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Neonatal transfusion practices

Naomi L C Luban, M.D

Chair, Laboratory Medicine and Pathology, Director, Transfusion Medicine/ Donor Centre,
Children's National Medical Centre, Washington, USA

The diagnosis and treatment of sick infants and children requires a broad knowledge of physiology, biochemistry, genetics and the application of sophisticated testing and treatment options. One of these options is transfusion of blood and blood products. Transfusion of the infant, especially the premature infant, and sick child, especially those with major organ dysfunction, requires careful consideration of their unique metabolic, hepatic and renal clearance mechanisms. Guidelines that direct the indications for transfusion differ from those in adults. Non-invasive measures of oxygen delivery and oxygen offloading may assist in guidelines for red blood transfusion. Metabolic complications from massive transfusion and/or the manipulation of blood products must also be considered. Dosing guidelines and apheresis techniques require special attention to the growing child's changing body mass and plasma volumes. Lastly, there are both infections and noninfectious risks of transfusion unique to the pediatric patient. Neonatal transfusion practices must be guided by the unique physiology of the infant.

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Novel platelet therapies and platelet additive solutions

Anneke Brand *, Jean-Louis Kerkhoffs, Bert Tomson

Leiden University Medical Center & Sanquin Bloodbank Region Southwest

Platelet transfusions are intended to prevent or treat bleeding during episodes of thrombocytopenia. However, few clinical studies have been performed to establish platelet transfusion triggers or the increments that must be obtained to reach this aim. Bleeding time measurements to evaluate the function of platelets are considered unreliable and are generally abandoned. Consequently, the indication and evaluation of platelet transfusion treatment is based on surrogate parameters such as platelet count and post-transfusion platelet increment.

Similarly, products prepared for platelet transfusions ideally should contain viable platelets surviving in the recipient and exerting haemostatic function. Platelet survival studies, which require radioactive tracing, have been incidentally performed to validate product quality. Rather, many countries have developed national (European guidelines require pH and swirling) guidelines with surrogate criteria that should be fulfilled to consider a platelet product acceptable for transfusion. Again, very limited data on the relationship between pH and swirling capacity of platelet products and the post-transfusion recovery and survival are available, whereas in vitro-assays predicting platelet function of stored products are completely lacking.

In this virtual surrogate world of platelet supportive care we tried to answer some real questions: on the quality of innovative products, on allo-immunization and donor selection, on non-radioactive tracing of transfused allogeneic platelets and above all, why are patients bleeding.

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Maximising the blood supply in emergencies or during times of shortage

Judith Chapman

Blood Stocks Management Scheme, London

Blood shortages may occur for a number of reasons including major incidents, flu epidemics, the exclusion of a high proportion of donors because of the introduction of a new pre-donation test or because of a lack of volunteer donors.

The National Blood Service (NBS) of England and North Wales and hospitals have jointly developed blood and platelet shortage plans. These ensure that hospitals and the blood service work together in a consistent, integrated framework giving patients equal access to available blood or platelets. The shortage plans have two key aims:- that the national pool of blood or platelets is available for essential transfusions for all patients and that overall usage is reduced to ensure the most urgent cases can receive the supply available. There are slight differences between the two plans, including the provision of a benchmarking framework for red cell but not platelet shortages.

Both plans suggest actions by the NBS and hospitals in three phases, 'normal', reduced availability (amber) and severe prolonged shortage (red). Every hospital is required to have a documented emergency blood management arrangement in place for each phase of the plan.

Actions to be taken in amber by hospitals for red cells include a reduction in normal stock holding levels and compliance with a daily hospital usage budget. Actions by the NBS include increased marketing activity and extending the opening times of blood collection sessions.

Actions to be taken in red by hospitals for red cells include further cuts in their inventory. Actions by the NBS include the declaration of a shortage and the activation of the emergency plan. For platelets a monitoring process will be introduced to track each unit issued to hospitals.

The red cell and platelet shortage plans should help to ensure that in the event of reduced availability blood and platelets will be available to the maximum number of patients.

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Management in isolated settings – Antarctica

Roland Watzl M.B.;B.S.

Medical Officer, Polar Medicine Unit, Australian Antarctic Division, Hobart

The Polar Medicine Unit of the Australian Antarctic Division, based in Kingston, Tasmania, provides comprehensive medical support for Australia's Antarctic program. This support includes medical services on Antarctic shipping, at permanent stations, and at remote field camps. Occasionally, medical assistance is given to other nations' Antarctic programs when requested.

The Australian Antarctic program requires its participants to spend extended periods of time in the most remote reaches of our planet, at times isolated from the outside world for periods of up to 9 months. Medical evacuations do not constitute first line management and may in fact be impossible during winter. When possible, evacuation times are generally measured in weeks.

Immediate medical support whilst on expedition with the Australian Antarctic program is provided by a single Antarctic Medical Practitioner. Antarctic Medical Practioners work in an extreme environment and the sophistication of medical care that can be provided is necessarily limited.

A ready refrigerated supply of donor blood is not routinely available and blood transfusions, when required, rely on a walking blood bank and the use of donated whole blood in an emergency. This poses unique challenges compared to standard practice in mainland Australia.

The Polar Medicine Unit has in place risk minimization strategies to address transfusion challenges in Antarctica. These strategies will be described. A case study illustrating our practice will be provided.

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Maximising blood supply in emergencies or during times of shortage: Management in isolated settings; the military

Marcus Skinner

Wing Commander RAAF SR

The military areas of operations provide a challenging set of circumstances for the reliable provision of appropriate stocks of blood and blood products.. Australian defence health recognises that the reliable supply of blood products is essential for the provision of high quality emergency and definitive health care in peace and on operations.

In light of the changing military theatre of operations from warlike to peacekeeping to disaster response the availability of supply, storage and transport issues and the requirements for "exportation" of blood the ADF policy on blood transfusion has come under review. The technical requirements for storage of blood and blood products may be difficult to achieve in certain military environments.

Currently the primary source of supply for blood products to the ADF is the Australian Red Cross blood Service (ARCBS), even on overseas deployments. If this source cannot meet demand, current doctrine states that blood is to be collected from local ADF donors, or, alternatively, that "screened" blood from indigenous civilian or allied military sources is to be used.

An overview of the operational needs will be presented to show that the ADF may need to provide high level medical facilities on operational deployments and that the provision of blood products to these facilities can be a significant logistic burden. With the current ADF system, the need for extra blood products to cope with unanticipated casualties inevitably leads to enormous waste of those blood components with short shelf lives.

The use of deployed military personnel as directed blood donors for whole blood (for red cells or platelets) is problematic and will briefly be discussed. While all personnel are ideally screened for HIV, hepatitis B and hepatitis C before deployment, no test is 100% sensitive.

Mention of alternative clinical possibilities including the use of blood salvage, frozen blood products, and artificial red cells and platelets and the use of Factor VIIa.

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Red cell transfusions in the PICU

Naomi L C Luban, M.D

Chair, Laboratory Medicine and Pathology, Director, Transfusion Medicine/ Donor Centre,
Children's National Medical Centre, Washington, USA

Significant differences in blood transfusion practices are seen among pediatric critical care practitioners. Red cell transfusion thresholds are poorly defined and a multiplicity of factors influence a practitioner's decision to transfuse. These include patient age, low Pa O_2, high blood lactate, acute bleeding, surgical intervention, degree/extent of multisystem organ failure and mortality scores, like the PRISM or PELOD. Several large multicenter clinical trials in adult critical care have evaluated restrictive versus liberal transfusion strategies. Two neonatal studies also used a randomized approach with discrepant results. No randomized studies on children have been performed to date and methods to reliably assess oxygen delivery are lacking. A growing literature on increased morbidity and mortality relate directly to transfusion demands that well powered, randomized studies be performed which control for disease, age and comorbidities.

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Mannose-binding lectin; biology and therapeutic potential of an innate immune system - pattern recognition molecule

Eisen Damon

Infectious diseases physician, Royal Melbourne Hospital

Mannose-binding lectin (MBL) is an important, pattern recognition molecule of the innate immune system. Its primary role appears to be killing of a wide range of pathogens via the lectin complement pathway but it is also involved in other inflammatory pathways. Low MBL levels and C4 deposition function resulting from MBL2 structural gene and promoter polymorphisms have been associated with predisposition to severe infection but the best measure of MBL deficiency is undecided. The therapeutic potential of MBL replacement or supplementation therapy is being investigated using both plasma derived and recombinant material.

The frequency and significance of MBL deficiency will be illustrated using studies of MBL measures in Australian blood donors and associations with severe infection including blood stream infection, Legionnaires' disease and invasive infection in haematopoietic stem cell transplanted patients.

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RH Immune Globulin – past and future

John G Gorman MD

Clinical Professor of Pathology at NYU School of Medicine

It is difficult today to imagine the degree of concern Rh Haemolytic Disease (at one point causing 10% of all perinatal mortality in Victoria) had for Rh Negative women and their obstetricians between 1940 and 1970. Ironically, by 1960, Passive Antibody Immunosuppression (PAI) (the phenomenon whereby circulating specific antibody prevents active immunization to the same antigen) and the mechanism of action of Rh Immune Globulin, had been fully described in the literature, seen by Theobald Smith first in 1909 and well characterized by many workers since. In 1959 a medical book salesman presented me in with a free copy of Florey's General Pathology, 2nd Edition. Gladstone and Abraham's chapter

contained a very clear three-page exposition of PAI, which convinced Vincent Freda, William Pollack and me that Rh antibody would protect Rh-negative women from sensitisation. A very lucky break indeed. In 1960 we began our research, to obtain Rh antibody in an injectible form, to test it in Rh Negative male volunteers and then in unsensitized Rh Negative mothers at risk. In 1960, quite independently and unaware of PAI, Ronald Finn and Cyril Clark in Liverpool made an identical proposal. Studying foetal maternal haemorrhage in Rh Negative mothers with the just developed Kleihauer-Betke test, they were led to anti-Rh by wondering what agent would clear the Rh positive cells they found in those Rh negative mothers who later became sensitised. Successful transatlantic studies with Rh Immune Globulin, followed by its general application, led to the disappearance of Rh Haemolytic Disease over the next few years. For the future, as Abraham Lincoln said, "Eternal vigilance is the price of liberty", the task now is to continually improve systems that identify Rh negative mothers at risk and make sure they are protected.

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Transfusion in utero

Helen Savoia

The Royal Children's Hospital and The Royal Women's Hospital, Melbourne

In 1963, Liley performed the first intrauterine transfusion. This transfusion, of red cells into the peritoneal cavity of a fetus severely affected by haemolytic disease due to anti D antibodies can be seen as one of the major breakthroughs in improving the morbidity and reducing the mortality of this disease. Liley's breakthrough was also the very beginning of the field of fetal therapy.

Today, intrauterine transfusion comprises both transfusion into the peritoneal cavity and intravascular transfusion via percutaneous puncture of the umbilical vein. Compared with intraperitoneal transfusion, intravascular transfusion has lower procedure-related morbidity and mortality rates, especially in fetuses with hydrops.

The major indications for in utero transfusion of red cells is anaemia due to haemolytic disease (mainly immunization to the D and Kell antigens) and anaemia due to fetal parvovirus infection. Rare indications for red cell transfusion are other causes of anaemia such as major feto-maternal haemorrhage. In utero transfusion of platelets is used in the management of some cases of alloimmune thrombocytopenia.

The fetus as a transfusion recipient must be seen as an immunocompromised patient; at risk of transfusion transmitted viral infection such as CMV and at risk of graft-versus host disease. Transfusion volume is also a critical consideration. Transfusion is often undertaken with results of maternal but not fetal pretransfusion testing. In cases of haemolytic disease, red cells negative for the implicated antigen and matching an extended maternal phenotype are often used.

In haemolytic disease fetal monitoring and hence the determination of need for transfusion has become non-invasive with the widespread use of middle cerebral artery doppler as an indicator of fetal anaemia.

The experience of intrauterine transfusion at the Royal Women's Hospital Melbourne in recent years will be presented.

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Clinical audit: Process, improvement and patient safety

Naomi L C Luban, M.D

Chair, Laboratory Medicine and Pathology, Director,Transfusion Medicine/ Donor Centre,
Children's National Medical Centre, Washington, USA

Audit is a system of investigation, evaluation, measurement and continuous assessment that provides a means to improve a process or practice. Clinical audits are broad defined and can involve direct observation, analysis of computerized processes and large database mining. Often a guidance or set of criteria must be established before a clinical audit can be performed. In pediatrics, transfusion guidance has been established by concensus often without randomized trials to guide practice. Transfusion audits can reflect local, national or international practices and can be used for benchmarking and evidence-based decision making. Q-probe from CAP and other national blood services have spearheaded transfusion audit methods. In this session, we will review kinds of audits, their ultimate usefulness, and tools to use in the quest for continuous quality improvement.

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Audit in New Zealand

Richard Charlewood

New Zealand Blood Service, Auckland, New Zealand

Background

As well as supplying blood components and products, New Zealand Blood Service (NZBS) also operates six of the country's largest blood banks. This environment lends itself to audit of clinical transfusion practice. In addition, because NZBS is a not-for-profit Crown enterprise, the District Health Boards (DHBs) are charged for blood components and products obtained through NZBS. This motivates the DHBs to understand their demand of blood components and products and they have been supportive of audit work.

Method

NZBS employs six Transfusion Nurse Specialists (TNSs) (5.8 FTE), one situated in each of its blood banks. NZBS has agreements with each of the six DHBs covering the TNS role, in effect, double-badging the TNSs as DHB employees. The TNSs have a high visibility and credibility within the DHBs based on their educator, liason and change management functions. Each year collective audits involving these DHBs and, in some cases, other DHBs, are undertaken by the TNSs, co-ordinated by a Transfusion Medicine Specialist, on different aspects of transfusion medicine. In addition local audits are undertaken, some of which act as pilots for the larger collective audits. These audits take place as part of a more general service of demand management, including monthly blood utilisation reports and retrospective data analyses.

Results

In the last two years, five collective audits have been undertaken. These have covered overnight transfusion practice, cryoprecipitate use and non-use, Intragam P use, irradiation of cellular blood components and platelet use. These audits have concentrated on issues around

clinical practice as well as appropriateness of use. The audit reports are provided to the hospital transfusion committees in draft form for comment, to allow the DHBs an opportunity to provide input into the audit conclusions. The final reports are circulated to the hospital transfusion committees and CEOs of all 21 DHBs.

Conclusion
The partnership between NZBS and the DHBs has enabled audit work to provide useful insight into blood component and product use in New Zealand. This has, to a large extent, reassured clinicians and managers of the appropriateness of use and helped concentrate improvement in areas shown to have problems.

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Immunomodulatory aspects of transfusions

Anneke Brand *, Leo van de Watering, Marloes Waanders
Leiden University Medical Center & Sanquin Blood Bank region Southwest

In the nineteen-seventies, transfusion related immuno-modulation (TRIM) was mainly studied to explore and understand the clinical observation that pretransplantation blood transfusions ameliorated rejection of a subsequent organ graft from the same donor or a third party donor. For this aim animal experiments were performed in mice to baboons. Although the clinical observations in humans were widely reproduced in these animal models, the allogeneic donor cells (generally purified mononuclear cells or spleen cells) used were not representative for blood products and the mechanism remained undetermined.

In the nineteen-eighties it was hypothesized that suppression of the allogeneic response, beneficial for transplantation, maybe deleterious for cancer patients. To reject malignant cells expressing tumour antigens in the context of Human Leukocyte Antigens (HLA) may require effector cells that could be suppressed by blood transfusions in a similar fashion as the allogeneic response. Although this indeed was the case in animal models measuring metastasis of inoculated tumour cells, human studies to investigate this effect were of poor quality and hundreds of observational, often retrospective studies, yielded contradictory results. This generated believers and non-believers until today.

Meanwhile, a definite role of leukocytes present in blood products on the induction of HLA allo-antibodies was recognized and clinical trials investigating the role of leukocyte depletion of red cell transfusions were designed. Currently thirteen trials on immunomodulatory effects of leukocyte-containing transfusions exploring different endpoints have been performed. Surprisingly, the best evidence for TRIM caused by the presence of leukocytes in blood transfusions is on the innate immune response enhancing infections and mortality in critically ill patients. Again the mechanism is speculative.

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Transfusion considerations in critically ill patients

Craig French
Director of Intensive Care, Western Health, Melbourne

Transfusion of allogenic packed red blood cells (RBC) is common in Intensive Care medicine; approximately 20% of patients admitted to Australasian Intensive Care Units receive a RBC transfusion. The determinants of which patients to transfuse has generated considerable debate in the last decade. The drivers for debate include: safety concerns, in particular the transferral of infectious material such as human immunodeficiency virus and bovine spongiform encephalopathy; concern that RBC transfusion in some way induces a immunosuppressed state that predisposes patients to infection- so called “transfusion related immunomodulation”; and with a decreasing donor pool the need to reduce unnecessary or inappropriate RBC transfusion.

The TRICC study published in 1999 challenged traditional RBC transfusion practice in intensive care. This prospective randomised controlled trial demonstrated no difference in outcome in for patients in whom the transfusion threshold was 70g/L compared with those whose transfusion threshold was 100g/L. As a result of this trial many clinicians now wait until the haemoglobin concentration is 70g/L before transfusing. The TRICC trial however does not provide sufficient evidence in a number of important subgroups of critically ill patients: post operative care, children, and patients with an acute coronary syndrome. Nevertheless in response to this trial, and observational studies suggesting worse outcomes in transfused patients, a restrictive strategy has been widely recommended and adopted.

It may however be time to re-evaluate the restrictive strategy. A recently reported observational study (the SOAP study) demonstrated that blood transfusion was not associated with increased mortality in multivariate analysis or propensity matching. The reasons for this reduction remain uncertain. The most popular theory involves the increased use of leucodepleted blood. The widespread use of leukodepleted blood may have impacted on the risks associated with blood transfusion. Storage lesion has also been implicated as a potential cause harm related to blood transfusion. Currently most Australasian Intensive Care Clinicians utilise a transfusion threshold of 70 g/L and administer non-leucodepleted red blood cells with a median age of 18 days. We are now left asking whether a transfusion threshold of 100g/L with leucodepleted “fresh” blood will lead to improved patient outcomes.

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Pregnancy and venous thromboembolism

Saskia Middeldorp

The risk of venous thromboembolism is increased during pregnancy and the postpartum period and is estimated to be approximately 1 in 1000 pregnancies. In western countries, pulmonary embolism is the leading cause of maternal death. In pregnant women, risk factors for venous thromboembolism are similar as in non-pregnant patients and include surgery (i.e. caesarion section), immobilization, a personal or family history of venous thromboembolism, hereditary thrombophilia, and an increased body weight. Several aspects of venous thromboembolism in pregnant patients deserve attention. The diagnostic work-up for a suspected deep vein thrombosis or pulmonary embolism appears more complicated in pregnant women. For the treatment of antepartum venous thromboembolism, effects of anticoagulants on mother and fetus should be taken into account. Management of anticoagulants close to delivery requires a multidisciplinary approach to the pregnant patients with recent thrombosis. Finally, many uncertainties exist with respect to the optimal management of women who are considered at high risk for pregnancy-associated venous thromboembolism. These include women with a personal history of venous thromboembolism, as well as known carriers of inherited thrombophilia or women with a strong family history for venous thromboembolism. In this lecture, an overview of the available evidence of these various aspects as well as practical issues will be discussed.

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Iron homeostasis and the pathophysiology of haemochromatosis

Nancy C. Andrews[1] *, Paul J. Schmidt, Franklin W. Huang, Diedra M. Wrighting, Tapasree Goswami

[1] Dean for Basic Sciences and Graduate Studies and the Leland Fikes Professor of Pediatrics, Harvard Medical School, Boston, Massachusetts

Genetic hemochromatosis is caused by mutations in genes encoding HFE, transferrin receptor-2 (TFR2), hepcidin, hemojuvelin (HJV) or ferroportin. Loss of function mutations in HFE and TFR2 cause adult onset hemochromatosis. Loss-of-function mutations in HJV and hepcidin cause severe, early onset hemochromatosis. We and others have shown that all of these diseases result from perturbation of a hepcidin/ferroportin regulatory axis that normal controls iron export from absorptive intestinal cells and tissue macrophages. Hepcidin is a circulating hormone that controls systemic iron homeostasis. Ferroportin is a key cellular iron transporter that is downregulated by hepcidin binding. Hemochromatosis-associated mutations in ferroportin are believed to interfere with its regulation by hepcidin. The functions of the proteins encoded by HFE, TFR2 and HJV were not obvious, but all were inferred to be involved in regulation of hepcidin production. With collaborators, we showed that HJV acts as a co-receptor for bone morphogenetic proteins (BMPs). HJV interacts with BMP receptors and BMP ligands to activate SMAD proteins that directly induce hepcidin expression. We asked whether HFE and TFR2 might also participate in this signal transduction pathway. We found that both HFE and TFR2 associate with HJV in a stable protein complex. HFE acts to amplify BMP signaling, presumably as part of a larger complex including the hemochromatosis-associated proteins and BMP receptors. TFR2 prevents the release of a soluble form of HJV that has been shown by others to inhibit hepcidin expression, suggesting that its function in the complex is to stabilize HJV. Our observations provide an explanation for the similar clinical features of genetic hemochromatosis disorders due to mutations in these five genes.

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Albumin: A retrospective review of post-market pharmacovigilance data. Impact of manufacturing improvements on clinical safety

Darryl Maher *, Yan Che, Fiona Wilson, Clare Schwarz

CSL Limited, Bioplasma Division, Broadmeadows, Victoria 3047, Australia

Aim: Since 1988, four generations of iso-oncotic albumin products and three generations of hyperoncotic albumin products have been manufactured and supplied by CSL Bioplasma. During this time a number of manufacturing improvements have been made, including the addition of viral reduction and chromatographic fractionation processes. The aim of this study was to investigate whether the manufacturing changes made to CSL Bioplasma's albumin products between 1988 and 2005 had an impact on their clinical safety, by evaluating the incidence of reported suspected Adverse Drug Reactions (ADRs).

Methods: Australian ADR data were retrieved from CSL Bioplasma's pharmacovigilance database. The incidence of total, hypotensive and other ADRs were expressed as a proportion per 100,000 bottles distributed. The levels of monomer, dimer, aggregates and prekallikren activator (PKA) in albumin batches at release were measured by the British Pharmacopeia methods and the records retained in the Laboratory Information Management System (LIMS).

Results: More than 3.7 million bottles of albumin were distributed in Australia in the specified period. The incidence of ADRs are summarised in Table 1. There were no cases of suspected viral transmission and only two reported deaths involving the earlier generation

products.

Table 1. Incidence of total, hypotensive and other adverse drug reactions. (ADRs per 100,000 bottles distributed)

Products	Years Distributed	Total ADRs	Hypotensive ADRs	Other ADRs
SPPS	1988 - 1991	14.1 (11.3 – 17.3)	9.6 (7.3 – 12.4)	4.5 (3.0 – 6.5)
NSA 5%	1992 - 1995	15.7 (11.9 – 20.4)	8.8 (6.0 – 12.5)	6.9 (4.5 – 10.2)
ALBUMEX 4/5 (1VI)	1995 - 2000	6.7 (5.1 – 8.5)*	6.6 (5.0 – 8.6)	0.1 (0.0 – 0.7)*
ALBUMEX 4 (2VI)	2000 - 2005	1.5 (0.8 – 2.6)*	1.1 (0.5 – 2.0)*	0.5 (0.1 – 1.2)*
NSA 20%	1989 - 1995	11.5 (8.2 – 15.7)	6.6 (4.2 – 9.9)	4.9 (2.9 – 7.8)
ALBUMEX 20 (1VI)	1995 - 2000	1.2 (0.3 – 3.5)#	0.4 (0.0 – 2.3)#	0.8 (0.1 – 2.9)
ALBUMEX 20 (2VI)	2000 - 2005	1.7 (0.6 – 3.6)#	0.3--- (0.0 – 1.5)#	1.4 (0.5 – 3.2)

* and # indicate $p < 0.0001$ when compared to SPPS and NSA 20% respectively.

The improvements in the manufacturing process resulted in a consistent increase in albumin purity and decrease in dimer, aggregates and PKA contents, compared to the 1st and 2nd generation products SPPS and NSA respectively.

Conclusions: Post-market pharmacovigilance data collected over an 18 year period supports the view that successive manufacturing improvements have significantly improved the clinical safety profile of human albumin products manufactured by CSL Bioplasma.

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Use of liquid thawed plasma improves utilization of fresh frozen plasma (FFP)

G.T. Magrin[1] *, N. Waters[2], E.M. Wood[2], A.M. Street[1], M. Cole-Sinclair[1]

[1] Haematology Unit, Alfred Hospital, Melbourne, VIC

[2] Australian Red Cross Blood Service (ARCBS), VIC

Background

Since November 2004, The Alfred blood bank has routinely relabelled thawed FFP as Liquid Thawed Plasma (LTP) and extend its shelf life by 4 days (= total 5 days from thawing). 4 units of group AB LTP are available at all times. ARCBS has documented that coagulation factor levels in thawed plasma stored up to 5 days at refrigerated temperature are well maintained. At 5 days, levels of FV are 0.75±0.13 U/mL, FVII 0.85±17 U/mL and FVIII 0.56±0.15 U/mL with vWF Ag (94±27%) and fibrinogen (275±50 mg/dL) unchanged at 5 days[1]. LTP may be used to treat coagulopathies other than FVIII deficiency (AABB).

Aim

To reduce the time taken to supply plasma and reduce wastage of FFP, once thawed.

Method

Review of data from ARCBS web-based wastage reporting system and hospital computer on wastage and time to supply for urgent use, of FFP and 5-day LTP.

Results

Wastage of FFP due to discard 24 hr post-thaw has reduced from 2.4% of plasma issues in 2003 to 0% in 2006 = average saving 11 units/month = approx 132 units plasma/year at our hospital alone. Time to thaw 4 units FFP using current method is 18 minutes so availability of LTP allows immediate issue. This strategy also reduces stress on laboratory staff, has been well received by The Alfred Trauma Service and is now a recommended strategy for support of Trauma Services.[2]

Conclusions

Availability of LTP reduces supply time for emergency use, has greatly reduced FFP wastage and has improved workflow in the blood bank laboratory.

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Thawed cryo with a five day shelf life?

Neil Waters *, Erica Wood, Wayne Alford, Georgeta Constantin, Mary Anne Neal, Shane Winzar, Nicole Hudson, Kim Boeters

Australian Red Cross Blood Service, Melbourne, Australia

Aim

We investigated 5 day storage of thawed cryoprecipitate (cryo) at 2-6°C. Currently, post-thaw expiry of cryo is only 6 hours. Ability to store

cryo for extended periods would allow greater flexibility and reduce product wastage.

Method

Whole blood (WB) and apheresis (APH) cryoprecipitate (WB, n=10x group O, 10xA, 10xB; or APH n=6xO, 2xA, 8xB) were thawed on day 0 in a 37^{o}C water-bath. Some from each group, n=18 WB (6xO, 6xB, 6xA); n=10 APH (4xO, 1xA, 5xB) were sampled immediately (Group I) while the remainder (Group II) was left at room temperature for 4h before initial sampling. All products were then stored at 2-6^{o}C for 5 days. Before subsequent samplings, units were brought to 37^{o}C to re-dissolve any precipitates. Samples were tested for FVIII (d0, 1, 2, 3, 4, 5) fibrinogen (d0, 1, 3, 5) and vWF (d0, 1, 3, 5).

Results

All products remained within Council of Europe (CoE) product specifications for fibrinogen, FVIII and vWF (Table). There was no significant difference between group I and II products.

Table: Results, Day 5

	Fibrinogen mg/Unit Mean ± SD	FVIII IU/Unit Mean ± SD	vWF IU/Unit Mean ± SD
Whole Blood Cryo	355 ±84	101±38	246±93
Apheresis Cryo	862 ±216	167±49	466±104
Cryo specification (CoE)	>140	>70	>100

Conclusion

After 5 days refrigerated storage, mean levels of coagulation factors remain well above CoE specification and are adequate for haemostasis. (ref. AABB Technical Manual 2005). In Australia in 2006, cryo is almost only ever used for fibrinogen replacement. These data show that cryo could be stored for up to 5 days post-thaw when used for this purpose, which would improve flexibility, reduce supply time in emergencies, and minimise wastage. Further work is in progress to investigate whether functional changes in coagulation factors occur during extended storage.

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Impact of haemoglobin deferral on the subsequent donation behaviour of blood donors

Tessa Hillgrove*[1], Kathleen Doherty[1] , Vivienne Moore[2], Philip Ryan[2]

[1] Australian Red Cross Blood Service, Adelaide, SA

[2] University of Adelaide, Adelaide, SA

Aim

To determine whether deferral due to low haemoglobin reduces the frequency of post -deferral donation events.

Methods

Whole blood (WB) donors deferred for low Haemoglobin (Hb) in August and September of 2004 (n=1015) were surveyed by letter 6 months after deferral. Donation records for deferred and non deferred WB donors donating in the same period (n=1896) were extracted from the Data Warehouse. Donation frequency prior to and after eligibility to return was compared using Symmetry (asymptotic), Wilcoxon signed-rank test, and paired t-tests. Probability of first return was estimated by the Kaplan-Meier method and Cox regression analysis was used to estimate hazard ratios of return

Results

37.8% of deferred donors failed to return once eligible, compared to 42% of the comparison population (p=0.057). Donors deferred on first donation attempt did not have a significantly higher non return rate (66%) than non-deferred new donors (60%). Deferred donors donated an average of 2.07 times in the 12 months before deferral, falling to 1.5 once eligible to return (p=0.00). In contrast, the comparison group donated significantly less frequently than deferred donors (1.20/12mth) with no significant difference in frequency over the corresponding donation periods (1.24/12mth). Return rates of donors deferred for low Hb were not significantly different to the non deferred population

(p=0.16).

Conclusion

Donors deferred for low Hb donate more frequently prior to deferral than non deferred donors suggesting a relationship between donation frequency and deferral risk. Deferral reduced return rates by an average of 0.5 donations per year to a level equivalent to that of the non-deferred donor population. This equates to an average loss of 1 donation for the deferral period and an additional loss of one donation in the post deferral period.

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Evaluation of gambro BCT trima accel plasma reduced leuco-depleted platelets resuspended in T-sol or PAS3M

Kathleen Doherty *, Ros Elias, Anthony DeConno, Tanya Buckerfield, David Jones, Suzanne Candy, Ben Saxon

Australian Red Cross Blood Service, Adelaide, SA

Aim

To evaluate quality and in vitro function of Gambro BCT Trima Accel Plasma Reduced Leuco-Depleted Platelets (dry platelets) resuspended in different additive solutions.

Method

A protocol for the preparation and resuspension of leucoreduced platelets was developed in association with Gambro and platelets were prepared and resuspended in either T-Sol (Baxter) or PAS3M (MacoPharma). Platelets were assessed at days 1 and 6 post collection for routine quality parameters including pH, platelet count/unit, platelet concentration, leucocyte contamination, volume, microbiological contamination and for functional parameters, ADP induced shape change and CD62P expression. A total of 54 platelets were resuspended in T-Sol and 18 platelets were resuspended in PAS3M. Both double and single collections were assessed. All collections were initially performed using a Yield Scaling Factor of 1.0. This was altered in an attempt to improve actual yield in relation to target during the course of the study.

Results

Of platelets resuspended in T-Sol, 2/20 single collections failed to meet platelet concentration criteria at YSF 1.0, vs 1/18 at YSF 0.9, 2/13 double collections failed to meet platelet count/unit criteria at YSF 1.0, and 1/10 single units collected in PAS3M did not meet platelet count criteria. 2/13 double collections exceeded pH at expiry. Despite this platelet products met quality acceptance criteria when resuspended in either T-Sol or PAS3M. The mean platelet activation levels were significantly lower at day 6 post collection when platelets were resuspended in PAS3M (12.5%) in comparison to T-Sol (23.6%) and plasma (21.8%). Platelets in T-Sol also showed a net reduction in shape change response over the storage period of 39% compared to 19.4% in PAS3M resuspended platelets and 24.5% in platelets resuspended in Plasma.

Conclusion

Gambro Trima methodology for the preparation of dry platelets results in a product which meets ARCBS quality criteria. Resuspension of platelets in PAS3M offers improved in vitro performance over the storage period. Further refinement of the process is underway to improve yield.

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Screening for haemolysis after Intragam®P Infusion

Rebecca Crockett[1], Mary Gaskell *, Robin Filshie, Danielle Hedley

[1] St. Vincent's Hospital Melbourne, VIC

In 2003, sixteen adverse events related to Intragam®P therapy were reported to the Commonwealth Serum Laboratory over a three month period. During one month in 2004, two haemolytic reactions related to Intragam®P therapy were recorded at St Vincent's Hospital Melbourne.

One patient received four consecutive doses of 24-36g Intragam®P The second patient received five consecutive doses of 36g Intragam®P. Both patients had a significant drop in Hb and required transfusion. The direct antiglobulin tests (DAT) were positive with anti-A eluted. In response to these two cases, a haemolytic screening program for Intragam®P and Sandoglobulin® patients was initiated.

For all A, B and AB patients receiving Intragam®P or Sandoglobulin® over three to five consecutive days, a haemoglobin and DAT +/- elution were requested to be performed at baseline and on day three and the final day of treatment.

Nineteen group A or AB patients and one group B patient were involved during the initial haemolytic screening program and were tested on forty-two occasions over twelve months. All patients eventually tested DAT positive post infusion, and in Group A or AB patients anti-A was eluted in 90% of cases, but no haemolytic reactions requiring transfusions were found.

It was found that a positive DAT with anti-A eluted following Intragam®P or Sandoglobulin® therapy was not a predictor of significant haemolysis and the screening program was modified. For A, B and AB patients only, a full blood count is required at baseline, and an Hb on day three and five.

As the haemolytic screening program continues, we hope that in combination with other diagnostic screening, clinical signs and symptoms, we will be able to continue to detect early signs of haemolysis so as to minimise risk and adverse outcomes for our patients.

ANZSBT Masterclass

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A test for prions – impacts and ethics

Marc Turner

Clinical Director, Edinburgh & South East Scotland Blood Transfusion Centre, New Royal Infirmary, Edinburgh, UK

There are considerable challenges in the development of peripheral blood screening assays for prions. There is no conventional immune response or detectable DNA associated with these diseases, and therefore most research groups and manufacturers have focused on PrP^{TSE} detection as a surrogate for infectivity. Despite the significant challenges involved in achieving the levels of sensitivity likely to be required detect sub-clinical disease, several manufacturers are now bringing forward potentially useful assays. Nevertheless considerable concerns remain including the potential for relatively low specificity of first generation assays, the need for confirmatory assays to discriminate true from false positives, the uncertain clinical implications of true positivity and the likely adverse psychological and social impact on both individual donors who test positive and more broadly on donor recruitment and retention. An evaluation algorithm has been developed which balances the need to carry out initial assessment on human brain/spleen spiked peripheral blood and TSE infected animal peripheral blood samples as a prelude to assessment on rare peripheral blood samples from patients and a specificity panel of blood donors. Significant scientific, medical and ethical issues remain to be addressed.

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European experience in management of TRALI

Bjarte G. Solheim

The National Hospital, Oslo, Norway

Transfusion related acute lung injury (TRALI) and ABO-mismatched transfusions are the leading transfusion related causes of death in the developed World. Serological, biochemical and haemovigilance data from Europe have added to the understanding and management of TRALI, which is an under reported and under recognised adverse effect.

TRALI is closely associated with leukocyte reactive antibodies in donor plasma. The antibodies are mostly directed against granulocytes and HLA Class I and Class II antigens, but also platelet specific antibodies have been reported as causative agents. However, leukocyte reactive antibodies are not always detectable. In these cases a “two event model” has been suggested where the patient’s leukocytes are first primed by underlying infection, surgery or trauma, and TRALI then provoked by activated lipids, cytokines or leukocyte reactive antibodies below detection level in donor blood products. TRALI has mostly been recognised as a rare but life threatening complication, however, mild and sub-clinical cases compromising pulmonary gas exchange are probably frequent.

TRALI is in general associated with plasma containing blood products, and plasma transfusion is the most common cause. However, red blood cells or platelets in additive solution with low plasma content can also cause TRALI. Storage of blood products, particularly if not leukocyte depleted, increases the risk. Screening for leukocyte reactive antibodies with sensitive techniques or deferral of women or transfused donors will reduce the risk for TRALI with plasma containing blood products, but would compromise the availability of blood donors significantly.

Hemovigilance data from Europe indicate that TRALI is not induced by solvent/detergent treated (SD) plasma. So far more than 10 million units of SD plasma have been transfused without documented cases of TRALI, and it has been shown that neither HLA or granulocyte antibodies nor activated lipids are detectable in the most widely used product, Octaplas. Thus, the production process of SD-plasma not only ensures standardised viral inactivated plasma with reduced frequency of allergic adverse events, but also results in TRALI safe products.

ANZSBT – Supply Management

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The constraints and opportunities for effective blood supply management across the blood supply

chain

Judith Chapman *, Rob Hick, Clive Hyam
Blood Stocks Management Scheme, London

There has been renewed interest in blood inventory management for a number of reasons not least the possibility of shortages associated with a diminishing donor base. Effective blood inventory management relies on an understanding of the many stakeholders in and influences on the blood supply chain. The stakeholders include the voluntary blood donor, the blood service, the hospital laboratory, clinicians and prescribers and the potential recipient and the influences include stock management practice in the hospital and blood service, and logistics management.

Data collection related to the blood supply chain provides information on the donor, blood collections, processing and testing, issues to hospitals, and inventory levels and wastage. This data can be used to ensure that the blood supply chain is managed effectively, that patient requirements are met, blood and blood components are transfused appropriately and wastage is minimized.

The Blood Stocks Management Scheme (BSMS) is an UK-wide scheme collecting online red cell and platelet inventory, issue and wastage data from hospitals and the UK blood services. In return they have access to data and associated charts. The data is also analysed by the BSMS team and used to make recommendations on inventory management practice.

In the commercial environment businesses invest heavily in information technology (IT) to facilitate easy, accurate data collection. This enables them to identify where problems may exist, e.g. inefficiencies in the management of the supply chain and potential areas for growth through customer profiling. The IT associated with the blood supply chain is often unfit for purpose making it difficult to obtain all the required information, particularly in relation to the recipient. This has the potential for problems in blood supply chain management e.g. incorrect demand forecasting leading to inaccurate blood collection planning with subsequent inappropriate inventory levels which may result in shortages or overstocking and associated increased wastage.

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Interim emergency blood management plan

Dr Ian Kerridge, Dr Philippa Hetzel *
National Operations Manager, Australian Red Cross Blood Service

Purpose
To provide an overview of the proposed interim Emergency Blood Management Plan (EBMP), including feedback received on the February 2006 version of the proposed EBMP and an outline of the revisions that are proposed to the EBMP.

Background
ARCBS, following significant consultation with health professionals, and government representatives, developed a draft EBMP dated February 2006. Subsequently the National Blood Authority (NBA) has released a Request for Tender for the *Provision of Contingency Planning Service*. However it is recognised that there is still a need to implement an interim national EBMP, pending the finalisation of the National Blood Supply Contingency Plan by the NBA. The ARCBS has since sought feedback on the February 2006 draft EBMP from the NBA, Department of Health and Ageing and by members of the Jurisdictional Blood Committee. The ARCBS has subsequently revised the EBMP to incorporate the feedback received.

Overview of Interim Emergency Blood Management Plan
There are three stages of the EBMP: Normal, Alert and Activate. These stages are evaluated both by jurisdiction and nationally. The inventory stages will be calculated for two categories of blood groups: group O and total all groups.

The stages of the interim EBMP will be first considered on an individual state and territory basis where the stages will be triggered by combined ARCBS and hospital inventory levels. National implementation will be triggered by either one jurisdiction being in Alert or Activate stage for a defined period of time or if multiple jurisdictions are in the Alert or Activate stage.

Within the Activate stage there are three levels which include options to be used in the event of major shortage and to ensure that appropriate controls and planning have occurred well before such systems might need to be used. Consultation has continued with TGA and other stakeholders, to ensure that activities would operate within the approved regulatory framework. A number of strategies which might be applied in such circumstances are being considered and include options such as restriction of transfusion activity, relaxation of donor selection criteria and blood importation.

ANZSBT – Supply Sufficiency

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Self sufficiency in the 21st Century

Bjarte G. Solheim
The National Hospital, Oslo, Norway

The principle of self sufficiency for blood and blood products is advocated by both WHO, the Council of Europe and the European Community both for ethical and epidemiological reasons. This principle has been challenged by the fractionation industry who argues that today the fractionated pathogen inactivated plasma products from viral infection screened blood donations can be regarded as safe with respect to disease transmission, and that a global market makes is impossible to account for the plasma source. However, emerging blood borne infections, and the fact that all pathogen inactivation methods have limitations, challenges the industry standpoint. The methods are only validated against known infectious agents, and have particular limits with regard to small non lipid enveloped viruses and spores. The risk involved with the infectious prion proteins has been highlighted by vCJD. In this context the European Commission Scientific Committee on Emerging and Newly Identified Health Risks has recently published an Opinion on: The Safety of Human-derived Products with regard to Variant Creutzfeld-Jakob Disease, where they underline: “that European Community Member States maintain the principle of regional blood supply structures, and national surveillance systems and international information exchange”.

In Norway a National self sufficiency model based on contract fractionation of plasma was implemented in 1988. The blood banks retain the property of the plasma, pay for the fractionation process, and distribute the fractionated plasma proteins to hospitals and the Norwegian market. So far we have had five European tenders and four contract prolongations. Three to five bidders per tender made it possible to select quality, safety and yield. An overcapacity on the fractionation market helped in the negotiation of favourable prices. Close collaboration with clinicians and the Norwegian Haemophilia Society in the choice of products, has secured the success of the programme. Both the WHO and the World Haemophilia Association are advocating the principles applied in the Norwegian self sufficiency model.

ANZSBT – Presidential Symposium

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Are all types of leucodepleted red cell concentrates equivalent?

Kristen Glenister*, Rosemary Sparrow
Research Unit, Southbank, Victoria, Australian Red Cross Blood Service.

The accumulation of cytokines in blood products is likely to contribute to the risk of adverse transfusion reactions. Leucocyte depletion of red cell concentrates (RCC) via specific filters prevents the accumulation of leucocyte derived cytokines, but less is known about the effect on cytokines from other sources.

Methods
In this study we used cytokine antibody microarrays to simultaneously investigate 79 cytokines, chemokines and growth factors in fresh and stored RCC. Factors that appeared accumulate during storage were quantified (by ELISA) in RCC that had been leucocyte reduced by buffy coat removal or by three different types of leucocyte depletion filter (OptiPure and Sepacell (Baxter) and Imuflex (Terumo)).

Results
Several cytokines were identified that have not previously been studied in relation to transfusion medicine. Although the leucocyte content of the three types of pre-storage leucocyte filtered RCC was not significantly different, the platelet content and level of plasma carryover were significantly different between filter types. These differences are due to a combination of processing constraints and filter characteristics. Not surprisingly, these product differences influenced the accumulation of platelet and plasma derived factors. For example, RANTES is a platelet derived cytokine that has been implicated in adverse transfusion reactions. The concentration of RANTES was significantly different between three types of leucocyte filtered RCC, and some units contained levels of RANTES that are reportedly capable of attracting and stimulating immunological responses by allogeneic leucocytes.

Conclusion
These results suggest that leucocyte-filtered RCC can have distinctly different cytokine milieu, depending in the type of leucocyte-depletion filter used. This could have ramifications for susceptible groups of transfused patients.

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Comparison of automated antibody identification using the Autovue Innova and Resolvigen 3 software with manual Biovue antibody identification

D Roxby *, M Phillips, K Kraft
Transfusion Service, Flinders Medical Centre, Bedford Park, South Australia

Introduction
Manual antibody identification relies heavily on the skill of the person reading the tests and interpreting those results. Fully automated

antibody identification procedures support this expertise and reduce the degree of manual intervention required, thereby enhancing accuracy of antibody identification (Ab ID). A computer assisted Ab ID system, fully integrated with an automated blood bank instrument, was compared with manual Ab ID procedures.

Method

Using the ORTHO AutoVue® Innova, routine pre-transfusion or antenatal samples with positive antibody screens were identified using ORTHO BioVue® AHG polyspecific cassettes and 3% Surgiscreen red cells. 308 consecutive samples with positive antibody screens from medical, surgical and obstetric patients were tested by manual and automated antibody identification techniques. Nine routine pre-transfusion samples with negative antibody screens were used as negative controls.

All samples with positive antibody screens were fully investigated using our standard manual antibody investigation protocol prior to automated antibody identification on the AutoVue Innova. Both methods employed BioVue AHG polyspecific cassettes and ORTHO 3% Resolve® Panel A and Panel B where necessary. For the manual protocol, all reaction grading, interpretations and antibody exclusions were carried out manually. Reaction grading was performed automatically on the AutoVue Innova and the results uploaded to the antibody identification software. The computer assisted antibody identification software Resolvigen 3 (Technosoft srl) subsequently performed interpretations and exclusions using reaction scores, test phase, dose effect of zygosity and antigen expression variability. Most probable antibodies were listed including a comment regarding the degree of fit for the data as well as non-exclusions.

Results

308 patient's samples were tested using both manual and automated protocols. Seven samples were excluded because of spurious results due to white cell related antibodies. 301 samples contained red cell antibodies of which 252 were a single specificity and 49 contained a mixture of antibodies. Where necessary, in those samples in which the presence of a particular antibody could not be conclusively excluded using the initial manual or automated results appropriate additional investigations were performed. There was complete agreement between manual and automated results in 300 samples. In one sample only the automated results indicated the presence of an extra antibody, anti-E, in a mixture of anti-D+K. No false positive results were detected in the nine negative controls tested.

Conclusion

Traditional manual techniques for identifying antibodies are time consuming, labour intensive and include the potential for technical and interpretational errors. Completely automated antibody identification performed on the ORTHO AutoVue Innova integrated with Resolvigen 3 showed a very high correlation with the manual technique.

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The NZBS national haemovigilance programme – one year's experience

Simon Benson * , Dr Peter Flanagan

New Zealand Blood Service, Auckland, New Zealand

On 1 May 2005 New Zealand Blood Service (NZBS) introduced a national haemovigilance programme.

The programme, which embraces Council of Europe requirements, is modelled on similar schemes in the UK and Ireland and collects data on the prevalence of all types of transfusion-related adverse events not only so-called transfusion reactions.

Hospital blood banks notify NZBS of the occurrence of events using a dedicated national haemovigilance form. Data from these forms are entered into a Microsoft Access™ database for subsequent analysis and reporting. If more detailed information is indicated additional event-specific forms are sent to the hospital concerned.

All events recorded in the database are reviewed by a 'Haemovigilance Steering Group' to ensure the validity and consistency of data. During the period 1May 2005 to 30 April 2006, 410 events, received from 40 hospitals (both public and private), were subsequently included in the database.

Whilst the majority of events have been non-haemolytic febrile transfusion reactions (NHFTR) or allergic reactions (48.5% and 32.2% respectively) other events include 'transfusion associated circulatory overload' (TACO; 2.9%), 'incorrect blood component transfused' (IBCT; 3.7%), 'transfusion associated acute lung injury' (TRALI; 3.2%) and delayed transfusion reactions (2.7%).

The Haemovigilance Programme appears to have gained acceptance within the New Zealand transfusion sector with each of the country's 21 District Health Boards represented in the cases reported. However to overcome undoubted under-reporting of events, especially those not causing an observable 'reaction' in the patient, there is still much effort required in raising awareness of the programme not only for blood bank staff but also for nurses, doctors and quality personnel.

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Immunomodulatory responses of allogeneic neutrophils (PMNs) to stored red blood cell (RBC) products

MF Veale *, KA Payne, T Georgakopoulos, G Healey, K Glenister, RL Sparrow

Research Unit, Australian Red Cross Blood Service, Melbourne, Australia

RBC transfusion has been implicated in adverse patient outcomes. Both pro-inflammatory and immunosuppressive mechanisms have been suggested and are collectively referred to as Transfusion-related immunomodulation (TRIM). Although the wider use of pre-storage WBC (white blood cell) filtered product has reduced the incidence of TRIM, it has not eliminated its other effects, suggesting that other mechanisms other than WBC factors must operate.

Aim

In this study we used *in vitro* functional assays to represent the response of a transfusion recipient's (responder) immune cells to RBC products and investigated the influence of residual WBCs and storage of the RBC transfusion product on responses by fresh allogeneic PMNs.

Methods

Buffy coat poor, hard-spun (HS) and leucocyte filtered (LF) RBCs were prepared using standard blood bank procedures. Samples were collected from RBCs on day 1, 14, 28 and 42 at product expiry. Cytokine release was determined by incubating fresh ABO-compatible responder PMNs isolated from normal donors, with stored RBC supernatants. Culture supernatants from responder PMNs were assessed by enzyme-linked immunosorbent assay (EIA) or cytokine-antibody microarrays. Induction of CD11b and CD54 on PMNs following incubation with RBC was determined by flow cytometry. Interaction of RBCs from stored RBC products with responder PMNs was investigated by a continuous flow perfusion assay.

Results

Supernatants from HS-RBCs induced CD11b and CD54 expression and cytokine release from responder PMNs including IL-8 and MIP-1β. The adherence of stored LF-RBCs to fMLP-activated PMNs increased with increasing storage time and PMNs pre-incubated with supernatant from stored HS-RBCs showed increased adherence of RBCs compared to untreated controls.

Conclusion

Our results suggest that factors in addition to WBC content of RBC products play a role in TRIM. The nature of the storage-related changes for the increased adhesion of stored RBCs to responder PMNs warrants further investigation.

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A gift in good health: blood donor selection and risk factors for transfusion –transmissible viral infection

Mark N. Polizzotto *, Erica M. Wood, Simon D.J. Gibbs, Helen Ingham and Anthony J. Keller

Donor and Product Safety Team, Australian Red Cross Blood Service.

Background

Selection of voluntary donors who are at low risk of transfusion-transmissible viral infection (TTVI), via pre-donation screening interview, is central in maintaining the safety of Australia's blood supply.

Aim

To explore donor selection and risk factors in allogeneic donors found to have a TTVI.

Methods

Identification of allogeneic donors who met selection criteria but were found to have a TTVI, with assessment of potential infective risk factors by follow-up interview.

Results

6.3 million donations were tested between January 2000 and June 2006; of these, 1449 donations (0.02%) tested positive for a TTVI and were discarded. This comprised 818 donations (56%) positive for Hepatitis C (HCV); 605 (42%) positive for Hepatitis B (HBV); 18 (1%) positive for HIV; and 20 (1%) positive for Human T-cell Lymphotrophic Virus (HTLV). Ten were positive for HBV and HCV; one for HCV and HIV; and one for HCV and HTLV.

Potential infective risk factors for each donor were re-assessed by a trained counsellor, and were able to be identified in 1158 cases (80%); 509 donors (44%) had more than one potential risk factor. The most common identified risks included country of birth and parental (especially maternal) ethnicity (n=682, 26%); tattoos or piercings (n=448, 18%, occurring median 16 years previously, range <1–45 years); and undisclosed intravenous drug use (IVDU; n=302, 12%, median 12 years previously, range <1–30 years). The relative importance of these risks varied between infections. For HBV, country of birth and parental ethnicity contributed 71% of identified risk (n=626), followed by sexual contact with individuals from outside Australia (n=44, 5%) and tattoos/piercings (n=43, 5%). For HCV, tattoos/piercings contributed 26% of identified risk (n=409), followed by IVDU (n=301, 19%). For HIV, undisclosed male-to-male sex within 12 months contributed 33% of identified risk (n=4), followed by sex with a sex worker (n=2, 17%), while for HTLV the major identified risks were at-risk household contacts and sex with individuals from overseas (combined n=8, 61%).

Conclusions

These findings affirm the effectiveness of current stringent donor selection criteria in excluding donors who are at risk of transfusion-

transmissible viral infection. No infective risk factor could be identified in 20% of donors with TTVIs. The major identified risk factors for infections other than HIV were temporally remote, particularly tattoos/piercings and IVDU for HBV/HCV, and vertical transmission for HBV.

ANZSBT – Masterclass

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Autoimmune haemolytic anaemias

Anneke Brand
Sanquin Blood Bank, The Netherlands

Acquired haemolytic anaemia is a rare disease that can run a mild to life-threatening course.

The most frequent cause is antibodies against erythrocytes. The appearance of such antibodies can be associated with identified (secondary) or unknown (idiopathic) immune suppression. Recently the incidence of AIHA increased associated with immune suppression with newly developed drugs and stem cell transplantation.

Clinical case-oriented diagnostic and therapeutic problems will be discussed in this class which can be attended by beginning as well as experienced colleagues with interest in immunohaematology.

ANZSBT – Current Regulatory Issues

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Assuring quality and safety of haematopoetic progenitor cells – development of appropriate regulatory provisions

Jeff Szer
Professor/Director, Department of Clinical Haematology & Bone Marrow Transplant Service,
Royal Melbourne Hospital

The subject of the regulation of cellular and tissue therapeutics recently has risen to high levels of consciousness in many clinicians who have been using these cells for a long time. Haemopoietic stem cells were the earliest used therapeutically and remain the most widely used engraftable cellular product in clinical medicine: in Australia and New Zealand in 2004, there were 1313 transplants performed in 44 different hospitals. The clinical use of these cells now extends into the 8th decade of life and 34 patients over the age of 70 were the beneficiaries of such treatment. Regulators have in mind the need to minimise (or preferably abolish) risk to recipients associated with the production and dispensing of cellular products while clinicians have focussed largely on the clinical risks associated with transplantation procedures themselves. While it is clear that these clinical risks of transplantation far outweigh any potential risks associated with the manufacture of the cells, the regulators would find themselves not fulfilling their duty if potentially unsafe products were allowed to find their way into patients. Accordingly, a prolonged period of discussion between the Therapeutics Goods Administration and interested stakeholders began in 2003 while all parties were made aware of the respective needs of the other groups. Key clinical participants in this process have been the Bone Marrow Transplant Scientists Association of Australia and later, the incorporation of the Bone Marrow Transplant Society of Australia and New Zealand allowed BMT clinicians to participate formally. The end result of this process has been the construction of a new set of standards to be published eventually under the auspices of the National Pathology Accreditation Advisory Council which will make clear the processes required for the collection, processing, storage and issue of minimally manipulated haemopoietic progenitor cell products and the requirements for obtaining a licence from the TGA for this purpose. Participants in the process were the TGA, NPAAC, NATA and clinicians and scientists involved in stem cell transplantation. The document is based on the FACT/JACIE standards and should be internationally acceptable while allowing for specific Australian (and New Zealand) conditions. This process is a demonstration of the success of wide collaboration, sufficient time for all parties to understand all of the ramifications of decisions and ultimately, common sense.

ANZSBT – Free Communications 2

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Sample and request form labelling errors – introduction of a NZBS national database

Simon Benson *, Dr Peter Flanagan
New Zealand Blood Service, Auckland, New Zealand

New Zealand Blood Service (NZBS) manages the blood banks in six of New Zealand's largest hospitals between them responsible for the major proportion of the country's pretransfusion testing.

The international transfusion literature have shown that labelling errors and misidentification associated with pretransfusion samples significantly increases the risk of transfusion errors, particularly transfusion of incompatible or 'wrong' blood.

On 1 May 2006 NZBS introduced a national procedure, at its blood banks, for the collection of data regarding errors associated with pretransfusion sample and request form labelling. A list of errors required to be reported has been created based on NZBS sample and request form labelling requirements, in turn based on requirements of the ANZBST 'Guidelines for pretransfusion testing' (2002). The occurrence of these errors is routinely recorded by each blood bank on a national NZBS form and data subsequently entered into a Microsoft Access™ database for analysis and reporting. Additional errors are recorded where this is required by individual hospitals but are not included in the wider analysis of data.

During the period 1 May 2006 to 30 June 2006, 1341 requests with the defined errors in sample and/or request form labelling were received. Of the 1398 specific errors reported 81.9% were due to the five most prevalent errors, namely: patient details - discrepancy between sample and form (20.2%), sample not signed (19.2%), missing/incomplete details (15.7%), sticky label on sample (13.7%) and declaration not signed (13.2%).

The NZBS sample and request form labelling errors database is starting to yield useful data and from this data it is hoped to gain an understanding of the nature and scope of labelling errors seen in the six NZBS blood banks. This knowledge will provide a unique opportunity for raising the awareness of what errors are occurring, awareness which will hopefully precipitate a reduction in numbers.

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Blood Services in Banda Aceh, Indonesia, after the Boxing Day tsunami 2005

David Jones

Australian Red Cross Blood service

The Indonesian province of Nanggroe Aceh Darussalam (Aceh) (NAD) was struck by a devastating Tsunami on 26th December 2004. Blood Services in several towns, notably the city of Banda Aceh, were severely compromised by flood water and debris.

In June 2005 the Australian Red Cross Blood Service, via the Global Advisory Panel (GAP), (current chair Dr Robert Hetzel), was asked to provide a scientist to assist with a review of blood services in the Aceh region. The ensuing report and recommendations would be presented to the Indonesian Blood Service (Palang Merah Indonesia, PMI) with a view to helping shape the future blood service in the region and also help direct the future involvement of the Australian Red Cross and the GAP in the area.

In September 2005 the ARCBS delegate arrived in Banda Aceh to work with an ARC delegate already in situ and a scientist from the PMI, to assess the blood service in the region.

Eleven centres covering an area of 57,365 km^2 and a population of 4 million were visited and assessed in their abilities to provide a quality blood service. Assessments included: equipment; grouping; crossmatching; virology testing; donor interviews; documentation and use of non renumerated donors

Conclusion

These audits raised awareness of transfusion practice standards in both public and private health organisations. The results provide an important tool for use in engaging stakeholders in local targeted, relevant transfusion improvement initiatives. The data arising from these audits will also inform the future work program of our state-wide BeST program.

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Implementing universal leucocyte depletion

Neil Beckman

NBS, Birmingham, England and ARCBS, Melbourne, Victoria

Aim

Universal leucocyte depletion (LD) of blood components requires fundamental changes to blood collection and processing. The National Blood Service (NBS) was required to implement this policy by the UK Department of Health. The objectives were to implement the most appropriate and robust operational solutions, a supporting procurement mechanism and widespread understanding and acceptance of the strategy.

Methods

Formal risk and health and safety assessments were performed to identify concerns. Validation procedures, acceptance criteria and standard leucocyte counting and monitoring methodologies were developed. Specifications for LD, red cell and platelet filtration losses and filtration times were assigned. LD methodologies were adopted, when validated, leading to a phased introduction of LD. Systems were introduced to monitor and collate LD results by the use of standard software files and blood pack faults, in conjunction with the

manufacturers. Modes of LD failure were identified and methods of assessing the performance of a LD process developed. Contingency measures in the event of a process failure were documented.

Results

The NBS implemented universal LD by November 1999. The LD specification was that >99% of components should have <5x106 leucocytes/unit with 95% confidence. In 2006 this was augmented with the additional Council of Europe requirement that >90% of components should have $<1x10^6$ leucocytes/unit. For Jan-Jun 2000, the failure rate at a specified limit of $5x10^6$ leucocytes/unit for apheresis platelets, pooled platelets, whole blood filtered SAG-M and red cell filtered SAG-M was 0.46, 0.11, 0.15, and 0.16% respectively and for Jan-Mar 2006, 0.17, 0.03, 0.06 and 0.04% respectively.

Conclusions

Implementation required considerable resources. The main problems were the initial poor performance of some LD systems, poor manufacture quality of blood packs, the use of 'cutting edge' methodologies and the changes to infrastructure and process flow. Results have improved over time with experience and improved LD systems.

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Implementation of best practice guidelines in Victoria and Tasmania

K. Botting [1], N. Boyce [2], C. French[3], A. Holian [4], L. McNicol [5], H. Savoia [6] *

[1] Department of Human Services, Melbourne, Victoria, Australia
[2] Australian Red Cross Blood Service, Melbourne, Victoria, Australia
[3] Western Health, Melbourne, Victoria, Australia
[4] Bayside Health, Melbourne, Victoria, Australia
[5] Austin Health, Melbourne, Victoria, Australia
[6] Royal Children's Hospital, Melbourne, Victoria, Australia

Introduction

The Better Safer Transfusion (BeST) program, Department of Human Services Victoria, aims to improve transfusion safety and appropriateness of use of blood and blood products within hospitals. The foundation for the work is the translation of national best practice guidelines into everyday transfusion practice.

Method

A series of audits of prescription and administration practices were conducted over a three-month period to:

1. determine contemporary patterns of usage of fresh frozen plasma (FFP) and alignment with the National Health and Medical Research Council/Australian and New Zealand Society of Blood Transfusion (NH&MRC/ANZSBT) Guidelines 2001
2. determine if blood management and red cell transfusion in orthopaedic patients are aligned to NH&MRC/ANZSBT 2001 Guidelines and if effective alternative treatments are being used
3. determine if blood product administration policies and procedures were available, appropriate and practised within hospitals and consistent with ANZSBT/Royal College of Nursing Australia Guidelines 2004.

Results

FFP data	Red cells in orthopaedic patients	Administration protocols and practice
21 sites, 553 transfusion episodes	20 sites, 607 episodes of care	88 sites provided protocol data 79 sites submitted prospective practice data (1,329 episodes)
65% of episodes consistent with guidelines	32% transfusion rate 79% of transfusion episodes aligned with guidelines (for 'clinical triggers' of transfusion)	95 % had protocols, up to 64% were incomplete.
Spectrum of conditions treated was similar to previous reports	Blood conservation strategies were not commonly applied in elective surgery (6% pre-operative autologous donation, 10% salvage)	Opportunities exist for practice improvements eg 80% recorded post-transfusion observations.

Conclusion

These audits raised awareness of transfusion practice standards in both public and private health organisations. The results provide an important tool for use in engaging stakeholders in local targeted, relevant transfusion improvement initiatives. The data arising from these audits will also inform the future work program of our state-wide BeST program.

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NAIT: Time for action!

Nicole Staples[1,2] *, Annette Hughes[1], John Lown [1], Susan Weightman[2]

[1] Transfusion Medicine Unit, PathWest Laboratory Medicine, Royal Perth Hospital, Perth, WA, Australia
[2] ARCBS, Perth, WA, Australia

Introduction

Neonatal alloimmune thrombocytopenia (NAIT) is a serious condition of the fetus and newborn caused by maternal antibodies to fetal platelet antigens affecting 1:1100-2000 pregnancies. Severe, occasionally fatal, intracranial haemorrhage occurs in 10-20% of those affected. Treatment of affected neonates includes HPA compatible platelets, if available, and/or intravenous immunoglobulin.

Aims

A WA NAIT Laboratory Action Group was established in 2005. The aim of this group was to optimise laboratory processes relating to NAIT including:

- Improve communication between clinical staff, hospital laboratories, Platelet Reference Laboratory and ARCBS
- Record detailed patient information
- Provide timely, matched platelet support
- Raise awareness of the condition and provide educational material
- Create a WA NAIT Register to record incidence and outcomes.

Results

Actions include:

- Implementation of Laboratory Investigation Form submitted by referring hospital for all NAIT investigations, with maternal, paternal and neonate's information: blood groups, ethnicity, maternal platelet counts, previous pregnancies, clinical presentation and treatment of neonate.
- Creation of WA NAIT Register to record information from Laboratory Investigation Form, laboratory results and incidence and outcome of NAIT.
- Maternal HPA antibody details entered on the WA Antibody Register (established 1976 to record all red cell antibodies in WA).
- Patient information: letter, antibody register card, and information booklet explaining significance of platelet antibodies in pregnancy.

13 cases of NAIT were confirmed January 2005-June 2006: anti-HPA 1a (10), anti-HPA 5b (2), anti-HPA 1b (1). 1 neonatal ICH death was recorded. 2 cases were repeat pregnancies of known alloimmunised mothers (anti-HPA 1a).

Conclusion

Formation of the WA NAIT Action Group has greatly improved inter-laboratory communication resulting in a coordinated approach to NAIT investigations and supply of compatible platelets. Information booklets have increased awareness of NAIT. WA NAIT Register should provide useful information to contribute to better understanding of the condition and treatment outcomes.

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Blood prescription forms & informed consent – overcoming the obstacles

Susan McGregor[1] *, Chris Hogan[1,2]

[1] Western, Sunshine & Williamstown Hospitals (Western Health)
[2] Royal Melbourne Hospital (Melbourne Health)

Background

The ANZSBT and Royal College of Nursing Australia Guidelines for the Administration of Blood (2004), and the NHMRC Clinical Practice Guidelines (2001) recommend clinicians obtain informed consent prior to the transfusion, and the clinical indication be recorded in the

medical record.

A retrsopective audit of records of sixty inpatients who received transfusion at Western Hospital between December 2004 and March 2005 revealed the clinical indication was recorded in only 58% of episodes. No documentation of a discussion with the patient regarding the risks and benefits or consent was located in any audited records.

Aim

To improve the documentation of indication, and documentation of a discussion regarding the risks and benefits of transfusion, the Western Health Transfusion Committee developed a new Blood Prescription Form. This form incorporated three essential elements: the order to transfuse/administer, the clinical indication, and confirmation of a discussion regarding the risks and benefits, and agreement or refusal of the transfusion by the patient/guardian. Provision was made for any emergency situation.

Method/Process

The form was trialled over one month in a surgical ward. Education sessions were conducted with nursing and medical staff, and patient information brochures provided. Audit of the records of sixteen patients who had been transfused showed 100% of episodes had appropriate clinical indications, and documentation of a discussion of the risks and benefits.

A recommendation was then made to the Clinical Governance Committee for health service wide implementation of this Blood Prescription Form. This was declined after resistance to a consent process by several senior Committee members. Following numerous submissions and presentations to this Committee by the Chair of the Transfusion Committee and Transfusion Nurse, the form was finally approved. A multi-faceted educational intervention, compromised of education sessions, posters, and web-based guidelines and procedures, was conducted prior to implememtation.

Results

A retrospective audit of the medical records of twenty inpatients transfused in June/July 2006 showed a significant increase in the number of transfusion episodes with clinical indications documented (90%), and of documentation of a discussion of the risks and benefits of transfusion (85%).

Conclusion

Early results indicate that the introduction of our Blood Prescription Form is likely effective in improving documentation of clinical indications for transfusion, and documentation of a discussion between clinicians and patients of the risks and benefits, and consent or refusal to transfusion.

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Managing the risk of transmission of variant Creutzfeldt-Jakob Disease (vCJD) by blood and tissues

Marc Turner

Clinical Director, Edinburgh & South East Scotland

Blood Transfusion Centre, New Royal Infirmary, Edinburgh, UK

Variant Creutzfeldt Jakob disease was first identified in the UK in 1996 on account of its atypical clinical features and young age of onset. The clinical, neuropathological and experimental data all suggest that this is the same strain of disease as Bovine Spongiform Encephalopathy and different from that of sporadic or familial CJD. In light of this, a number of precautionary measures have been taken by Blood Services worldwide in order to reduce the risk that the disease may be transmitted by blood or tissues. The description of 3 such transmissions over the past few years reinforces the wisdom of a precautionary stance. However in assessing the current risk there remain a number of key uncertainties. Although the incidence of clinical vCJD is now falling in the United Kingdom (UK) there is an important discrepancy between the number of future cases projected on that incidence and the prevalence of sub-clinical vCJD predicted on the basis of a retrospective study of tonsil and appendix samples in the UK. The best mathematical models now suggest that around 1 in 10,000 UK blood donors may be sub-clinically infected although only a minority may go on to develop clinical disease. The concentration, temporal and spatial distribution of infectivity in peripheral blood of such patients is uncertain and can only be estimated by extrapolation from animal models. In the face of such uncertainties, evaluating the impact of existing risk reduction measures and the need for further measures is problematic. A number of donor deferral strategies have been implemented in the UK and elsewhere, but are crude risk management tools and have an adverse impact on the donor base. Significant progress is being made in development of peripheral blood screening assays but significant challenges exist in trying to reach appropriate levels of sensitivity and specificity and in knowing how to manage the implementation of such an assay in such a way as to protect public health whilst minimising the adverse impact on donors and the blood supply. Two companies have now developed prion reduction filters which could significantly reduce the risk of transmission of disease. However the evaluation of these devices is problematic in that it has be carried out on spiked brain homogenates or endogenous infected animal blood, the relevance of which to the human situation is uncertain. The evaluation and implementation of these further risk reduction measures is likely to pose further very significant challenges to Blood Services worldwide. In the meantime the best available risk reduction measure remains optimal clinical transfusion practice.