ANZSBT ORAL ABSTRACTS PRESENTED AT THE HSANZ/ANZSBT/ASTH WITH APSTH ANNUAL SCIENTIFIC MEETING, MELBOURNE, 28-31 October 2012

Sunday 28 October

ANZSBT Symposium 1: Transfusion Trials for Clinical Practice

Clinical Trials in Transfusion Medicine

Larry J Dumont
The Geisel School of Medicine at Dartmouth, Lebanon, NH USA

Aim
We will review key questions on the safety and efficacy of transfusion practice, highlight recent and ongoing clinical trials, and discuss barriers to the implementation of new methods and practices.
Results
Contemporary dogma is that transfusion practice should be informed and guided by the best available evidence. Although blood products have been used for decades, there remain areas where evidence is weak or lacking to support current practice. Progress has been made in understanding the role of white cells in alloimmunisation and transfusion reactions, platelet dose effectiveness in hypoproliferative thrombocytopenia, antibody mediated TRALI, plasma and platelet use in trauma, methods to reduce the risk of transfusion acquired sepsis, effective test strategies for infectious disease screening, RBC transfusion triggers in adult critical care and others. Questions still remain regarding transfusion triggers, dose, prevention of adverse events, and prevention of transfusion transmitted infectious diseases. As we scan the patient population served by transfusion medicine (such as, neonatology, trauma, neurology, pediatric intensive care, cardiac surgery, and hematologic oncology), it is apparent that one size does not fit all. Evidence across all patient groups is needed. Where solutions seem to be within our grasp, such as pathogen reduction, implementations are hampered because of uncertainties related to adverse events. Clinical trials have been opened world-wide to address some of these points.
Conclusion
Important evidence has been provided in recent clinical trials, and important trials have been launched. There remain open questions. Collaborative effort is necessary to identify and overcome barriers to gaining important evidence and timely implementation of solutions.

Keywords clinical trial, evidence based medicine

Conflict of interest No

Sunday 28 October
ANZSBT Symposium 1: Transfusion Trials for Clinical Practice

Patient Outcomes and Red Blood Cell Storage: the Clinical Studies

Christopher P Stowell
Massachusetts General Hospital & Harvard Medical School, USA

Aim

The aim of this lecture is to provide a broad overview of the clinical studies which have been carried out to determine the effects of RBC storage on patient outcomes. In addition, the design of several ongoing, randomized, controlled clinical trials addressing this issue in critical care patients and cardiac surgery patients will be reviewed.

Results

One of the most controversial topics in our field in recent years has been the question of whether or not the transfusion of stored RBC has adverse effects on patients. It has been proposed that the numerous changes which are known to occur to RBC during storage impair their function when transfused and, furthermore, be actively deleterious. A large number of retrospective clinical studies, and a few prospective studies, have been carried out to address this issue, but the results have not been conclusive. Within the past few years, several randomized clinical trials addressing the effect of RBC storage on patient outcomes have been initiated. In this session, the speaker will summarize our current understanding of this issue based on the results of published clinical studies, and describe several ongoing randomized, controlled clinical trials which have been a designed to provide an answer to this question.

Conclusion

Although it is firmly established that the RBC changes during storage, we remain in a state of clinical equipoise on the question of whether or not these changes affect patients in a clinically significant way.

Keywords – RBC storage, RCT, equipoise

Conflict of Interest – none

Sunday 28 October
ANZSBT Symposium 2: Transfusion Safety Today and the Future

What Have We Learned From Haemovigilance?

TRIP Dutch National Hemovigilance and Biovigilance Office, The Netherlands

Aim

- To review results from implementing a national haemovigilance reporting system, based on the Dutch experience
- To note lessons concerning the most trequently reported transfusion hazards
- To recognise strengths and limitations of national haemovigilance data

Introduction

The national hemovigilance office in The Netherlands commenced data collection in 2003.

Methods

The hemovigilance office is run by a foundation governed by representatives of professional societies. It captures reports all types of transfusion reaction, both serious and non-serious, and incidents in the transfusion chain. Expert review is in place for all serious reports. For serious transfusion reactions and errors reporting to the healthcare inspectorate is mandatory under EU legislation; this can be effected using the TRIP a digital reporting system.

Results

Participation by hospitals has run at over 95% since 2006. The annual number of reports has shown a slight continued rise since then to 2601 in 2011, for an overall rate of 3.9/1000 blood components distributed. The largest categories are those of new allo-antibody formation, febrile non-hemolytic transfusion reactions and minor allergic reactions. The annual rate of serious reactions is approximately 0.15 per 1000 components distributed. A drop in TRALI reports was observed following implementation of male-only plasma. The most frequent serious reactions in 2011 were other reaction (reactions not meeting criteria for recognised reaction categories), anaphylactic reaction and transfusion-associated circulatory overload. The overall rate of reported incorrect blood component transfused was 0.07/1000 components. This has dropped from 0.09/1000 in 2009.

Discussion and conclusion

Collecting information about transfusion reactions and errors in the transfusion chain has highlighted the risks associated with blood transfusion. Hemovigilance data capture is subject to variable and under-reporting. Only some adverse reactions can be prevented.

Keywords reporting system, transfusion error, adverse reaction
Conflict of interest None

Sunday 28 October
HSANZ/ANZSBT/APSTH Workshop 7: Goldilocks and the 3 Platelets

Platelets in MPD Clinical Syndromes and Management

Claire Harrison
Guy's and St Thomas' Hospitals, London, UK

A raised platelet count, bleeding or thrombosis are often the first manifestation of a myeloproliferative disorder (MPD) triggering an investigation and indeed all of these issues may also guide management decisions for these patients. A raised platelet count may also be a manifestation of other clinical states such as myelodysplasia or iron deficiency. How can we best reach a more certain diagnosis of MPD? In this session we will also discuss the role of platelets in the pathogenesis of clinical complications of the MPDs – innocent bystander or smoking gun ? In particular for essential thrombocythaemia our management has been driven by the height of the platelet count.

In collaboration with colleagues in Australia, New Zealand, Ireland and France since 1997 we have been accruing patients into the Primary thrombocythaemia -1 trial. With well over 1000 patients entered this trial is now yielding important insights into this disease from pathogenesis, diagnostics, impacts of newer molecular markers, prognostic factors and treatment decisions. I will share the latest information from this trial and data from other authors in this session.

Keywords Platelet, MPD, Thrombosis

Conflict of interest Received speaker fees from Novartis, Shire, Cellgene, Sanofi Avensis; consultancy work for YM Bioscience, S*Bio, Sanofi Avensis and research funding from Shire and Novartis.

Sunday 28 October
HSANZ/ANZSBT/APSTH Workshop 7: Goldilocks and the 3 Platelets

Platelet Function Defects

Paul Harrison
Oxford Haemophilia & Thrombosis Centre, Churchill Hospital, Oxford University Hospitals NHS Trust, Oxford, UK

Inherited platelet defects are a heterogeneous group of rare bleeding disorders presenting with a classical mucocutaneous bleeding pattern. They may be difficult to diagnose and manage (and are likely to be under-diagnosed). They are generally characterised by a range of molecular defects affecting either platelet function and/or number. Most defects result in deficiencies and/or dysfunction within platelet receptors (e.g. GPIb-IX-V, Bernard-Soulier syndrome and integrin αIIbβ3, Glanzmann thrombasthenia), defects in receptors for agonists (e.g. $P2Y_{12}$, collagen and thromboxane receptors), various signalling pathways, cytoskeletal proteins, alpha and dense granule contents and procoagulant activity. With Chediak-Higashi, Hermansky-Pudlak, Wiskott-Aldrich and Scott syndromes the molecular defect also affects other cells. There is a failure of platelet production in Familial thrombocytopenia that sometimes results in macrothrombocytopenia (e.g. MYH9-related diseases). Diseases of platelet production can also interfere with the development and function of major organs. Acquired platelet defects are most commonly caused by the administration of various anti-platelet drugs e.g. aspirin/NSAID's. Numerical and/or functional platelet disorders are also prevalent amongst patients with abnormal bleeding and may be clinically indistinguishable from other haemostatic disorders, particularly von Willebrand disease (VWD). An evaluation of patients with abnormal bleeding symptoms requires objective clinical assessment of bleeding history, a physical examination and if appropriate a suitable panel of platelet function investigations. Laboratory testing can identify a low platelet count, abnormal platelet size and morphology, the loss or abnormal functioning of receptors, downstream signalling pathways, storage organelles, or enzymatic activities essential for platelet adhesion, activation, aggregation and procoagulant activity. A full diagnosis is only complete when the genetic mutation(s) have been defined for each patient although the molecular basis of some defects remains to be fully characterised. Platelet disorders can also sometimes co-exist with other coagulation factor defects or VWD. Laboratory investigations of platelet number and function are therefore recommended in any patient where bleeding symptoms are not fully explained by standard clinical laboratory investigations.

Keywords Blood Platelet Disorders/diagnosis, Platelet Function

Conflict of interest Consultant for Sysmex UK, Research Grants from Eli Lilly and Siemens Diagnostics. Wife is an employee of IL-UK.

Sunday 28 October
HSANZ/ANZSBT/APSTH Workshop 7: Goldilocks and the 3 Platelets

Platelet Support: Best Practice in Malignant Haematology

Terry B Gernsheimer
Puget Sound Blood Center, University of Washington School of Medicine, Seattle, Washington, USA

Platelets, along with reactive vasoconstriction, are the first response to bleeding and the need to maintain haemostasis. Without adequate numbers of platelets to preserve vascular endothelial integrity spontaneous bleeding occurs, and when tissue is damaged, bleeding occurs more readily and may be uncontrollable. Since storage of platelets for transfusion became possible in the 1960's investigators have sought the optimum strategy to prevent bleeding in thrombocytopenic patients with haematologic malignancy.

The two main variables in the approach to platelet transfusion have been the "transfusion trigger" or "threshold" at which platelets should be administered, and the appropriate dose of platelets necessary to maintain vascular integrity while minimizing exposure. More recently, whether platelet transfusions could be postponed or avoided until signs of bleeding occur has been explored as a potential management option.

This session will review the most recent data on the transfusion management of the patient with haematologic malignancy and thrombocytopenia. Alternative strategies, including the use of antifibrinolytic agents and thrombopoietic receptor agonists, will be discussed.

Keywords Platelet transfusion, thrombocytopenia, platelet alloimmunization

Conflict of interest No

Sunday 28 October
ANZSBT Symposium 3: Age of Red Cell - Blood Storage Lesion

Stored Red Blood Cells: Old or Vintage?

Christopher P Stowell
Massachusetts General Hospital & Harvard Medical School, USA

Aim

The aim of this lecture is to review the biochemical and structural changes that occur in RBC during storage under conventional blood bank conditions including some of the studies done in animal model systems to assess the functional impact of these storage-related changes.

Results

RBC stored under conventional blood bank conditions undergo numerous biochemical change such as reduction in the levels of intra-erythrocytic 2,3-diphosphoglycerate, adenosine triphosphate and nitric oxide (and its adducts). These observed changes have generated physiologically plausible hypotheses about how they might affect the ability of the RBC to function once transfused. For example, a decrease in the 2,3-DPG level would decrease the P_{50}, and perhaps impair oxygen unloading. NO-depleted RBC might not be able to maintain the degree of vasodilatation required to permit adequate blood flow to the tissues. In addition, numerous changes in the structure and characteristics of the RBC plasma membrane have also been described, including the loss and oxidation of membrane lipids and proteins and the rearrangement of some membrane constituents. These changes are accompanied by the formation of microvesicles and a loss of membrane elasticity which could interfere with the movement of the RBC through the microcirculation. Evidence from animal model systems also suggests that stored RBC do not function as well as native RBC. These studies have pointed out the importance of blood viscosity and sheer stress for maintaining microvascular blood flow, although differences in the biology of RBC from different species, notably in the pace of their “aging”, warrant some caution in extrapolating these data to the clinical setting.

Conclusion

The biochemical and morphological changes which occur to RBC during storage have led to the formulation of several hypotheses about how they might affect their function, and some data from animal model systems support these hypotheses.

Keywords – RBC storage, biochemical changes, membrane changes

Conflict of Interest – none

Sunday 28 October
ANZSBT Symposium 3: Age of Red Cell - Blood Storage Lesion

What Research is Telling Us About the Storage Lesion

Rosemary Sparrow
Research and Development, Australian Red Cross Blood Service, Melbourne, Victoria, Australia

The current concerns about the 'age of blood' has encouraged renewed interest in laboratory-based research to better understand the biological effects of storage on red cell components and the potential implications of the red cell storage lesion on transfusion outcomes. Despite decades of research, it is clear that there is still much to learn about the basic biology of red cells together with the effects of manufacturing and storage. It is also clear that red cells are not just oxygen-delivery vehicles, but rather they contribute to blood dynamics through interaction and modulation of other blood elements.

This presentation will highlight some of the new approaches being used by researchers to better understand the red cell storage lesion and how these research findings may offer new insights into the potential in vivo responses of transfusion recipients.

Keywords red cells, storage lesion, transfusion

Conflict of interest No

Monday 29 October
ANZSBT Presidential Symposium

O025

Effects of Short Term Temperature Excursions on Irradiated Platelet Concentrates

Kelly Winter, Lacey Johnson, Matthew Kwok, Tanja Hartkopf-Theis, Samantha Reid, Denese Marks
Research and Development, Australian Red Cross Blood Service, Sydney, NSW, Australia

Aim
Platelets stored outside the acceptable temperature range (20-24 °C) for any length of time during processing, transportation or storage are usually discarded. However, there is currently limited published data on the effects of short excursions outside this range on platelet quality. The aim of this study was to evaluate the *in vitro* quality of irradiated platelets following temperature excursions below or above their optimal storage temperature.
Methods
Whole blood derived pooled platelet concentrates prepared in 28 % plasma/SSP+ were gamma-irradiated with 25-50 Gy on day 1 and then exposed to temperatures of either 18 °C or 28 °C for 3 hours without agitation (n=10) on day 2. Before and after the temperature excursions, platelets were stored under standard conditions at 22 °C with agitation. Platelet concentrates were sampled on day 1 prior to the temperature excursion, day 2 after the excursion, then on days 5 and 7. Platelets were tested using an array of *in vitro* assays designed to test platelet quality and functionality. Irradiated platelet concentrates stored at 22 °C with agitation served as a reference.
Results
Following a 3 hour excursion at 18 °C there were no differences in the measured *in vitro* quality parameters compared with reference irradiated platelet concentrates ($p>0.05$). In contrast, irradiated platelet concentrates stored at 28 °C for 3 hours displayed increased glucose consumption and lactate production immediately following the temperature excursion on day 2 ($p<0.001$ and $p=0.002$ respectively). However, there were no changes in ADP and collagen aggregation, hypotonic shock response, annexin V and viability ($p>0.05$).
Conclusion
Short term temperature excursions for 3 hours at 18 or 28 °C had little effect on *in vitro* platelet quality. This information may be of use when deciding the fate of a specially matched (e.g. HLA-matched) platelet component that has been stored outside the recommended temperature range for short periods of time.

Keywords platelets, temperature, irradiated
Conflict of interest No conflict of interest to disclose

Monday 29 October
ANZSBT Presidential Symposium

O026

Glucose-containing Additive Solution Supports Platelet Recovery and *In Vitro* Quality Parameters Following Cryopreservation

Lacey Johnson, Kelly M. Winter, Diana Vidovic, Shereen Tan, Denese C. Marks
Research and Development, Australian Red Cross Blood Service, Sydney, Australia

Aim
Platelets for transfusion are typically stored at 20-24 °C for up to 5 days. However, the shelf-life can be extended to 2 years when frozen at -80 °C in 5-6% dimethylsulfoxide (DMSO). Platelets are frozen in a hyperconcentrated state to minimise residual DMSO concentration in the transfused product. Consequently, these platelets require reconstitution upon thawing, which is typically carried out using a unit of plasma. However, reducing the plasma content in platelet products may provide both operational and clinical benefits. As such, the aim of this study was to determine whether the use of a glucose-rich additive solution (PAS-G) could replace plasma in the preparation and reconstitution of a cryopreserved platelet product, whilst maintaining *in vitro* platelet quality.

Methods
DMSO (5% final concentration) was added to buffy coat-derived pooled leukoreduced platelet concentrates on day 2 following whole blood collection. The platelets were then hyperconcentrated by centrifugation (1250 x g) and frozen at -80 °C. The cryopreserved platelet units (n=12) were thawed at 37 °C, reconstituted in a unit of PAS-G (Pall Corporation) and stored at 22 °C with agitation. Platelet recovery and *in vitro* quality were examined prior to freezing, immediately after thawing and at 6 and 24 hours post-thaw.

Results
The platelet recovery after thawing was greater than 70%, with each unit containing an average of $252.5 \pm 35.9 \times 10^9$ platelets. The frozen platelets displayed a reduction in the surface expression of several key platelet receptors, including GPIbα and GPIIb. Further, freeze/thawing induced the expression of the platelet activation markers CD62P, CD63, annexin V and increased the secretion of multiple cytokines. Importantly, platelets were still capable of *in vitro* aggregation in response to both collagen and ADP, despite a measurable loss in activity.

Conclusion
Preparation and reconstitution of cryopreserved platelets in PAS-G maintains post-thaw platelet recovery and *in vitro* quality for up to 24 hours, without the need for supplementation with plasma. This data supports a novel use for a new generation platelet additive solution and may lead to future improvements to cryopreservation techniques.

Keywords Cryopreservation, platelet concentrate, dimethylsulfoxide
Conflict of interest No conflict of interest to disclose

Monday 29 October
ANZSBT Presidential Symposium

O027

Identification of Potential Dendritic Cell and Monocyte Inflammatory Biomarkers to Predict Patient Outcomes in the Transfusion Setting

Melinda M Dean[1], Luke D Samson1[1,2], Robert L Flower [1,2]
[1]Research and Development, Australian Red Cross Blood Service, Brisbane QLD Australia, [2]Queensland University of Technology, Brisbane QLD Australia

Aim
The basis for poor outcomes in some patients post transfusion remains largely unknown. In addition, there is evidence that the age of blood components transfused significantly affects patient outcomes. An in vitro whole blood model of transfusion was utilised to investigate potential myeloid dendritic cell (DC) and monocyte inflammatory markers that may predict patient outcomes in the transfusion setting.
Methods
ABO-compatible leukodepleted packed red blood cells (PRBC) were cultured with freshly collected "recipient" whole blood at 25% blood-replacement-volume for 6hrs. PRBC were stored at 4°C and utilised in the transfusion model at various time points during storage until expiry (Day (D) 2, 14, 28 and 42). In parallel, LPS or Zymosan (Zy) were added to model infection. Recipients were maintained for the duration of each PRBC time course (2 recipients, 4 PRBC units, n=8). Recipient DC and monocyte production of IL-6, IL-10, IL-12, TNF-α, IL-1α, IL-8, IP-10, MIP-1α, MIP-1β, MCP-1) were determined via flow cytometry. Changes in immune response were calculated by comparison to a parallel "no transfusion" control (Wilcoxin matched pairs, 95% CI). Influence of storage age was calculated using ANOVA.
Results
Exposure to PRBC resulted in significant suppression of DC and monocyte inflammatory responses. In particular DC and monocyte production of MIP-1α and IL-1α were significantly reduced, regardless of PRBC storage. Storage-independent PRBC-mediated suppression of DC and monocyte IL-1α was also evident in cultures co-stimulated with Zy. In addition, a significant reduction in both DC and monocyte TNF-α, IL-6, MIP-1α, MIP-1β and IP-10 were evident following PRBC exposure in co-culture with either LPS or Zy as models of infection. PRBC storage attenuated monocyte TNF-α production when co-cultured with LPS ($P<0.01$).
Conclusions
The complexity of the transfusion context was reflected in the whole blood approach utilised. Modulation of DC and monocyte inflammatory response was largely independent of PRBC storage. Significant suppression of DC and monocyte immune regulators may contribute to poor patient outcomes. We propose TNF-α, IL-1α, IL-6 and MIP-1α as potential biomarkers of patient outcomes post-transfusion.
Keywords Dendritic Cell, Monocyte, Immune Suppression, Blood Transfusion
Conflict of interest No conflict of interest to disclose

Monday 29 October
ANZSBT Presidential Symposium

O028

Variation in Transfusion Practice in Cardiac Surgery: A Report from the Australian and New Zealand Society of Cardiac and Thoracic Surgeons (ANZSCTS) Cardiac Surgery Database

Zoe McQuilten[1,2,3], Nick Andrianopoulos[1], Erica Wood[1,2,3], Merrole Cole-Sinclair[4] John McNeil[1], Peter Cameron[1], Christopher Reid[1], Julian Smith[1,3] and Louise Phillips[1] on behalf of the Australian and New Zealand Society of Cardiac and Thoracic Surgeons (ANZSCTS) Steering Committee.
[1]Monash University, [2]Australian Red Cross Blood Service, [3]Monash Medical Centre and [4]St Vincent's Hospital, all in Melbourne, Victoria, Australia

Aim
To measure variation in transfusion of red blood cells (RBC), platelets (PLT), fresh frozen plasma (FFP) and cryoprecipitate (CRYO) in cardiac surgery.
Methods
Procedures on all adult patients who underwent cardiac surgery from January 2005 – December 2011 at 25 Australian hospitals as recorded in the ANZSCTS database were included. Summary statistics and multiple logistic regression were used to examine variation and possible association of patient and hospital level factors with the following transfusion outcomes: one or more RBC, PLT, FFP and CRYO and 5 or more RBC from surgery until hospital discharge.
Results
In 43482 recorded procedures 55% were isolated coronary artery bypass graft (CABG), 17% were isolated valve, 11% were CABG and valve, and 17% were other procedures. Rates of transfusion following adjustment for patient and procedure factors varied across hospitals for one or more RBC from 22% to 67%, 5 or more RBC 5% to 25%, one or two RBC 10% to 34%, one or more PLT 11% to 39%, one or more FFP 11% to 48% and one or more cryoprecipitate 1% to 20%. The difference in transfusion rates was not accounted for by hospital level factors (odds ratio,95%confidence interval) including for one or more RBC: private vs. public (0.7,0.2 – 2.4), non-teaching vs. teaching (1.3,0.4 – 4.5), or state (1.5,0.9 – 2.7)
Conclusions
Substantial variation in transfusion of all blood components and large volume RBC transfusion was identified and remained even after adjustment for patient-level factors. Hospital-level factors examined did not account for the observed différences between institutions. Further work to elucidate factors contributing to this variation and how it may influence patient outcomes is warranted.
Keywords Transfusion, Cardiac surgery
Conflict of interest No

Monday 29 October
ANZSBT Presidential Symposium

O029

Clinical Coding Data to Describe Critical Bleeding - Lottery or Mother Lode?

AJ Zatta[1], Z McQuilten[1,2], N Aoki[1], L Stevenson[3], K Badami[4], K Davis[5], N Andrianopoulos[1], P Cameron[1], J Isbister[6], L Phillips[1], E Wood[1] *on behalf of the Massive Transfusion Registry Steering Committee*
[1]Monash University [2]Australian Red Cross Blood Service and [3]Blood Matters Program, Victorian Department of Health, all in Melbourne, VIC [4]New Zealand Blood Service, Auckland [5]Royal Adelaide Hospital, Adelaide, SA [6]University of Sydney, Sydney, NSW, Australia.

Background

Clinical coding data, collected primarily for hospital funding, are increasingly being studied to understand blood utilisation according to clinical demand.

Aim

To examine the validity of using clinical coding data to determine types of critical bleeding events (CBE) requiring massive transfusion (MT)

Results

Data regarding MT indications were collected from medical records for 282 patients from 33 hospitals across Australia & New Zealand. Data collectors categorised types of CBEs into defined bleeding contexts (Table 1). Admission DRG and ICD10 codes were extracted separately. ICD10 coding logic, using diagnosis and procedure codes, was developed to assign patients a bleeding context. The DRGs were similarly grouped. Both ICD10 and DRG were compared against the data collectors' interpretation. Excellent agreement was found between the bleeding context assigned by data collectors and ICD coding logic. In contrast, poorer agreement was achieved between data collectors and DRG.

Bleeding context derived from medical record (*n*)	**Observed agreement with the medical record**	
	of ICD10 coding logic	**of DRG classifications**
Trauma (46)	91.3%	56.5%
Cardiac surgery (34)	88.2%	52.9%
Obstetric haemorrhage (43)	97.7%	95.3%
Vascular surgery (43)	69.8%	62.8%
Liver surgery (6)	50.0%	0.0%
Gastrointestinal haemorrhage (64)	82.8%	8.8%
% Agreement (kappa value)	**82.6% (0.79)**	**53.7% (0.48)**

Table 1: Agreement between bleeding context identified from different data sources

Conclusions

ICD10 coding logic developed for the Massive Transfusion Registry is reliable and sufficiently accurate to broadly categorise CBEs.

Keywords Critical Bleeding, Massive Transfusion, Clinical Coding Data
Conflict of interest This research was partially supported by CSL Biotherapies. The company had no role in analysing the data or preparing the abstract.

Monday 29 October
ANZSBT Symposium 5: Pathogen Inactivation and Blood Safety

European PI Experience

Emma Castro
Centro de Transfusión de Cruz Roja Española en Madrid, Spain

Background

The current paradigm of safety is the implementation of laboratory screening methods and restrictive donor criteria. Pathogen inactivation is a proactive way to manage pathogens before they enter the blood supply because it impedes the replication of a wide range of viruses, bacteria and parasites within plasma, platelets, or red blood cells.

PI State of the Art

There are two different technologies that inactivate viruses in plasma (Solvent Detergent -S/D - and Methylene Blue) another two for the inactivation of a wide range of viruses bacteria and parasites in platelets and plasma (INTERCEPT TM from Cerus Corp. and Mirasol from Terumo BCT). Theraflex UVC for platelets from Macopharma is under development. With respect to red cells, Cerus has developed a system based on S-303, that is under clinical trials at this moment and it is committed for the development of a new system for whole blood. Terumo BCT is also developing a new system for the treatment of whole blood.

S/D Plasma: It was introduced in Germany in 1992 and nowadays is in use in 15 EU countries. More than 12,015,969 bags have been used to treat 4,005,323 patients during the last 20 years without relevant side effects.

Methylene Blue plasma: Intended for individual treatment of FFP units. It is in routine use for more than 12 years in 8 EU countries and more than 5.5 million of units have been transfused without remarkable side effects.

INTERCEPT TM for Platelets and Plasma: The system is in routine use in more than >100 centers in 17 countries (12 in UE) and there are ongoing evaluations in 11 countries (incl. Australia and Malaysia). More than 1,300,000 PI platelets and plasma transfusions. Haemovigilance have demonstrated that no relevant side effects occur.

Mirasol-for Platelets and Plasma: CE marked in 2002. It is in use in 50 centers in 16 countries (7 within EU). Nowadays > 24,000 platelets and >34,000 units of FFP have been transfused, without remarkable side effects.

Theraflex UVC for Platelets: The device obtained the CE mark in 2009. Clinical trial Phase II/III is planned for 2013.

Conclusion

Pathogen inactivation systems are widely implemented in Europe with thousands of PI platelets and plasma transfusions without remarkable side effects. This means that the goal of «zero risk» is coming ever closer.

Keywords Transfusion transmitted infectious diseases; Pathogen Inactivation;
Conflict of interest Author is member of the Scientific Advisory Board of Macopharma. The author's Blood Centre has been awarded Centre of Excellence by Cerus Corporation.

Monday 29 October
ANZSBT Masterclass: "There were three dames from Quebec .." Limericks and rare red blood cell phenotypes

"There Were Three Dames from Quebec .." Limericks and Rare Red Blood Cell Phenotypes

Christopher Stowell
Massachusetts General Hospital & Harvard Medical School, USA

Aim
The aim of this lecture is to review the H deficient RBC phenotypes from the perspective of the Transfusion Service.

Results
The speaker will review the serological work-ups of several patients with H-deficient phenotypes, the molecular basis for these phenotypes, and how such cases can be managed at the level of the transfusion service.

Conclusion
"Chance favors only the prepared mind.." Louis Pasteur.

Keywords – Bombay, H-deficient RBC

Conflict of Interest – none

Tuesday 30 October
ANZSBT Free Communications 1

O078

A New Method of Testing for Anti-IgA Antibodies in Adverse Transfusion Reactions

Katie Havelberg, Gail Pahn, Bruce Dawkins, Mark Burton, Greg Jones
Australian Red Cross Blood Service

Aim
The presence of anti-IgA in a transfused patient can result in an adverse transfusion reaction presenting with allergic or anaphylactic reactions. These reactions can range from uncomfortable to life-threatening. Historically, results from anti-IgA testing were not available for up to one month in our laboratory, due to a range of testing constraints. We have developed a fluorescent microbead-based test for anti-IgA1 and anti-IgA2 antibody detection. This method is fast, reliable, allows a rapid result turn around and is much less labour intensive than the previous in-house ELISA method.

Method
The method utilises a simple immunocomplex reaction. This reaction takes place on an antigen-coated polystyrene microbead. Flow cytometry detects anti-IgA that is bound to the coated microbeads, using a fluorescent detector antibody. Anti-IgA1 and anti-IgA2 can be detected separately but simultaneously in the same reaction tube. A number of samples were evaluated using the new method, and compared with the results from in house ELISA and commercial ELISA and PaGIA methods.

Results
The microbead method detected 100% of antibodies that were detected in either one or all of the in-house ELISA, commercial ELISA and PaGIA methods. Three positive samples had varying results using each of the comparison methods, with the beads being the only method able to detect the antibody in all three samples. This suggests that the bead method has a higher sensitivity than the other methods. Following successful validation, the anti-IgA microbead method has been utilised for routine testing within our laboratory for the past 12 months.

Conclusion
The results of the validation testing were satisfactory, with all parameters meeting the acceptance criteria. The use of the new assay has resulted in a reduction in both time and labour involved in testing for anti-IgA antibodies, and consequently a faster result turn-around time. Investigations can be completed within 48 hours of a transfusion reaction – providing a result that is more useful for clinicians in their decisions regarding further treatment, including the use of IgA deficient blood products if necessary.

Keywords Anti-IgA, Adverse Transfusion Reaction
Conflict of interest No conflict of interest to disclose

Tuesday 30 October
ANZSBT Free Communications 1

O079

Sero-prevalence of Antibodies to *Leptospira* Among Blood Donors in High-risk Areas of Queensland

Helen Faddy[1], Vanessa Racloz[2], Colleen Lau[2], Robert Flower[1], Philip Weinstein[3]
[1]Research and Development, Australian Red Cross Blood Service; [2]School of Population Health, University of Queensland; Brisbane, Qld. [3]Barbara Hardy Institute, University of South Australia, Adelaide, SA

Aim
To examine the sero-prevalence of antibodies to *Leptospira spp* in blood donors residing in high-risk areas of Queensland.
Methods
A total of 498 plasma samples were collected from blood donors residing in high-risk areas of northern Queensland, based on notification rates of leptospirosis (including Ingham, Innisfail, Mareeba, Tully, Cairns, Townsville and Brisbane) during 2009 and 2011. All samples were tested for the presence of antibodies to 22 leptospiral serovars by microscopic agglutination. Samples with a titre of 1:400 or higher against any serovar were described as serologically suggestive of a recent infection, while samples with a titre greater than 1:50 were described indicative of previous infection.
Results
Of the 498 plasma samples tested, none had antibody titres suggestive of a recent infection. However, seven donors (1.41% 95%CI: 0.37 – 2.44%) had titres suggestive of previous infection.
Conclusion
Leptospirosis is an acute febrile illness, with concomitant bacteraemia, and transfusion transmission of *Leptospira* is possible. Infection is relatively uncommon in Australia, however, higher rates of infection are observed in northern Queensland. Management of the risk of transfusion-transmitted leptospirosis at the Australian Red Cross Blood Service involves total product restrictions for 3 months following a diagnosed infection, as well as product use restrictions for abattoir workers. Blood component quarantine or recall for donors reporting any illness within 7 days of donation and bacterial contamination screening are additional safety measures. In this study, we did not find evidence of recent infection in Queensland blood donors residing in high-risk regions. Collectively, our study provided novel data to underpin evidence-based risk assessment and policy development relating to *Leptospira* and the safety of the Australian blood supply, and supports the appropriateness of our current relevant donor selection policy.

Keywords Sero-prevalence, blood safety, leptospirosis
Conflict of interest No

Tuesday 30 October
ANZSBT Free Communications 1

O080

Alterations in Red Blood Cell (RBC) Band 3 and 4.1R Proteins Effect Viability During Storage

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Maintaining RBC shape, deformability and elasticity involves complex interactions between protein 4.1R, transmembrane protein band 3 and the cytoskeletal network. Band 3 and 4.1R are crucial to the maintenance of RBC structure and function, including RBC membrane phospholipid asymmetry, membrane integrity and viability.

Aim

The purpose of this project was to monitor the RBC changes occurring in band 3 and 4.1R, and to correlate these with viability during RBC storage and aging.

Methods

Leukocyte-depleted RBCs ($n \leq 6$) were processed according to standard Blood Service procedures. Samples were collected aseptically at day 1, 14, 28 and 42. Standard haematological parameters were tested. At each time point, density fractionated young and old RBCs and ghosts were prepared. RBC shape and size were measured by flow cytometry (FCM). Changes to band 3 were determined using a fluorescent dye, eosin-5-maleimide (EMA) and the mean fluorescence intensity (MFI) was measured using FCM. RBC viability over storage was measured using calcein a fluorescent vital dye. The changes to the 4.1R protein in RBC ghosts was determined by using SDS-polyacrylamide gel electrophoresis and Coomassie Blue and silver staining. Densitometric analysis was performed using an Image Quant analyser. Results were statistically analysed using ANOVA.

Results

RBC size increased over storage and differences to surface complexity were greatest between young and old RBCs ($p<0.05$). EMA MFI decreased significantly at day 14 in young and old RBCs, suggesting changes to band 3 distribution in the RBC membrane ($p<0.01$). Calcein MFI decreased in all RBCs over storage with significant differences between young and old RBCs ($p<0.001$) suggesting that RBC viability and membrane integrity decrease over storage. Changes to the 4.1R in old RBCs suggest that alterations occur to the cytoskeletal network of proteins.

Conclusion

These results suggest that RBC membrane alterations that occur in band 3 and 4.1R during storage and aging and may contribute to decreases in RBC viability.

Keywords band 3, protein 4.1R, red blood cells
Conflict of interest No

Tuesday 30 October
ANZSBT Free Communications 1

O081

Older Stored Red Blood Cells Promote Increased Adhesion of Fresh Allogeneic Leucocytes with Endothelial Cells

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Aim
Transfusion of older red cells (RBCs) has been linked to poorer clinical outcomes in which endothelial perturbation may be implicated. Using *in vitro* EC flow perfusion and *ex vivo* perfused vessel models designed to simulate *in vivo* blood transfusion, this study investigated the interaction of allogeneic leucocytes (representing the patient's cells) and endothelial cells (ECs) (representing the patient's blood vessel wall) that were pre-treated with stored RBCs or their supernatant.
Methods
RBCs were prepared by standard Blood Service procedures. Samples were collected during 42 days of storage. Human ECs were cultured on perfusion slides (EC-perfusion assay). Fresh murine aortic vessels were mounted in a customised perfusion chamber. ECs/vessels were pre-perfused at 37°C with stored RBCs, RBC supernatant or medium alone. Fresh allogeneic whole blood (WB) was obtained from healthy volunteers and neutrophils (PMNs) were isolated for the EC-perfusion assays. PMNs were perfused across the ECs at 0.5 dyne/cm^2 and PMN adhesion recorded by a CCD camera (n=8 experiments). For the *ex vivo* vessel model (n=5), WB was fluorescently labelled with Vybrant-DiI dye and perfused through the vessel at 0.12mL/min. Leucocyte adhesion to the vessel wall was recorded by 10 sec-videos of two fields of view taken over 15 min by a CCD camera fitted to the fluorescence microscope. Unpaired t-tests and ANOVA determined significance.
Results
ECs pre-perfused with supernatant or RBCs from RBC units stored for >35 days resulted in increased PMN adhesion compared to control (for supernatant pre-perfusion, 17±2 vs 6±1 PMNs/field; $p<0.0002$) (for RBCs, 23±3 vs 6±1 PMNs/field; $p<0.002$). For the vessel model, vessels pre-perfused with 42 days-stored RBCs resulted in increased leucocyte adhesion (13±2 vs 2 ±0.5 leucocytes/field; $p<0.001$).
Conclusion
Exposure of ECs to stored RBCs or RBC supernatant promotes increased interaction of allogeneic leucocytes with ECs in our *in vitro* transfusion models. These findings may potentially lead to better understanding the effects of stored RBCs on EC interactions, which may be implicated in poorer clinical outcomes.
Keywords red blood cells, endothelial cells, leucocytes
Conflict of interest No

Tuesday 30 October
ANZSBT Free Communications 1

O082
Weak D Type 1, 2 and 3 in the Western Australian Patient Population

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Aim
To determine the proportion of weak D types 1, 2 and 3 using TaqMan PCR in serologically identified weak D samples in a Western Australian patient population.
Method
60 patient samples sent for routine blood grouping reacting with anti-D at a grading <4 in Diaclon ABO/D gel cards (Biorad), were further evaluated using a panel of twelve monoclonal anti-D reagents (Alba Bioscience, Scotland) to differentiate weak D from partial D. Molecular analysis of the weak D samples to characterise weak D type 1, 2 and 3 was performed by TaqMan realtime PCR using custom TaqMan (Assay-by-DesignSM, Applied Biosystems) MGB primer-probe mixes for the specific amplification of *RHD* and exclusion of *RHCE*. DNA sequencing of exons 1, 6 and 9 was performed using previously described primers[1]
Results
The percentage of patients in the Western Australian population identified as weak D type 1, 2 or 3 by TaqMan PCR are shown in Table 1. The serological reactivity patterns with monoclonal anti-D were variable for all weak D types.
Table 1:% of patients identified as weak D types 1, 2 or 3 using TaqMan PCR.

Molecular Characterisation by TaqMan	% Patients (n=60)
Weak D Type 1	40 (24)
Weak D Type 2	50 (30)
Weak D Type 3	5 (3)
Unknown	5 (3)

Conclusion
Weak D type 2 was the prevalent allele in the Western Australian population contrasting with many other geographical locations where type 1 is reported to predominate. Although 95% of patients serologically identified as weak D were confirmed as weak D type 1, 2 or 3 significant heterogeneity in anti-D reactivity was observed.

[1] Wagner F, Frohmajer A, & Flegel W. RHD positive haplotypes in D negative Europeans. BMC Genetics 2009 2:10.

Keywords weak D, monoclonal anti-D, TaqMan PCR **Conflict of interest** No

Tuesday 30 October
ANZSBT Free Communications 1

O083

Clinically Significant DEL-associated *RHD* Alleles Exist Within the Australian RhD Negative Blood Donor Panel

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[1]Research and Development and [2]Red Cell Reference Laboratory, Australian Red Cross Blood Service, Australia

Aim

RBC donations with weakly expressed RhD antigen, or 'DEL' donations, are typed and managed as RhD negative. r'r and r"r donors have been genotyped, and 8 DEL-associated *RHD* alleles have been characterised. DEL-associated alleles which have been reported to immunise RhD negative patients, *1227G>A* and *hom IVS5-38del4*, have been detected. As a result of these initial findings, the study was continued to define the frequency of these types in the RhD negative donor panel

Method

gDNA from r'r and r"r donors (*n*=1026) was screened for *RHD* exon 4, 5, 10 by qPCR. Donors with a *RHD* signal were SNP analysed using a DNA microarray to fully characterise the *RHD* allele.

Results:

Donor Group	*N*	*RHD* Alleles
1: Carry *RHD* alleles not expected to be immunogenic	53/1026	*Non-functional RHD alleles*
2: Carry potentially immunogenic DEL-associated alleles	21/1026	*RHD-CE(4-9)-D; IVS3+1G>A; IVS3+2T>A; M295I; 94insT; 1177C*
3: Carry DEL-associated alleles reported to be immunogenic	9/1026	*1227G>A and hom IVS5-38del4*

Using qPCR and SNP data, the r'r and r"r donors tested were divided into groups of different risk of RhD immunogenicity. Group 1 donors, 5.17% (95% CI: 3.81–6.52%), carry non-functional *RHD* alleles that do not encode for the RhD antigen and are not expected to be immunogenic. RBC donations from Group 2 donors, 2.05% (95% CI: 1.18–2.91%), are potentially immunogenic as donors carry a DEL-associated allele predicted to express a DEL phenotype. Group 2 alleles have not been reported to immunise RhD negative patients. Donors from Group 3, 0.88% (95% CI: 0.31–1.45%), do carry DEL-associated alleles that have been reported to immunise.

Conclusion

Clinically significant DEL alleles *1227G>A* and *hom IVS5-38del4* were detected in 0.88% of an Australian r'r and r"r blood donor sample. To reduce the risk of DEL immunisation, policy in relation to the issue of these DEL donors should be developed.

Keywords: RhD; DEL; immunise
Conflict of interest: No

Tuesday 30 October
ANZSBT Free Communications 2

O084
Lessons from the Albumin Quarantine 2012

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Aim
Information was collated from BloodSafe Transfusion Nurses and key transfusion personnel from South Australian public and private sectors regarding the quarantine of Albumin. The experience and learnings from the Albumin quarantine process in South Australia 2012 have been summarised.

Results
The quarantine highlighted a number of issues

- Imprest (official and unofficial)
- Traceability
- Communication to and within the organisations
- Clear lines of responsibilities for acting upon communication
- Cases where it was used (or not)
- Roles of transfusion nurse, transfusion service provider and transfusion committee involvement in the process.
- Human factors can still corrupt sound processes

Conclusion
The profile of Albumin being a blood product and it's traceability requirements were raised within some organisations. It also reinforced the hospitals role in managing blood and blood products safely and efficiently. Imprest levels of Albumin official (and other) have been reassessed and modified. As a result of this experience communication lines have been tested and reassessed along with responsibilities clarified, allowing for more succinct future communications if the need arises. The role of the transfusion nurses varied depending upon which hospitals they supported. Despite some hospitals handling the process extremely well human factors can still intervene.

Keywords Albumin, quarantine, transfusion nurses
Conflict of interest No conflict of interest to disclose.

Tuesday 30 October
ANZSBT Free Communications 2

O085

Does the Duration of Blood Storage Impact on the Prognosis of Critically Ill Patients - A Multicentre Observational Study?

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Aim

To assess the impact of Red blood cells (RBC) storage duration on the outcomes of patients hospitalised in intensive care unit (ICU).

Methods

This retrospective multi-centre study was conducted over a 10-year period. All adults admitted to ICU in two tertiary hospitals who received at least one RBC were included. The impact of storage duration of the RBC (or age of blood) on ICU and hospital mortality and length of stay (LOS) was evaluated using the mean, maximum and minimum ages of blood divided into deciles. A multivariate analysis was performed adjusting for potential confounders. Subgroup analysis was performed on patients with no RBC transfusion prior to ICU and patients who received leukodepleted RBC exclusively.

Results

Between 2001 and 2011, 8416 patients were transfused with a median of 4 (IQR=2-7) units per patient. The overall ICU and hospital mortality was 10% and 26%, respectively. The mean age of the first RBC unit received per patient was 18.1±8.5 days and was lower for the survivors compared to the non-survivors (17±0.2 days versus 18.3±0.1 days, p=0.0001). In multivariate analysis adjusting for factors associated with the risk of death on univariate analysis (Apache 3 score, admission category type, number of RBC units received, study centre and year), neither the mean, maximum or minimum age of RBC was associated with mortality. Similar results were obtained for the subgroup analyses. However, the age of the oldest RBC and the mean age were both independently associated with an increased ICU and hospital LOS, in the overall population and in the sub-groups analyses.

Conclusion

In this large study, RBC storage duration was not associated with mortality but was independently associated with ICU and hospital LOS. These results support the need for a multicentre randomised trial to determine whether, compared to standard care, transfusion of the freshest available RBC leads to clinically relevant benefits.

Keywords age of blood, critically ill patients, outcome

Conflict of interest Nothing to disclose

ANZSBT Free Communications 2

O086

Validation of Transfusion Laboratory Information System Data is Important in Data Linkage Studies: Results from a Validation Study

Zoe McQuilten[1,2,3], Nick Andrianopoulos[1], Joanne Enticott[1], Erica Wood[1,2,3], Merrole Cole-Sinclair[1,4], John McNeil[1], Peter Cameron[1], Julian Smith[1,3], Christopher Reid[1], Louise Phillips[1] on behalf of the Australian and New Zealand Society of Cardiac and Thoracic Surgeons (ANZSCTS) Steering Committee

[1]Monash University, [2]Australian Red Cross Blood Service, [3]Monash Medical Centre and [4]St Vincent's Hospital , all in Melbourne, Victoria

Aim

Data from transfusion laboratory information systems (LIS) are increasingly being linked with clinical data to inform transfusion practice. Accurate data are essential for correct estimates of the risks and benefits of transfusion and appropriate interventions. However studies to validate data for this purpose are lacking. This study aimed to validate LIS data against the Australian and New Zealand Society of Cardiac and Thoracic Surgeons ANZSCTS Cardiac Surgery Database (CSD).

Methods and Results

Data regarding transfusion episodes from surgery until discharge date in all patients who underwent cardiac surgery at 6 Victorian sites in 2008 were analyzed.

During the study period, 2689 patients underwent cardiac surgery. LIS data were extracted on 2685 patients for 2709 procedures and matched to CSD. Kappa value (95% Confidence Interval) for agreement between LIS and CSD was 0.76 (0.74-0.79) for transfusion of one or more red blood cell (RBC) unit, 0.71 (0.67-0.74) for 5 or more RBC units and 0.83 (0.80-0.85), 0.86 (0.84- 0.89), 0.83 (0.80-0.87) for one or more doses of platelets, fresh frozen plasma or cryoprecipitate, respectively. Total number of mismatches for any RBC unit between LIS and CSD was 321 (12%) and for 5 or more RBC units 235 (9%). In 55 (2%) procedures, the difference in RBC units transfused was outside limits of agreement on Bland-Altman plot. Compared with the patient medical record, 54 (98%) had missing RBC data in the LIS dataset. Problems identified included discrepant patient identifiers, the data query used and incorrect dates recorded in the LIS extract.

Conclusion

There was very good to excellent agreement between LIS and CSD data on transfusion episodes, supporting use of LIS for data linkage purposes. In those cases with a large discrepancy between the two data sources, the most common cause of error was inaccurate data extraction from the LIS.

Keywords Transfusion, data, cardiac surgery

Conflict of interest No

Tuesday 30 October
ANZSBT Free Communications 2

O087

Has Transfusion Practice Improved in Australian Hospitals? Evidence from the Blood Matters Program Audits

Linley Bielby, Lisa Stevenson, Jo Perillo, Bridget Glazebrook, Erica Wood
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Aim
The audit aimed to determine whether health services had a blood administration policy that is consistent with national guidelines and that everyday transfusion practice at the health service adheres to the policy.
Method
In 2011, 155 public and private hospitals across Victoria, Tasmania, Northern Territory and Australian Capital Territory were invited to participate in a comparative audit (2005&2007). The process included a desk top audit of existing blood transfusion policy alignment to guidelines related to specimen collection, labelling, consent, patient identification (ID), observations and adverse reaction management. A prospective bedside observational audit of 30 transfusion episodes including: location, patient consciousness, ID, monitoring, documentation and adverse event management. Data were entered electronically by participants.
Results
Eighty-five hospitals responded, 69 public (81%) and 15 private hospitals (17%), 1 no longer provided transfusions. All sites had a hospital-wide transfusion policy, improving from 66% and 84% respectively in 2005 & 2007. Eighty-two hospitals reported 1595 transfusion episodes. Transfusions mainly took place between 8am-8pm (90%) and most patients (95%) wore ID bands. Patients were not asked to confirm ID at 34 hospitals; as high as 70% at one, and 40% at four others. Generally documentation remained the same or improved. Adverse effects associated with transfusion were reported by 23/82 hospitals, 16% had no documentation of the event compared to 30% (2007), and 48% no documentation of reporting to the laboratory.
Conclusion
Transfusion practice has improved in hospitals contributing to the audits. The quality of hospital policies available to guide clinical practice has seen ongoing improvement from 2005 to 2011. There are still areas where practice can be improved, such as the reporting and management of adverse events, and more vigilant patient identification

Keywords Policy, practice, patient identification, transfusion safety
Conflict of interest No conflict of interest.

Tuesday 30 October
ANZSBT Free Communications 2

O088
Procedural Adverse Events in Transfusion: What Do We Know?

Marija Nedeljkovic[1,2], Lisa Stevenson[1,3], Bridget Glazebrook[1,3.], Linley Bielby[1,3], Erica Wood[1,2,3] on behalf of the STIR expert group
[1] Australian Red Cross Blood Service, [2] The Royal Melbourne Hospital & [3] Blood Matters Program - Victorian Department of Health, Melbourne, Vic, Australia

Aim/Background
The Victorian Serious Transfusion Incident Reporting (STIR) haemovigilance system that also includes reporting from Tasmania, Northern Territory and ACT, was established in 2007 after a successful pilot. Incident data related to transfusion are reviewed with the aim to identify potential areas for improvement and focus strategies for prevention. Procedural adverse events related to transfusion at the hospital end of the transfusion chain account for a large proportion of these incidents.

Method
Reports from January 2007 to March 2012 were reviewed, utilising the categories of incorrect blood component transfused (IBCT), wrong blood in tube (WBIT) and near miss for procedural incidents.

Results
A total of 992 incidents were reported to STIR over this time, of which 42% were procedural adverse events. The majority of these were WBITs and other types of near miss events where there is a potential for harm. There were 67 IBCTs (7%), including 5 ABO incompatible red cell transfusions, which contributed to serious harm for patients.
The majority of these errors occurred during the ordering and prescribing of blood products (21.5%), in the laboratory (22%) and at the bedside (21.5%), with patient/product identification as a key issue with all types of events. Factors contributing to errors included lack of awareness by junior doctors of patients' special requirements for blood products, poor communication between staff, failure to follow procedures regarding bedside pre-transfusion checks, and environmental conditions predisposing to risk, such as storage of blood in satellite fridges.

Conclusion
A large number of these process-related incidents are preventable. Near miss events provide valuable learning opportunities as they occur more frequently than actual harm events, and are preceded by the same patterns of error as adverse events causing harm. Given the complexity of hospital-based transfusion practice, interventions to improve transfusion safety aimed at this part of the transfusion chain depend on a combined approach, including staff training, simplifying procedures relating to transfusion and monitoring of performance standards.

Keywords Transfusion, Errors, STIR **Conflict of interest** No

Tuesday 30 October
ANZSBT Free Communications 2

O089
Predicting the Probability of Red Cell Transfusion in Surgical Patients

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Objectives
To predict the probability of red cell transfusion in patients undergoing cardiothoracic, colorectal and orthopaedic surgery based on pre-operative factors.
Methods
A linked electronic database developed for SA public hospitals using clinical, epidemiological and transfusion data was used. Admissions for a range of major surgical procedures over between January 2009 and June 2010 were included. Pre-operative variables including age, sex, type of surgery and haemoglobin [Hb] (up to 8 weeks prior to date of surgery) were analysed using logistic regression to model the probability of red cell transfusion.
Results
A total of 2821 surgical admissions including primary total arthroplasty of the hip [THR] (530), primary total arthroplasty of the knee [TKR] (643), right sided colorectal surgery (332), left sided colorectal surgery (305), coronary artery bypass grafting [CABG] (621) and on-bypass valve replacement surgery (390) were identified. The independent predictors of transfusion were older age (≥65 years: odds ratio [OR] = 1.7; 95% confidence interval [CI] = 1.4-2.1, p =0.001), female sex (OR = 1.4; 95% CI =1.1-1.8, p <0.001) as well as type of surgery and Hb level. Compared with TKA, the OR of transfusion was higher with left sided colorectal surgery (OR = 2.0; 95% CI =1.4-2.9, p <0.001), THR (OR = 2.3; 95% CI =1.7-3.2, p <0.001), valve replacement surgery (OR = 14.1; 95% CI =9.9-20.1, p <0.001) and CABG (OR = 14.8; 95% CI =10.6-20.6, p <0.001). The model showed that the odds ratio of transfusion was significantly higher if the pre-operative Hb was between 100 -110 g/L (OR -11.9 95% CI = 7.6 to 18.6, p <0.001) compared to a pre-operative Hb >140 g/L. Graphs showing the predicted probability of transfusion derived from the model (based on age, sex, type of surgery and pre-operative Hb) can be used in pre-operative assessment.
Conclusion
Based on the findings from the model, a number of preoperative factors can be used to better assess the probability of transfusion in individual patients. The results, after further validation, could be used to help target and prioritise patient blood management (PBM) initiatives.
Keywords: red cell transfusion, major surgery, pre-operative haemoglobin
Conflict of interest: No

Recipients' Perceptions of Red Cell Transfusions and Anti-D Administration

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New Zealand Blood Service, New Zealand

Aim
The primary aim was to ascertain whether patients were satisfied with the information received before the administration of the blood component/product and what concerns they had about blood transfusions.
Method
Using a combined modified version of a questionnaire by Gray & Murphy (1993) and Horne, Hankins & Jenkins (2001) patients at eight main hospitals in New Zealand were interviewed by Transfusion Nurse Specialists.
Results
356 red cell recipients and 191 Anti-D recipients were interviewed. All recipients were aware of having received either red cells or Anti-D. All recipients of Anti-D felt part of the decision making process whereas only 87% of those receiving red cells felt part of the process. Anti-D recipients were less concerned about receiving a blood product. The primary concern voiced by both groups was of contracting a viral infection. Anti-D recipients voiced no concerns post transfusion whereas 7% of red cell recipients still had concerns. Those patients who received written information were statistically less concerned about receiving blood transfusions compared to those who received verbal information only.
Conclusion
This survey provides a useful picture of the perceptions of various groups of patients receiving two different blood products. The results are relevant to the practice of transfusion medicine in New Zealand and provide a baseline of patient's perceptions toward blood transfusions. Results indicate that both Anti-D and red cell recipients were less likely to have concerns if given written information about their transfusion. However a significant minority of red cell recipients felt they weren't involved in the decision making process.

Keywords Consent, perception, satisfaction
Conflict of interest No

Tuesday 30 October
ANZSBT: Ruth Sanger Oration

The Marvellous Land of Oz - 2030

Ken Davis
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In the Wonderful Wizard of Oz, Dorothy, Scarecrow, Tin Woodman, and Cowardly Lion followed the yellow brick road [YBR] on their first adventure. In the Munchkin Forest it was broken by two deep crevices, and nearer the Emerald City a river cuts through it. In the Marvellous Land of Oz, Tip and Jack Pumpkin head followed another branch of this road as they rode the Sawhorse from the Gillikin Country to the Emerald City.

The road is famous, paved with smooth yellow bricks, which connects various sections of the Land of Oz to the Emerald City. It is broad, but not straight. It wanders over hill and dale. It's smooth except in a few places where bricks have crumbled or been removed, leaving holes. Following any stretch of the yellow brick road is a hazardous journey.

The YBR could well describe the many roads and directions that transfusion medicine has taken and is an analogy that may still be relevant as we attempt to look forward to 2030 and beyond. For many years we have awaited a range of new technologies to provide suitable alternatives or substitutes in lieu of some of our current treatment options. Success in bringing R&D to a therapeutic alternative has occurred with the recombinant clotting proteins FVIII , FIX and FVIIa. In the area of red cell alternatives and specific recombinant antibodies, we have seen promising developments slowed, halted or abandoned.

Are we being overly optimistic in anticipating that the fields of protein chemistry, genetic manipulation, cryobiology and large scale manufacture of artificial red cells or platelets in bioreactors will provide a new array of safe, cost-effective therapeutic alternatives?

Whether the rate of exponential development will continue at the pace of the last 20 years is yet to be seen.

Tuesday 30 October
ANZSBT Symposium 8: Platelet Storage

Evaluation and Characterization of Cryopreserved Platelets

Larry J Dumont[1], Jose Cancelas[2], Ann Galan[3], Gines Escolar[3], Kathy Grindle[1], Melissa Barber[1], Michelle Dumas[1], Sharry Baker[1], Sue-Ann Connary[1], Kathleen Grindle[1], Rene Geissler[1]
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[3]Serv Hemoterapia-Hemostasia, Hospital Clinic, Barcelona, Spain

Aim
The availability of 22°C stored platelets is severely limited in some settings. Our objectives were to develop a cGMP manufacturing process for 6% DMSO frozen platelets (CPP), and to characterize the *in vivo* and *in vitro* performance of CPP including storage stability at -80°C.
Results
We performed a randomized, Phase 1 study analysing platelet viability and *in vitro* function in consenting healthy subjects. CPP were prepared from apheresis platelets (AP) suspended in 6% DMSO, concentrated and placed at ≤ -65°C for 7 to 13 days, thawed at 37°C and resuspended into 25mL 0.9% NaCl. Autologous recovery and survival of CPP were determined and compared to fresh autologous platelets as a control. CPP 24-hour recovery (41.6±9.1%) was lower than AP (74.2±18.5%, $p<0.0001$) and did not meet the current FDA criterion. CPP had diminished survival compared to fresh platelets (6.8±2.1 vs. 8.2±1.3 days, respectively, $p=0.018$), but did meet and exceed the FDA criterion for survival. *In vitro* tests of CPP stored up to 6 months revealed CPP retained 77±6% of AP platelet yield, showed increased platelet associated P-selectin (72±10%), reduced responses to agonists, and platelet microparticle content of 2.8x10E6 per unit. Platelet coverages for platelet depleted whole blood in the Impact-R and Baumgartner perfusion chamber were restored by CPP in a dose dependent manner. Compared to 5-day old plasma stored platelets, CPP were more efficient at enhancing fibrin formation on vascular surfaces approaching that of whole blood. Clot viscoeleastic properties were evaluated in the TEG and ROTM devices, and thrombin generation by F1+2 and response in the calibrated automate thrombogram.
Conclusion
While 24-hour recovery does not meet FDA criteria for liquid stored platelets, the CPP survival of circulating platelets was surprisingly high and exceeded the FDA criteria. CPP retains a measure of adhesive functions and clot viscoelastive properties. These data support proceeding with additional studies to evaluate the clinical effectiveness of CPP.
Keywords cryopreservation, platelet, recovery
Conflict of interest No

Tuesday 30 October
ANZSBT Symposium 8: Platelet Storage

Platelet Storage: What Are We Doing in Australia?

Denese C Marks
Research and Development, The Australian Red Cross Blood Service

Platelets are the primary cellular mediators of haemostasis. In Australia over 130,000 platelet donations are supplied to hospitals every year for life-saving transfusions, most frequently for oncology patients or surgery and trauma. The shelf-life of fresh platelets is currently limited to 5 days due to the potential for bacterial contamination and development of the platelet storage lesion, which impair the quality of a platelet concentrate upon storage beyond 5 days. This presents a major challenge for managing a platelet inventory, and extension of the platelet shelf-life would be highly advantageous.

One way of prolonging the shelf-life of platelets is cryopreservation, allowing platelets to be stored frozen for up to 2 years. Cryopreserved platelets are not currently an approved blood component in Australia. There is, however, an unmet demand for such a product in remote and regional areas where platelets are either discarded due to infrequent demand or not immediately available in emergency situations. Similarly, cryopreserved platelets could be utilised by the Australian Defence Force (ADF) on deployments to austere environments where fresh blood products cannot be readily supplied.

The Netherlands Military Blood Bank has been using cryopreserved platelets since 2001 for peacekeeping and peace enforcing missions abroad, and they have been shown to be safe, effective and efficient in supporting combat casualty care. The ADF plans to adopt a similar capability for use in their deployments. The Australian Red Cross Blood Service has been working closely with the ADF to develop processes for producing and supplying deep frozen blood products, including cryopreserved platelets, based on published methods and those used by the Netherlands Military.

This presentation will highlight the methods we have been evaluating for freezing and thawing platelets, with emphasis on resuspension solutions and their effect on platelet quality. Some changes that occur to intracellular signalling will also be presented.

Keywords Platelet storage lesion, cryopreservation
Conflict of interest No

Tuesday 30 October
ANZSBT Symposium 8: Platelet Storage

Frozen Products in Remote Environments

Anthony Holley
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Haemorrhage is a potentially reversible cause of trauma deaths. The concept of haemostatic resuscitation, characterised by transfusion of blood products in an immediate and sustained fashion is well established. Early transfusion with red blood cells, platelets and plasma in a 1:1:1 ratio appears beneficial. This paradigm demands products be readily available in austere environments. Investigation into synthetic products has failed to provide a viable alternative. Refrigerated liquid products are limited by short shelf lives, while fresh, warm whole blood has significant draw backs. Deep freezing is able to substantially extend the shelf life of blood products required for resuscitation, facilitating practical resupply.

	Viable Storage Times	
	Standard Liquid Blood	**Deep Frozen Blood**
Red Blood Cells	42 days at 4^{o}C	10 years at -80^{o}C
Platelets	5 days at 22^{o}C	2 years at -80^{o}C
Fresh Frozen plasma	1 years at -30^{o}C	7+ years at -80^{o}C

Deep frozen blood product production requires cryopreservation with glycerol in the case of erythrocytes and dimethyl sulphoxide for the preservation of platelets. These agents protect the biological elements from the destructive potential of deep freezing. Prior to transfusion the products must be washed/prepared including removal of cryopreservatives. The development of a deep frozen blood product supply could substantially enhance the ability to provide high quality critical care for injured service personnel on deployment or civilians in remote centres. This presentation will describe the processes, training, Dutch/Australian experience and potential pitfalls of adopting "deep freezing" technology in the military environment.

Keywords Frozen blood products, military, remote
Conflict of interest No

Transfusion in the Vulnerable Trauma Patient

Herbert Schöchl
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Uncontrolled bleeding is the second most common cause of death following severe trauma just exceeded by major brain injury. Traditionally blood loss, consumption of coagulation factors and dilution of the remaining coagulation proteins has been assumed as the major components of trauma induced coagulopathy (TIC). Moreover, hypothermia and acidosis are well known contributors of coagulopathy and frequently observed upon emergency room admission. Additionally primary hyperfibrinolysis has been identified recently as an additional important driver of TIC. Uncompressible diffuse microvascular bleeding results in increased transfusion requirements and is strongly associated with poor outcome. To avoid exsanguination the concept of “damage controlled resuscitation” has been implemented in military and civilian trauma centres. This concept addresses blood pressure control to minimise blood loss by “popping the clot”, minimal prehospital volume therapy to avoid dilutional coagulopathy and aggressive rewarming. Furthermore early and consequent haemostatic therapy has been proven effective in avoiding and treating trauma related coagulopathy.
One of the core problems is to identify those patients early upon admission who are at risk for massive transfusion (MT). It has been shown that unnecessary exposure to FFP or platelet concentrates is associated with important side effects such as acute lung injury, transfusion related immune modulation and pathogen transmission. There is sound evidence that patients receiving less than 10 red blood cells within the first 24h do not benefit from early high ratio plasma or platelet transfusion. Therefore an early stratification regarding the potential risk of receiving MT is highly warranted. MT predictive scores based on both anatomical findings and rapidly available laboratory data, such as haemoglobin and the base deficit were developed in order to assess the risk of the individual patient for MT. Our group showed recently that thromboelastometric measurements are potentially useful to identify massive bleeders within 10 minutes upon ER admission. Patients with clot amplitude of 0 – 3 mm in the fibrin polymerization test (FIBTEM) showed an 85% risk for MT. The receiver characteristics operation curve was 0.83 which is similar to other published MT predictive scores. These retrospective data clearly have to be confirmed and validated in prospective studies.

Keywords Coagulopathy, trauma, risk stratification
Conflict of interest HS received speakers fees from CSL Behring and TEM international

Tuesday 30 October
ANZSBT Symposium 9: Transfusion Reactions in the Vulnerable Patient

Neonatal Exchange Transfusion – Challenges in the Modern Era

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Aim
To describe morbidity and mortality associated with exchange transfusion in a 21st century tertiary neonatal unit.
Results
Sixty four exchange transfusions (ETs) were performed in 51 infants over a 10 year period, an average of 6.4 ETs per year. This compares with over 100 a year performed in this hospital in the 1960's. Thirty-six (71%) infants were Rhesus isoimmunised and 6 (12%) had ABO incompatibility. The highest SBR prior to ET was 782 µmol/l. Of the 39 infants not on respiratory support prior to ET, 6 (15%) required mechanical ventilation afterwards; these infants were significantly more acidotic during the ET compared with those who were never ventilated (mean pH 7.309 and 7.153 respectively, mean difference -0.156, 95%CI -0.196 to -0.116, $p<0.001$). The three infants with the most severe hyperbilirubinaemia are known to have significant neurodevelopmental sequelae. Four (8%) infants died before a month of age.
Conclusion
Exchange transfusion is becoming a rare procedure in neonatal practice. Short term morbidity related to ET is common. Despite advances in neonatal care, an infant who undergoes ET remains at significant risk of dying in the neonatal period.

Keywords Neonate, exchange transfusion, complications

Conflict of interest No

Tuesday 30 October
ANZSBT Masterclass: RBC storage advances and metabolomics

RBC Storage Advances and Metabolomics

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Aim
Understanding the cause and effect relationship between red blood cell (RBC) collections, processing and storage (including age); the RBC phenotype; and clinical outcomes is central to many R&D initiatives and investigations. Our aim is to examine the changes in the RBC metabolomics profile and identify candidate biochemicals and/or processes that may correlate to clinic outcomes and may be amendable to either screening and selection or to interventions in RBC for transfusion.
Results
Broad metabolomic fingerprints covering over 270 metabolites from various RBC will be presented for discussion. These conditions include aerobic & anaerobic storage, storage times up to 6 weeks, various donors, gamma irradiated, and RBC treated with rejuvenation methods. The major RBC pathways of glycolysis, pentose phosphate, purine salvage, and glutathione homeostasis will be considered. Significant variations are observed between various RBC treatment methods and between individual donors. In a preliminary pilot study, levels of a few metabolites correlated with the autologous RBC recovery observed in four selected study subjects.
Conclusion
These observations suggest that candidate metabolites and/or pathways may be identified for hypothesis driven studies evaluating the effects on clinical outcomes. Understanding the larger metabolic profile picture within the RBC may inform the mechanistic understanding of the RBC storage lesion.

Keywords RBC, metabolomics, storage

Conflict of interest LJD has received research support and/or consulting fees from New Health Sciences, Fenwal, and Citra Labs.