

Strategic Blood Forum 2010

The Australian Red Cross Blood Service convenes an annual Strategic Blood Forum, providing clinical and government stakeholders an update on our activities, particularly those related to patient safety and service issues. The meeting is an opportunity to obtain feedback from our clinical colleagues and representatives from professional societies and the specialist colleges regarding areas of priority for them.

This year's Forum was held in Sydney on Wednesday 10 February.

This edition of *MediLink* focuses on specific issues discussed during the Forum.



Blood Storage Lesion and Age of Transfused Components: Implications for Recipient Safety and Blood Availability

Dr Rosemary Sparrow and Dr Pip Hetzel

Red blood cell (RBC) transfusion is a critical part of the health industry, with over 800,000 units of RBCs issued by the Blood Service annually. This represents approximately 87% of the total fresh blood components issued by the Blood Service.

RBCs are prepared from whole blood donations and are suspended in a simple preservative solution which allows the RBCs to be stored refrigerated until needed for transfusion. The RBC storage systems used in Australia are licensed for storage of RBCs for up to 42 days following blood collection. This shelf-life limit is governed by a US Food and Drug Administration (FDA) regulation which specifies that, when transfused, 75% of stored RBCs in a single RBC unit must still be circulating 24 hrs after transfusion.

This criterion was based on studies conducted in the 1980s on healthy normal volunteers transfused with their own (autologous) stored RBCs. How applicable this criterion is to sick patients who receive volunteer donor (allogeneic) RBCs is an open question.

During refrigerated storage of RBC units, the RBCs undergo numerous, complex physical and chemical changes, collectively referred to as the "RBC storage lesion", which impacts on their function and survival. Although much is known about these changes, there is still a lot that is not well understood.

Concerns have been raised by the clinical community about the age of blood at transfusion and this continues to be an area

of active discussion and debate. A number of clinical studies have been published that suggest that transfusion of older stored RBCs is associated with poorer outcomes for patients compared to fresher RBC units, more particularly for certain patient groups. Other studies have not supported these findings. Most of the studies are retrospective, observational studies and were not specifically designed to address the question of age of blood. Differences in timeframes for analysis, manufacturing approaches and component quality may also be contributing to differences in these studies where red cells might be non-leucoreduced, buffy coat reduced or leucodepleted, and these differences are not always qualified. Prospective, randomised controlled trials are underway overseas to address this question, but are not due to report for several years.

The age at supply of red cell components is directly influenced by red cell demand, inventory holdings and donor attendance patterns.

continued overleaf

DISCLAIMER This newsletter has been prepared by Transfusion Medicine Services at the Australian Red Cross Blood Service, a division of the Australian Red Cross Society. Every endeavour has been made to ensure the contents are correct and accurate at the time of publication, however, the medical environment is constantly changing and information herein may become out of date. The information in this publication is provided as a general guide only and should not be used to replace professional advice.

Medilink questionnaire

Included in this issue is a questionnaire to help us update our mail list and review our modes of communication. Please take the chance to update your details, add any colleagues who might like to join the mail list, and give us your feedback on how you like to read your news and information from the Blood Service.

Thank you for taking the time to let us know.

Over the past year, the Blood Service has implemented a number of strategies aimed at reducing the red cell age at supply, including:

- ❖ Strengthening our statistical forecasting capabilities for supply trends to enable more timely adjustment of collection and production plans in response to fluctuations in clinical demand
- ❖ Changes to the age mix of red cells supplied to Approved Health Providers
- ❖ Introduction of a Last In First Out (LIFO) inventory management practice for group AB Rh(D) positive and group B Rh(D) positive red cells, and
- ❖ Improved marketing performance and donor (and public) education regarding blood group and linking this to patient need.

Further improvement opportunities are under investigation and development, including:

- ❖ Implementation of a donor relationship management system which will allow improved planning and system capability to target specific donors by blood group depending upon clinical demand
- ❖ Agreeing an upper and lower limit for red cell inventory which will drive the average age at supply
- ❖ Reviewing red cell issuing policies and procedures, including further modelling and piloting of LIFO inventory management practices
- ❖ Modelling of the potential impact of reducing the red cell shelf-life to 35 days, and
- ❖ Working in collaboration with hospitals and transfusion laboratories to explore age at transfusion and options for alternative red cell inventory management practices. ■

Implementation of Hepatitis B Nucleic Acid Testing (NAT): Change in Blood Component Safety

Ms Sue Ismay

The Australian Red Cross Blood Service collects approximately 1.2 million blood donations per year, each of which is screened for human immunodeficiency virus (HIV), hepatitis B virus (HBV), hepatitis C virus (HCV) and human T lymphotropic virus (HTLV) to prevent transfusion transmission of these infectious agents. In addition to highly sensitive viral antibody screening methods used to detect the body's immune response to these infections, in June 2000, nucleic acid testing (NAT) for HIV-1 and HCV was implemented as a further measure to reduce the risk of transfusion-transmitted infection in Australia. The implementation of this technology markedly reduced the infectious window period (i.e. the time between initial infection and detection of the virus) for HIV-1 and for HCV.

Because of these significant improvements in blood safety, NAT for HIV-1 and HCV using first generation semi-automated testing platforms has been readily adopted by blood services worldwide and has rapidly become recognised as international best practice for blood donor screening. However, the industry benchmark is changing with the recent availability of fully automated NAT screening platforms that can now significantly improve both laboratory process control and laboratory

efficiency, allow for screening by individual donation and provide a testing platform that gives the Blood Service the ability to rapidly implement new NAT assays (for example dengue or West Nile virus) with minimal impact on the laboratory. In addition, the second generation NAT assays now incorporate the simultaneous detection of HBV along with HIV-1 and HCV.

Consequently, the Blood Service performed a comprehensive evaluation of the benefits and performance of these new automated NAT systems and will implement the Novartis Procleix TIGRIS and Ultrio assay in the individual donation format.

The implementation of HBV NAT at the individual donation level will provide an improvement in blood safety by reducing the infectious window period.

Table 1 shows the change in infectious window period (WP), the percentage of window period closure and the residual risk estimates for HBV following the implementation of NAT.

Options are being developed for managing component inventory at the time of implementation and the Blood Service is on track to implement uniform automated HIV-1, HCV and HBV NAT on all blood donations using the Procleix TIGRIS and Ultrio assay by mid-2010. ■

Table 1

Virus	Assay	NAT Pool Size	Infectious WP (Days)	% WP Closure	Estimate of Residual Risk
HBV	HBsAg	No NAT	38		1 in 739,000
	ULTRIO	1	24	37.6%	Less than 1 in 1 million

Conference Diary

2010 Transplant Society of Australia and New Zealand Annual Scientific Meeting

23–25 June, Manning Clark Centre, Australian National University, Canberra, Australia
www.tsanz.com.au/meetings/index.asp

XXXIst International Congress of the ISBT

26 June–1 July, Berlin, Germany
www.isbt-web.org/berlin/default.asp

XXIII International Congress of the Transplantation Society

15–19 August, Vancouver, Canada
www.transplantation2010.org

RCPA Evidence Based Pathology Seminar

6 September, Sydney, Australia
http://www.rcpa.edu.au/static/File/Asset%20library/public%20documents/Events/09_2010/Evidence_Based_Pathology.pdf

8th Australian Conference for Safety & Quality in Health Care

6–8 September, Perth, Western Australia
www.aaqhc2010.org.au

HAA 2010 – The Annual Combined Scientific Meeting of HSAZ, ANZSBT & ASTH

17–20 October, Sky City Convention Centre, Auckland, New Zealand
www.haa2010.org

Hepatitis B Nucleic Acid Testing: Implications for Lookback

Dr Anthony Keller

Screening the blood supply for hepatitis B in Australia which began in 1971 has relied on progressively more sensitive testing for hepatitis B surface antigen (HBsAg). Nevertheless, transfusion transmission of hepatitis B does still occur, albeit rarely, with four cases documented in Australia since 2000.

The current risk for transfusion-transmitted hepatitis B, based on modelling, is approximately 1: 739,000 per unit transfused, which compares well with international figures. The recent availability of nucleic acid testing (NAT) for hepatitis B, which is incorporated into a triplex assay (for HIV-1, HCV and HBV), will improve safety by allowing earlier detection of potentially infectious donations in the window period. A reduction of the window period from approximately 38 to 24 days is predicted.

In addition, the HBV NAT will detect cases of chronic hepatitis B which are HBsAg

negative using the current screening test. These chronic infections are called occult hepatitis B infections (OBI). The prevailing opinion is that the majority of OBIs represent past HBV infections that have been controlled rather than completely cleared by the immune system, but a minority may represent carriers where HBsAg has disappeared over time. In both cases, HBV DNA is invariably at low concentration (<100 IU/mL) and fluctuates during the course of infection. This can lead to intermittent detection even where the most sensitive NAT, performed at the individual donation level, is used. While anti-HBc testing may be able to detect these individuals, there are substantial problems with the specificity of this screening test, which is further exacerbated by the lack of a confirmatory test.

It is predicted that 50% of donors with OBI will have some detectable anti-HBs. Those donors with anti-HBs levels greater

than 10 IU/mL are extremely unlikely to be infectious, and those with a level greater than 100 IU/mL are considered not to be infectious.

Using Canadian data and applying these to Australian donors, it is predicted that a small number of potential new and repeat donors with OBI will be identified. This will have implications for donor counselling and lookback. Donations collected from new donors with OBI will be discarded. Repeat donors identified with OBI will require donor triggered lookback to be undertaken.

The implications for fractionated products have been considered in consultation with the Therapeutic Goods Administration (TGA), the National Blood Authority (NBA), the Department of Health and Ageing (DOHA) and CSL, and a paper with detailed recommendations has been submitted to governments for approval. ■

Clinical Impact of Measures to Reduce Bacterial Contamination of Blood Components in Australia

Dr Erica Wood, Dr Marija Borosak and Dr Janet Wong

Bacterial contamination of blood components remains an important residual infectious hazard of transfusion, and a challenge for blood services, transfusion laboratories, treating clinicians and haemovigilance programs. The spectrum of bacterial contamination outcomes ranges from fatal sepsis to detection of bacteria on routine component surveillance testing without apparent consequence. Reduction in clinical events is the ultimate goal of measures to reduce bacterial contamination. However this is quite difficult to measure, because of absence of meaningful denominator data for transfusion events, and lack of standard international case definitions and terminology for clinical and laboratory features, components and processes, detection methods and reporting, making comparisons difficult both between countries and over time.

Measures to reduce the risk of bacterial contamination include:

- ❖ Donor selection and health screening, with special attention to risks for acute or chronic bacterial infection, with donor deferral as necessary.
- ❖ Optimising the donation process, including improvements in skin cleansing procedures, selection of collection method and diversion of initial volume away from the collection bag.
- ❖ Improvements in component manufacturing, with environmental monitoring and attention to time and temperature restrictions at all stages of the process, supported by product quality control testing.
- ❖ Use of apheresis platelets to minimise exposure to donor skin flora.
- ❖ Pathogen reduction technologies (PRT), which are now in routine use for platelets

and plasma in some countries, but are generally less advanced for red cells.

New methods are awaited with interest.

- ❖ Attention to proper storage and handling procedures.
- ❖ Efforts to promote more appropriate and evidence-based clinical practice.

Undoubtedly, a combination of interventions contributes to improve bacterial safety of transfusion. In Australia, the Blood Service has nationally standardised donor skin and environmental disinfection procedures. Routine use of diversion pouches during blood collection has been in place nationally since 2006. In international studies, this intervention has been shown to reduce bacterial contamination of both whole blood and components by between 40 and 88%, with the major reduction being seen in skin flora. Routine pre-release surveillance testing of platelets is now widely practised internationally and was introduced in Australia in April 2008.

continued overleaf

From 23 April 2008 to 30 November 2009, the Blood Service has screened a total of 187,991 platelet components (136,466 pooled platelets [73%] and 51,525 apheresis platelets [27%]) for bacterial contamination.

Table 1 shows the number of:

- ❖ Initial machine positives
- ❖ Confirmed positives
- ❖ Machine false positives
- ❖ Other false positives, and
- ❖ Indeterminate (i.e. a sample that had an initial positive result but follow-up testing could not be completed due to unavailability of sample) results as a percentage of pooled platelets, apheresis platelets and total platelets tested.

Propionibacterium species (which are not usually considered clinically significant) continue to be the organisms most commonly identified in confirmed positive platelet components, accounting for approximately 79% of cases. Figure 1 shows the range of organisms identified in confirmed positive samples between 23 April 2008 and 30 November 2009.

Table 2 shows the fate of the components related to these confirmed positive samples.

57% of the pooled platelets and 13% of the apheresis platelets had already been transfused at the time of the initial machine positive result. In a small number of cases, associated red cells and/or plasma had also been transfused. Overall, 9% of all the components produced from confirmed positive donations had already been transfused at the time of the initial machine positive result. A further 33% of the components had been issued to transfusion laboratories but not yet transfused.

The organisms identified in the majority of these transfused components were *Propionibacterium* species, followed by *Corynebacterium* species. *Propionibacterium* species were the only organisms detected in 91% of the transfused platelets.

The Blood Service has worked closely with hospitals and transfusion laboratories related to implementation of this new safety measure, including to follow-up initial machine positive results and components

Table 1

Result	Pooled Platelets	Apheresis Platelets	Total Platelets
Initial Machine Positives	1.13%	0.95%	1.08%
Confirmed Positives	0.12%	0.05%	0.10%
Machine False Positives	0.84%	0.79%	0.82%
Other False Positives	0.10%	0.05%	0.08%
Indeterminates	0.07%	0.07%	0.07%

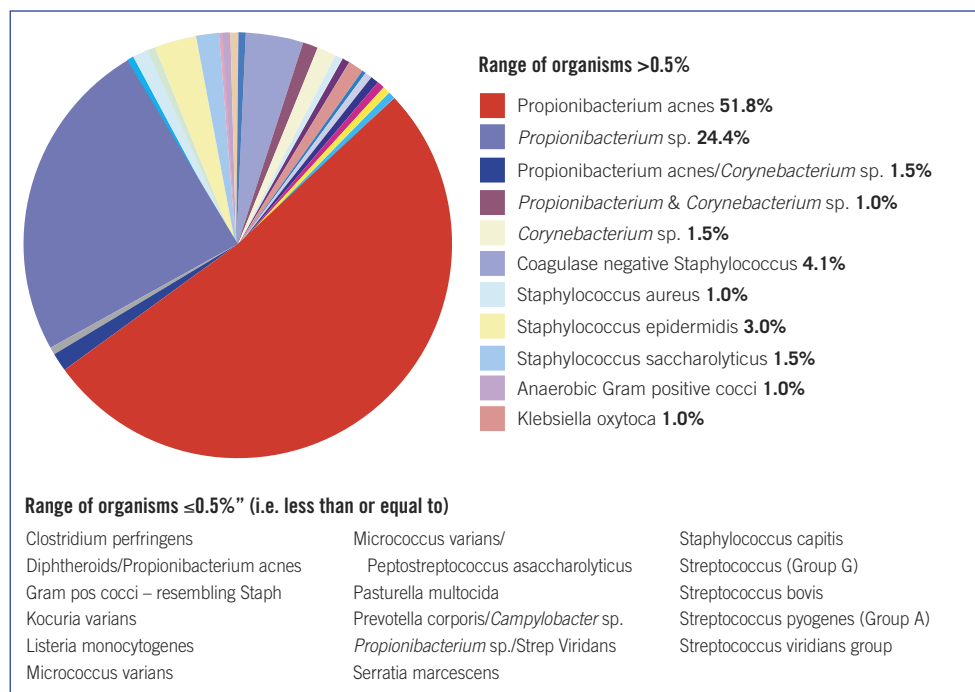


Figure 1 The range of organisms identified in confirmed positive samples between 23 April 2008 and 30 November 2009.

Table 2

Component	Issued to Transfusion Laboratory				Discarded at Blood Service		Total
	Transfused		Recalled				
Pooled Platelets	98	57%	31	18%	44	25%	173
Apheresis Platelets	5	13%	7	18%	27	69%	39
Red Cells	17	2%	207	30%	468	68%	692
Plasma	21	3%	284	40%	408	57%	713
Cryoprecipitate	0	0%	3	19%	13	81%	16
All Components	141	9%	532	33%	960	59%	1633

Table 3

Calendar year	2006	2007	2008	Jan–Jun 2009	Total
Total bacterial suspected	36	43	36	20	135
Total bacterial confirmed	5 (2 RC, 3 PLT) 1 fatality (PLT)	3 (1 RC, 2 PLT) 1 fatality (PLT)	0	0	8

transfused prior to availability of testing results. Experience to date is that there has been a decrease in reported cases of clinical sepsis due to platelets, with no confirmed or high probability cases since introduction of platelet bacterial screening (see Table 3).

The Blood Service is conducting research into PRT for platelets and closely monitoring international developments in this area.

Ongoing efforts are required to improve knowledge and management of transfusion-

related bacterial contamination. Without awareness of transfusion as a cause of potentially fatal sepsis, cases will not be recognised and treated promptly. Delay in recognition is reported to be associated with worse outcomes and also hampers reporting to haemovigilance programs. Correct handling of components for investigation of suspected bacterial contamination is also extremely important to prevent external contamination. ■

TRALI and Risk Reduction Strategies

Dr Joanne Pink and Dr Marija Borosak

Transfusion-related acute lung injury (TRALI) is a clinical diagnosis of non-cardiogenic pulmonary oedema due to acute lung injury related to transfusion of plasma-containing blood components. It often occurs in the setting of multiple pathologies in sick patients who may already have other disease or injury to the lung. In this setting, TRALI is classified as 'possible' as clinically it can be difficult to truly determine whether deterioration at a particular time point is related to the patient's underlying condition or to a transfusion-related event.

TRALI is now the most common cause of transfusion-related death reported to the US Food and Drug Administration (FDA) and the UK Serious Hazards of Transfusion (SHOT) system. While the literature reports a range of clinical scenarios and the aetiology remains incompletely understood, in many cases there has been an association between the implicated components in TRALI cases and female donors who have had one or more pregnancies or donors (male and female) who have been previously transfused. Females are more likely to have HLA or granulocyte (HNA) antibodies than males, due to exposure to fetal antigens during pregnancy.

However, TRALI can occur in the absence of antibodies. Over recent years, there has been increasing evidence supporting the role of bioactive lipids or substances in the aetiology of TRALI and a two-hit theory; the first hit being a change to the lining of the blood vessels in the lungs of sick patients resulting in adherence of neutrophils, and the second being the activation of these neutrophils by substances in the blood component, with the release of oxidases and proteases which damages the blood vessels and makes them leaky.

It is likely that TRALI is the culmination of a complex interplay of various donor, blood component and patient-related factors and thus, effective prevention will require a multi-faceted approach.

Table 1 Transfusion reactions reported to the Australian Red Cross Blood Service by calendar year January 2006 until June 2009

Calendar year:	2006	2007	2008	Jan-Jun 2009	Total
Total Transfusion Reactions	135	151	197	129	612

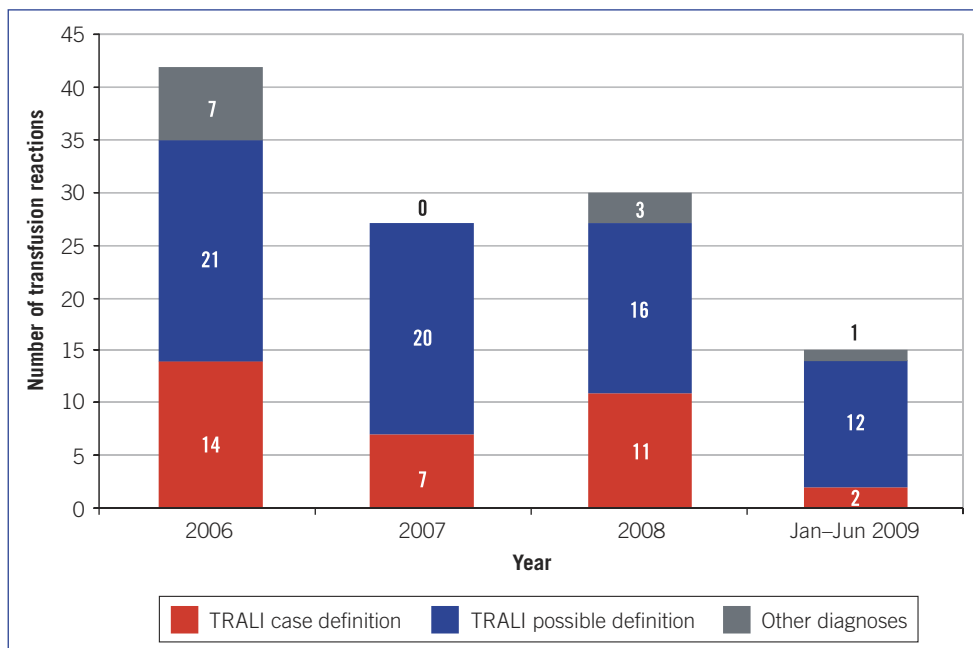


Figure 1 TRALI reporting by calendar year, January 2006 until June 2009.

The Blood Service has implemented a number of strategies to reduce the risk of TRALI including:

- ❖ a deferral strategy for donors implicated in TRALI
- ❖ about 97% of frozen clinical plasma components are sourced from male donors
- ❖ about 80% of apheresis platelets are sourced from male donors, and
- ❖ pooled platelets are resuspended in additive solution.

The Blood Service also has an active TRALI research program and is concurrently evaluating options to further reduce the risk of TRALI including:

- ❖ additional donor selection questions e.g. previous pregnancy
- ❖ testing for HLA/HNA antibodies, and
- ❖ resuspending apheresis-derived platelets in additive solution.

It is important to note that while transfusion-related adverse event reporting to the Blood Service has been increasing (Table 1), perhaps reflecting growing awareness of the importance of identification and monitoring of transfusion reactions and participation in developing haemovigilance activities, TRALI rates have reduced or stabilised since mid 2007 when male-predominant clinical plasma became available (Figure 1). ■

Pathogen Inactivation of Blood Components

Dr Denese Marks

The current multilayered approach to ensure blood safety includes donor selection and deferrals, screening for infectious disease markers by serological testing (ELISA) and nucleic acid testing (NAT), leucodepletion, gamma irradiation and bacterial contamination screening. However, concern remains regarding emerging pathogens for which a screening assay does not exist. There is still a residual risk of platelet bacterial contamination despite the introduction of screening, and bacterial contamination continues to result in blood component wastage. Despite highly sensitive tests, infected donors may not be identified due to the post-infection window period before many transfusion-transmitted infections can be detected. Pathogen reduction technology (PRT) could potentially be added to this suite of measures to give an extra layer of safety and reduce these risks.

continued overleaf

Several pathogen reduction technologies have been developed to improve the safety of blood products. Two of the most promising technologies inactivate pathogens by targeting nucleic acids. The INTERCEPT system uses a combination of ultraviolet (UV) light and amotosalen, a psoralen compound that must be removed during processing by a compound adsorption device, as it is highly toxic. The INTERCEPT system has been adopted in many European blood centres. However, there is concern regarding the long-term effect of transfusing psoralen-treated blood products, despite over 300,000 treated blood products being transfused.

The Mirasol system uses a combination of riboflavin and UV light. Riboflavin is a natural product found in many foodstuffs, which has been used in combination with UV light to treat jaundice in neonates for several decades. Both systems have been found to be effective in reducing contamination with Gram-positive and Gram-negative bacteria as well as viruses including HIV, West Nile virus and B-19 parvovirus. Some parasites such as Leishmania and T. cruzi, which causes Chagas' disease, are also inactivated. However, these systems do not inactivate prions due to their mode of action.

PRT systems currently only accommodate treatment of plasma or platelets, and pathogen reduction systems to treat red cells are currently in development. These technologies also have the added benefit of inactivating white blood cells due to their mode of action. Treatment of blood components with PRT has been shown to cause some loss of functional activity. The cost of implementing these systems must also be considered against the potential benefits.

The Australian Red Cross Blood Service has been closely following the development of PRT, and has now commenced an evaluation of the Mirasol system for treatment of platelets. The aim of this evaluation is to examine platelet quality of PRT-treated platelets during storage. The ability of this system to inactivate white blood cells has also been investigated. ■

Research and Development at the Blood Service

Dr David Irving

Over the past two to three years, the focus of R&D at the Blood Service has moved from one that was primarily investigator driven to a more applied approach, specifically aimed at aligning research priorities with the strategic requirements of the Blood Service – conducting “leading edge research to meet the needs of patients”.

Broadly, research projects are conducted within the following strategic areas:

- ❖ **Donor and community research** – in which projects are designed to provide outcomes that will assist in the understanding of the motivators for current and potential future donors. For example, we are researching what motivates groups such as generation Y and people from a diverse range of ethnic backgrounds. In addition, we are conducting research into the effectiveness of different types of marketing communications, non-financial incentives and appointment scheduling on behaviour outcomes, such that these findings can then be taken into account when designing donor recruitment (and retention) programs.
- ❖ **Applied and developmental research** – in which experimental programs are designed to provide outcomes that will improve operational efficiencies and the safety of our blood products. Projects include studies on alternatives to plasma for the storage of platelets; development of robust protocols for the cryopreservation and thawing of platelets and the evaluation of technologies that can be used for broad spectrum inactivation of pathogens in blood components (platelets in the first instance). Research into the development of diagnostic tests to detect infectious agents such as those that cause dengue fever is also underway.

❖ **Transfusion science research** – in which longer term research programs are undertaken in the areas of red blood cell science, transfusion immunobiology and molecular diagnostics. Such research is aimed at generating knowledge that has the potential to be translated into more applied research at a later date. Of particular significance in this area is research aimed at investigating the changes that occur to red blood cells during storage and the development of experimental models to study transfusion-related acute lung injury (TRALI), a significant, potentially life-threatening adverse event associated with transfusion.

❖ **Clinical research** – the Blood Service is increasing its activities in clinical research whereby evidence is gathered from the clinical setting in order to identify potential improvements in clinical practice. Included in this area are projects aimed at developing a better understanding of patterns of transfusion practice by linking data from a number of existing or newly developed data registries and the conduct of clinical trials of novel procedures that also could lead to improvements in practice. ■

International Benchmarking Data: Australia in Perspective

Dr Sally Thomas and Sandra Boyd

The Blood Service participates in annual benchmarking with a number of international blood networks. Through this benchmarking we are able to compare our activities with other relevant blood services, and benefit from best practice exchange. The two principal networks are the Alliance of Blood Operators (ABO) which comprises American, European, Canadian and Australian blood services, and the Asia Pacific Blood Network (APBN) which represents nine regional countries.

Benchmarking areas are selected to reflect our key stakeholder requirements,

and include patient, hospital, donor, organisational efficiency and public measures. The two strategic objectives identified in the patient measures are to:

1. Reduce the residual risk of transfusion, and
2. Ensure the appropriate use of blood.

Australia compares favourably in terms of initiatives and practices to reduce the residual risk of transfusion, with the implementation in recent years of bacterial detection for platelets, leucodepletion, management strategies for transfusion-related acute lung injury and nucleic acid testing. The Blood Service also continuously monitors new developments internationally to ensure this position is maintained.

There is continued interest in the appropriate utilisation of blood and blood products, with heightened concern in most blood services about the potential growing gap between red cell demand with ageing populations and donor availability and the impact of 'the red cell storage lesion' on usage. Significant variation in utilisation rates is observed across benchmarked countries, and a recent workshop was held at the Regional Congress of the International Society of Blood Transfusion (ISBT) in Nagoya to better understand the data and potential for improving appropriate utilisation by sharing international practice. With reported red cell "issue" rates ranging from 21 to 61 per 1000 population, there is a need to understand what data is being reported, how to differentiate between issued, produced and "used", what the appropriate blood unit measure is – a litre, or a unit, or a volume, and what influences utilisation rates and how they relate to patient outcomes.

Experience from other countries provides some insight into possible influences on utilisation rates, and these are examined in three key areas of data collection, country demographic and individual patient profiles, and the organisational system in which the blood service operates. By better understanding these aspects, we are better able to identify those initiatives which support appropriate utilisation, and can be considered for use in the Australian context. ■

Clinical Demand Drivers for Intravenous Immunoglobulin

Dr Marija Borosak, Dr Erica Wood and Dr Joanne Pink

Intravenous Immunoglobulin (IVIg) is a precious resource made from plasma donations and is the main driver of plasma fractionation in many countries, with growth increasing year on year (Figure 1). Within Australia, the Blood Service collects plasma from volunteer, non-remunerated donors, which is fractionated into a range of plasma-derived products, including IVIg. Currently Australia is not self-sufficient in IVIg, and imported IVIg products supplement domestic supply.

The *Criteria for the clinical use of intravenous immunoglobulin in Australia* (implemented in March 2008) identifies clinical conditions where IVIg can be provided under the National Blood Agreement, if qualifying criteria are met. The introduction of the Criteria now ensures more equitable access to IVIg across Australia.

The introduction of the *Criteria* for IVIg use has led to a period of change in diagnostic classification for patients, as well as, increased use of IVIg due to changes to disease indications, and has provided a consistent framework for assessment of all IVIg requests across jurisdictions. Factors affecting state-based differences

in use are complex, multi-factorial and warrant further evaluation, especially in the areas of disease burden and prevalence. Better understanding of the impact of initiatives that potentially change access arrangements, such as the establishment of regional infusion centres, is also warranted.

Population growth, ageing and changes in weight have the potential to have significant impact on IVIg demand in the future. Future drivers in demand will include changes in clinical indications, alternate dosage regimes and availability of new immunosuppressive or immunomodulatory agents for a range of conditions. Other areas of future work include clinical studies exploring optimal IVIg dosing regimens (for example longitudinal patient outcomes in the context of dose modifications, such as 0.2g/kg versus 0.4g/kg dosing in acquired hypogammaglobulinaemia). The Blood Service has already piloted evaluation of lean body weight dosing, and further careful outcome studies will also be important. These initiatives may have significant impacts on IVIg use due to the current trends seen in obesity in the developed world. ■

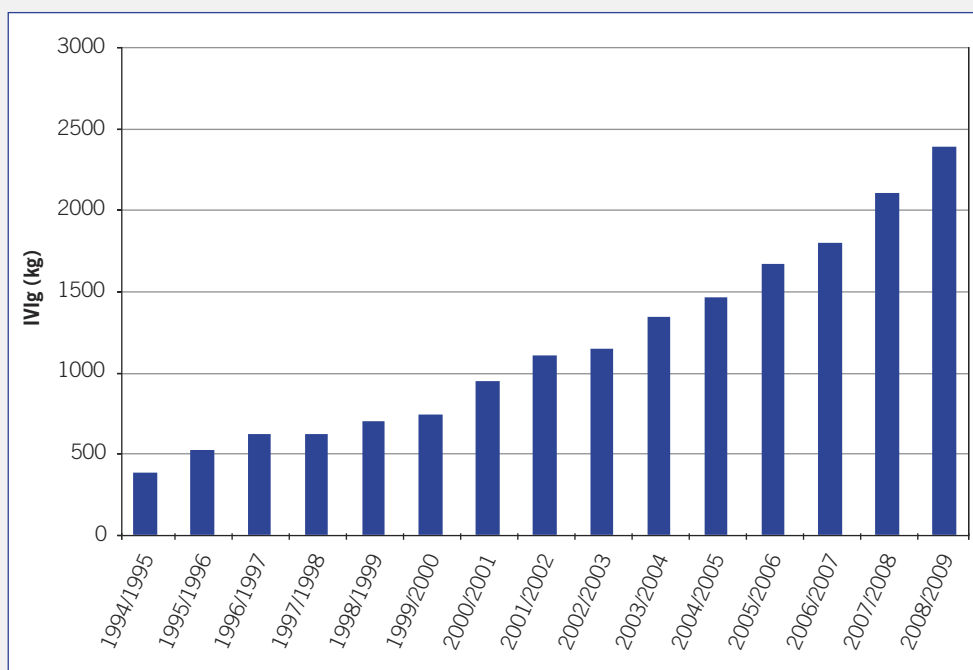


Figure 1 IVIg growth by financial year over the last 15 years

Residual Risk Estimates for Transfusion-Transmitted Infections

The Blood Service publishes estimates of the residual risks of transfusion-transmitted infections in the every edition of *Medilink* as a service to clinicians to guide transfusion decision-making and informed consent processes.

Blood Service estimates of residual risk of transfusion-transmitted viral infection are based on published models and represent the median risk estimate derived using three models. These estimates are updated annually. It should be noted that, as the order of magnitude of these risks is very small, the calculated median risk estimate may fluctuate from year to year.

The risk estimates for HIV, HCV and HBV presented in Table 1 are based on Blood Service data from 1 January 2007 to 31 December 2008. The risk estimate for HTLV I/II is based on data from 1 January 2004 to 31 December 2008.

There have been no reported cases of transmission by transfusion of classical Creutzfeldt-Jakob Disease (cCJD) and retrospective studies suggest that the possibility of such transmission of cCJD is remote.¹

To date, there have been no reported cases of vCJD in Australia. In the UK, there have been a small number of reported cases of putative transfusion transmission since 2004. In Australia, as a precaution, people who have spent a cumulative period of six months in the UK between 1 January 1980 and 31 December 1996 and/or had a transfusion in the UK between 1 January 1980 and the present time are not accepted as blood donors.

When considering the significance of specific risks, it is often useful to compare them to the risks associated with everyday living. The risk estimates listed above are very small when compared to everyday risks (refer to the Calman scale opposite). The chance of dying in a road accident, for example, is about 1 in 10,000 per year.

Reference

1. Dorsey et al. Lack of evidence of transfusion transmission of Creutzfeldt-Jakob disease in a US surveillance study. *Transfusion* 2009; 49: 977–984.

Table 1 Residual risk estimates for transfusion-transmitted infections

Agent and testing standard	Window Period (Days)	Estimate of residual risk 'per unit' ^a
HIV (antibody + NAT)	9	Approximately 1 in 5.4 million
HCV (antibody + NAT)	5.4	Approximately 1 in 2.7 million
HBV (HBsAg)	38	Approximately 1 in 739,000
HTLV I & II (antibody)	51	Approximately 1 in 17.5 million
Variant Creutzfeldt-Jakob Disease (vCJD) [No testing]		Possible. Not yet reported in Australia. See section to the left.
Malaria (antibody)	14	1 in 4.9 million to 1 in 10.2 million

^a The risk estimates for HIV, HCV and HBV are based on Blood Service data from 1 January 2007 to 31 December 2008. The risk estimate for HTLV I/II is based on data from 1 January 2004 to 31 December 2008.

Viral estimates: Seed CR, Kiely P and Keller AJ. Residual Risk of Transfusion-transmitted Human Immunodeficiency Virus, Hepatitis B Virus, Hepatitis C Virus and Human T Lymphotropic Virus. *Intern Med J* 2005; 35(10): 592–8.

Malaria: Seed CR. Residual Risk Estimates for Transfusion-transmitted Malaria (TTM). Australian Red Cross Blood Service DPARC: November 9/10 2005 meeting.

Non-Viral Serious Risks of Blood Transfusion

The most frequently reported serious or fatal complications of blood transfusion are bacterial contamination, transfusion-related acute lung injury (TRALI) and ABO incompatibility (the later mostly due to preventable patient or sample identification errors). Other serious risks associated with transfusion, based on overseas estimates, are outlined in Table 2.

Table 2 Reported Non-Viral Serious Risks of Blood Transfusion

Adverse reaction	Risk per unit transfused (unless specified)
Bacterial sepsis* – Platelets – Red cells	At least 1: 75,000 At least 1: 500,000
Haemolytic reactions – Acute – Delayed	1: 12,000 to 77,000 1: 4,000 to 9,000
Anaphylaxis – IgA deficiency	1: 20,000 to 50,000
Fluid overload/cardiac failure	Up to 1% of patients receiving transfusions
Transfusion-related acute lung injury	1: 5,000 to 190,000
Transfusion-associated graft versus host disease	Rare

* Clinically apparent reactions

Source: Blood Service *Blood Component Information Booklet 2009*. Available at <http://www.manual.transfusion.com.au/admin/file/content13/c6/BCI%202009.pdf>

The **CALMAN Chart** (Calman 1996[†]) for explaining risk (UK risk per one year)

Negligible:	< 1,000,000 e.g. death from a lightning strike
Minimal:	1:100,000 – 1:1,000,000 e.g. death from a train accident
Very low:	1:10,000 – 1:100,000 e.g. death from an accident at work
Low:	1:1000 – 1:10,000 e.g. death from a road accident
Moderate:	1:100 – 1: 1000 e.g. death from smoking 10 cigarettes per day
High:	> 1:100 e.g. transmission of chickenpox to susceptible household contacts

[†] Calman K. The Health of the Nation. *Br J Hosp Med* 1996; 56: 125–6.

medilink is published by Transfusion Medicine Services at Australian Red Cross Blood Service to update health professionals with the latest news and research relating to transfusion. It is published in tandem with our electronic newsletter, *Med e-News*, which is distributed in the months between Medilinks. If you or your colleagues would like to be added to either of these mailing lists, please email details to [Lisa Reid I Reid@arcbs.redcross.org.au](mailto:Lisa.Reid@arcbs.redcross.org.au)

An archive of *Medilink* and *Med e-News* can be accessed at www.transfusion.com.au

Medilink is printed with vegetable-based inks on 55% recycled and 45% elemental chlorine-free (ECF) sustainable plantation fibre.

Australian governments fully fund Red Cross for the provision of blood products and services to the Australian community.