BLOOD ISSUES

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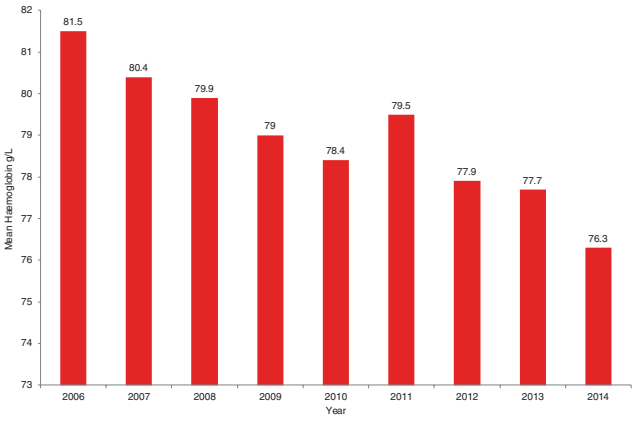
NZBS 10TH ANNUAL HAEMOVIGILANCE REPORT 2014 – A SUMMARY

The NZBS is responsible for all aspects of the transfusion process, from donor to recipient. This includes the national Haemovigilance Programme that monitors untoward events during blood donation and along the transfusion chain. The 10th Annual Haemovigilance Report for New Zealand marks a decade since monitoring began in 2005. The success of the programme relies heavily on the support of doctors, nurses and laboratory staff completing and submitting forms for adverse events. NZBS is most appreciative of this.

Patient blood management guidelines reflect an increasingly restrictive red cell transfusion policy. This has led to a gradual reduction in mean pretransfusion haemoglobin value to 76g/L in the recipients of red cells reported to NZ Haemovigilance in 2014.

FIGURE 1 ANNUAL MEAN PRETRANSFUSION HAEMOGLOBIN CONCENTRATION 2006 – 2014



The change in local clinical practice has contributed to a 16% decline in the number of annual red cell transfusions and annual total blood component use in NZ since 2010. The rate of decline is however falling, with only a further 1% drop in annual red cell transfusions during 2014. A similar plateau is appearing in the use of fresh frozen plasma.

FIGURE 2 ANNUAL NUMBER OF BLOOD COMPONENTS TRANSFUSED 2009 – 2014

Blood Component	2009	2010	2011	2012	2013	2014	% Change 2014 compared to 2010
Total Red Cells	125,819	124,643	117,820	114,746	105,229	104,271	-16.3%
Total Platelets	13,381	13,616	13,257	13,783	13,388	12,601	-7.5%
Total Fresh Frozen Plasma	20,001	17,872	16,863	16,724	13,703	13,551	-24.2%
Cryoprecipitate	2,869	2,951	3,228	3,745	4,167	4,198	42.3%
Cryodepleted Plasma	517	486	751	670	508	514	5.8%
Total Components	**162,587**	**159,568**	**151,919**	**149,668**	**136,995**	**135,135**	**-15.3%**

Largely as a result of these changing demand-patterns for fresh blood components, the number of reported transfusion events has declined by 24% since 2010.

During 2014, there were 463 reported events involving 434 patients. Of these, 106 events were excluded as their causes were considered to relate to the patient's underlying condition rather than to the transfused component. The remaining 357 events having imputability scores ≥3 were further evaluated. Events are assigned a severity score using a scale from 1 to 4; grade 1=minor (patient may have received treatment however lack of such would not have led to permanent damage or impairment), grade 2=severe (patient required hospitalisation or prolongation of hospitalisation; patient required treatment to preclude permanent damage or impairment), grade 3=life threatening (patient required major medical intervention such as vasopressor support, intubation or transfer to an intensive care unit to prevent death), grade 4=death. The majority (93%) of adverse events in 2014 were grade 1 and were predominantly febrile non-haemolytic transfusion reactions (FNHTR) or allergic events. Severe and life-threatening events were predominantly due to transfusion-associated circulatory overload (TACO) or allergic reactions. There was one grade 4 event where TACO resulted in the death of a patient.

TABLE 1 TRANSFUSION-RELATED ADVERSE EVENTS (IMPUTABILITY ≥3) 2014 BY EVENT TYPE AND SEVERITY

Event Type	Severity				Total
	Grade 1	Grade 2	Grade 3	Grade 4	
FNHTR	187	1		188	
Allergic	76	5	2		83
IBCT	20				20
DSTR	19				19
UCT	15	3	1		19
TACO	2	9		1	12
TAD	3	1			4
AHTR	2	1			3
DHTR	3				3
Hypotensive	2	1			3
Near Miss	2				2
TRALI		1			1
Total	**331**	**22**	**3**	**1**	**357**
Percentage	92.7%	6.2%	0.8%	0.3%	

FNHTR febrile non-haemolytic transfusion reaction; IBCT incorrect blood component transfused; DSTR delayed serological transfusion reaction; UCT unclassifiable transfusion reaction; TACO transfusion-associated circulatory overload; TAD transfusion-associated dyspnoea; AHTR acute haemolytic transfusion reaction; DHTR delayed haemolytic transfusion reaction; TRALI transfusion-related acute lung injury.

However, annual use of fractionated plasma products, predominantly intravenous immunoglobulin (IVIg), continues to rise in New Zealand. A similar trend is occurring internationally, as there is an increasing spectrum of conditions where IVIg-immunomodulation may be beneficial. Rising local demand for IVIg has contributed to the steady increase in plasmapheresis collections and the annual number of plasmapheresis donations has more than doubled since 2010. Apheresis procedures are associated with a high frequency of donor adverse events and among these are events related to hypocalcaemia from citrate anticoagulant in donors undergoing plateletpheresis. In 2014, a national protocol was introduced for the calcium supplementation of plateletpheresis donors. Following this, and compared to data from 2013, there has been a reduction by 33% in the number of events due to citrate toxicity.

Blood transfusion in NZ is very safe. Severe adverse events, predominantly allergic reactions and circulatory overload (TACO), are reported for 0.02% of components transfused and in 0.09% of transfusion recipients. Transfusion-related acute lung injury (TRALI) and infection are very rare events. No cases of human immunodeficiency virus (HIV) or hepatitis C (HCV) transfusion-transmitted infection have been reported in New Zealand since testing was introduced in 1986 and 1992 respectively and the rates of infected donations are now so low that modelling is required to derive the risk to recipients. The following table demonstrates current residual risk estimates for HIV, HCV and hepatitis B (HBV) using infectious serology results from first time and repeat NZ donors.

TABLE 2 RESIDUAL RISK ESTIMATES FOR HUMAN IMMUNODEFICIENCY VIRUS, HEPATITIS B AND HEPATITIS C TRANSFUSION-TRANSMITTED INFECTION IN NEW ZEALAND

Infection	Mean Risk	95% Prediction Interval
HIV	1 in 9.2 million	1 in 2.5 – 32.8 million
Hepatitis C	1 in 6.9 million	1 in 3.6 – 12.5 million
Hepatitis B	1 in 0.8 million	1 in 0.4 – 1.4 million

Although the modelled risk for HBV is greater than for HCV and HIV, the true risk to patients is more difficult to establish. This is because the model for calculating HBV risk does not take the prevalence of donor occult HBV infection nor recipient HBV immunity into account.

Bacterial contamination in platelets can result in sepsis with the associated morbidity occasionally leading to death and as such continues to be a serious risk of transfusion. Bacteria will either enter the component at the time of venepuncture or more rarely arises due to an occult infection in the donor but can also enter due to a breach of the closed system during processing. Internationally, the contamination rate of platelets identified using the Bac-T-Alert culture system is reported to be between 0.02 – 0.3% (1 in 5,000 – 3 in 1,000). During 2014, confirmed positives from testing at day 2 of storage occurred at a rate of 0.07% (1 in 1464), indicating that NZBS systems compare well with other blood service organisations.

References:
Source: NZ Blood National Haemovigilance Programme Annual Report 2014. www.nzblood.co.nz

Post Implementation Monitoring of Extended Life Platelets

The nationwide implementation of platelet components with a 7 day shelf life is complete and extended life platelets (ELP) are now a standard NZBS component. The extension of platelet shelf life has been made in conjunction with the implementation of a comprehensive bacterial screening programme. The combination will enhance the safety of platelet components by reducing the risk of bacterial contamination while the extended shelf life will allow improved utilisation of platelet components. The results of post implementation monitoring are presented below.

Clinical Evaluation of Day 6 and Day 7 Extended Life Platelet Components

Following a pilot implementation in the Auckland region of extended life platelets (ELP) with a shelf life of seven days, a clinical evaluation of the response to transfusion of day six and seven platelets was undertaken at Auckland City Hospital.

Over a 7 week period, the clinical notes related to 59 transfusion episodes involving 61 platelet units administered to 34 haematology/oncology patients and babies in neonatal units were retrospectively evaluated by NZBS Transfusion Nurse Specialists. The transfusion of one or more day six or seven platelet units during a four hour period was considered a transfusion episode and evaluated for clinical efficacy. The measures assessed were changes in bleeding pattern, time to next transfusion, corrected platelet count increment (CCI) and proportion of transfusions with CCI > 7 x 10^9/L (a level considered clinically acceptable). Any documented adverse effects were noted. To assess whether 'older' components are associated with any change in the frequency of adverse events or with any reduction in their ability to control bleeding, the results were compared to a similar evaluation performed in 2009 following the introduction of apheresis platelets in platelet additive solution (PAS).

Platelet units transfused were a mix of apheresis (21), pooled (31) and neonatal units (9). The indication for transfusion was bleeding prophylaxis in 65%, pre-procedural in 11% and therapeutic in 24% of episodes. Bleeding was present pre-transfusion in 16 (26%). Of these, bleeding reduced or stopped in all but one,

with the remaining episode showing no change. No cases showed any deterioration in bleeding. An acceptable mean CCI of 12.4 x 10^9/L was calculated and 74% of transfusions demonstrated a CCI > 7 x 10^9/L. A single adverse reaction, namely transfusion-associated circulatory overload (TACO), was noted.

The evaluation did not show any increase in adverse events or change in clinical efficacy with the use of day six and seven platelets when compared with the previous evaluation of apheresis platelets suspended in PAS. As such, the new ELP components appear to be safe and efficacious. Further post-implementation monitoring, including the NZBS Haemovigilance Programme, has not identified any concerns with the use of these platelets.

Component Quality Monitoring Data for Platelet Components

The presence of platelet swirl is a qualitative assessment of platelet function where the absence of the swirling phenomenon has been reported as predictive of a poor transfusion outcome. Platelet swirl can be observed by gentle agitation of the platelet bag in front of a light source; viable non-activated platelets are discoid in appearance and will scatter the incident light in different directions resulting in a moving opalescence or swirling phenomenon.

All platelet components are visually inspected at the hospital blood bank to confirm the presence of swirl immediately prior to issue to the designated recipient. In the absence of swirl, the platelet component is discarded. Comparable results of swirl testing for the 3 months prior to implementation of the extended shelf life with those for 3 months post implementation provides an indirect confirmation that platelet components issued at day 6 or 7 of their shelf-life continue to be viable.

Platelet pH at expiry is sensitive to storage conditions and is a potential marker of platelet deterioration during the shelf life period. The pH testing of expired platelets was increased following implementation of ELP, with results meeting requirement of the NZBS component monograph. Lower pH values have been recorded in platelets resuspended in plasma (i.e. components intended for use in neonates) as opposed to platelet additive solution (PAS) and this area is being actively monitored.

Bacterial Screening

The extension of platelet shelf life was implemented together with introduction of a mandatory day 2 pre-release bacterial screening programme on 100% of platelet components using the Bac-T-Alert culture system and involving the use of both aerobic and anaerobic bottles. Post implementation monitoring also includes day 8 culture of expired units. Monthly reports from the results of bacterial screening include data both nationally and from individual sites within NZBS. These give a breakdown of the number and frequency of Bac-T-Alert machine reactive results and the number and frequency of confirmed bacterial culture positives, together with identification of the bacterial species. The final fate of platelet components associated with both machine reactive and confirmed culture positive samples is monitored. In addition, a clinical review is performed of all clinical cases where implicated platelet components have been transfused. Reassuringly, since the introduction of ELP in December 2015, no increase in confirmed day 8 positives has been seen.

Seroprevalence and Incidence of Hepatitis E Virus Infection in New Zealand Blood Donors

Hepatitis E virus is a major cause of hepatitis globally, particularly in developing countries in Africa and Asia where HEV is endemic. In developed countries, including New Zealand, the epidemiology of HEV infection is not fully understood and while most cases are thought to be associated with travel to endemic countries, there are increasing reports of sporadic autochthonous (locally acquired) infection. While the route(s) of transmission remain uncertain for the majority of these autochthonous infections, transmission via blood transfusion is increasingly being considered as an important, albeit rare, route.

Hepatitis E virus (HEV) is a small non-enveloped positive-stranded RNA virus. There are four major genotypes (HEV genotypes 1-4: HEV-1, HEV-2, HEV-3 and HEV-4) known to infect humans. The four genotypes have different geographical distributions, major transmission routes and pathogenicity. For example, HEV-1 and HEV-2 commonly infect humans, whereas HEV-3 and HEV-4 infect not only humans but a broader host range, including domestic pigs, wild boar, deer and other animals. In general, infections caused by HEV are mild and self-limiting in immune-competent individuals, but subfulminant or fulminant hepatitis can occur following infection of 'at risk' groups including the elderly, pregnant women and immunocompromised patients.

In ensuring the provision of safe blood and blood products, NZBS monitors international developments and assesses their relevance to the New Zealand situation. With only limited contemporary data on the seroprevalence of HEV in the New Zealand population and no data on the detection of HEV RNA in New Zealand blood donors, the Ministry of Health provided funding to ESR, the Institute of Environmental Science and Research, to undertake a study on the prevalence and incidence of HEV in New Zealand blood donors. The purpose of this study was to provide information that would enable NZBS to develop

an evidence-based policy in the event that either regulatory requirements for HEV testing of plasma pools emerge, or to enable alignment with other blood services commencing testing strategies to reduce the risk of HEV transmission.

Specifically, the aims of this study were to: (i) determine the contemporary seroprevalence of HEV in blood donors, and (ii) assess the incidence of HEV infection (as measured by HEV RNA detection) in New Zealand blood donors. The study was performed on NZBS samples collected during 2014 and 2015. The seroprevalence of anti-HEV IgG antibodies in 1,013 New Zealand blood donors was determined using two commercial enzyme-linked immunosorbent assays (ELISA) kits. The prevalence of HEV RNA in over 5000 blood donations was determined using reverse transcription real-time quantitative PCR (qPCR) in minipools of eight donations. In addition, 103 individual samples that were anti-HEV IgG positive by either of the commercial ELISA kits were tested for the presence of HEV RNA.

Key findings of the study were:

- The prevalence of anti-HEV IgG in the New Zealand blood donors was 7.8%, comparable with other developed countries.
- The presence of anti-HEV IgG was significantly correlated with increasing age.
- Seroprevalence did not differ significantly between males and females, nor across any of the selected five geographic regions comprising urban and rural areas within New Zealand.
- No HEV RNA was detected in any of the samples tested.

This study, the largest to date to assess HEV seroprevalence in New Zealand, provides valuable baseline information on the prevalence and incidence of HEV infection in New Zealand blood donors. The results of the study will assist NZBS in determining the appropriateness of introducing targeted or universal testing of blood donations for HEV RNA. The study authors recommend that future work should include assessment of risk factors for HEV exposure in New Zealand, including food-borne exposure.

NZBS Transfusion Medicine Handbook 3rd Edition 2016

The third edition of the NZBS Transfusion Medicine Handbook is expected to be available from late April this year. This provides information on the products and services provided by NZBS. While retaining a familiar format, the content has been updated to reflect current local and international clinical guidelines. New topics include preoperative iron supplementation, massive transfusion protocol (MTP), autologous serum eye drops (SED), and non-vitamin K-dependent oral anticoagulation (NOAC). Evidence continues to evolve and the Handbook has been provided as a complement to obtaining specialist advice.

An electronic version will be available on the NZBS website (www.nzblood.co.nz). Printed copies should be available from your local Blood Bank or Transfusion Nurse Specialist. Additional copies can be obtained free of charge. Please contact jillian.sinden@nzblood.co.nz, giving your contact details.

Zika Virus and the Safety of New Zealand's Blood Supply

Recent media interest in the on-going epidemic of Zika virus inevitably raises questions around the security of the New Zealand blood supply. NZBS has a well-developed set of measures aimed at managing the risk of transfusion transmissible infection associated with international travel. The arbovirus donor deferral measures implemented during late 2014 provide security against a wide range of mosquito borne infections including Zika virus. Potential recipients of blood products in New Zealand can be reassured that the risk of transfusion transmission of Zika virus by blood products is being effectively managed.

Zika virus is a mosquito-borne virus transmitted by Aedes mosquitoes. The same mosquito also transmits three other vector-borne diseases (dengue, chikungunya and yellow fever) across tropical and subtropical regions around the world. Since late 2014 prospective donors who have travelled to 'at risk' areas for these infections have been deferred for 28 days following departure from the area. Current outbreaks of Zika infection are occurring in countries that are known to be endemic for dengue virus. The Aedes mosquito is not present in New Zealand and so local transmission of the virus will not occur.

Zika virus is a member of the Flavivirus family. These enveloped viruses are highly susceptible to the virus inactivation steps included in the manufacture of plasma products. This includes immunoglobulin, coagulation factor and albumin products. Any virus that enters a plasma pool will be destroyed during the manufacturing process.

Further information on the NZBS response to the infection including advice to prospective donors who have travelled overseas is available on the NZBS website (www.nzblood.co.nz/news/2016/update-zika-virus-and-the-safety-of-new-zealands-blood-supply/).