BLOOD ISSUES

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NZBS Introduces a New Blood Component – 'Platelets in Additive Solution'

For many years red cell components have been suspended in 'additive solutions' rather than plasma. The additive solution utilised by NZBS is called SAG-M. This contains saline, adenine (helps to maintain red cell ATP levels improving red cell survival), glucose (a source of nutrient for the red cell) and mannitol (adjusts osmotic pressure and avoids haemolysis). Additive solutions have improved the overall flow characteristics of the red cell components enabling more rapid infusion in urgent clinical settings. They have also increased the amount of plasma available for fractionation purposes thereby reducing overall costs of blood services.

In recent years there has been increasing interest in adopting a similar approach to platelet components. A number of countries in Europe have been providing platelet components suspended in additive solutions for several years. They are also widely used in Australia. The clinical performance of platelets suspended in additive solution is equivalent to that of platelets suspended in plasma. Published data indicates that platelet increments might be slightly lower for platelets suspended in additive solution than for those in plasma. Haemostatic performance is however the same and for regular platelet recipients there is no change in the interval between transfusions.

Platelets in additive solution provide two main benefits to blood services. Both arise because of the reduction in the amount of plasma in the final component.

The first benefit is a significant reduction in the frequency of transfusion reactions. Haemovigilance data from New Zealand shows that the frequency of reports of transfusion reactions associated with platelet and FFP transfusion is significantly higher than that seen with red cell components. Overseas data shows that the frequency of transfusion reactions is significantly less when the platelets are suspended in additive solution. The reduction applies mainly to allergic and febrile reactions. These can be particularly problematic in regular recipients of platelets. The reduction in the frequency of reactions simply reflects the lower volume of plasma present in the final component.

Secondly, the use of additive solutions results in more plasma being available for fractionation. NZBS estimates that full implementation of platelets in additive solution, for both pooled and apheresis platelets, might release a further 5 tonnes of plasma for fractionation. This represents a 10% increase over current levels and also reduces the number of plasmapheresis procedures required to meet plasma requirements with a consequent reduction in overall costs. This is particularly beneficial to NZBS because the demand for Intragam P continues to grow at a rate of about 7% per annum.

During the last two years NZBS has been progressing systems to enable implementation of platelets in additive solution in New Zealand. Medsafe have now approved the new component and NZBS will begin formal validation in November 2010. Platelets in additive solution will be progressively implemented at all NZBS manufacturing sites over the next year. This will initially apply to pooled platelet components and subsequently to apheresis platelets. NZBS will issue the component in response to standard requests for platelet components. At this stage no change is planned for neonatal platelet components which will continue to be provided suspended in plasma.

NZBS Implements National Policy on the Provision of CMV Antibody Negative Blood Components

Cytomegalovirus (CMV) is a ubiquitous herpes virus. In immuno competent individuals primary infection is often asymptomatic. The frequency of infection, defined by the presence of antibody, increases with age. Approximately 60% of previously untested donors in New Zealand are positive for the antibody. CMV infection can be life threatening in susceptible immunocompromised individuals. This includes transplant recipients, patients with severe immunodeficiency disorders, the foetus and low weight premature neonates and pregnant women. Routine monitoring for CMV by PCR post transplant with the early initiation of specific anti-viral therapy has significantly reduced morbidity and mortality in this setting.

CMV, a cell associated virus, is readily transmitted by transfusion of cellular components from infected donors. CMV is a cell-associated virus.

Efforts should be made to reduce the likelihood of transmission by transfusion in susceptible individuals. This primarily involves CMV antibody negative patients and transplants involving CMV antibody negative donor and recipient pairs. Reactivation of CMV can occur in immunosuppressed CMV antibody positive patients and grafts from CMV antibody transplant donors can also lead to infection.

Blood Services can reduce the risk of transmission of CMV by blood components in two ways:

1. **The use of CMV antibody negative components:**

   Overall, this strategy appears to be associated with a more than 90% reduction in the risk of transfusion transmitted CMV in high-risk recipients. However it fails to prevent a low residual rate of transmission of approximately 1.2-1.5%, likely to be due to donation during the "window" period following infection, before the development of a detectable antibody response.

2. **The removal of white cells from components:**

   This is most effective when pre-storage leucodepletion is undertaken in controlled settings. As with CMV antibody testing, leucodepletion appears to result in a greater than 90% reduction in the risk of transfusion transmitted CMV in high risk recipients but it fails to prevent a low residual rate of transmission of approximately 2.1-2.5%, probably mediated by persistent or recurrent plasma viraemia in the donor, allowing infective virus to traverse the filter.

The Council of Europe Guide to the Preparation, Use and Quality Assurance of Blood Components identifies that neither method nor the combination can completely avoid transmission from the occasional case of CMV viraemia in the early stage of acute infection. There is no consensus on the requirement for ongoing CMV antibody screening in blood services, such as NZBS, that undertake universal leucodepletion of blood components. While some services, especially those in areas that have a high prevalence of CMV have ceased testing, others believe that the combination approach may confer some additional safety.

During late 2009 NZBS undertook a consultation process seeking comment on a draft policy for the future provision of CMV antibody negative blood components in New Zealand. The draft policy was developed in conjunction with clinical haematologists and solid organ transplanters across New Zealand. The policy aims to introduce a nationally consistent approach on this controversial issue. Feedback on the draft policy was positive and NZBS is now progressively implementing this on a DHB by DHB basis.

The key elements of the policy are shown below:

NZBS will adopt the following approach to avoidance of transfusion transmitted CMV infection:

1. Standard blood components that have undergone pre-storage leucodepletion offer a high level of safety for all immune competent recipients.
2. Haemopoeitic stem cell and organ transplant recipients will routinely be provided with standard pre-storage leucodepleted blood components. These provide a high level of safety with respect to avoidance of transfusion transmitted CMV infection.
3. Pregnant women, regardless of their CMV antibody status, will routinely be provided with standard pre-storage leucodepleted blood components. These provide a high level of safety with respect to avoidance of transfusion transmitted CMV infection.
4. Blood components manufactured for intra-uterine and neonatal use will continue to be CMV antibody negative. This recognises the particular vulnerability of these groups and the difficulty of undertaking routine CMV surveillance in these settings.
5. CMV antibody negative components will continue to be provided for individual patients following discussion and agreement between the specialist responsible for the patient's care and a member of the NZBS Medical team. This will require the addition of a specific protocol within the NZBS Blood Management System (Progesa). Such requests should be made in sufficient time to ensure that adequate numbers of suitable components are easily available.

This approach is consistent with policy developed by the American Association of Blood Banks and by the Joint UKBTS/NIBSC Professional Advisory Committee.

This policy will be reviewed in the future if compelling new evidence becomes available from clinical trials addressing this issue.

NZBS has recently commenced implementation of the new policy. The NZBS clinical team will work closely with local clinicians to ensure that those patients who continue to require CMV antibody blood components continue to have access to them.

XMRV – A New Transfusion Transmitted Infection?

New Zealand Blood Service (NZBS) has been closely monitoring international developments in relation to Chronic Fatigue Syndrome and its possible relationship to Xenotropic Murine Leukaemia Related Virus (XMRV) since the initial report by Lombardi and colleagues published in Science in October 2009.

Lombardi reported that XMRV was isolated from peripheral blood mononuclear cells in 67% of patients with Chronic Fatigue Syndrome compared to 3.7% of healthy controls. The virus was also present in the plasma.

Considerable scientific uncertainty exists in relation to the implications of these findings for the safety of the blood supply. Studies from the United Kingdom and the Netherlands have been unable to replicate the United States data produced by Lombardi. However a recent study by Harvey Alter from the US National Institutes of Health (NIH) has confirmed the original findings.

There is currently no data to indicate that the virus is transmitted by transfusion and whether pre-storage leucodepletion might reduce or eliminate this risk. Studies are currently being designed in the US and elsewhere to address these questions.

Blood Services internationally have taken steps to reduce the risk of transfusion transmission of the virus. Potential donors reporting a history of Chronic Fatigue Syndrome are being permanently deferred from donating blood. In line with this, NZBS introduced this permanent deferral in April 2010 extending the previous two year deferral following recovery from CFS to a permanent deferral. The situation will continue to be closely monitored.

Further reading:

1. Lombardi VC, Ruscetti FW et al (2009) Science 236 : 585-9
2. Lo SC, Pripuzova N et al, (2010) Proc Natl Acad Sci USA online early view August 2010.

Residual Risk of Virus Transmission via Transfusion

Despite highly sensitive screening methods there is a small residual risk of transmission of major blood borne viruses for blood product recipients, particularly if the donation is collected during the window period (time between infection and the first detectable viral marker). An analysis of the residual risk of viral infection from blood component transfusion in New Zealand, using mathematical modelling, has recently been undertaken by Dr Richard Charlewood from NZBS. The analysis utilised systems originally developed by Schreiber and colleagues in the United States[1].

The key parameters utilised in the analysis are shown below.

Virus	Window Period	Donations	Average Donation Interval
HBV	38 days	541,426	152 days
HCV	7.4 days	1,413,490	204 days
HIV	9 days	1,413,490	204 days
HTLV	51 days	105,726	N/A

The residual risk estimates are shown in the table below. Equivalent data from the English National Blood Service and Australian Red Cross Blood Service is also provided.

	Risk per 10^6 donations			
Virus	New Zealand	Australia	UK	*p*
HBV	3.4 (0.9-13.0)	0.75	1.84	0.25
HCV	0.4 (0.1-3.5)	0.28	0.029	0.39
HIV	0.2 (0.0-3.2)	0.14	0.1	0.92
HTLV	0.4 (0.0-37.1)			

The New Zealand data is comparable to that in Australia and the UK. Confidence intervals are wide reflecting the low level of risk. This is further supported by the absence of reports of transmission of HIV or HCV since beginning antibody testing for HIV in 1985 and HCV in 1992.

The model assumes window period donations represent the dominant source of risk of transmission of the virus by transfusion. This is likely to be correct for HIV and HCV but is not likely for Hepatitis B where occult infection is, in our clinical experience, the more likely cause and not reflected in these calculations. However no cases of hepatitis B transmission attributable to transfusion have been reported following the introduction of HBV DNA testing (NAT testing) in September 2007.

[1] Schreiber GB, Busch MP, Kleinman SH et al. The risk of transfusion-transmitted viral infections. N Engl J Med. 1996 June 27; 334(26):1685-1690

An Audit of Bedside Transfusion Practice in 8 New Zealand Hospitals

Background

The most basic principle of patient care during transfusion is to ensure patient safety. Enormous efforts are made to ensure the product is safe, but the bedside process is, in many ways, the most vulnerable point in the transfusion. The administration of blood to the wrong patient or the failure to identify a developing transfusion reaction early enough may lead to major morbidity or death.

The Serious Hazards of Transfusion (SHOT) and The New Zealand Blood Service (NZBS) haemovigilance programme receive reports of adverse transfusion reactions and incidents such as incorrect blood component transfused and 'near miss' events. Annual reports from both schemes highlight that errors in bedside checking are a major contributor to the number of reported incidents.

The published 'Guidelines for the Administration of Blood and Blood Components and the Management of Transfused Patients' by The British Committee for Standards in Haematology (BCSH), and 'The Guidelines for the Administration of Blood Components' by the Australian and New Zealand Society of Blood Transfusion (ANZSBT) have offered recommendations for minimising the risk. These recommendations are the basis of present hospital policy for the transfusion of blood and blood products.

Aim of Audit
The aim of this audit was to determine the level of adherence to the Australian and New Zealand Society of Blood Transfusion (ANZSBT) guidelines with the administration of resuspended red cells at patients' bedsides at North Shore, Auckland, Middlemore, Waikato, Palmerston North, Wellington, Christchurch and Dunedin public hospitals.

Method
Episodes from a spread of specialties were collected prospectively by the Transfusion Nurse Specialist (TNS) at each site, both as the transfusion took place by direct observation and later from the patient's clinical records after the transfusion had been completed. Patients in an operating theatre or undergoing a rapid massive transfusion were not included in the audit. A list of bare essential safety checks was compiled and each episode compared to this list.

Results
Patient identity checks were generally performed well when assessed against the ANZSBT guidelines. Notable exceptions included failing to ask patients to state their identity (45% compliance overall), neonates (33%) and day cases (57%) not wearing identification wristbands. Clerical checks were conducted well but the presence of an additional form with handwritten unit numbers and blood groups used in some sites appeared to distract from checking the unit against the compatibility label and introduced the risk of transcription errors. The two person bedside check of a unit against the patient and prescription was performed variably, with one hospital failing this step in almost a quarter of transfusions audited. Checking patient vital signs revealed confusion over the role of pulse oximetry versus observed respiratory rate. The patient was observed for the first 15 minutes of the transfusion in only 86% of cases. Only 60% of adverse reactions were reported to blood bank. Post-transfusion documentation was well performed except for failure of staff to counter-sign the prescription in one site and a lack of records of transfusion times at several hospitals. Transfusion duration was over 4 hours in up to 10% of transfusions. Only 67% of transfusions met the requirements of a set of bare essential safety checks, with up to five omissions per transfusion.

Comment
Some of the key areas for improvement identified by this audit include:

- identifying in hospital policy how neonates and outpatients will be identified for transfusion, and in particular, whether and how wristband labels will be applied.
- removing transcription of blood unit numbers and blood groups onto forms accompanying blood from Blood Banks.
- training that the two-person checks must occur at the bedside.
- clarifying in hospital policy the role of pulse oximetry vs respiratory rate in monitoring transfusion.
- reinforcing that the patient must be closely observed for the first 15 minutes of each unit transfused.
- educating that all adverse reactions need to be reported to Blood Bank.
- improving documentation, in particular the signature to show the blood component has been transfused as well as when it was transfused.
- ensuring red cells should be transfused in less than four hours other than in exceptional circumstances due to the risk of bacterial contamination.
- considering providing day-case transfusion recipients with a contact card for obtaining advice in case of a delayed transfusion reaction.
- encouraging DHBs to work together to establish nationally consistent processes and documentation. NZBS will be happy to support this development.

2009 Annual Haemovigilance Report

The 2009 Haemovigilance report is now available on the NZBS website (www.nzblood.co.nz). The report contains information on adverse events associated with transfusion in New Zealand during 2009. Hard copies can be obtained on request (please contact jillian.sinden@nzblood.co.nz).

A summary of the key findings from the report will be included in the next edition of Blood Issues.