Leucocyte Depletion for Neonatal and Paediatric Care

The Impact of Leucocyte Depletion of Allogeneic Transfusion Products on Neonatal and Paediatric Groups

Transfusion Transmitted Cytomegalovirus Infection (TT-CMV)
Cytomegalovirus (CMV) is known to be transmitted by blood transfusion. Several observations support the hypothesis that CMV is transmitted within leucocytes which contaminate donated blood products:1

- the high incidence of CMV infection associated with the receipt of granulocyte transfusions
- the removal of leucocytes from blood components significantly reduces or eliminates TT-CMV
- infectious virus is readily isolated from granulocytes and monocytes, subsets of leucocytes

Unlike other transfusion-transmitted viral infectious, CMV is understood to be transmitted in a latent, non-infectious state and reactivated after transfusion into the recipient. In immunocompetent patients, TT-CMV usually manifests as seroconversion without an accompanying illness, or presents as a flu-like syndrome. However, TT-CMV in low birth weight premature infants, or immunocompromised patients, can result in fever, pneumonia, hepatitis, gastrointestinal disease, encephalitis, pericarditis and/or pancytopenia with significant morbidity and mortality.2

Preterm low birth weight neonates who are born to CMV-seropositive mothers may have passively acquired antibodies, but will not have developed cellular immunity against the virus. This is particularly relevant as preterm infants are being resuscitated at lower and lower gestation ages, where no protective levels of maternal antibodies prior to birth have been acquired.3,4

Most guidelines recommend the provision of CMV-safe blood to children under 12 months of age.6,7 In surveys of the transfusion practices of AABB institutional members, 93% of 438 respondents provided CMV-safe components to at least some neonates, with 83% using CMV-safe blood for all neonates regardless of birthweight or CMV serostatus.6,9

Transfusion During Pregnancy
The consequences of acquiring a CMV infection during pregnancy are serious. 40% of women experiencing primary CMV infection during pregnancy give birth to infants with congenital CMV infection (Figure 1), who may develop handicaps such as deafness and neurological problems.10 It may therefore be prudent to provide CMV-safe blood components to women requiring blood antenatally and for intrauterine transfusions.

Figure 1
Congenital CMV Infection
Filtration Solution

CMV-Safe Blood Components
The European Committee on Blood Transfusion in the “Guide to the preparation, use and quality assurance of blood components” has advised that high risk patients, such as transplant recipients, patients with severe immunodeficiency, foetuses transfused in utero, CMV seronegative pregnant women, and low weight and premature neonates should receive blood components either from CMV seronegative donors or leucodepleted components to reduce the risk of CMV transmission and disease. The Committee notes that while some blood services in high seroprevalence areas have ceased CMV antibody screening, others have combined antibody screening and leucodepletion in the belief that doing so may confer additional safety. This conclusion was reached after analysis of data showing that leucocyte depletion by filtration effectively reduces the risk of TT-CMV to that equivalent to CMV screened negative products.12-17

The largest study to date12 involved adult bone marrow transplant patients and demonstrated that the CMV-safe blood components can be delivered by effective filtration; infection rates within 249 patients receiving screened seronegative blood components was 0.8% (2/249), whereas CMV infection rates within 247 patients receiving unscreened leucocyte depleted blood components was 1.2% (3/247). There was no significant difference in infection rates between the two groups.

Blood Transfusion Immunoulation
It is well known that recipients of perioperative allogeneic transfusions have increased rates of bacterial infections.15,26 The exact underlying mechanisms responsible for this type of transfusion-associated immunosuppression remain elusive, although active research is being undertaken.27 One notable aspect is that allogeneic transfusion causes immune deviation toward the secretion of cytokines which downregulate cellular immunity, this may well explain the altered clinical outcomes in several different clinical settings.

A striking observation is that between transfusions and increased infection rates are associated with prolonged lengths of hospital stay.28-32 This transfusion effect has been shown to be independent of other parameters measured (bleeding, anaemia, age, pre-existing medical comorbidity, etc). The neonatal and paediatric populations are often immunocompromised and the unintentional immunosuppressive effects of allogeneic transfusion may only compound this predicament.

Reduced Immunosuppressive Effects
Leucocyte depletion will reduce the associated immunosuppressive risks where allogeneic transfusions are required. Jensen et al 33 (Figure 2) showed that when leucocyte depleted blood was transfused both surgical and healthcare-associated infections were significantly reduced; wound infection rates fell from 12 to 0%, intraabdominal abscesses from 5 to 0% and pneumonia from 23 to 3%. This corroborates her group’s previous findings.34

Patients transfused with buffy coat poor blood (BCPB), n = 142, developed significantly (P < 0.005) more infectious complications related to the surgical procedure (18.3%), than patients transfused with leucocyte depleted blood (LDB; 0%), n = 118, or non-transfused patients (NT; 0.6%), n = 326. Hospital acquired infections also developed at a significantly (P < 0.01) higher rate in patients receiving BCPB (36.6%), than in the LDB group (14.4%), or the NT group (7.1%).

Van de Watering et al,35 (Figure 3) demonstrated that, by leucocyte depleting the allogeneic blood products transfused to cardiac patients, it is possible to significantly reduce their mortality rate. Significant reductions in the development of multi-organ failure and subsequent mortality were the most notable.

Patients scheduled for cardiac surgery (n = 914) were randomly allocated to receive either buffy coat poor red cells (BCPB), fresh filtered red cells (FF – leucocyte depletion was completed within 24 hours of donation), or stored filtered red cells (SF leucocyte depletion was completed at 6 – 20 days post donation). Evaluation of mortality over 60 days revealed a significant difference (P = 0.001) between the BCPB and leucocyte depleted groups (FF and SF = LDB), particularly in the number of patients who died of noncardiac causes, such as multiorgan failure (P = 0.001).

In addition, recent literature suggests that leucoreduction may be effective in reducing the risk of transmission of a number of noteworthy transfusion-transmitted infectious agents, including herpesviruses, retroviruses, bacteria, protozoa and prions.36

### Figure 2

Wound Infection Rates

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<thead>
<tr>
<th></th>
<th>BCPB</th>
<th>LDB</th>
<th>NT</th>
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<tbody>
<tr>
<td>% Infection Rate</td>
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<tr>
<td>Surgical Infection</td>
<td>7.8%</td>
<td>4.6%</td>
<td>3.3%</td>
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<tr>
<td>Hospital Acquired Infection</td>
<td>2.3%</td>
<td>1.0%</td>
<td>0.3%</td>
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</tbody>
</table>

### Figure 3

Comparison of Causes of Patient Deaths

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<thead>
<tr>
<th></th>
<th>BCPB</th>
<th>LDB</th>
<th>NT</th>
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</thead>
<tbody>
<tr>
<td>Number of Patient Deaths</td>
<td></td>
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<td></td>
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<tr>
<td>Overall Mortality</td>
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<td></td>
<td></td>
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<tr>
<td>Cardiac Related</td>
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<td></td>
<td></td>
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<tr>
<td>Multi-Organ Failure</td>
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<tr>
<td>Anastomotic Dehiscence</td>
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<td>2.3%</td>
<td>1.0%</td>
<td>0.3%</td>
<td></td>
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<tr>
<td>0.3%</td>
<td>0%</td>
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HLA Alloimmunisation
Antibodies against HLA class I antigens are a major cause of non-haemolytic febrile transfusion reactions and refractoriness to platelets. The production of these antibodies occur following exposure to functional allogeneic leucocytes. The ability of neonates to produce significant antibody concentrations may be limited due to their functionally immature B lymphocytes. However, it has been documented that multiply transfused babies can produce antibodies and the more donors babies are exposed to, the more likely they are to be strongly positive for anti-HLA antibodies.

Due to the problems associated with finding compatible cross match negative blood and/or organs, it is reasonable to consider preventing alloimmunisation in patients who may in the future go on to require prolonged blood product support, require bone marrow transplantation or solid organ transplant. Because it is frequently impossible to discern at the outset which infants and children may ultimately require such treatment in the course of their lives, some experts advise leucocyte reduced blood for all transfusion recipients.

Reduction of Alloimmunisation
There is a considerable amount of data to support leucocyte depletion as a means of preventing alloimmunisation and subsequent clinical sequelae (Table 1).

Table 1.
Rate of Alloimmunisation

<table>
<thead>
<tr>
<th>Author</th>
<th>Patient Group</th>
<th>Standard Transfused Group</th>
<th>Leucocyte Depleted Transfused Group</th>
</tr>
</thead>
<tbody>
<tr>
<td>TRAP Study</td>
<td>Acute Myeloid Leukaemics</td>
<td>13%</td>
<td>3%</td>
</tr>
<tr>
<td>Killick et al</td>
<td>Aplastic Anaemics</td>
<td>18%</td>
<td>12%</td>
</tr>
<tr>
<td>Adamzik et al</td>
<td>Leukaemics</td>
<td>27%</td>
<td>0%</td>
</tr>
<tr>
<td>Oksanen et al</td>
<td>Acute Myeloid Leukaemics</td>
<td>38%</td>
<td>17%</td>
</tr>
<tr>
<td>Saarinen et al</td>
<td>Paediatric Leukaemics</td>
<td>30%</td>
<td>0%</td>
</tr>
<tr>
<td>Bedford-Russell et al</td>
<td>Neonates</td>
<td>30%</td>
<td>0%</td>
</tr>
</tbody>
</table>

Table 2.
Efficiency of Leucocyte Depletion

<table>
<thead>
<tr>
<th>Leucocyte Depleted Blood Group (n = 19)</th>
<th>Standard Blood Group n = 23</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gestation (weeks)</td>
<td>29 (24 – 35)</td>
</tr>
<tr>
<td>Weight (g)</td>
<td>950 (675 – 2240)</td>
</tr>
<tr>
<td>Number of Transfusions</td>
<td>8 (2 – 35)</td>
</tr>
<tr>
<td>Positive HLA- Antibody Detection</td>
<td>0 (0%)</td>
</tr>
</tbody>
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Haemonetics Filters
High efficiency leucocyte depletion filters provide red cells, platelets and plasma transfusion products with residual counts significantly below the European Guidelines.

Summary
Leucocytes in allogeneic blood transfusions have been shown to increase patient risks of morbidity and mortality. There is evidence to show that leucocyte depletion through filtration of blood products protects patients against:
- Transfusion-associated CMV infection and reactivation
- Immunosuppression and infection
- HLA alloimmunisation and subsequent clinical sequelae
References


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