Introduction.

Simple red cell transfusions are most commonly used to correct acute blood loss and hypovolaemia in preterm and term neonates, as well as the correction of anaemia of prematurity. Exchange transfusions may be used to correct severe anaemia, and to treat hyperbilirubinaemia and polycythaemia. This policy is directed at practices used to avoid red cell transfusions, criteria for red cell transfusion and the practicalities of red cell transfusion.

Incidence

All infants admitted to JSN between 1996 to 1998 that were born < 27 weeks gestation required red cell transfusions, with the median number of transfusions per infant ranging from 7 at 24 weeks to 4 at 26 weeks gestation. Transfusion requirements decrease substantially after 26 weeks and are uncommon after 29 weeks gestation.

Table 1: Median number of red cell transfusions by gestational age at birth:

<table>
<thead>
<tr>
<th>Gestation: (weeks)</th>
<th>24</th>
<th>25</th>
<th>26</th>
<th>27</th>
<th>28</th>
<th>29</th>
<th>30</th>
</tr>
</thead>
<tbody>
<tr>
<td>Red cell transfusions (median)</td>
<td>7</td>
<td>4</td>
<td>4</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

Figure 1: Incidence simple red cell transfusion by gestation in surviving preterm neonates admitted to JSN between 1996 to 1998:
Risk factors

Anaemia in the neonate may result from:

1. **Peripartum**: blood loss -
   - foetal-maternal haemorrhage
   - vasa praevia
   - tight nuchal cord
   - occasionally with antepartum haemorrhage and
   - placental abruption

2. **Early** -
   - iatrogenic blood loss from frequent blood sampling, and

3. **Intermediate**: *Anaemia of prematurity* resulting from
   - Rapid rate of body growth
   - Short red blood cell survival
   - Reduced erythropoietin production in preterm infants

4. **Late (post discharge)**:
   - anaemia of prematurity (due to iron deficiency
   - *Isoimmunisation* (most commonly rhesus)

Normal haemoglobin levels in neonates

**Table 2:**

<table>
<thead>
<tr>
<th>Age</th>
<th>GA / birth weight</th>
<th>Hb (g/l)</th>
<th>PCV %</th>
</tr>
</thead>
<tbody>
<tr>
<td>birth</td>
<td>24</td>
<td>140</td>
<td>40</td>
</tr>
<tr>
<td></td>
<td>28</td>
<td>145</td>
<td>45</td>
</tr>
<tr>
<td></td>
<td>34</td>
<td>150</td>
<td>47</td>
</tr>
<tr>
<td></td>
<td>term</td>
<td>168</td>
<td>53</td>
</tr>
<tr>
<td>3 days</td>
<td>28-32</td>
<td>175</td>
<td>54</td>
</tr>
<tr>
<td></td>
<td>32-36</td>
<td>190</td>
<td>59</td>
</tr>
<tr>
<td></td>
<td>36-40</td>
<td>190</td>
<td>59</td>
</tr>
<tr>
<td></td>
<td>term</td>
<td>190</td>
<td>59</td>
</tr>
<tr>
<td>2 months</td>
<td>&lt;1000g</td>
<td>70</td>
<td></td>
</tr>
<tr>
<td></td>
<td>1000-1500g</td>
<td>80 (70-114)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>1500-2000g</td>
<td>95 (80-114)</td>
<td></td>
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</tbody>
</table>

Consequences

Benefits
Clinical studies have been unable to determine unambiguous benefits of red cell transfusion and precise criteria for transfusion. The following may assist in clinical decision making:

1. **Effect on weight gain:**
   - Minimal effect on weight gain was shown in two controlled trials of transfusion (to keep Hb > 100g/L or transfused at mean Hb 115 g/L)  

2. **Breathing patterns in stable preterm infants:**
   - A controlled study found that benefit from red cell transfusion in 1 3 month old preterm infants with haematocrit < 30 was predicted by presence of heart rate > 152 bpm, apnea/bradycardia or lactic acidosis.
   - A controlled study comparing albumin and red cell transfusion in preterm infants with a mean Hb < 10g/L found no difference in the reduction of clinically significant apnea between the two groups.
   - Uncontrolled studies (before and after) have suggested a reduction in apnea from red cell transfusion.

3. **Heart rates, oxygen consumption and cardiac outputs of stable preterm infants:**
   - A controlled study in stable preterm infants with Hb < 10g/L found no change in heart rate, cardiac output or central venous oxygen tension difference in infants transfused red cells compared to infants transfused albumin.
   - Several uncontrolled studies have shown reductions in heart rate and cardiac output after transfusion.

4. **Subclinical tissue acidosis:**
   - An uncontrolled trial of red cell transfusion in ventilated preterm infants < 1500g (mean hct = 33 pre transfusion) demonstrated an increase in regional oxygen delivery and tissue pH in contrast to colloid infusion, which had no effect.
   - A controlled trial showed a reduction in serum lactate in transfused anaemic (HCT < 29) infants with BPD or apnoea/bradycardia.

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**Harms**

Potential adverse consequences of neonatal blood transfusion include:

1. **Volume overload** avoided by awareness of potential, avoidance of rapid transfusion rates in isovolaemic neonates and use of frusemide where indicated. Partial exchange may be indicated for infants with heart failure (infants with cardiac disease, hydrops or polycythaemia)

2. **Immunosensitisation** shown in an RCT to be avoided by use of leucocyte depletion filter

3. **Graft versus host disease** rare complication of neonatal transfusion with usually fatal outcome - avoided by irradiation

4. **Metabolic derangement**
   - **Hyperkalaemia** avoid rapid transfusion with old blood in infants at risk (< 27 weeks gestation and < 72 hours age or with renal impairment)
   - **Hypocalcaemia** monitor with large volume transfusions
   - **Hypomagnasaemia** monitor with large volume transfusions

5. **Transmission of infection** - The risk of seronegative infective blood donation calculated by the Victorian Red Cross Blood Bank (data from 1994 to 1995) was 1) HBV 6.45 per million donations; 2) HCV 4.27 per million donations; and 3) HIV 0.79 per million donations.
   - **Cytomegalovirus** risk reduced to < 1% by use of CMV negative blood and/or leucocyte depletion filters.
   - **Other viruses** - Hepatitis B virus, hepatitis C virus, HIV and HTLV1/2 viruses donors routinely screened

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**Diagnosis**

**Criteria for neonatal blood transfusion**
Criteria of blood transfusion are arbitrary. Unequivocal benefits of red cell transfusion have not been demonstrated in randomised trials \(^1\)\(^{16}\).

Consider red cell transfusion for neonates (term or preterm) and infants < 4 months of age if:

- Haemoglobin < 120 g/L (hct < 36) and severe pulmonary or heart disease
- Acute blood loss > 10% of blood volume and evidence of cardiovascular compromise
- Haemoglobin < 80 g/L in a stable newborn infant, or
- Haemoglobin < 9-10 g/l, low reticulocyte count (<2%) and symptomatic of anaemia

In infants > 4 weeks of age, testing should include a reticulocyte count. Infants with reticulocyte counts > 2% are unlikely to suffer increasing anaemia.

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**Pre-transfusion testing and patient identification**

Pre-transfusion testing is undertaken to provide suitable blood for a patient which will not cause a haemolytic transfusion reaction, and which will have an adequate life span after transfusion.

**This is achieved by -**

1. Accurate identification of patient at time of collection of specimen (hand label specimen tubes and transfusion order).
2. Ascertaining patients ABO + Rh group in order to provide ABO + Rh compatible blood.
3. Having in place an independent Check Group System so that blood is not released for the patient before group is checked.
4. Screening the materanl sample
5. Crossmatching suitable units and having a second person check the crossmatch paper work before release of the blood, if possible.
6. Requiring two persons (medical officer or nurse and one other) to ensure the correct unit of blood is given to the correct patient, and that this is documented in the patients notes.

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**Treatment**

**RPAH Blood Bank guideline for Neonates**

Blood transfusion:

1. Inform the parents of need for transfusion
2. In stable preterm infants: give packed red cells 20 mls / kg \(^{23}\) over 4 hours with frusemide 1 mg/kg IVI at beginning of transfusion
3. For acute blood loss: give whole blood or pack red cells 20 mls / kg or volume of estimated blood loss titrated to infants response to transfusion (correction of tachycardia)
4. Use CMV negative blood
5. Use irradiated blood
6. Use a leucocyte depletion filter
7. Ensure all blood bank procedures are adhered to

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**Prevention of need for transfusion**

1. Delayed cord clamping controlled trials in premature infants have failed to show an increase in infants haematocrit or reduction in rate of intraventricular haemorrhage with delayed cord clamping \(^{17-20}\)
2. Minimise iatrogenic losses appropriate microsampling with return of the unused blood used to clear the line of fluid and use of non-invasive monitoring should reduce red cell transfusion requirements
of premature infants.

3. Autologous transfusions although feasible it is difficult to collect, store and ensure sterility and identification of autologous blood

4. Erythropoietin (rhEPO) it is not possible at present to recommend the routine use of rhEPO in preterm infants. Evidence from at least 20 RCTs of rhEPO to date have shown: 1, 21
   - RhEPO and iron results in short term improvements in marrow erythroid cellularity, blood reticulocyte counts and improvements in haematocrits
   - RhEPO reduces the numbers of infants receiving blood transfusion and the number of transfusions received by premature infants.
   - However, benefits of rhEPO are limited by:
     - Reduced effect in sick, extremely premature infants who are the recipients of most transfusions,
     - Need for early transfusion is not affected by use of rhEPO. Most extremely premature infants receive early blood transfusion
     - New practices of reducing donor exposure limit the exposure of preterm infants to multiple donors
     - Risk of infection or adverse event resulting from blood transfusion is low
     - Continued use of rhEPO requires subcutaneous injections

Reducing exposure to multiple donors use of dedicated donor packs

- Use of multiple paediatric transfer packs allows infants to be multiply transfused from the same donor pack and limits infant exposure to multiple donors 21
- Use of blood with expiry times < 35 days facilitates use of multiple transfusions from a single donor the potassium level in the supernatant, although potentially reaching levels of 50-80 mmol/L, only expose the infant to 0.5 mmol potassium per 20 mls of blood safe if given over hours 1, 22

Directed transfusion

An audit of blood donations to the NSW Red Cross Blood Transfusion Service showed a non-significant trend to increased rates of hepatitis B and C infection in directed donations compared to the volunteer homologous donations. Although not feasible acutely for urgent transfusion of sick neonates, if requested may be obtained for transfusion of stable preterm infants.

If parents express a wish to donate blood for their own child, the procedure is:

1. Order a group and Coombs on the neonate
2. Order group, antibody screen, haemoglobin, haemolysin screen and CMV test on parent for testing at RPAH
3. Assess the suitability of the parent (see below). If the mother has antibodies and/or the baby has a positive direct antiglobin test then the situation must be discussed with a Haematologist.
4. An appointment is made by ringing Maureen Ingram, Autologous Clinic, Red Cross 9229 4444. At this time the parent will have to answer preliminary questions on the telephone to assess suitability.
5. The doctor looking after the baby must complete a directed donation form. You should stipulate if you require the unit to be made into a packed cell.
6. Inform Blood Bank, RPAH to expect a directed donation for the infant.
7. The parent will be required to fill out the Donor Declaration Form at Red Cross prior to collection. Routine donor screening is performed at Red Cross at the time of collection, and it can take up to 3 working days for the donor unit to be cleared. Units found to be positive for any infectious markers are unsuitable.

Notes:

1. If parent is same ABO and Rh group as the infant then he/she would be suitable. If the baby is group A or B and the parent is group O, Rh compatible, then he/she would need to be haemolysin-free and the units made into packed cells. If the baby is Rh negative and parent Rh positive, then
he/she would be unsuitable.
2. All donations from parents must be irradiated.
3. Blood should be CMV negative, however the Neonatologist looking after the baby may elect to take responsibility for using CMV positive blood and ensure that it is filtered prior to use in the Nursery, to reduce the risk of transmission.
4. The haematologists have strong reservations about the use of maternal blood for neonates because of the possibility of white cell or platelet antibodies in the mother's serum, which are not detected by routine testing. Ideally any maternal blood should be washed at Red Cross prior to transfusion. This would limit the collection to only one transfusion with a 24-hr expiry and could not be arranged quickly or out of normal working hours. The Neonatologist looking after the baby may elect to take responsibility for using unwashed maternal blood.
5. All paternal donations must be fully cross-matched against infant's serum and against maternal specimen if applicable.
6. The cost of directed donations is $250 to the patient.

Key Points

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References


randomized study of 10 vs 20 cc/kg. *Pediatrics*. 104: **S3**: 739.

Last Reviewed: June, 2000