10.2: Neonatal transfusion

Neonates are defined as infants up to 28 days after birth. Most neonatal transfusions are carried out in low birth weight preterm infants treated on neonatal intensive care units (NICUs). Transfusion triggers in neonates are controversial and mainly based on expert clinical opinion, although recent randomised controlled trials of ‘liberal’ versus ‘restrictive’ red cell transfusion policies in very low birth weight preterm babies are starting to influence clinical guidelines.

10.2.1: Neonatal red cell exchange transfusion

Neonatal red cell exchange transfusion is mainly used in the treatment of severe hyperbilirubinaemia or anaemia in babies with HDFN. It removes antibody-coated neonatal red cells and reduces the level of plasma unconjugated bilirubin (the cause of bilirubin encephalopathy). The steep decline in the incidence of HDFN following the introduction of maternal anti-D Ig prophylaxis, more effective antenatal monitoring and treatment, and the use of intensive phototherapy and intravenous immunoglobulin postnatally has made red cell exchange transfusion an uncommon procedure that should only be performed in specialist units by experienced staff. A ‘double volume exchange’ (160–200 mL/kg) removes around 90% of neonatal red cells and 50% of bilirubin.

The Blood Services produce a special red cell component for neonatal exchange transfusion (Table 10.3). It is ordered in specially by hospitals when required and close collaboration between the clinical team, hospital transfusion laboratory and blood service is essential. The component should be warmed to 37°C immediately before transfusion. It should be irradiated if this requirement does not cause clinically important delay in provision (irradiation is essential if the baby has received IUT).

Table 10.3 Red cells for neonatal exchange transfusion
Plasma reduced with haematocrit of 0.5–0.6 (NHSBT 0.5–0.55) to reduce the risk of post-exchange polycythaemia

In CPD anticoagulant

Less than 5 days old

Irradiated (essential if previous IUT)

CMV negative

Sickle screen negative

Usually produced as group O (with low-titre haemolysins)

RhD negative (or RhD identical with neonate) and Kell negative

Red cell antigen negative for maternal alloantibodies

IAT crossmatch compatible with maternal plasma

10.2.2: Large volume neonatal red cell transfusion

Large-volume transfusion, equivalent to a single circulating blood volume (approximately 80 mL/kg), is mainly used in neonatal cardiac surgery. The component supplied (mean unit volume 294 mL) is in SAG-M anticoagulant (see Chapter 3) and has the same specification as that used for neonatal ‘top-up’ transfusions. It should be transfused less than 5 days from donation to reduce the risk of hyperkalaemia. Irradiated blood is required in babies with known or suspected T-cell immunodeficiency, such as DiGeorge syndrome, in which case the blood should be transfused within 24 hours of irradiation.

10.2.3: Neonatal ‘top-up’ transfusion

Repeated small-volume ‘top-up’ red cell transfusions (up to 20 mL/kg) are commonly carried out in preterm babies, mainly to replace losses from repeated blood testing exacerbated by reduced red cell production (‘anaemia of prematurity’). Up to 80% of preterm babies weighing less than 1500 g at birth are transfused at least once. Indications for transfusion in this group have largely been based on the Hb concentration combined with the cardiorespiratory status of the baby (e.g. requirement for oxygen or ventilatory support)
and factors such as weight gain, although the evidence base is weak. The new British Committee for Standards in Haematology (BCSH) Transfusion Guidelines for Neonates and Older Children (https://b-s-h.org.uk/) suggest the transfusion thresholds summarised in Table 10.4.

Table 10.4 Summary of BCSH recommendations for neonatal top-up transfusions

<table>
<thead>
<tr>
<th>Postnatal age</th>
<th>Suggested transfusion threshold Hb (g/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Ventilated</td>
</tr>
<tr>
<td>First 24 hours</td>
<td>&lt;120</td>
</tr>
<tr>
<td>Week 1 (days 1–7)</td>
<td>&lt;120</td>
</tr>
<tr>
<td>Week 2 (days 8–14)</td>
<td>&lt;100</td>
</tr>
<tr>
<td>Week 3 (day 15 onwards)</td>
<td></td>
</tr>
</tbody>
</table>

Several randomised controlled trials have addressed the risks and benefits of liberal or restrictive red cell transfusion policies in very low birth weight infants. A systematic review by the Cochrane Collaboration in 2011 found a modest reduction in exposure to transfusion in the restrictive transfusion groups and no significant difference in mortality, major morbidities or survival without major morbidity. The approximate lower limits used to define a ‘restrictive’ transfusion policy in these trials are shown in Table 10.5. Although many experts now favour a restrictive transfusion policy (Venkatesh et al., 2013), it is important to note the Cochrane Review comment that ‘the safe lower limits for haemoglobin transfusion thresholds remain undefined, and there is still uncertainty regarding the benefits of maintaining a higher level’. Further large clinical trials are advocated, especially to address the issues of longer term (including neurodevelopmental) outcomes and cost-effectiveness. Most local guidelines are closer to the restrictive thresholds used in the trials.

Table 10.5 Approximate capillary Hb transfusion thresholds used for ‘restrictive’ transfusion policies in studies evaluated by the Cochrane Review

<table>
<thead>
<tr>
<th>Postnatal age</th>
<th>Respiratory support</th>
<th>No respiratory support</th>
</tr>
</thead>
<tbody>
<tr>
<td>Week 1</td>
<td>115 g/L</td>
<td>100 g/L</td>
</tr>
<tr>
<td>Week 2</td>
<td>100 g/L</td>
<td>85 g/L</td>
</tr>
<tr>
<td>Week 3</td>
<td>85 g/L</td>
<td>75 g/L</td>
</tr>
</tbody>
</table>
Many neonatal red cell transfusions are given to replace losses from frequent blood sampling. This can be reduced by avoiding non-essential tests, using low-volume sample tubes, validated near patient testing, micro-techniques in the laboratory, and non-invasive monitoring where possible. Donor exposure can also be reduced by allocating single donor units, split into ‘paedipacks’, to babies predicted to need more than one transfusion episode within the expiry date of the donation. This requires close collaboration between the clinical team and blood transfusion laboratory.

The specifications for neonatal/infant small-volume red cells for transfusion are shown in Table 10.6. The typical transfusion volume is 10–20 mL/kg (higher end of dose for severe anaemia or bleeding) administered at 5 mL/kg/h. Top-up transfusions in excess of 20 mL/kg are not recommended because of the risk of transfusion-associated circulatory overload (TACO).

During the first 4 months of life ABO antigens may be poorly expressed on red cells and the corresponding ABO antibodies may not have yet developed (making confirmation by ‘reverse grouping’ unreliable). Maternal IgG ABO antibodies may be detected in neonatal plasma. Wherever possible, samples from both the mother and infant should be tested for ABO and RhD grouping, an antibody screen should be performed on the larger maternal sample, and a direct antiglobulin test (DAT) on the infant’s sample. Because of the significant risk of ‘wrong blood in tube’ errors due to misidentification, the infant’s blood group should be verified on two separate samples (one of which can be a cord blood sample) as recommended for adult patients, providing this does not delay the emergency issue of blood. If there are no atypical maternal antibodies and the infant’s DAT is negative, top-up transfusions can be given without further testing during the first 4 months of life. Details of pretransfusion testing in neonates and infants are given in the 2013 BCSH guidelines for pre-transfusion compatibility procedures in blood transfusion laboratories (https://b-s-h.org.uk/). Irradiated neonatal components are indicated if the infant has previously received IUT or has a proven or suspected T-cell immunodeficiency disorder.

Table 10.6 Red cells for small-volume transfusion of neonates and infants

<table>
<thead>
<tr>
<th>Haematocrit 0.5–0.7</th>
</tr>
</thead>
<tbody>
<tr>
<td>In SAG-M anticoagulant/additive solution (approximately 20 mL residual plasma)</td>
</tr>
<tr>
<td>Up to 35 days from donation</td>
</tr>
<tr>
<td>Group O (or ABO-compatible with baby and mother) and RhD negative (or RhD compatible with the neonate)</td>
</tr>
<tr>
<td>In practice, many hospitals use O RhD negative</td>
</tr>
<tr>
<td>CMV seronegative for neonates</td>
</tr>
</tbody>
</table>

10.2.4: Neonatal platelet transfusions
Severe thrombocytopenia (<50×10^9/L) is a common finding in infants treated on NICUs, especially in sick preterm neonates (NAIT is discussed in section 10.1). There is no clear correlation between the severity of thrombocytopenia and major bleeding, such as intraventricular haemorrhage, suggesting other clinical factors are important. Audits show that, contrary to many published guidelines, the majority of platelet transfusions are given as ‘prophylaxis’ in the absence of bleeding. A randomised trial is comparing transfusion thresholds of 25 and 50×10^9/L. Meanwhile, an example of suggested transfusion thresholds is given in Table 10.7. Single donor apheresis platelets manufactured to neonatal specifications are used. They should be CMV-negative and ABO RhD identical or compatible with the recipient. A typical dose is 10–20 mL/kg.

Table 10.7 Suggested transfusion thresholds for neonatal prophylactic platelet transfusion (excluding NAIT)

<table>
<thead>
<tr>
<th>Platelets &lt;20 or 30×10^9/L</th>
<th>In the absence of bleeding</th>
</tr>
</thead>
<tbody>
<tr>
<td>Platelets &lt;50×10^9/L</td>
<td>Bleeding, current coagulopathy, planned surgery or exchange transfusion</td>
</tr>
<tr>
<td>Platelets &lt;100×10^9/L</td>
<td>Major bleeding, major surgery (e.g. neurosurgery)</td>
</tr>
</tbody>
</table>

10.2.5: Neonatal FFP and cryoprecipitate transfusion

Normal neonates have different, age-related values for common coagulation screening tests compared to older children and adults. This complicates the diagnosis of ‘coagulopathy’. At birth, vitamin-K-dependent clotting factors are 40–50% of adult levels and are lowest in preterm infants. The prothrombin time (PT), thrombin time (TT) and activated partial thromboplastin time (APTT) may be longer, although overall haemostatic function may be normal. In addition, most laboratories rely on published neonatal reference ranges, which may differ from those using local analysers and reagents. Disseminated intravascular coagulation (DIC) is common in sick neonates and haemorrhagic disease of the newborn due to vitamin K deficiency may cause major bleeding in babies who have not received appropriate vitamin K prophylaxis at birth.

Sick neonates in intensive care are commonly transfused with fresh frozen plasma (FFP), which carries a significant risk of serious acute transfusion reactions (see Chapter 5). The 2009 National Comparative Audit of the use of FFP (http://hospital.blood.co.uk/safe_use/clinical_audit/national_comparative/index.asp) confirmed that, contrary to published guidelines, 42% of FFP transfusions to infants were given ‘prophylactically’ in the absence of bleeding, on the basis of abnormal clotting tests. BCSH guidelines recommend that FFP should be used for:

- Vitamin K deficiency with bleeding
- DIC with bleeding
- Congenital coagulation factor deficiencies where no factor concentrate is available (Factor V deficiency)

The dose of FFP is usually 12–15 mL/kg. The degree of correction is unpredictable and clotting tests should be repeated after administration.
FFP should not be used as routine prophylaxis against peri/intraventricular haemorrhage in preterm neonates (evidence from a randomised controlled trial), as a volume replacement solution, or just to correct abnormalities of the clotting screen.

Cryoprecipitate is used as a more concentrated source of fibrinogen than FFP and is primarily indicated when the fibrinogen level is <0.8–1.0 g/L in the presence of bleeding from acquired or congenital hypofibrinogenaeemia. The usual dose is 5–10 mL/kg.

FFP for neonates (and all patients born on or after 1 January 1996) is imported from countries with a low risk of vCJD and is pathogen-inactivated. Methylene blue inactivation is used by the UK Blood Services and commercial pooled solvent detergent treated FFP is also available. It should be ABO identical with the recipient or group AB (group O FFP should only be given to neonates of group O).

10.2.6: Neonatal granulocyte transfusion

There is no conclusive evidence from randomised controlled trials to support the use of granulocyte transfusions in neutropenic, septic neonates. Current guidelines do not recommend their routine use in the absence of further prospective studies.

10.2.7: T-antigen activation

Occasional severe haemolytic reactions have been reported in neonates or infants receiving blood or FFP containing anti-T antibodies. The T-antigen may be exposed on the surface of neonatal red cells by neuraminidase-producing bacteria such as Clostridium spp., often in association with necrotising enterocolitis (NEC). As T-antigen activation is often found in healthy neonates and severe haemolysis is very rare, the need to screen neonates with NEC and make special components available remains controversial and is not performed in many countries. Red cells in SAG-M, containing only small amounts of plasma, are regarded as safe. All non-essential transfusions of FFP and platelets should be avoided. If low-titre anti-T components are regarded as essential, platelets in platelet suspension medium can be used and methylene blue treated FFP with a low titre of anti-T may be available from the Blood Services.