10.1: Fetal transfusion

The most common indications for intrauterine transfusion (IUT) are red cells for prevention and treatment of fetal anaemia due to haemolytic disease of the fetus and newborn (HDFN) or parvovirus infection and platelets for neonatal alloimmune thrombocytopenia (NAIT). This is a highly specialised area of medical practice requiring close collaboration between experts in fetal medicine, haematology and blood transfusion, and rapid access to blood counting. Even in the most expert hands IUT carries a risk of fetal death of 1–3% per procedure and fetomaternal haemorrhage may cause further sensitisation and worsening of HDFN.

10.1.1: Intrauterine transfusion of red cells for HDFN

Maternal aspects of the management of HDFN are covered in Chapter 9. The objective of red cell IUT is to prevent or treat life-threatening fetal anaemia (hydrops fetalis) and allow the pregnancy to continue to a stage where a viable baby can be delivered (ideally at least 36 weeks gestation). High-risk pregnancies are monitored by weekly fetal Doppler ultrasound scans to measure middle cerebral artery peak systolic velocity, an indication of the severity of fetal anaemia, and regular ultrasound monitoring of fetal growth. Fetal blood sampling is indicated if severe anaemia before 24 weeks gestation is suspected, if there has been a previous intrauterine death, or if there is a rapid increase in maternal red cell alloantibody levels.

Guidelines for IUT vary between specialist units but published indications include a haematocrit of <0.25 between 18 and 26 weeks of gestation and <0.3 after 26 weeks. The target haematocrit after IUT is usually around 0.45. To balance the competing risks of fetal anaemia and the hazards of invasive IUT procedures, the transfusion programme is started as late as possible and the frequency of transfusion is reduced by giving the maximum safe volume of a special red cell component with a high haematocrit (Table 10.1). Transfusion volume is calculated by the fetal medicine specialist using a formula based on the haematocrits of the donor blood and fetus, the estimated feto-placental blood volume and the target haematocrit. The component is warmed to 37°C immediately before transfusion. Whenever possible, red cells for IUT are requested well in advance of the planned transfusion, in close communication with the Blood Services. In extreme emergencies, where delay in obtaining special IUT blood would be life-threatening, blood from a neonatal exchange transfusion unit or paedipack should be used (irradiated if time allows) but not maternal blood. The SHOT Annual Report 2012 included a neonatal death from transfusion-associated graft-versus-host disease (TA-GvHD) when non-irradiated non-leucodepleted maternal red cells were used for an urgent IUT (http://www.shotuk.org/shot-reports/report-summary-and-supplement-2012/). Babies who have received IUT should be transfused with irradiated cellular blood components until 6 months of post-gestational age.

Table 10.1 Red cell component for IUT
Plasma reduced (haematocrit 0.7–0.85)

In citrate phosphate dextrose (CPD) anticoagulant (theoretical risk of toxicity from additive solutions)

Leucocyte-depleted

Less than 5 days old (to avoid hyperkalaemia)

Cytomegalovirus (CMV) antibody negative

Sickle screen negative

Irradiated to prevent TA-GvHD (shelf life 24 hours)

Usually group O with low-titre haemolysins (or ABO identical with the fetus)

RhD and Kell negative and red cell antigen negative for maternal alloantibodies

Indirect antiglobulin test (IAT) crossmatch compatible with the mother’s plasma

10.1.2: Intrauterine transfusion of platelets and management of NAIT

The IUT of platelets is used in the treatment of severe fetal thrombocytopenia due to platelet alloimmunisation (neonatal alloimmune thrombocytopenia – NAIT). NAIT is the platelet equivalent of HDFN. Maternal alloantibodies to antigens on fetal platelets cause fetal and/or neonatal thrombocytopenia with a high (10%) risk of intracerebral haemorrhage. Nearly all cases are caused by antibodies to HPA-1a (80–90% of cases), HPA-5b or HPA-3a. The mother is negative for the implicated platelet antigen and NAIT is diagnosed by demonstrating the platelet alloantibody in maternal serum. The diagnosis is most often made when an otherwise healthy neonate presents with purpura and an isolated severe thrombocytopenia. Subsequent ‘at risk’ pregnancies should be managed in a fetal medicine centre as prenatal management is rapidly evolving (Peterson et al., 2013 [http://www.ncbi.nlm.nih.gov/pubmed/23384054]). Management is influenced by any history of previous fetal losses and their timing. Fetal blood sampling and platelet transfusion carry a significant risk of life-threatening haemorrhage (suitable platelets should always be immediately available when fetal blood sampling is performed). There is an increasing trend to use a non-invasive approach with maternal intravenous immunoglobulin and steroids and to avoid fetal transfusion where possible. Hyperconcentrated platelets for IUT are specially prepared by the Blood Services (see Table 10.2) and transfusion should be
planned in advance. The transfusion volume is determined from the fetal and platelet concentrate platelet count and estimated feto-placental volume. Platelets are transfused more slowly than IUT red cells because of a risk of fetal stroke.

**Table 10.2 Platelets for intrauterine transfusion**

<table>
<thead>
<tr>
<th>HPA-compatible with maternal alloantibody</th>
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<tbody>
<tr>
<td>Hyperconcentrated to at least $2000 \times 10^9$/L</td>
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<tr>
<td>Irradiated</td>
</tr>
<tr>
<td>CMV negative</td>
</tr>
</tbody>
</table>

Neonates with suspected or proven NAIT who are severely thrombocytopenic ($<30 \times 10^9$/L) should be transfused with HPA-compatible platelets. HPA1a/5b negative platelet units are usually available ‘off the shelf’ from the Blood Services. Neonates with intracranial haemorrhage (ICH) or a previous affected sibling with ICH are transfused at a threshold of $50 \times 10^9$/L. If HPA-compatible platelets are not available in a clinically relevant time frame, random donor neonatal platelets should be transfused and will produce a temporary platelet increment in most cases. Spontaneous recovery of the platelet count usually occurs within 1 to 6 weeks as maternally derived antibody levels fall. For babies with persistent severe thrombocytopenia, intravenous immunoglobulin improves the count in around 75% of cases, but response is often delayed for 24–48 hours.