CHAPTER 7

PAEDIATRICS AND NEONATOLOGY

Key points

1. Evidence suggests that restrictive rather than liberal haemoglobin thresholds for red blood cell (RBC) transfusions are efficacious and safe in both neonates and children.

2. Outside the setting of massive or exchange transfusion, the indications for plasma are very limited.

3. Restrictive use of platelet transfusions is also recommended.

7.1 Introduction

This chapter addresses the indications and practical considerations of transfusion of red cells, platelets, plasma and cryoprecipitate in neonates, older infants, children and adolescents. The general aspects of safe preparation and administration of blood are covered elsewhere. This information will therefore not be repeated here, except to highlight areas where special attention and/or special procedures are required when administering transfusions to paediatric patients. Neither will the full range of treatments required for the disorders discussed be covered; it is assumed that clinicians will always strive to provide specific treatment for the underlying disorder leading to the need for transfusion.

Learning outcomes

After reading this chapter, the reader should be able to:

1. List the causes of neonatal anaemia
2. Know when to transfuse and manage hyperbilirubinaemia by exchange transfusions
3. Understand principles of red cell transfusion in patients with sickle cell disease and thalassaemia
4. Manage red blood cell transfusions in sickle-cell disease and thalassaemia patients
5. Understand the practical aspects of red blood cell (or whole blood) transfusion
6. Know when to transfuse platelets, and understand the practical aspects
7. Know when plasma transfusions are indicated, and understand the practical aspects

7.2 Anaemia and red blood cell/whole blood transfusions

Since whole blood (WB) is the only RBC-containing product available in many low-income countries (LIC) and low/middle-income countries (LMIC), we will use the generic term RBC transfusion to refer to a transfusion of an RBC concentrate or a WB unit. For most patients (other than those with sickle-cell disease or thalassaemia), the only appropriate indication for an RBC transfusion is to correct an inadequate (or to avoid an imminent inadequate) oxygen-carrying capacity caused by an inadequate RBC mass that cannot be corrected, in a timely manner, by safer treatments. In this case, the goal of transfusion is to relieve the indication for transfusion and not necessarily to achieve a normal haemoglobin concentration.

Neonatal period (up to 4 months of age)

The mean haemoglobin concentrations at birth of babies born at term, 32 weeks gestation and 28 weeks gestation are 16.5 g/dl, 15 g/dl and 13.5 g/dl respectively. In a term neonate, anaemia at birth is defined as a haemoglobin concentration below 13.5 g/dl; the lower limits of normal for preterm infants are somewhat lower and vary according to gestational age at birth.

Anaemia at birth

Anaemia present at birth may be the result of haemolysis, blood loss or bone marrow failure.

Haemolysis is most often due to haemolytic disease of the newborn (HDN), a chronic, in-utero immune process due to fetal–maternal blood group incompatibility. RhD incompatibility is the most frequent cause of clinically significant HDN whereas other blood group incompatibilities (for example, Kell) are only occasionally the cause. Although ABO fetal–maternal blood group incompatibility is common, this does not usually result in anaemia at birth. Rarely, congenital haemolytic or aregenerative anaemias may cause anaemia at birth.

Blood loss can be antenatal or intrapartum. Antenatal blood loss is most often chronic and is due to transplacental fetal–maternal transfusion or twin–twin transfusion. Intrapartum blood loss is usually acute and may be external (for example, placenta previa, ruptured umbilicus or vasa previa), internal (for example, subperiosteal, subgaleal, intracranial or adrenal haemorrhage, traumatic fracture, extensive bruising or extravasation), or transplacental when umbilical cord obstruction prevents adequate venous return, resulting in fetal–placental transfusion. The haemoglobin level immediately after acute blood loss at delivery is normal but falls within a few hours after fluid equilibration restores blood volume.

Bone marrow failure is uncommon. It may be caused by antenatal infection (for example, rubella or parvovirus B19) or rare genetic diseases (for example, Diamond-Blackfan anaemia).

Postnatal anaemia

All infants show a decline in haemoglobin concentration, known as physiologic anaemia, in the first 8–10 weeks of life when erythropoietin production is transiently low. Haemoglobin concentration in term infants may fall to 9.5-10 g/dl; in preterm infants, these levels may fall to as low as 6–8 g/dl.

Delayed umbilical cord clamping should be performed in both term and preterm neonates who do not require immediate resuscitation. Delayed umbilical cord clamping increases the Hb level at delivery thereby increasing the infant's iron reserves which in turn decreases the nadir of physiologic anaemia and delays or prevents iron deficiency later in infancy. Delays of 1 and 3 minutes deliver about 20 ml/kg and 30 ml/kg of blood, respectively, to the newborn. Umbilical cord milking should be considered if the neonate's gestational age is at least 28 weeks and the clinical condition precludes delayed cord clamping (e.g. need for immediate resuscitation).

In addition to physiologic anaemia, anaemia after birth reflects the level of haemoglobin at birth, the amount of blood drawn for laboratory tests (iatrogenic anaemia), and haemolysis or postpartum haemorrhage, if present. Prevention of iatrogenic anaemia includes limiting blood sampling and using small blood collection containers and micromethods for laboratory studies.

The routine use of erythropoietin to decrease transfusions in preterm infants is not currently recommended.

Indications for RBC transfusions in neonates

Recommended guidelines for RBC transfusions to neonates vary, although, recent guidelines generally suggest quite restrictive haemoglobin thresholds. Suggested guidelines are shown in Table 7.1 (*1*, *2*).

Table 7.1. Suggested indications for neonatal transfusions[a]

Acute blood loss	≥ 10% TBV and signs of decreased oxygen delivery
	≥ 20% TBV
Chronic anaemia[c]	Moderate–significant mechanical ventilation and Hb ≤ 10 g/dl[b]
	Minimal mechanical ventilation and Hb ≤ 8 g/dl[b]
	Supplemental oxygen without mechanical ventilation and Hb ≤ 7 g/dl
	No supplemental oxygen, no signs of anaemia and Hb ≤ 7 g/dl and reticulocytes ≤ 100×10^9/L

TBV – total blood volume; term neonates = 85 ml/kg; preterm neonates = 100 ml/kg.

[a] Table does not apply to neonates with ongoing haemolysis.

[b] Adapted from reference (*1*); some guidelines (*2*) suggest slightly higher thresholds particularly in preterm neonates born < 32 weeks gestation.

Hyperbilirubinaemia and exchange transfusion

Worldwide, severe hyperbilirubinaemia, i.e. total serum bilirubin > 428 µmol/L (25 mg/dl) places hundreds of thousands of newborns at high risk of death or incapacitating long-term disability (kernicterus) due to acute bilirubin encephalopathy (ABE). The underlying cause of severe hyperbilirubinaemia is most often haemolysis due either to HDN or G6PD deficiency. Non-haemolytic risk factors for severe hyperbilirubinaemia include prematurity, infection, dehydration and caloric deprivation, birth trauma, enclosed blood collections, and family or sibling history of severe neonatal jaundice. Often there are multiple causes.

Newborns with haemolytic disease are at risk of ABE and kernicterus at lower levels (≥ 342 µmol/L or 20 mg/dl) than healthy term infants who may tolerate serum bilirubin levels up to 428 µmol/L (25 mg/dl). Critically high total bilirubin levels for preterm newborns have not been firmly established. The risk of kernicterus is high for all infants with bilirubin levels ≥ 513 µmol/L (30 mg/dl) and is increased by prematurity, haemolysis, sepsis, acidosis, hypoxaemia and hypoalbuminaemia, or exposure to drugs that displace indirect bilirubin from albumin. The threshold for initiating phototherapy depends upon postnatal age, the rate of total bilirubin rise and individual risk factors, and is generally 103–120 µmol/L (6–7 mg/dl) below the critical threshold for exchange transfusion.

The purpose of neonatal exchange transfusion (ET) is to prevent or treat ABE by rapidly removing unconjugated bilirubin from the circulation and tissues. If immune haemolysis is present, ET will also remove sensitized RBCs and plasma antibodies. ET is urgent whenever there are clinical signs of ABE or when total serum bilirubin reaches critical levels above which the risk of ABE is known to be high.

Thresholds for initiating phototherapy and ET are detailed in the *American Academy of Pediatrics Clinical practice guideline* (*3*). Although unconjugated indirect bilirubin is the neurotoxic agent, it is important to note that these guidelines are based on total serum bilirubin (indirect (unconjugated) + direct (unconjugated) bilirubin). The thresholds reflect optimal conditions in high-income countries (HIC); in LIC and LMIC with limited resources, treatment thresholds may need to be lowered based on the anticipated rate of bilirubin rise, personnel and equipment available, and expected delays in setting up equipment or obtaining blood.

An isovolumetric double-volume ET can be performed using the push-pull method via the umbilical vein (see Box 7.1) or simultaneously using the umbilical artery for blood removal and the umbilical venous line for blood infusion (*4*). The umbilical venous catheter is inserted only far enough to get good blood return and should be removed after the ET unless a second exchange is anticipated soon afterwards. If so, fluid must be continuously infused through a well-secured umbilical catheter to prevent blood stasis and clotting.

Box 7.1. Neonatal exchange transfusion (ET) procedure using a single blood vessel[a]

1. Give nothing by mouth during and for at least 4 hours after ET. Empty the stomach if the infant was fed within 4 hours of the procedure.
2. Closely monitor vital signs including heart and respiratory rates, temperature and pulse oximetry before, during and after ET. Have resuscitation equipment ready.
3. Using sterile technique, insert umbilical venous line just far enough to get good blood return (in a term infant about 5 cm from the level of the abdominal wall). Secure the line with tape or surgical suture.
4. Prewarm blood only if an approved, quality-controlled warmer is available. Do not use a water bath.
5. Exchange 10–15 ml increments in full-term infants and smaller volumes in preterm infants. Each cycle should be performed slowly, over about 4 minutes.
6. Agitate the blood unit intermittently to prevent red cell sedimentation.
7. If there is electrocardiogram (ECG) evidence of hypocalcaemia (prolonged Q-T intervals) or, if no ECG is available, clear clinical signs (jitteriness or tremor, especially with stimulation) slowly give 1–2 ml of 10% calcium gluconate solution intravenously. Flush tubing with normal saline before and after calcium infusion. Monitor for bradycardia during calcium infusion.
8. To complete a two-volume ET, transfuse 160–180 ml/kg for a full-term infant and 200 ml/kg for a preterm infant.
9. Send the last aliquot of blood withdrawn to the laboratory for determination of haemoglobin or haematocrit, blood glucose, total bilirubin, potassium and calcium, and group and crossmatch.
10. Post-exchange, continuously infuse a glucose-containing intravenous fluid to prevent hypoglycaemia.

[a] See the text for choice of blood product to use and reference (*4*) for further details about exchange transfusion.

At least two people are needed to perform an ET: one to perform the exchange and the other to record each infusion/withdrawal of blood, track the volume of blood exchanged and continuously monitor vital signs. ET should be performed by trained personnel in a location where monitoring and resuscitation equipment is available. Intensive phototherapy should be started as soon as possible while preparations for ET are underway, continued during the exchange, if possible, and continued after completion of the exchange.

A double-volume ET replaces approximately 85% of the infant's blood volume and lowers the total bilirubin level by approximately one half of the pre-exchange level. Following ET, the total bilirubin level rises to approximately two thirds of the pre-exchange level. Additional ET may be necessary.

For ABO incompatibility the ideal blood product for ET is reconstituted WB prepared by removing the supernatant fluid from a group O RBC concentrate and adding an equal volume of group AB plasma or plasma of the same ABO group as the patient. Where this cannot be easily or properly prepared, group O WB may be used, preferably a unit with low-titre anti-A/B. For other indications, WB or reconstituted WB of the patient's ABO group should be used. In the case of blood group incompatibility (other than ABO), the WB or RBC concentrate should be antigen-negative for the implicated antibody.

Potential complications of ET are summarized in Box 7.2.

Box 7.2. Potential complications of exchange transfusion[a]

Cardiovascular

- Portal vein thrombosis, other thromboemboli
- Blood vessel injury
- Dysrhythmias
- Volume imbalance
- Cardiorespiratory arrest
- Electrolyte and metabolic imbalances
- Hyperkalaemia
- Hypernatraemia
- Hypocalcaemia
- Hypoglycaemia
- Acidosis

Haematological

- Anaemia/polycythemia
- Thrombocytopenia

Infectious

- Sepsis
- Transfusion-transmitted infections

Miscellaneous

- Air emboli
- Necrotizing enterocolitis

[a] See also reference (*4*).

Older infants and children/adolescents

The WHO definitions of anaemia in infants and children are shown in Table 7.2 (*5*). WHO does not use separate definitions for normal haemoglobin concentrations according to ethnicity although it is now accepted that the lower limits of normal for haemoglobin concentrations in black persons are approximately 5–10% lower in childhood and 10–15% lower in adulthood than those of Caucasians. These differences are important when considering the presence or absence of anaemia but are not significant when considering the need for transfusion.

Table 7.2. WHO haemoglobin levels to diagnose anaemia at sea level (g/L)

Population	Non-anaemia (g/L)	Anaemia		
		Mild (g/L)	Moderate (g/L)	Severe (g/L)
Children 6–59 months of age	≥ 110	100–109	70–99	< 70
Children 5–11 years of age	≥ 115	110–114	80–109	< 80
Children 12–14 years of age	≥ 120	110–119	80–109	< 80
Non-pregnant women (15 years of age and above)	≥ 120	110–119	80–109	< 80
Pregnant women	≥ 110	100–109	70–99	< 70
Men (15 years of age and above)	≥ 130	110–129	80–109	< 80

Adapted from reference (*5*).

A systematic analysis of the global prevalence and burden of anaemia (as determined by years lived with disability) from 1990 to 2010 published in 2014 (*6*), using definitions of anaemia and its severity similar to those published by WHO, reported the overall global prevalence of anaemia in 2010 to be 32.9% (mild 18.4%, moderate 13.5%, severe 1.1%). The prevalence and burden of anaemia are inversely related to country income levels, with the highest burden in the LIC of sub-Saharan Africa (SSA). In all regions of the world, the burden is highest in women and children under 5 years of age, and those under 5 years had the least favourable changes between 1990 and 2010. Globally, iron-deficiency anaemia (IDA) is the most common etiology, while other causes of anaemia vary widely by geography, age and sex. For children in LIC and LMIC, the commonest causes of anaemia, after IDA, are malaria, hookworm infection (categorized separately from IDA) and haemoglobinopathies.

Indications for RBC/WB transfusions in general paediatric patients

Evaluation of an anaemic patient

Ideally decisions on RBC transfusion should be based on objective measurements of inadequate systemic and/or regional oxygen delivery. Unfortunately, such measurements are not readily available, even in high-resource settings. Thus, the haemoglobin concentration is the single most important laboratory measurement in determining the need for transfusion. A haemoglobin level should be obtained prior to any RBC transfusion. Except in a patient with extreme pallor, even experienced clinicians are not always able to accurately estimate haemoglobin concentration from a physical examination. Studies in low-resource settings have shown that not obtaining, or possibly not following up on ordered haemoglobin testing, can lead to inappropriate administration of RBC transfusions (*7*). While inappropriate use of RBC transfusions is a concern, equally or even more concerning, are the number of severely anaemic children in LIC and LMIC who do not receive RBC transfusion in a timely manner. Several studies from SSA have shown that critically ill children who present to acute care units with haemoglobin concentrations less than 5 g/dl are at risk of increased mortality if not transfused within 8 hours of presentation (*7, 8*). The reasons for not administering transfusions to these children are multifactorial: the main reason, unfortunately, is the lack of available blood. However, there are also reports that suggest that the lack of transfusion may, in some cases, be due to the failure to recognize the presence of severe anaemia.

Although haemoglobin concentration is a critical factor in deciding whether to administer an RBC transfusion, it is rarely the only factor to consider. Otherwise healthy adults and children have an impressive capacity to increase oxygen delivery to tissues as haemoglobin levels decrease, particularly if the decrease occurs slowly. Children with chronic anaemia, such as IDA due to inadequate iron intake or hookworm infection, may tolerate haemoglobin concentrations below 4–5 g/dl without need for transfusion if iron supplementation plus other treatments, as appropriate, can be

assured. By contrast, in situations such as acute haemorrhage without volume replacement, a seemingly "moderate" degree of anaemia may require urgent transfusion.

In determining the need for RBC transfusion in a child with severe (and sometimes moderate) anaemia, the following clinical factors should be considered:

- general state of health: well, mildly–moderately ill or critically ill
- nutritional status
- haemodynamic stability
- likely timeframe for the development of the anaemia: acute, subacute or chronic
- likely etiology: is correction possible with treatment other than blood transfusion?
- comorbidities that could affect adaptation/tolerance to anaemia and/or response to other treatments
- symptoms and signs to suggest that the anaemia is compensated or uncompensated.

Other questions to ask are:

- If the child is bleeding or has a history of bleeding, is the bleeding controlled or ongoing? What is the extent of the blood loss?
- Is there a need for an invasive procedure under general anaesthesia and/or is the child at risk of significant blood loss?

Up until the late 1990s, guidelines for the administration of RBC transfusions (in all age groups) were based on expert opinion as almost no evidence-based data were available. In HIC, these guidelines generally recommended transfusion at haemoglobin thresholds that studies performed over the past two decades have shown to be inappropriately liberal (i.e. they recommended using haemoglobin thresholds for transfusion that are unnecessarily high) thus exposing patients to transfusion risks without any observable benefit. Although most of these studies were performed in adult patients, it is reasonable to assume that paediatric patients, beyond the neonatal period, should be able to tolerate haemoglobin levels at least as low as those found to be safe in adult patients and, indeed, the few studies carried out in children have confirmed this.

Unlike the liberal guidelines for RBC transfusions that were used until relatively recently in HIC, the WHO guidelines for transfusion in acutely ill children have been much more restrictive – haemoglobin < 4 g/dl or haemoglobin 4–6 g/dl and clinical signs of complicated or decompensated anaemia – although also not evidence-based (*9, 10*). This is probably because the WHO guidelines were targeted more towards clinicians in LIC and LMIC where the blood supply is much more limited and where the risks of transfusion (particularly from transfusion-transmitted viruses and possibly also from errors) are higher than in HIC. With the development of evidence-based guidelines in HIC that recommend more restrictive use of RBC transfusions, the two approaches are converging.

A group of investigators from three SSA countries (Malawi, South Africa and Zimbabwe) have proposed a paediatric transfusion protocol for use in under-resourced environments. This protocol is based on the WHO guidelines but offers

more specific guidance with respect to the definition of complicated anaemia and adds a third category for children with severe malnutrition (for whom transfusions should be used more sparingly) (*7*). The definitions of complicated anaemia are shown in Table 7.3 and a comparison of the previous WHO guidelines with the 2010 paediatric blood transfusion protocol is summarized in Table 7.4.

Table 7.3. Comparison of definitions of complicated or uncompensated severe anaemia in children[a]

WHO 2001[b]	Clinical features of hypoxia i.e. acidosis or impaired consciousness
	Hyperparasitaemia (malaria) > 20%
WHO 2013[c]	Clinically detectable dehydration
	Shock
	Impaired consciousness
	Heart failure
	Deep, laboured breathing
	Hyperparasitaemia (malaria) > 10%
Suggested modification of WHO definitions[d]	Any respiratory distress
	Cool peripheries + capillary filling time ≥ 3 seconds
	Impaired consciousness (Ballantyne score ≤ 4)
	Prostration (≥ 1 year, alert but unable to sit; < 1 year, unable to drink or breastfeed)

[a] In each definition, only one criterion is required.

[b] Adapted from reference (*9*).

[c] Adapted from reference (*10*).

[d] Adapted from reference (*7*).

Table 7.4. Comparison of suggested modifications for a paediatric blood transfusion protocol with the WHO transfusion guidelines[a]

	Protocol comparison	
	WHO transfusion guidelines (WHO, 2001)	**Modified protocol**
No severe malnutrition		
Transfuse all children if:	Hb < 4 g/dL	Hb < 4 g/dL
Transfuse "complicated anaemia" patient also, if:	Hb = 4–6 g/dl	Hb = 4–6 g/dl
Volume of transfusion	20 ml/kg whole blood (or equivalent RBC volume)	20 ml/kg whole blood (or equivalent RBC volume)
	Give first 5 ml/kg red cells more rapidly to relieve the acute signs of tissue hypoxia	
Duration of transfusion	Complete transfusion in 4 hours	If complicated anaemia: first half in 1 hour and second half over 2 hours
		If uncomplicated anaemia: transfuse over 4 hours

	Protocol comparison	
	WHO transfusion guidelines (WHO, 2001)	**Modified protocol**
Severe malnutrition		
Transfuse all children if:	Not mentioned as a separate category	Hb < 4 g/dl
Transfuse "complicated anaemia" patient also, if:		Hb = 4–6 g/dl not for routine transfusion
Volume of transfusion		Decision made on individual clinical basis: 10 ml/kg whole blood (or equivalent RBC volume)
Duration of transfusion		Transfuse over 4 hours

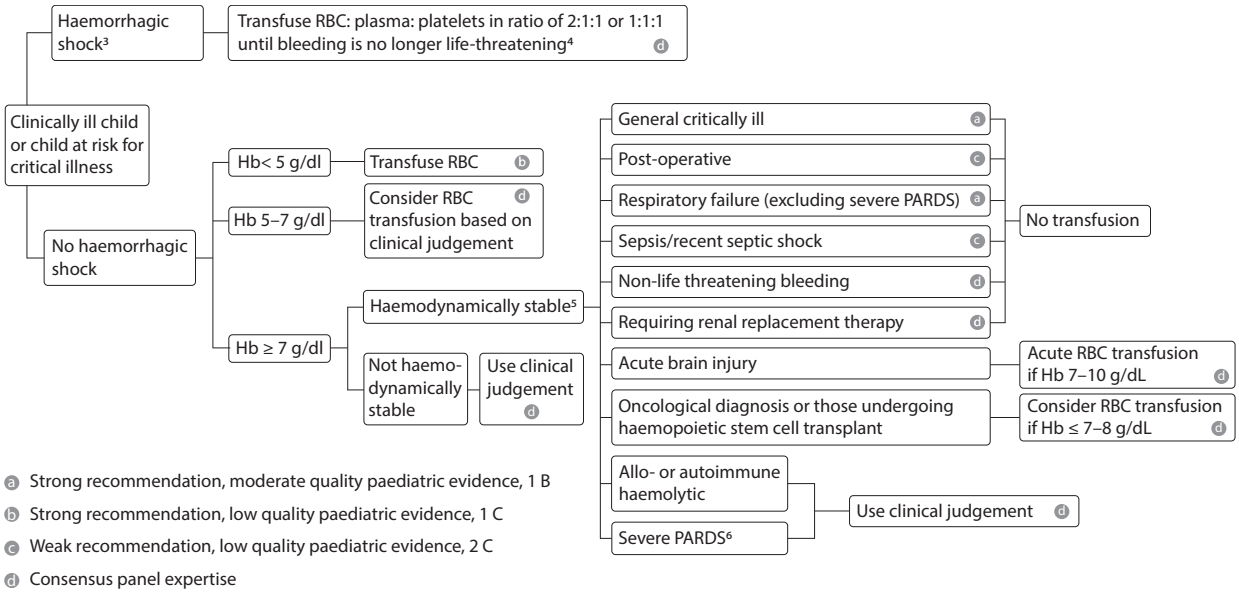
Hb, haemoglobin; RBC, red blood cell.

[a] Modified from reference (*7*). For definitions of complicated anaemia see Table 7.3. Severe malnutrition is defined as pitting oedema of both feet or severe visible wasting.

Note: These recommendations apply to acute or critically ill children; they may not necessarily apply to children with chronic anaemia or children with sickle-cell disease or thalassaemia (refer to text).

In 2018, a group of paediatric critical care physicians from Canada, Europe, South Africa and the United States published a series of guidelines for RBC transfusions in critically ill paediatric patients (*11*). Where possible these guidelines were evidence-based; where that was not possible, expert-based consensus statements were developed. The guidelines produced by this group are summarized in Fig. 7.1.

Figure 7.1. Transfusion and Anaemia Expertise Initiative (TAXI) recommendations for transfusion in critically ill children[1,2]



Hb: haemoglobin | PARDS: paediatric acute respiratory distress syndrome | RBC: red blood cell.

[1] Adapted from reference (*11*).
[2] Does not include children with sickle-cell anaemia (SCA), thalassaemia or cardiac disease; for children with SCA, see text and Tables 7.5 and 7.6; for children with thalassaemia see text and reference (*14*); for children with cardiac disease see reference (*11*).
[3] Severe bleeding in patients at risk of exsanguination.
[4] If available, may use whole blood instead.
[5] Haemodynamically stable = mean arterial pressure not more than 2 SD < normal for age and cardiovascular support not increased for at least 2 hours.

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RBC transfusions in patients with sickle-cell disease

Several studies and consensus documents have addressed the indications for RBC transfusion in patients with homozygous haemoglobin S (HbS) disease or HbS/β^0 thalassaemia (*12, 13*). For the sake of brevity, we refer to these two conditions together as sickle-cell anaemia (SCA). Indications for transfusion in other sickle-cell disease (SCD) conditions have not been studied and decisions on transfusion in patients with those conditions will not be specifically addressed. However, in general, for these conditions, the more the patient's phenotype resembles that of a SCA patient or the more severe the complication or potential complication, the more likely it is that the patient will benefit from an approach similar to that used for SCA patients.

RBC transfusions in patients with SCA may be given for acute or chronic complications and in either case may be simple transfusion(s) or ET(s), either manual or automated exchange.

The three reasons to administer an RBC transfusion in a patient with SCA are:

1. to increase tissue oxygenation;

2. to decrease viscosity by diluting the relative amount of HbS-containing RBCs;

3. to suppress endogenous erythropoiesis.

In acute situations, the main reason(s) for RBC transfusion is/are the first or the first and second. The main goal of chronic transfusion programmes is the third. For all situations, the goal with respect to post-transfusion haemoglobin should be to attain a total haemoglobin concentration of about 10–11 g/dl. It is important not to raise the haemoglobin above this level as this may lead to complications of hyperviscosity (including stroke). If the transfusion goal is to suppress endogenous erythropoiesis, then an additional goal is to decrease the HbS concentration below 30%.

Transfusions are not indicated for the treatment of uncomplicated painful crises and are also unlikely to be helpful in the acute treatment of priapism or isolated kidney injury, in the preoperative preparation for very low-risk surgical interventions not requiring general anaesthesia, or in patients with asymptomatic chronic anaemia due to chronic hypersplenism.

The indications and recommended transfusion type in acute situations are summarized in Table 7.5. Transfusion modalities (for either acute or chronic transfusions) are compared in Table 7.6 and the procedure for performing a manual ET is summarized in Box 7.3. In acute situations where a simple transfusion is recommended but the patient has a haemoglobin level ≥ 9 g/dl, a partial ET (often manual) should be performed. Alternatively, if an ET is recommended but cannot be carried out (either manually or by automated exchange) then a simple transfusion should be given provided that this can be done without raising the total haemoglobin concentration above 10-11 g/dl. If that is not possible, then every attempt should be made to transfer the patient to a centre where an ET can be performed. In situations where an ET is recommended but the patient's haemoglobin is very low, a simple transfusion should be given initially, and the patient re-evaluated for consideration of a subsequent ET.

Table 7.5. Indications for episodic (acute) red blood cell (RBC) transfusions in sickle-cell anaemia (SCA) patients (*12,13*)

Indication	Transfusion type
Aplastic crisis	Simple transfusion
Acute symptomatic blood loss or severe anaemia	Simple transfusion
Acute splenic sequestration	Simple transfusion[a]
Acute hepatic sequestration	Simple or exchange transfusion
Complicated painful crisis (i.e. drop of Hb ≥ 2 g/dl from baseline or Hb < 5 g/dl)	Simple transfusion
Mild to moderate ACS not responding to antimicrobials and other supportive treatment	Simple transfusion[b]
Severe ACS, i.e. an oxygen saturation < 90% despite supplemental oxygen	Exchange transfusion[c]
Prior to medium-risk surgery	Simple transfusion[b]
Prior to high-risk surgery	Exchange transfusion[c]
Multisystem organ failure	Simple or exchange transfusion
Acute intrahepatic cholestasis	Simple or exchange transfusion
Acute ischaemic stroke	Exchange transfusion[c]
Acute mesenteric "girdle" syndrome (acute sickling in the mesenteric vascular bed, liver and lungs)	Exchange transfusion[c]

Hb: haemoglobin | ACS: acute chest syndrome

[a] The RBC transfusion volume should be < 50% of the usual transfusion volume as RBCs sequestered in the spleen will return to the circulation.

[b] If the Hb ≥ 9g/dl, then a partial exchange transfusion should be performed.

[c] If an exchange transfusion cannot be performed then a simple transfusion should be given providing that this can be done without raising the total Hb concentration above 10–11g/dl. if the patient's Hb is very low then a simple transfusion should be given initially, and the patient re-evaluated for consideration of a subsequent exchange transfusion.

Table 7.6. Comparison of transfusion modalities in sickle-cell anaemia patients

	Simple transfusions	Manual exchange transfusions	Automated exchange transfusions
Convenience	Available in any transfusing facility	No special equipment required	Can only be performed in a major centre with specialized equipment and staff
	No special equipment and only basic training required	Additional training required	
Venous access	Ordinary single venous access	Requires two venous lines	Requires central venous access or two large-bore venous lines
Number of units required	1–2 units – enough to raise Hb level to 10 g/dl	More than for simple transfusion but less than for automated exchange	More than for manual exchange (8–12 units per exchange in an adult)
Iron accumulation	Inevitable over time with multiple transfusions	Occurs, but with less net gain than with simple transfusion	Does not usually occur

Box 7.3. Procedure for performing a manual exchange transfusion

Note: If haemoglobin (Hb) concentration is < 80 g/L, perform a simple transfusion before proceeding to a manual exchange transfusion.

Prior to beginning the procedure

1. Weigh the patient.
2. Ensure that the patient has two well-functioning large-bore venous accesses.
3. Calculate the patient's red cell mass that will be removed:
   - total blood volume removed × patient's haematocrit (expressed as a fraction).
4. Calculate the amount of blood to transfuse (*Note*: It is important to know the type of red blood cell (RBC) product available – refer to Table 7.7.)
   - red cell mass removed/haematocrit (expressed as a fraction) of blood unit.

Example of calculation for volume to transfuse: 30 kg child with haematocrit of 0.25, removing a total of 20 ml/kg, using whole blood with haematocrit of 0.40: (30 kg × 20 ml × 0.25)/0.40 = 375 ml. This will give a post-exchange haemoglobin (Hb) level that is approximately the same as the pre-exchange Hb. If a slightly higher post-exchange Hb is desired, then a slightly larger transfusion volume can be given.

First step: *Phlebotomy with simultaneous isovolaemic saline replacement*

- Phlebotomy: over 15–20 minutes, from one of the venous lines remove 10 ml/kg (up to a maximum of 500 ml total).
- Volume replacement: using the other IV access, simultaneously infuse the same volume of saline as the volume of blood being removed.

Second step: *RBC transfusion while performing a second phlebotomy*

- Phlebotomy: over 15–20 minutes, from one of the venous lines remove 10 ml/kg (up to a maximum of 500 ml total).
- Transfusion: using the other IV access, beginning at the same time as the phlebotomy, transfuse the calculated amount of blood over 30 minutes (or slightly longer if aiming to raise the post-exchange Hb level).

30 minutes post-procedure

- Do a complete blood count and obtain results rapidly.
- If the post-exchange Hb level is < 90 g/L, perform an additional transfusion if required.
- If the post-exchange Hb level is > 110 g/L, perform a phlebotomy if required.

In high-resource settings, chronic transfusion therapy, i.e. a programme of regular transfusions (approximately every 3–4 weeks), in order to maintain a HbS level below 30%, is recommended for primary stroke prevention in children 2–16 years old with confirmed abnormal (> 200 cm/sec) transcranial Doppler (TCD) velocities in any of the large cerebral arteries and for secondary stroke prevention in children who have had a previous stroke. Selected children (with no previous history of stroke) with abnormal TCDs but no severe vasculopathy may transition to hydroxyurea (HU) therapy after 1–2 years of transfusion therapy. Chronic transfusion therapy can be accomplished using simple transfusions or manual or automated exchange transfusions. Unfortunately, in many parts of the world, chronic transfusion therapy is either not available, not feasible, or is available but without the possibility of iron chelation therapy to prevent the inevitable and potentially fatal consequences of iron overload. In these settings it is reasonable to consider replacing transfusion therapy with, or transitioning from initial transfusion therapy to, HU at maximal tolerable doses.

Previously, patients with recurrent severe acute chest syndrome and/or recurrent disabling painful events were placed on chronic transfusion programmes. Most such patients can now be successfully managed with HU. The use of chronic transfusions in infants with severe or recurrent acute splenic sequestration is controversial. Many physicians will place such patients on a chronic transfusion programme until 2–4 years of age when a splenectomy will be performed.

Where possible, patients with SCD should receive RBC units that have been matched for the five most common Rhesus antigens (D, C, E, c, e) and the Kell antigen to decrease the risk of RBC alloimmunization (*14*). Some, although not all, experts also recommend that patients on chronic transfusion programmes should receive blood that is HbS negative (*14,15*). In addition to the transfusion complications described elsewhere, in SCA patients it is important to be aware that a delayed haemolytic transfusion reaction can present with a clinical picture of a painful episode occurring 1–2 weeks post-transfusion. In rare cases, SCD patients may experience hyperhaemolysis after an RBC transfusion. This is a potentially fatal reaction usually occurring within 7 days of transfusion in which there is haemolysis of both transfused RBCs and recipient RBCs leading to a lower haemoglobin level than before transfusion. It may or may not be associated with alloimmunization. In addition to supportive therapy, it is important to avoid further transfusion and treat the patient with high-dose IV corticosteroids and, if available, intravenous immunoglobulin, erythropoietin (if reticulocytopenic) and possibly eculizumab. Following the acute episode, patients not already on HU therapy should begin HU.

Thalassaemia patients

Thalassaemias are a heterogeneous group of genetic disorders characterized by a reduced production of globin chains of haemoglobin and ineffective erythropoiesis. Children with β-thalassaemia major require regular transfusions every 3–4 weeks if they are to survive. Maintaining a nadir haemoglobin concentration of 90–100 g/L before transfusion is usually sufficient to achieve adequate suppression of erythropoiesis and prevent disease-related complications. However, iron overload will develop over time and, if untreated, will lead to endocrine failure, liver disease and ultimately to cardiac failure, which is the major cause of death.

Some children have an intermediate form, called non-transfusion-dependent thalassaemia. They have residual β-chain synthesis but might require transfusions periodically and they will develop iron overload with time even if they are never transfused. Children with more severe β-thalassaemia intermedia may benefit from regular transfusions. This should be considered in children with growth failure, skeletal deformities or extramedullary erythropoietic masses.

With appropriate diagnosis of transfusion-related haemosiderosis by magnetic resonance imaging and timely chelation, affected children can now live well into adulthood. Several iron chelators are available. Deferoxamine (DFO) has been in use since the 1970s and is effective in reducing liver and cardiac iron overload. However, its infusion modality (prolonged daily subcutaneous infusion) is cumbersome and may affect adherence and quality of life. Deferiprone is a bidentate oral iron chelator introduced in the late 1990s. It improves both liver and cardiac overload in β-thalassaemia major patients. Deferasirox is a tridentate oral chelator introduced in the early 2000s and has been shown to be effective in treating both transfusion-dependent and non-transfusion-dependent thalassaemia. Both oral chelators can be used in combination with DFO (*16*).

7.3 Practical aspects of RBC/WB transfusion

RBC products

RBC-containing products include WB and RBC concentrates prepared either by removing approximately three quarters of the plasma/anticoagulant solution from the WB unit (traditionally known as “packed red cells”) or by removing

most of the plasma/anticoagulant solution from the WB unit and then resuspending the packed RBCs in an "additive" (nutrient) solution. Some characteristics of these products are summarized in Table 7.7. At the time of writing, there was no published study comparing WB with RBC concentrates for the treatment of anaemia in children. The choice of product is usually determined by what is available.

ABO group/Rh type

Except in emergency situations, WB and RBC units should be ABO group identical with the recipient, both for ease of ensuring ABO compatibility and for optimal inventory management. Acceptable substitutions for RBC concentrates are shown in Table 7.8. For WB, the same ABO blood group substitutions can be used but plasma compatibility should also be considered. This involves either performing a "minor compatibility" test (recipient RBCs with donor plasma) in addition to the usual "major compatibility" test (donor RBCs with recipient plasma) or using blood with low anti-A and anti-B titres when transfusing group O WB to recipients who are not themselves group O.

RhD-positive patients may receive RhD-positive or negative blood, although most RhD-negative blood should be reserved for RhD-negative patients, especially for females of childbearing age. RhD-negative patients should receive RhD-negative blood, but in extreme emergencies RhD-positive blood may be administered; a life-saving transfusion should not be withheld due to the lack of RhD-negative RBCs.

Table 7.7. Comparison of RBC-containing products

Product	Composition	Approximate haematocrit	Approximate volume[a] (ml)	RBCs per transfusion	
				Transfusion volume (ml/kg)	RBCs per transfusion (ml/kg)
Whole blood in CPD, CP2D or CPDA-1	RBCs Plasma[b] 200–250 ml Platelets[c]	0.40	500–550	20[e]	8
RBCs in CPD, CP2D or CPDA-1	RBCs Plasma[b] 50– 70 ml	0.75[d]	250	10	7.5
RBCs in additive solution	RBCs Minimal plasma[b] Additive solution 100 ml	0.60[d]	330	15	9

CPD, citrate-phosphate-dextrose; CP2D, citrate-phosphate-double dextrose; CPDA-1, citrate-phosphate-adenine anticoagulant-preservative; RBCs, red blood cells.

[a] In some South-East Asian countries 350 ml of whole blood (WB) is collected in 49 ml of anticoagulant-preservative solution, giving a total volume for a WB unit of approximately 400 ml. Volumes for RBC units will thus also be proportionately smaller, but the haematocrit levels should be similar.

[b] Plasma plus anticoagulant solution.

[c] Number equivalent to that in one platelet unit prepared from WB; platelets kept in cold storage may be efficacious for the treatment of bleeding (but not prophylaxis) for up to 14 days (*17*).

[d] Haematocrit varies with amount of plasma/anticoagulant removed. Values shown are those obtained with centrifugation; if "settling" by gravity without centrifugation is used, then the haematocrit levels will be considerably lower (e.g. 0.50–0.55) as well as the RBC content/ml.

[e] The usually recommended WB transfusion volume of 20 ml/kg should raise the Hb concentration (in a non-bleeding patient) by approximately 2.7 g/dl. The equivalent volume of RBC concentrates with haematocrits of 0.75, 0.60 and 0.55 are 10.7 ml/kg, 13.3 ml/kg and 14.5 ml/kg, respectively.

The white blood cell content varies according to production method and whether pre-storage leukoreduction is performed. Granulocytes are non-functional 12–24 hours after collection.

Table 7.8. Blood group substitutions in paediatric patients

Blood component	Recipient ABO group	Substitution blood group when isogroup component not available	Extreme emergency and/or when unable to confirm patient's blood group
RBC concentrate	O	none	Males: O pos Females: – first choice: O neg – second choice: O pos
	A	O	
	B	O	
	AB	first choice: A or B second choice: O	
Whole blood	O	None	Males: O pos Females: – first choice: O neg – second choice: O pos Ideally use O-low titres
	A	O with low-titre anti-A/B (O-low titres)	
	B		
	AB	first choice: A or B second choice: O-low titres	
Frozen plasma or fresh frozen plasma	O	first choice: A or B second choice: AB	first choice: AB second choice: A
	A	AB	
	B	AB	
	AB	none	
Platelets	O	first choice: A or B second choice: AB	first choice: AB second choice: A or B third choice: O (O-low titres) Do not pool units of different ABO groups
	A	AB	
	B	AB	
	AB	none	
Cryoprecipitate	O	Any	All ABO groups are acceptable. May pool units of different ABO groups (but then do not indicate an ABO group on the label)
	A		
	B		
	AB		

- Always try to use the same blood group as that of the patient.
- Group O neg red cell concentrates are compatible with all groups but should be used judiciously because of their short supply.
- Group AB plasma/platelets are compatible for all plasma/platelet transfusions but should be used judiciously because of their short supply.
- In patients weighing < 10 kg avoid non-isogroup plasma/platelet transfusions unless components can be volume-reduced or are known to have low anti-A/B titres.

Storage age/product manipulation

RBC units of any storage age can be safely used for small-volume transfusions (≤ 20 ml/kg) in neonates and children (*18,19*). For massive transfusion in neonatal or small paediatric patients blood stored for ≤ 7–10 days (or if only older units are available with the supernatant fluid removed) should be used, as the potassium content of older units may pose a risk of hyperkalaemia. Removal of additive solutions from RBC units stored in these solutions was previously considered prudent for massive transfusion in neonates but is no longer routinely performed (except for units >7–10 days old). Leukoreduction and irradiation of RBC units is discussed in Chapter 3.

Partial units

If an entire blood unit is not required for a neonatal or paediatric patient, ideally a partial unit should be used. Small "paediatric" units are sometimes prepared by the blood supplier (using a closed system to maintain unit integrity). Alternatively, the required volume can be removed from the full unit into a transfer pack at the transfusing facility. To prevent septic transfusion reactions resulting from possible introduction of bacteria at this step, this must either be done using a sterile connecting device that splices and re-channels tubing preserving sterility of the units (in which case the expiry date does not change) or the blood in both the transfer pack and the original bag must be transfused with 24 hours of entry into the unit (with storage at 2–6 °C until transfusion).

Aliquots for neonates may also be prepared in a syringe, using specialized neonatal syringe sets with built-in filters. Blood in the syringe must be transfused immediately; if prepared using a sterile connecting device the blood in the original unit retains its original expiry date, otherwise it expires 24 hours after entry into the unit.

Complete information about the unit (blood group, unit number, expiry date and time) must appear on a label on the transfer pack or syringe and, if prepared non-sterilely, the revised expiry date and time must be indicated on the original unit.

Transfusion volumes

Within a given jurisdiction the clinician needs to know which RBC products are available in order to determine optimal transfusion volumes for small patients, i.e. those patients receiving less than one full blood unit. Traditional recommendations have been to administer WB transfusions of 20 ml/kg and RBC transfusions of 10 ml/kg. However, as can be seen in Table 7.7, the amount of an RBC unit that must be given to deliver the same red cell mass as WB 20 ml/kg depends upon the haematocrit of the RBC component and is often more than 10 ml/kg. For RBC concentrates in additive solution, 15 ml/kg should be given in order to assure an adequate haemoglobin increase. For patients with severe malnutrition, who are at increased risk of volume overload, only half these volumes should be given.

Transfusion rate/blood administration

RBC/WB transfusions must be completed within 4 hours of issue of the blood unit from the transfusing facility's blood bank. Recommendations for the transfusion rate are included in Table 7.4. If a patient is unable to tolerate the required volume within this timeframe a diuretic may be administered before transfusion and/or the total amount to be transfused can be divided into separate bags in the blood bank and administered in separate aliquots (following the guidelines mentioned above).

A blood administration set that includes a 170–260-micron filter (or other approved blood transfusion filters of smaller size) must be used. Ideally an infusion pump should be used to ensure the correct infusion rate. The catheter size should be the largest that can be reasonably inserted, at least a 22-gauge.

Drugs should not be administered simultaneously through the same intravenous line as transfusions. Normal saline is compatible with blood and may be simultaneously given if necessary; hypotonic solutions and Ringer's lactate must not be given through the same line as a blood transfusion.

Warming of RBC/WB solutions is not necessary for paediatric patients except when rapidly transfusing large amounts (> 15 ml/kg per hour) of cold blood through a central line. An approved blood warming device should be used.

7.4 Thrombocytopenia and platelet transfusions

The definition of thrombocytopenia is a platelet count (PC) below 140–150 × 10^9/L and is the same for all age groups, both males and females and for all ethnicities, except in the first week of life when the lower limit of normal is approximately 125 × 10^9/L.

Thrombocytopenia occurs frequently in preterm or ill neonates, in neonates with congenital infections and in neonates with perinatal asphyxia. These infants show a poor correlation between the PC and bleeding risk, suggesting that other factors are more important. The possibility of neonatal alloimmune thrombocytopenia (NAIT) should be considered in an otherwise well, term neonate with isolated moderate or severe thrombocytopenia (PC < 75–100 × 10^9/L) and in all other neonates with a PC < 50 × 10^9/L.

The commonest causes of thrombocytopenia in older infants and children are infections (in particular malaria, HIV and other viral infections), critical illness, disseminated intravascular coagulation (DIC), malignant disorders and their treatment, aplastic anaemia and immune thrombocytopenia (ITP). In high-resource settings thrombocytopenia is also common in patients undergoing cardiovascular surgery or on extracorporeal membrane oxygenation (ECMO).

Indications for platelet transfusions

Apart from one study in preterm neonates, published in 2019, there have been no randomized controlled trials of platelet transfusions (PT) specifically addressing indications for PT in paediatric patients (*17, 18*). Thus, guidelines for children are based on evidence from studies in adults (which have sometimes included some children) or, where such evidence is not available, on expert opinion. Generally accepted guidelines for PT in neonates and children are summarized in Box 7.4.

Box 7.4. Indications for platelet transfusions (PT) in neonates and children (*2, 17, 18*)

Neonates[a]

1. Neonatal alloimmune thrombocytopenia (NAIT) or suspected NAIT
   - Give prophylactic PT for a PC ≤ 30×10^9/L.
   - For invasive procedures, surgery or moderate or severe bleeding, use the recommendations for older infants and children as a general guide.
   - Use implicated-antigen-negative platelets where these are readily available, otherwise use random donor platelets; if using maternal platelets, they must be washed and irradiated.

2. Other neonates with thrombocytopenia
   - Give prophylactic PT for a PC ≤ 25×10^9/L
   - For invasive procedures, surgery or bleeding, use the recommendations for older infants and children as a general guide.

Older infants and children

1. Guidelines are based on adult literature and recommendations.

2. Hypoproliferative thrombocytopenia
   - Prophylaxis
     - Stable: PC ≤ 10×10^9/L (for non-reversible hypoproliferative thrombocytopenia consider a lower threshold or only therapeutic PT)
     - Increased bleeding risk (e.g. patient on anticoagulants, laboratory evidence of disseminated intravascular coagulation, sepsis): PC ≤ 20×10^9/L
   - Bleeding (due to or mainly due to thrombocytopenia)
     - minor: PC ≤ 10×10^9/L
     - moderate: PC ≤ 30×10^9/L
     - severe: PC ≤ 50×10^9/L
     - bleeding at a critical site (e.g. central nervous system): PC ≤ 100×10^9/L
   - Invasive procedures/surgery[b]
     - bone marrow aspirate/biopsy – no specific PC required
     - lumbar puncture: PC ≤ 40×10^9/L
     - percutaneous liver biopsy: PC ≤ 50×10^9/L
     - minor surgery at a non-critical site: PC ≤ 20×10^9/L
     - surgery at a critical site (e.g. central nervous system): PC ≤ $75–100 \times 10^9$/L
     - other surgery: PC ≤ 50×10^9/L

3. Immune thrombocytopenias (e.g. ITP, TTP/HUS)
   - Prophylaxis – PT is not indicated.
   - Bleeding – use PT only for severe/life-threatening bleeding.
   - Invasive procedures – decisions are to be made on an individual basis if other treatments not sufficient.

4. Other critically ill children with thrombocytopenia
   - Follow the recommendations in point 2 above as a general guide for PT.

PT, platelet transfusion; PC, platelet count; ITP, immune thrombocytopenia; TTP, thrombotic thrombocytopenia; HUS, haemolytic uraemic syndrome.

[a] Neonates with NAIT or suspected NAIT and neonates with PC < 50×10^9/L should undergo cerebral imaging to rule out the possibility of intracranial haemorrhage.

[b] For insertion and removal of central lines and for renal biopsy, refer to reference (*18*).

Practical aspects

Platelet products

There are three kinds of platelet products:

- platelets prepared from a standard WB donation; approximate volume 50 ml; platelets/unit ≥ 5.5×10^{10} platelets
- buffy coat pool; approximate volume 300–350 ml; platelets/pool ≥ 2.4×10^{11} platelets
- apheresis unit: approximate volume 200–250 ml; platelets/unit ≥ 2.4×10^{11} platelets.

Platelets/unit are an approximation and will vary between jurisdictions.

Usually only one or two platelet products are produced by a blood supplier. Blood suppliers who produce platelets from standard WB donations may pool 4 or 5 units under sterile conditions.

ABO group/Rh type

Ideally platelet units should be of the same ABO group as the recipient. Permissible substitutions are shown in Table 7.8. Whenever possible, group O platelets should be avoided for non-group O infants and children unless they can be volume-reduced (which can only be appropriately performed in specialized centres) or the units have low titres of anti-A/B. Prophylactic use of anti-D may be considered in Rh-negative female patients receiving Rh-positive platelets but this is not generally considered necessary in male patients.

Platelet dosage and transfusion rate

The usual paediatric platelet dosages are:

- neonates: 10–15 ml/kg (up to 50 ml or 1 unit prepared from WB)
- infants 4–10 kg: 5–10 ml/kg (up to 50 ml or 1 unit prepared from WB)
- children and adolescents >10 kg:
  - single units from WB donations: 1 unit per 10 kg (so 1 unit if body weight is 10–19 kg, 2 units if weight is 20–29 kg, etc.) to a maximum of 4–5 units
  - pooled units (buffy coat pool or pool of 4–5 units prepared from WB): 5–10 ml/kg up to 1 pooled unit
  - apheresis unit: 5–10 ml/kg up to 1 unit.

Platelets should be administered at a rate that the patient can safely tolerate (over at least 1 hour, or more slowly to avoid administering a large bolus of cytokines quickly) and in all cases within 4 hours of issue from the transfusing facility's blood bank.

Other practical considerations

In jurisdictions in which only pooled or apheresis platelets are available, partial units may be transfused. They can be prepared using the RBC transfer bags, in which case they should be transfused immediately. If aliquots are withdrawn under sterile conditions, the original unit retains its original expiry date but if prepared non-sterilely the original unit expires in 4 hours. Where available, platelet storage transfer bags should be used; in this case if prepared under sterile conditions and transferring the amount of product indicated by the manufacturer, both the aliquot and the original

unit maintain the original expiry date. If not prepared under sterile conditions both expire in 4 hours. A standard blood administration set with a 170–260-micron filter must be used. Leukoreduction and irradiation of platelet units is discussed in Chapter 3.

7.5 Bleeding disorders other than thrombocytopenia and the transfusion of plasma components

After the neonatal period, the indications for plasma transfusions are the same in children as in adults. Here we discuss only plasma transfusions in neonates, haemorrhagic disease of the newborn and the treatment of children with known or suspected haemophilia A or B when factor concentrates are unavailable.

Plasma transfusion in neonates

Except for von Willebrand factor and Factor VIII, the reference values for coagulation and prothrombotic factors are lower in neonates (including those receiving prophylactic vitamin K) than in adults. The most marked difference is observed in the Factor IX level. Consequently, the reference values for routine coagulation tests, in particular, the activated partial prothrombin time are higher in the neonatal period than later in life. "Adult" levels are reached by about 6 months of age.

There is no good evidence on which to base guidelines on plasma transfusion in the neonate. Plasma transfusions should not be used for volume expansion nor to prevent intraventricular haemorrhage, nor should they be administered to neonates with abnormal coagulation test results, but who are not bleeding (*22*). Plasma should not be used as the infusion fluid in the treatment of polycythemia; saline is a cheaper and safer choice. For bleeding neonates with coagulation test results outside the neonatal reference ranges, decisions should be made on an individual basis, guided by indications for plasma transfusion in older children and adults.

The use of plasma in exchange transfusions is described above.

Haemorrhagic disease of the newborn

A transient decrease in vitamin K-dependent coagulation factors (II, VII, IX, X) occurs normally in neonates within 48–72 hours of birth and can lead to spontaneous bleeding in the first 2–7 days of life. Typically, bleeding is intracranial, intestinal or umbilical. Prophylactic administration of vitamin K – 1 mg intramuscularly at birth (or a repeated oral dosing schedule) – prevents this disorder (known as haemorrhagic disease of the newborn) in most neonates. However, in babies born outside hospitals and/or where systems are not in place to ensure that every newborn receives vitamin K, this still occurs. It is treated with vitamin K, 1–5 mg intravenously. Plasma transfusion is indicated if the bleeding is severe or life-threatening. Infants whose mothers take phenobarbital or phenytoin or certain anti-tuberculosis drugs are at risk later in the neonatal period; bleeding in these infants can be prevented by giving oral vitamin K daily for the first 2 weeks of life.

Treatment of children with known or suspected haemophilia A or B when factor concentrates are unavailable

Ideally all patients with haemophilia A or B should have access to treatment with recombinant or plasma-derived, virally-

inactivated factor concentrates. Where these are unavailable, treatment of active bleeding with plasma components will still be beneficial. Both fresh frozen plasma (FFP, plasma frozen within 8 hours of collection) and plasma frozen within 24 hours of collection (FP24) contain factors VIII and IX, at a concentration of approximately 1 IU/ml. Cryoprecipitate has no Factor IX but each unit should contain at least 80 IU of Factor VIII. If the patient has haemophilia B or a suspected but unconfirmed diagnosis of haemophilia, then plasma should be given. If a diagnosis of haemophilia A is confirmed, cryoprecipitate is preferable to plasma if available. The amounts to be given should be calculated using the recommended number of coagulation factor units for the type of bleeding and then administering the maximum amount/volume that the patient can tolerate.

Practical considerations for plasma transfusions

FFP and FP24 are interchangeable. Ideally FFP/FP24 units should be of the same ABO group as the recipient. Permissible substitutions are shown in Table 7.8. Rh type does not need to be matched.

Partial units, prepared after thawing and using the same transfer bags as for RBC transfusions, may be transfused. If aliquots are withdrawn under non-sterile conditions, the aliquot and the original unit must both be transfused within 24 hours of entry into the original unit. If prepared under sterile conditions, local regulations for permitted length of storage at 2–6 °C must be followed.

If the patient can tolerate the volume, a dose of 20 ml/kg should be given. A standard blood administration set with a 170–260-micron filter must be used. Only normal saline is compatible with FFP/FP24, although co-administration is not recommended.

Practical considerations for cryoprecipitate transfusions

ABO group and Rh type do not need to be matched.

In neonates and small children, a dose of 1–2 units per 10 kg body weight is used; in older children and adolescents the usual dose is 1 unit per 10 kg.

Only normal saline is compatible with cryoprecipitate. Normal saline can be used to dilute the thawed unit if necessary. When more than 1 unit will be given, a pool is usually prepared (see Table 7.8). Following thawing, local regulations for permitted duration of storage at 2–6 °C must be followed. A standard blood administration set with a 170–260-micron filter must be used for infusion.

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