Red Cell, platelet and blood component Transfusion in Neonates

University Hospitals of Leicester NHS NHS Trust

Trust ref: C165/2008

Contents

1. Introduction and who this guideline applies to;

Most neonatal transfusions are carried out in low birth weight preterm infants treated on neonatal intensive care units. Elective blood transfusion is given on the neonatal unit to treat or prevent the adverse effects of anaemia. Emergency blood transfusion is given to support the circulation in the acute situation such as fetomaternal haemorrhage, pulmonary haemorrhage, intraventricular haemorrhage, subgaleal haemorrhage, Disseminated Intravascular Coagulation (DIC). Urgent or semi emergency blood is given on the neonatal unit as an exchange transfusion to treat haemolysis or for toxin removal (e.g. bilirubin)
This guideline is aimed at all health care professionals involved in the care of infants within the neonatal service.

Aim

This document aims to provide information about;

- Parental assent (agreement) for transfusing blood and blood components
- How to document discussion of benefits and risks of blood components transfusion and Parental assent (BLEED audit Initiative)
- Recommended Red cell and Platelet transfusion thresholds
- Prevent wastage of blood components by careful assessment of need and adhering to blood components recommended storage and shelf life
- Trigger Massive haemorrhage protocol if consecutive blood transfusion totals > 40 ml/kg

Key points

- All blood and blood component transfusion-a medical team member should discuss the benefits and risks of transfusion with parents and complete Blood Transfusion Integrated Care Pathway & parental assent form (Tick, Stick and Sign) prior to transfusion (Refer to Appendix 1, 2, 3 & 4).
- In emergency situations give blood and complete parental assent retrospectively at the earliest opportunity.
- Elective RBC transfusions should not exceed 20 ml/kg and completed in 3 hours
- To report any adverse transfusion reactions and events to Transfusion laboratory as soon as possible. Complete Datix incident. Preserve all blood and blood component and transfusion giving set to help investigation
- NEC occurring within 48 hours of a baby receiving a blood transfusion needs to be reported via the electronic reporting system (SABRE).

Related UHL documents

- **Blood Transfusion UHL Policy** Trust ref: B16/2003
- **Alloimmune Thrombocytopenia UHL Neonatal Guideline** Trust ref: C3/2014
- **Exchange Transfusion and Dilution Transfusion UHL Neonatal Guideline** Trust ref: C21/2010
- **Platelet Transfusion UHL Childrens Hospital Guideline Trust ref: C42/2009**

Flowchart 1: Neonatal blood transfusion

2. Neonatal Blood Transfusion

2.1 Benefits of Transfusion

Blood transfusion may be life-saving in the acute situation but its role in 'anaemia of prematurity' is less clear. Many symptoms have been ascribed to anaemia. Unfortunately, most of these are common symptoms on the neonatal unit (apnoea, bradycardia, tachypnoea, poor feeding, poor weight gain) but there is little evidence that transfusion abolishes these symptoms. Lactate levels measure the degree of tissue perfusion and tend to decrease after transfusion but are quite variable [(1)]. Clearly at some level anaemia will start to have deleterious effects on the baby but the trend over the last few years has been for fewer transfusions and stricter guidelines with no obvious detriment [(2,3,4)].

2.2 Risks of Transfusion

Blood transfusion is very safe but there are risks which increase with multiple donors. Blood is screened for known blood borne infections and CMV negative blood is always supplied by the blood bank. The red cells are suspended in SAGM (or CPD) which reduces but does not completely exclude the risk of T-cell activation and acute haemolysis. Transfusion will switch off the baby's own erythropoiesis and measurement of a high reticulocyte count (75 $x10^9$/l) may obviate the need to transfuse. In certain circumstances where the cardiovascular status is unstable a transfusion may worsen cardiac failure and tissue perfusion. 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).

2.3 Acute Circulatory Decompensation due to fluid loss

Fluid loss from the circulation may be from haemorrhage or from capillary endothelial losses (particularly with sepsis). Calculations of whether to transfuse and which fluid to give (blood, platelets, FFP, albumin or crystalloid) will depend on the estimated blood loss, an estimate of continuing losses, evidence of end organ compromise and presence of disseminated intravascular coagulation. In this situation, Consultant advice should be sought. There is very little evidence base to support the choices except that with acute blood loss, stabilising the circulating blood volume is a more important priority than oxygen carrying capacity. If a baby is severely anaemic at delivery, there is always a supply of O negative blood kept in the Labour ward fridge (both at LRI and LGH). This can be given but should not be allowed to delay the fluid resuscitation.

2.4 Transfusion Decision Making

If there is concern about acute loss of circulating blood volume;

- Examine baby for poor circulation (pulse, Blood Pressure, peripheral perfusion, urine output)
- Examine baby for sites of blood loss (external, gut, brain, tissues, lungs)
- Check blood gas and lactate.
- Check iatrogenic losses
- Discuss with consultant if the assessment suggests that the baby is unstable or likely to become unstable.
- Discuss with consultant and trigger massive haemorrhage protocol if consecutive blood transfusion totals > 40 ml/kg [8]

2.5 Treating or Preventing Adverse Effects of Anaemia

The definition of anaemia is where the oxygen carrying capacity of the blood is the rate limiting step for tissue oxygenation. Clinically this may be hard to define and bears little relationship to haemoglobin concentration. There is very little evidence that keeping babies up to pre-determined haemoglobin levels influences long term

outcome but as it is easy to measure, this is the criterion taken by many other guidelines.

The normal haemoglobin at birth is 175 (+ or – 25) g/l. In term infants this falls over the first 3 months to a nadir of 90 g/l and then increases through infancy. In well preterm babies the fall in haemoglobin level is further and faster and is exacerbated by venesection. There is very little evidence base for transfusion practice and most national and international guidelines [5,6] are based on recommendation from experts (grade C).

If the baby has chronic symptoms which might relate to anaemia;

- Check the babies observations over time (persistent tachycardia, tachypnoea, Blood Pressure, perfusion)
- Examine the baby for signs of responsiveness, tone, cardio-respiratory function, weight and feeding
- Assess the iatrogenic blood loss
- Check Hb, lactate and reticulocyte count

A reticulocyte count of above 75 $x10^9$/l suggests that the baby is making enough new cells for the haemoglobin to rise over the next week. A persistent lactate of >2.3 mmol/l is abnormal and due to anaerobic tissue respiration. Poor tissue oxygenation is one cause. It is very variable even in stable neonates so is not a useful investigation in isolation.

2.6 Pre-transfusion testing

Wherever possible, samples from both the mother and infant should be obtained for initial ABO and RhD group determination. Details of pre-transfusion testing in neonates and infants are given in the 2013 British Society for Hematology (BSH) guidelines for pre-transfusion compatibility procedures in blood transfusion laboratories https://b-s-h.org.uk/guidelines/guidelines

Blood supplied by the blood bank is suspended in SAGM and is all CMV negative (blood for exchange transfusion by contrast is fresh, suspended in CPD, CMV negative, irradiated and supplied direct from Sheffield).

The blood is dispensed in pedipacks (about 45 ml) and some attempt is made to have repeat transfusions from the same donor to reduce the risk of blood borne infection.

2.7 Neonatal ‘top-up’ transfusion

Several randomized 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[9] 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.

Although many experts now favor a restrictive transfusion policy, it is important to note the Cochrane Review comment that 'the safe lower limits for hemoglobin 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.

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, and non-invasive monitoring where possible.

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).

There is no need to stop feeds during this time and furosemide is **not** routinely given.

Calculation for Top-up transfusion: Red Cells Desired Hb (g/l) - actual Hb x weight (kg) x 3 (Usually 10 to 20 ml/kg). Rate approx 5ml/kg/hr.

A haemoglobin concentration on its own is not adequate reason to transfuse (or not to transfuse). The new BSH Transfusion Guidelines for Neonates and Older Children (b-s-h.org.uk/guidelines/transfusion-for-fetuses-neonates-and-older-children)[5] suggest the transfusion thresholds summarized in Table 1.

Table 1. Summary of BSH recommendations for neonatal top-up transfusions

Postnatal age	Suggested transfusion threshold Hb (g/L)		
	Ventilated	On oxygen/CPAP	Off oxygen
First 24 hours	<120	<120	<100
≤Week 1 (days 1–7)	<120	<100	<100
Week 2 (days 8–14)	<100	<95	<75–85 depending on clinical situation
≥Week 3 (day 15 onwards)		<85	

NB arterial Hb is usually 10 g/l lower (simplified from Kirpalani et al 2006) [4]

2.8 Parental assent (Agreement) and BLEED initiative

Blood and blood component transfusions can be rarely associated with serious risks and side effects. Parents should be informed of any possible serious risks associated with proposed medical treatment even if these are rare, as failure to do so could be considered negligent.

All elective blood component transfusion- a medical team member should discuss the risks and benefits of transfusion with parents and complete parental assent form and blood transfusion integrated care pathway (Tick, Stick and Sign) prior to transfusion (Refer to Appendix 1, 2 & 3 for further details).

All emergency/urgent/out of hours blood component transfusion- Give blood and blood products as required and complete assent retrospectively at the earliest opportunity. A medical team member should discuss the risks and benefits of transfusion with parents and complete parental assent form and blood transfusion integrated care pathway (Tick, Stick and Sign).

2.9 Special Cases

Prior to surgery there may be an indication to transfuse particularly if the risk of bleeding is high. This and provision of blood intra-operatively should be discussed with the Surgeon and Anaesthetist as there may be individual variation in practice.

Babies with cyanotic congenital heart disease may need to be kept at a higher Hb level than normal to increase tissue oxygen delivery at low PaO_2.

In babies with 'heart failure' a transfusion may exacerbate the pulmonary oedema. In this situation the blood may be given over a longer period of time and furosemide considered.

2.10 Transfusion-associated NEC (TANEC)

The relationship between blood transfusion and necrotising enterocolitis in preterm babies is currently unclear. There is a legal requirement under EU Legislation to report any Serious Adverse Reactions to blood transfusions via the SHOT (Serious Hazards of Transfusion)/MHRA joint electronic reporting system, SABRE. This now includes any episodes of NEC occurring within 48 hours of a baby receiving a blood transfusion, and should be reported under the category of 'Uncategorised Complications of Transfusion', via SABRE (https://www.shotuk.org/reporting/)[7].

2.11 Neonatal red cell exchange transfusion

Neonatal red cell exchange transfusion is mainly used in the treatment of severe hyperbilirubinaemia or anaemia in babies with hemolytic disease of newborn (HDN). It removes antibody-coated neonatal red cells and reduces the level of plasma unconjugated bilirubin, the cause of bilirubin encephalopathy. A 'double volume exchange' (160–200 mL/kg) removes around 90% of neonatal red cells and 50% of bilirubin. For further details refer to relevant Exchange transfusion guideline.

2.12 Irradiation and Large volume neonatal red cell transfusion

Universal irradiation of blood products for neonates is NOT required. 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.

All blood for neonatal exchange transfusions (ET) should be irradiated if there is a previous history of IUT or if donation comes from first- or second- degree relative. For other neonates requiring ET, irradiation is recommended provided it does not cause undue delay.

Neonates who have received a previous IUT of either red cells or platelets should receive irradiated blood products until 6 months after their expected delivery date (40 weeks gestation).

All HLA-matched platelets or donations from first- or second- degree relative must be irradiated.

It is not necessary to irradiate red cells for routine “top-up” transfusions of premature or term infants unless there is a prior history of IUT, or the donation has come from a first- or second- degree relative

For full guidance please refer to BSH Guidelines https://b-s-h.org.uk/guidelines/guidelines/guidelines-on-the-use-of-irradiated-blood-components on the use of Irradiated Blood Components.

2.13 Neonatal platelet transfusions

Severe thrombocytopenia (<50×10^9/L) is a common finding in infants treated on NICUs, especially in sick preterm neonates. 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 Large, multicenter, randomized trial[10] involving preterm infants < 34 weeks with severe thrombocytopenia showed that more deaths, major bleeding, or both occurred when a higher prophylactic platelet-count transfusion threshold of 50,000 per cubic millimeter was used than when a threshold of 25,000 per cubic millimeter was used. Further reducing the transfusion trigger from 50,000 per cubic millimetre to 25,000 per cubic millimeter may prevent death or major bleeding in 7 of 100 preterm neonates with severe thrombocytopenia.

An example of suggested transfusion thresholds is given in Table 2. 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 for children under 15kg is 10–20 mL/kg.

Table 2: Suggested transfusion thresholds for neonatal prophylactic platelet transfusion (excluding NAIT)

Platelet Count ($\times 10^9$/L)	Clinical situation to trigger platelet transfusion in neonates
<25	Stable term or preterm infant with asymptomatic thrombocytopenia and no bleeding
26-50	Sick preterm infant with thrombocytopenia
<50	Term or preterm infant with symptomatic* thrombocytopenia and minor bleeding, coagulopathy or prior to surgery
<100	Term or preterm infant with symptomatic* thrombocytopenia and major bleeding or requiring major surgery (e.g. neurosurgery)

*Symptomatic thrombocytopenia-Bruising, petechie and bleeding in body systems (endotracheal tube, urine, stools, stoma losses)

2.14 Neonatal alloimmune thrombocytopenia (NAIT)

NAIT is the platelet equivalent of Hemolytic disease of Fetus and Newborn (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. For further information refer to NAIT guideline.

For Management of NAIT please see Alloimmune Thrombocytopenia UHL Neonatal Guideline

2.15 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.

The 2009 National Comparative Audit of the use of FFP https://nhsbtdbe.blob.core.windows.net/umbraco-assets-corp/14933/nca-audit_of_ffp_elsewheres2009.pdf 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. BSH 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)

In a well-baby INR > 2.0 should not prompt automatic FFP. Discuss with consultant.

The dose of FFP is usually 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 <1.0 g/L in the presence of bleeding from acquired or congenital hypofibrinogenaemia. The usual dose is 5–10 mL/kg.

3. Audit Standards

1. Parental assent (agreement) to transfusion documentation completed for all elective transfusions (100%)
2. Retrospective completion of parental assent (agreement) to transfusion for urgent/emergency/out of hours transfusions (100%)
3. Documentation of provision of information leaflet 'Will my baby need a blood transfusion) to parents (100%)
4. Documentation of discussion of risks and benefits of transfusion with parents (100%)
5. Platelet transfusion threshold in asymptomatic preterm infant < 34 weeks is < 25 x 10^9/L (100%)

4. References

1. Frey B, Losa M. Intensive Care Med. 2001;27:222-7 The value of capillary whole blood lactate for blood transfusion requirements in anaemia of prematurity.

2. Ramasethu J, Luban NLC. Semin Neonatol 1999;4:5-16. Red blood cell transfusions in the newborn.

3. Aher S, Malwatkar K, Kadam. Semin Fetal Neonatal Med 2008;13:239-47. Neonatal anaemia.

4.Kirpalani H, Whyte RK, Andersen C, et al J Pediatr. 2006;149:301-7. The premature infants in need of transfusion (PINT) study: A randomized controlled trial of a restrictive (low) versus liberal (high) transfusion threshold for extremely low birth weight infants.

5.BSH Transfusion Guidelines for Neonates and Older Children (b-s-h.org.uk/guidelines/transfusion-for-fetuses-neonates-and-older-children) (Accessed April 2024)

6. Fetus and Newborn Committee CPS. Can Med Assoc J 1992;147:1781-92. Guidelines for transfusion of erythrocytes to neonates and premature infants.

7. PHB Bolton-Maggs (Ed) D Poles et al, on behalf of the Serious Hazards of Transfusion (SHOT) Steering Group, The 2014 Annual SHOT Report (2015). Available at www.shotuk.org/shot-reports/ [accessed on 23rd May 2016]

8. Personal communication with Consultant hematologist Dr Hafiz Qureshi

9. Low versus high haemoglobin concentration threshold for blood transfusion for preventing morbidity and mortality in very low birth weight infants. Cochrane Review 2011

10. PlaNeT2. Randomized Trial of Platelet-Transfusion Thresholds in Neonates. N Engl J Med. 2019 Jan 17; 380(3):242-251

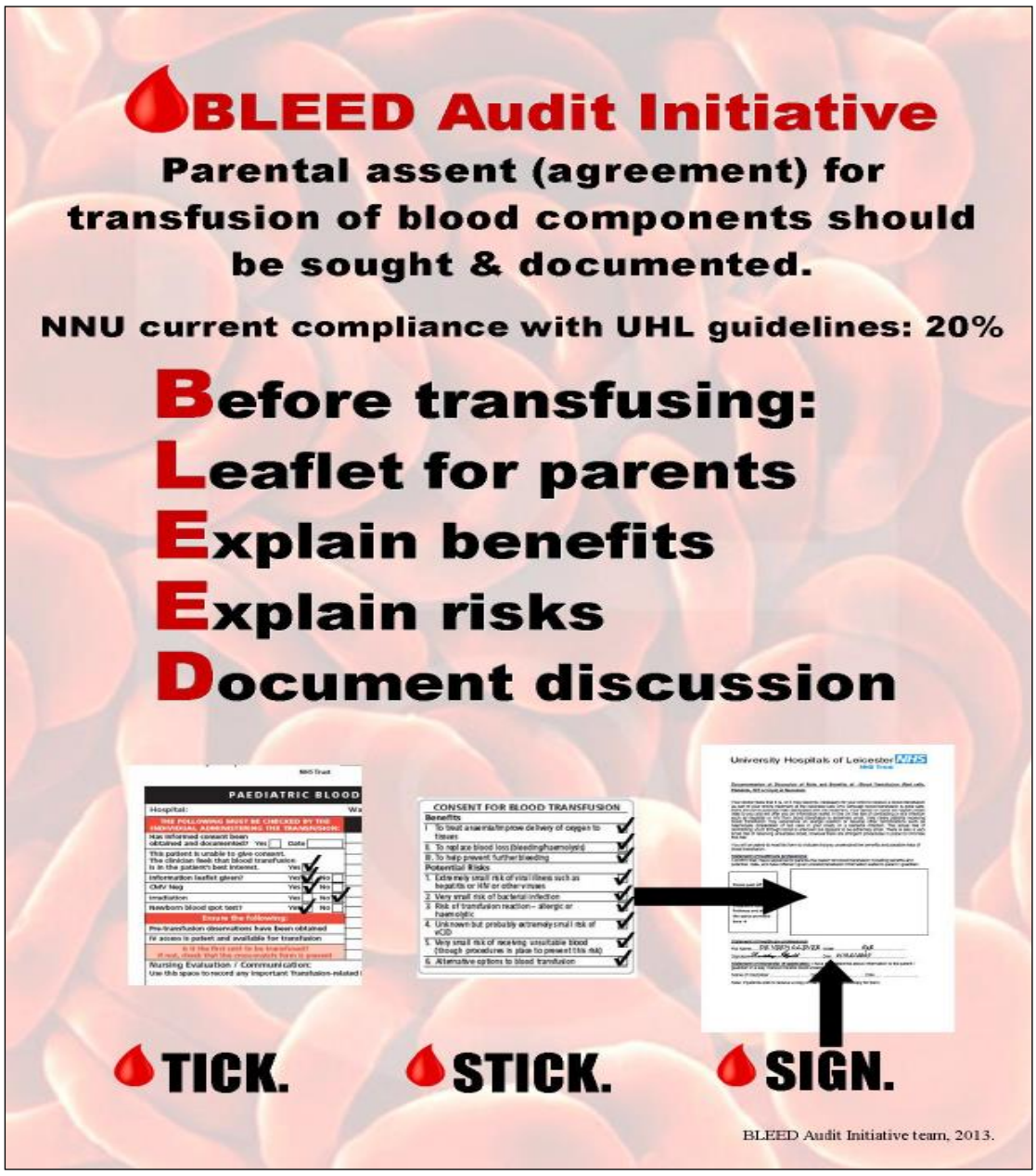
5. Key Words

Anaemia, Platelets, FFP, Albumin, Crystalloid

The Trust recognises the diversity of the local community it serves. Our aim therefore is to provide a safe environment free from discrimination and treat all individuals fairly with dignity and appropriately according to their needs.
As part of its development, this policy and its impact on equality have been reviewed and no detriment was identified.

CONTACT AND REVIEW DETAILS			
Guideline Lead (Name and Title) Original author: Wren Hoskyns, Reviewed by: Venkatesh Kairamkonda			Executive Lead Chief Medical Officer
Details of Changes made during review:			
Date	Issue Number	Reviewed By	Description Of Changes (If Any)
Oct 2008	1		New guideline
May 2016 - Jun 2016	2	guideline lead (REM)	Educational initiative information added (BLEED audit)
April 2018	3	Neonatal Guidelines Meeting	
April 2019	4	Neonatal Guideline Meeting Neonatal Governance meeting	Updated evidence added
Feb 2021	5	Neonatal Guideline Meeting	minor amendments
April 2024	6	Neonatal Guideline Meeting Neonatal Governance meeting UHL Women's Quality & Safety Board	Format update Reference & hyperlink update

Appendix 1: BLEED audit Educational Initiative



Appendix 2: BLEED Audit Initiative Frequently Asked Questions

BLEED Audit Initiative - FAQs:

A bit of background:

'Better Blood Transfusion' is an initiative from the Department of Health to improve the safety of blood component transfusions throughout the NHS. It was first launched in 1998, then reviewed in 2002 & 2007. Recent research into patient consent showed that:

- 95% of healthcare professionals think that patients should be given the opportunity to consent to a blood transfusion;
- 50% felt it should be compulsory.

It also raised concern that patients are given too little information about risks, benefits, alternatives & the right to refuse. In some cases they may not even be aware that they have had a transfusion, & then go on to donate blood themselves, when they should not (since 2004, you cannot be a blood donor if you have been a transfusion recipient, because of concerns about vCJD).

1. Why is consent/assent needed for transfusing blood components?

Patients have a right to information about their condition and the treatment options available to them; explaining potential risks involved is important in upholding the patient's right to dignity & autonomy.

There is currently no legal requirement to obtain consent for blood transfusion. However, patients should be told of any possible serious risks associated with their proposed medical treatment, even if these are rare, as failure to do so could be considered negligent.

2. What do current Guidelines say?

Both the British Committee for Standards in Haematology (BCSH) & UHL Guideline state that the minimum information documented should include:

- details of the information provided to the patient (or parent)
  - risks, benefits, alternatives to transfusion.
- written consent to proceed (Assent in Neonates)

3. What are the risks of blood component transfusion?

In the UK in 2011, approximately 2 million blood components were issued, and there were:

- No reported transfusion-transmitted infections;
- 8 reported deaths, (2 definitely related to transfusion, 6 possibly linked, including one death from necrotising enterocolitis following transfusion);
- 117 cases of major morbidity (the majority were acute transfusion reactions).

According to the Serious Hazards of Transfusion (SHOT) scheme, blood product administration in the UK carries a risk of death of 0.0027 per 100 components issued & risk of major morbidity of 0.0396 per 100 components issued.

4. Why Parental Assent (versus parental consent) in neonates?

Where a child is not competent, (as is obviously the case with neonates), then those with parental responsibility can provide parental assent (or 'agreement') for treatment. So in the case of neonatal blood component administration, we are seeking parental assent as a proxy for consent.

5. In an emergency?

As in all areas of medical practice, in an emergency treatment can be given without consent, which:

> 'is limited to what is immediately necessary to save life or avoid significant deterioration in the patient's health. However, you must still respect the terms of any valid advance refusal which you know about, or is drawn to your attention. You should tell the patient what has been done, and why, as soon as the patient is sufficiently recovered to understand'.

Afterwards, parents should be informed in a timely manner that their child has had a blood transfusion, given the information leaflet & this discussion documented as usual. If the parents are not present, this could be done over the telephone (where practically possible), & documented appropriately.

Appendix 3. How to document discussion & parental assent
(attach the sticker to the 'documentation of discussions@ form in the admission booklet)

6. How to document discussion & parental assent:

Prior to transfusion, a medical staff member should:

1. Give parents the leaflet **'Will my baby need a blood transfusion?'**

2. **Discuss with parents** the benefits & potential risks of blood product transfusion.

3. Complete **all the relevant tick boxes** on the front left-hand column of the Blood Transfusion Integrated Care Pathway (ICP).

TICK

4. Complete the '**Consent to transfuse' sticker,** found on the back of the ICP.

STICK

5. Attach the sticker to the '**Documentation of discussion of risks & benefits of blood transfusion in neonates'** form.

6. **Sign** the form (Last page of the admission booklet)

SIGN