AGE OF BLOOD - BACKGROUND

PURPOSE

The following information provides guidance on the age of fresh blood products provided by the blood bank at the Royal Children's Hospital (RCH) including specific patient populations.

RCH blood bank definitions:

- Neonatal patients:
  - Up to 28 days post expected due date
- Paediatric patients:
  - Infant – 1 to 12 months of age
  - Child – 1 to 12 years of age
  - Adolescent – 13 to 18 years of age

Shelf life of fresh blood products

Fresh blood products have a shelf life, or expiry date as follows:

Fresh blood product	Temperature	Shelf life
Red blood cells	2-6°C	42 days
Pedipak – red blood cells	2-6°C	35 days
Platelets*	20-24°C	5 days
Fresh Frozen Plasma (FFP)	-25°C	1 year
Extended Life Plasma	2-6°C	5 days from thawing
Cryoprecipitate	-25°C	1 year

* The Blood Service samples each platelet unit 24 hours after collection and screens them using both aerobic and anaerobic culture bottles. After sampling, they issue platelets as 'negative to date' and they continue to incubate for 3 days beyond their expiry. If a culture becomes positive, the screening equipment automatically flags this as 'initial machine positive' (IMP). As the testing process is quite sensitive, many IMPs turn out be false alarms.

If the platelets and/or their associated components (e.g. red cell or plasma) have already been transfused, the Blood Service contacts the RCH blood bank to recall the associated blood component. The on-call haematologist contacts the treating clinician to manage the patient with the knowledge of the preliminary result.

BACKGROUND

To align with local and international guidelines, the RCH Age of Blood guideline has been developed. In Australia red cell units can be stored up until 42 days. Red cell units stored for longer periods of time have decreased ability to deliver oxygen due to decreased levels of 2, 3-diphosphoglycerate, decreased nitric oxide metabolism and increased red blood cell (RBC) rigidity due to an altered RBC membrane. Recent guidelines and randomised controlled trials have reviewed the effect of transfusing fresh red cells compared with standard issue red cells. These show there is no evidence to demonstrate a benefit of transfusing fresh red cells, with no difference in mortality or morbidity in individuals receiving fresh red cells compared with individuals who receive standard issue red cells. A meta-analysis performed by Carson *et al* looking at the association between fresher versus standard issues blood on mortality in neonates and children and found no difference with a RR 0.99 (95% CI of 0.95 – 1.14). (Carson *et al, JAMA,* 2016) These studies were conducted in premature, very low-birth weight infants and children with anaemia in Africa. It is therefore recommended that neonates and children should receive RBC units selected at any point within their licensed dating period, rather than limiting patients to transfusion of only fresh red cell units.

These trials did not evaluate patients undergoing a massive transfusion or exchange transfusion, neonates undergoing intrauterine transfusions, children with haemoglobinopathies requiring chronic transfusion support or children at risk of hyperkalaemia. Neonates and children are at risk of metabolic complications from transfusion including hyperkalaemia, hypothermia, hypomagnesaemia, hypocalcaemia and acid- base alterations due to their higher transfusion to blood volume ratio. Fatal cardiac arrhythmias secondary to hyperkalaemia are reported in the setting of large volume transfusions during extra-corporeal life support (ECLS), cardiopulmonary bypass and neonatal exchange transfusions. For these reasons shorter storage durations may be considered in neonates and children receiving large volume red cell transfusion.

THE EVIDENCE

Neonates, Infants and Children

Trial	Study population	Study number	Intervention	Comparison	Volume of RBC	Primary outcome	Morbidity/mortality outcome
Fernandes da Cunha, 2005	VLBW infants (<1,500g)	n = 52	≤3 days	<28 days	15ml/kg	Not stated	**Death** 9/26 vs 10/26 (short vs long) RR 0.90; 0.44 – 1.85 **Respiratory distress syndrome** 25/26 vs 24/26 **NEC** 6/26 vs 4/26 (short vs long)
Strauss, 1996	VLBW infants (600 -1,300g)	n = 40	CPDA-I RBCs ≤ 7 days	AS- 1 RBCs ≤ 42 days	15ml/kg	Whether AS-1 RBC could safely supply all RBC needs	**Death** O/21 vs 1/19 (short vs long); RR 0.30; 0.01 – 7.02 **Transfusion reaction** 0/21 vs 1/19 (short vs long)
The ARIPI trial, Fergusson, 2012	Preterm infants <1250g	n= 377	< 7 days Mean 5.1 days (SD 2.0)	Standard issue Mean 14.6 days (SD 8.3)	Mean 14.18ml/kg (7.84) vs 14.05ml/kg (6.82) (short vs long)	Composite measure of death and major neonatal morbidities – NEC, ROP, BPD and IVH	**Death** 7/143 vs 5/143 (short vs long) RR 0.97; 0.61 – 1.54 **Composite measure of death and morbidity** Relative risk 1.00 (95% CI; 0.82-1.21)
Dhabangi, 2013	Children 6– 59 mth with severe malarial anaemia (Hb ≤ 50gL)	n = 74	1 - 10 days Mean 7.8 (±1.8) days,	21 - 35 days Mean 27.2 (±3.9) days	Mean 12.7ml/kg (±2.6) vs 12.7ml/kg (±2.2) (short vs long)	Lactic acidosis resolution by four hours after transfusion	**Death** 1/37 vs 0/37 (short vs long) RR 3.0; 0.13 – 71.34 **AEs** 2/37 vs 1/37 (short vs long)
TOTAL trial, Dhabangi, 2015	Children 6 – 60 mth with Hb ≤50 g/L and lactate ≥ 5 mmol/L	n = 290	1 to 10 days	25 to 35 days	10ml/kg	Lactate of 3 mmol/L or lower at 8 hours	**24-hour mortality** 5/145 vs. 3/145 (short vs long) RR 1.40; 0.45 – 4.31 **AE unrelated to transfusion** 16/145 vs 13/145 (short vs long) **AE related to transfusion** 1/145 vs 1/145 (short vs long)
Ongoing trials							
NCT01977547 - ABC PICU trial		Estimated enrolment , n = 1,538	≤ 7 days	Standard issue RBCs (expected 17-21 days).		New or Progressive Multiple Organ Dysfunction Syndrome	

ABC PICU - Age of Blood in Children in Pediatric Intensive Care Units , AE – adverse event, ARIPI - Age of Red Blood Cells in Premature Infants, BPD- bronchopulmonary dysplasia, Hb – haemoglobin, IVH – intraventricular haemorrhage NEC – necrotising enterocolitis, RBC – red bloods cells, ROP – retinopathy of prematurity, TOTAL- Tissue Oxygenation by Transfusion in Severe Anaemia With Lactic Acidosis

AGE OF BLOOD ISSUED AT RCH

The RCH blood bank will aim to provide blood products within the age range listed, however this may not always be possible due to issues such as donor availability or requirements that may take precedence, such as phenotype matched.

Patient group	Age of red blood cells on day of issue	Considerations
Neonatal exchange transfusion	< 5 days	Kell negative, CMV negative, Rh and phenotype matched
Intrauterine transfusion	< 5 days	Kell negative, CMV negative, Rh and phenotype matched
Paediatric large volume transfusion* - Cardiac surgery requiring cardiopulmonary bypass - ECLS - Craniofacial surgery	< 7 days	In an emergency, the blood bank scientist will issue the most appropriate unit available at that time
Paediatric – routine transfusion - Post-op surgical patient - Oncology patients - Solid organ transplantation	Standard issue	
Massive transfusion	Aim < 10 days	In an emergency, the blood bank scientist will issue the most appropriate unit available at that time
Chronically transfused patients - Congenital anaemia who are transfusion dependent - Haemoglobinopathies (sickle cell disease, thalassaemia) - Aplastic anaemia	Aim < 14 days	Patients with haemoglobinopathies are matched for Rh and Kell Extended phenotype matching for patients with alloantibodies. Extended phenotype matching may take precedence over age of red cells
Small volume (top up) neonatal transfusions	Standard issue	
Children and adolescents not included in any groups listed above	Standard issue	

* Equivalent to a single circulating blood volume (~80ml/kg)

ECLS – extracorporeal life support

BLOOD PRODUCT MODIFICATION

Irradiation:

- Platelets
    - Irradiated at the Blood Service, this does not affect the age of platelets at issue
- Red blood cells
    - Red blood cells may be irradiated at any time up to 14 days after collection, and stored for a further 14 days from the date of irradiation.
    - RCH irradiates just prior to issue to avoid issues related to storing irradiated red cells such as changes in potassium level and pH.