Paediatric Transfusion Guidelines

‘Tiny Transfusions’
Yorkshire and Humbar RTC meeting
Helen New

Consultant in Paediatric Haematology and Transfusion Medicine
Imperial College NHS Trust/NHSBT
Guidelines

BCSH

www.bcsghguidelines.com

Handbook of Transfusion Medicine

www.tsoshop.co.uk

Electronically soon on:
www.transfusionguidelines.org.uk/
Previous BCSH guidelines 2004

- What has changed since?
  - Evidence base
  - Components
  - SHOT paeds
  - NHSBT paeds group/BBTS paeds SIG

- New guidelines in preparation
  - clinical and lab sections
Risks vs benefits

- Who is transfused?
- What are the risks?
- What blood is used for children?
- How decide when to transfuse?
- How to prescribe?
UK National Comparative Audit
Age of paediatric recipients

Median (IQR) age estimated at 5 (1-12) years for 1294/1302 patients.

21% (279) < 1 year  8% (102) < 1 month
Age of neonatal recipients

Comparative Audit of the use of Red Cells in Neonates and Children 2010.
Paediatric transfused patients: reason for admission

- **Haematology/oncology**
  - 53% in Paeds red cell NCA 2010
Paediatric transfusion risks?

Component related: additives, K+  
Lee et al Transfusion 2014

Procedure related  
eg neonatal exchange transfusion

Neurodevelopmental effects?  
Liberal transfusions and ↓intracranial volume?  

Age of blood?  
ARI PI trial Fergusson et al JAMA. 2012 10;308:1443-51

NEC -?causal association

Haemovigilance: ‘SHOT’
Indications for transfusion?

Your blood is made up of four different things...

1. Saucer shaped red blood cells that carry a thing called oxygen around your body. Oxygen gives you lots of energy so you can run around in the playground.

3. Tiny egg-shaped platelets. They are needed when you fall over. They act like a plug to stop you bleeding if you cut yourself.

4. Plasma. That’s the liquid that all the other bits float in. It is mainly water but also contains food for your body to live off.

Blood would be useless without help from other bits of your body......
Figure 2  Hemoglobin concentrations and reticulocyte counts in preterm and term infants during the first 6 postnatal months. Median values and 95% confidence limits are indicated for each of 3 birth weight groups: >3000 g, 1501-2000 g, and 1000-1500 g.

From: Caroll and Widness  Seminars in Perinatology Volume 36, 2012 232 - 243
Iowa study

- 100 preterm infants, bw 500-1300g
- Hb stratification: respiratory status
- Primary endpoint: difference in transfusion number
  - not clinical

Bell et al Pediatrics 2005:115;1685-1691

PINT

- 451 ELBW infants < 48hrs age (<1000g)
- Hb stratification
  - respiratory status and postnatal age
- Composite clinical outcome

Kirpilani et al J Paediatr 2006:149;301-7
<table>
<thead>
<tr>
<th></th>
<th>Iowa (n=100)</th>
<th>PINT (n=451)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mean Hb g/dl</strong></td>
<td>8.3 vs 11.0</td>
<td>10.1 vs 11.2</td>
</tr>
<tr>
<td><strong>No transfusion</strong></td>
<td>10% vs 12%</td>
<td>5% vs 11%</td>
</tr>
<tr>
<td><strong>Death/brain injury</strong></td>
<td>16% vs 2%</td>
<td>31% vs 31%</td>
</tr>
<tr>
<td><strong>Longer term</strong></td>
<td>Approx 12 yr: Brain volumes in liberally transfused smaller than controls</td>
<td>18-21 mth -cognitive delay in restrictive group - post hoc</td>
</tr>
</tbody>
</table>

Whyte et al, Pediatrics 2009
Nopoulos et al, Arch Pedatr Adolesc Med 2011
<table>
<thead>
<tr>
<th>Postnatal Age</th>
<th>Respiratory Support</th>
<th>No Respiratory Support</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Haemoglobin g/l (Haematocrit %)</td>
<td></td>
</tr>
<tr>
<td>Week 1</td>
<td>115 (35%)</td>
<td>100 (30%)</td>
</tr>
<tr>
<td>Week 2</td>
<td>100 (30%)</td>
<td>85 (25%)</td>
</tr>
<tr>
<td>Week 3</td>
<td>85 (25%)</td>
<td>75 (23%)</td>
</tr>
</tbody>
</table>

• 1018 neonatologists,
• 11 countries
• scenarios for neonates < 1000g bw and/or < 28 wks gestational age

Figure 1  Thresholds for red cell transfusion for infants weighing <1000 g at birth and/or <28-week GA for each of the first 4 weeks of life given 5 different levels of respiratory support. Each box represents the interquartile range (25th-75th percentile). The median value intersects each box.
# Audit findings by postnatal age & respiratory status

<table>
<thead>
<tr>
<th>Postnatal age 0-1 days</th>
<th>Postnatal age 2-7 days</th>
<th>Postnatal age 8-28 days</th>
<th>Postnatal age &gt;28 days</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>Median (IQR) Hb</td>
<td>N</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Mechanically ventilated</td>
<td>187/201</td>
<td>11.6 (10.3-12.6)</td>
<td>195/200</td>
</tr>
<tr>
<td>• On CPAP</td>
<td>17/18</td>
<td>11.2 (9.4-12.2)</td>
<td>54/55</td>
</tr>
<tr>
<td>• On supplementary O₂</td>
<td>9/9</td>
<td>5.6 (4.8-9.9)</td>
<td>1/1</td>
</tr>
<tr>
<td>ANY OF THE ABOVE</td>
<td>213/228</td>
<td>11.5 (10.2-12.5)</td>
<td>250/257</td>
</tr>
<tr>
<td>OFF OXYGEN</td>
<td>9/13</td>
<td>7.9 (5.9-11.1)</td>
<td>9/13</td>
</tr>
</tbody>
</table>

What to recommend?

- Local guidelines
- within parameters set by Cochrane
- not too complex
- further studies
  - Effects of Transfusion Thresholds on Neurocognitive Outcome (ETTNO)
    - 920 VLWB infants randomised
### Draft new BCSH recommendations

<table>
<thead>
<tr>
<th>Postnatal age</th>
<th>Suggested transfusion threshold Hb (g/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Ventilated</td>
</tr>
<tr>
<td>1&lt;sup&gt;st&lt;/sup&gt; 24 hours</td>
<td>&lt; 120</td>
</tr>
<tr>
<td>≤ week 1 (day 1-7)</td>
<td>&lt; 120</td>
</tr>
<tr>
<td>week 2 (day 8 - 14)</td>
<td>&lt; 100</td>
</tr>
<tr>
<td>≥ week 3 (≥ day 15)</td>
<td>&lt; 100</td>
</tr>
</tbody>
</table>
Paediatric red cells

- TRI PI CU study 2007
  - Restrictive \( \leq 7 \text{ g/dl} \) vs Liberal \( \leq 9.5 \text{ g/dl} \)
  - organ dysfunction scores
  - 637 stable, critically ill children
  - mean age approx 38 mths
  - Restrictive: ↓ transfusions, no ↑ adverse outcomes

- Cardiac
  - Willems et al, TRI PI CU 2010
    - restrictive < 7 g/dl vs liberal 9.5 g/dl
    - MODS no difference
  - Cholette et al 2011: Cyanotic heart disease
    - restrictive < 9 g/dl vs liberal 13 g/dl
    - no significant difference in clinical outcomes
Recent guidelines

Red Blood Cell Transfusion: A Clinical Practice Guideline
From the AABB*

Jeffrey L. Carson, MD; Brenda J. Grossman, MD, MPH; Steven Kleinman, MD; Alan T. Timmough, MD; Morta B. Marques, MD; Mark K. Fung, MD, PhD; John B. Holcomb, MD; Orija Elish, MD; Lewis J. Kaplan, MD; Louis M. Katz, MD; Sunil V. Rao, MD; John D. Roback, MD, PhD; Aryeh Shander, MD; Aaron A.R. Tobian, MD, PhD; Robert Weinstein, MD; Lisa Grace Swinton McLaughlin, MD; and Benjamin Djulbegovic, MD, PhD, for the Clinical Transfusion Medicine Committee of the AABB


Recommendation 1: The AABB recommends adhering to a restrictive transfusion strategy (7 to 8 g/dL) in hospitalized, stable patients (Grade: strong recommendation; high-quality evidence).

- adult and paediatric for critical care

Recommendation 4: The AABB suggests that transfusion decisions be influenced by symptoms as well as hemoglobin concentration (Grade: weak recommendation; low-quality evidence).
Draft new BCSH guidelines
Red cell thresholds for older children

- **Acute paediatrics/PICU:** 70g/L
  - if symptomatic may consider higher

- **Cardiac Surgery**
  - **On cardiopulmonary bypass**
    - non-cyanotic: 70g/L
    - cyanotic: 90-100 g/L
  - **Post bypass**
    - non-cyanotic: 70 g/L (stable) – 90g/L (less stable)
    - cyanotic: 120 g/L (stable) – 140g/L (less stable)
Platelet transfusion in neonatal thrombocytopenia

- transfusion rates on NICU up to 9%
- varied thresholds, dose, follow-up

- little evidence
  - moderate thrombocytopenia (50-150 \( \times 10^9/\text{l} \)) not detrimental
    - Andrew et al, 1993 RCT
  - unclear < 50 \( \times 10^9/\text{l} \)

- PlaNeT 1 observational study
  - Mean pre-tx platelet count 27 (18, 36) range 2-59

Stanworth et al Pediatrics, 2009
Platelets for Neonatal Transfusion Study 2 (PlaNeT-2) - a randomised controlled trial of platelet transfusion thresholds 25 vs 50 x 10^9/L
New BCSH Guidelines
Neonatal platelets

- Platelet count < 20 - 30 x10⁹/l
  Neonates with no bleeding (NAIT if no bleeding and no family history of ICH: 30 x10⁹/l).

- Platelet count < 50 x10⁹/l
  Neonates with bleeding, current coagulopathy, surgery or exchange transfusion, infants with NAIT if previously affected sibling with ICH

- Platelet count < 100 x10⁹/l
  Neonates with major bleeding or requiring major surgery (e.g. neurosurgery)
FFP in paediatrics

- **Lack of evidence for FFP use**
  - Yang et al Transfusion 2012;52:1673-86

- **Prevention of neonatal IVH?**
  - Northern Neonatal Nursing Initiative Trial Gp Lancet 1996;348:229
  - prophylactic FFP for preterms at birth
  - no prevention of IVH, improved outcome at 2 yrs
FFP National Comparative Audit

Age ranges: 4635 - 16+; 114 - 1-15 yrs; 220 < 1 yr
Main reason for transfusion in Infants (< 1 yr old, n=220)
Neonatal coagulation ranges

- age and gestation related
- ‘INR’ & ‘APTR’ usually based on adult values

<table>
<thead>
<tr>
<th>Test</th>
<th>Post natal age</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Day 1</td>
</tr>
<tr>
<td>PT (secs)</td>
<td>13.0 (10.1-15.9)</td>
</tr>
<tr>
<td>APTT (secs)</td>
<td>42.9 (31.3-54.5)</td>
</tr>
<tr>
<td>Fibrinogen (g/l)</td>
<td>2.83 (1.67-3.99)</td>
</tr>
</tbody>
</table>

Figures for adults and healthy full-term infants during the first month of life

Data from M. Andrews et al, 1988, 1990. All infants had had vitamin k
FFP may be of benefit in neonates with active bleeding/prior to surgery who have abnormal coagulation

- PT or APTT > than 1.5 times the mid-point of the gestational and postnatal age-related reference range (taking into account local reference ranges where available)
- no evidence to support the use of FFP to try to correct abnormalities of the coagulation screen alone

- FFP should not be used for simple volume replacement

- Prophylactic FFP should not be administered to non-bleeding children with minor prolongation of the PT or APTT

THINK CAREFULLY
Prescribing transfusion volume

- mL NOT ‘Units’
- Neonates often 10-20ml/kg
- ‘Transfusion formula’
  - NB new Hb units (g/L – prev g/dL)

\[
\text{Volume to transfuse (mL)} = \frac{\text{Desired Hb (g/L)} - \text{actual Hb (g/L)} \times \text{weight (kg)} \times \text{Factor (4)}}{10}
\]

Eg 10 kg child, Hb 60 g/L, aim Hb 90 g/L

\[
\text{Volume to transfuse} = \frac{90 - 60 \times 10 \times 4}{10} = 120 \text{ mL} \quad \text{(ie 12 mL/kg)}
\]
National comparative audit – transfusion volumes

Neonatal transfusions: Median 18.7 mls/Kg (IQR 15.0-20.0), n=1144
24% (277/1144) >20.0 mls/Kg

Among very-low-birth-weight neonates is red blood cell transfusion an independent risk factor for subsequently developing a severe intraventricular hemorrhage?

Vickie L. Baer, Diane K. Lambert, Erick Henry, Gregory L. Snow, Allison Butler, and Robert D. Christensen

BCSH new recommendation: neonatal top-ups not > 20 ml/Kg to avoid the risk of volume overload
Patient identification

- Mother/baby
- ‘Baby’ Smith
- Twin/twin
- Two sample rule
Maternal sample for infants up to 4 mths

- Sample from both mother and infant for ABO and D compatibility
- Antibody screen on maternal sample
  - levels may be lower in baby
  - larger maternal sample
Neonatal exchange units

Group compatible with mother, neonate
  • antigen negative if maternal antibodies
Hct 0.5-0.6 (NHSBT 0.5-0.55)
< 5 days old
Anticoagulant: CPD
Irradiated, especially if previous IUT
CMV negative
Components

- **SaBTO recommendations re CMV neg**
  - neonates up to 44 weeks corrected gestational age

- **Neonatal / Infant Specification**
  - use up to 6 months

- **MB Cryo**
  - no AB
  - recommend group A alternative
    - note not HT tested
Large volume neonatal transfusion

- Pragmatic component for large vol with neo specification
- Not necessary for labour ward stock
- K+ issue recently highlighted
  - range of supernatant potassium levels
  - recommendation for cardiac perfusionists:
    - check bypass circuit K+ before attaching to patient
- Red book – up to 5th day after bleed date
Intra Uterine Transfusion (IUT)

- Hierarchy of recommended components depending on degree of urgency / component availability
  - Standard
  - ‘Urgent’
  - Emergency / Life-Threatening
## BCSH guidelines ‘Urgent’ IUT

<table>
<thead>
<tr>
<th>Option</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Request urgent irradiated IUT red cells from blood service</td>
<td>• Generally available in 4 hrs (6 hrs outside routine hours) for urgent situations unless there is a maternal antibody that requires sourcing of antigen negative blood.</td>
</tr>
</tbody>
</table>
| 2. Request urgent irradiated exchange red cells from blood service   | • If IUT red cells unavailable or take longer than clinically acceptable exchange units are the recommended alternative  
• **NB** 
  - Hct 0.5-0.55 (NHSBT) ie lower than standard IUT red cells  
  - still in CPD like IUT red cells |

_N.B. If exchange red cells are unavailable (rarely) or take longer than clinically acceptable it is reasonable to request an urgent irradiated paedipack._
Life threatening
- no time to request blood from blood centre
Not to use maternal blood
<table>
<thead>
<tr>
<th>Option</th>
<th>Notes</th>
</tr>
</thead>
</table>
| 1. Order standby irradiated paedipack from blood service when there is a known high-risk procedure | • Hct 0.5-0.7 approx  
• Red cells in SAG-M not CPD |
| 2. Keep non irradiated paedipack near FMU / labour ward | • Not irradiated, therefore is theoretical risk of TAGVHD - parents should be made aware  
• < 5 days old in line with the large volume neonatal transfusion recommendations  
• Non-irradiated doesn’t have automatic 24 hr expiry.  
• Hct approx 0.5-0.7, Red cells are in SAG-M not CPD |
| 3. Use adult flying squad blood | • Not irradiated  
• Not neonatal/infant spec blood (and may not be CMV neg) so not as suitable as a paedipack  
• Not necessarily < 5 days old – could therefore be K+ issues also. |
Optimal neonatal red cell usage:

Example Paedipack allocation algorithm
Check Patient Details and Transfusion Record

Never been transfused

Gestational age <33 w

Allocate and keep 6 packs from one adult donor

Gestational age >33 w

Allocate and keep 3 packs from one adult donor

Previously transfused

Units used or expired

Discuss likely future blood requirements

Tx-dependence unlikely

Allocate and keep 6 packs from one adult donor

Units still available and in date

Tx-dependence likely

Allocate and keep 6 packs from one adult donor

Issue units
Other areas included
- coagulation special situations
- cell salvage
- refusal of transfusion
- major haemorrhage

Haemoglobinopathies: separate BCSH
Acknowledgements

- Guideline writing group
  - Tony Davies – and slides
  - Carol Cantwell
  - Elizabeth Chalmers
  - Ruth Gottstein
  - Sylvia Hennem
  - Andrea Kelleher
  - Sailesh Kumar
  - Sarah Morley
  - Simon Stanworth

- BCSH Transfusion Taskforce
  - Sarah Allford

- Sounding board