Paediatric Transfusion Guidelines

'Tiny Transfusions'
Yorkshire and Humbar RTC meeting

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NHS Blood and Transplant

Guidelines

BCSH

www.bcshguidelines.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**

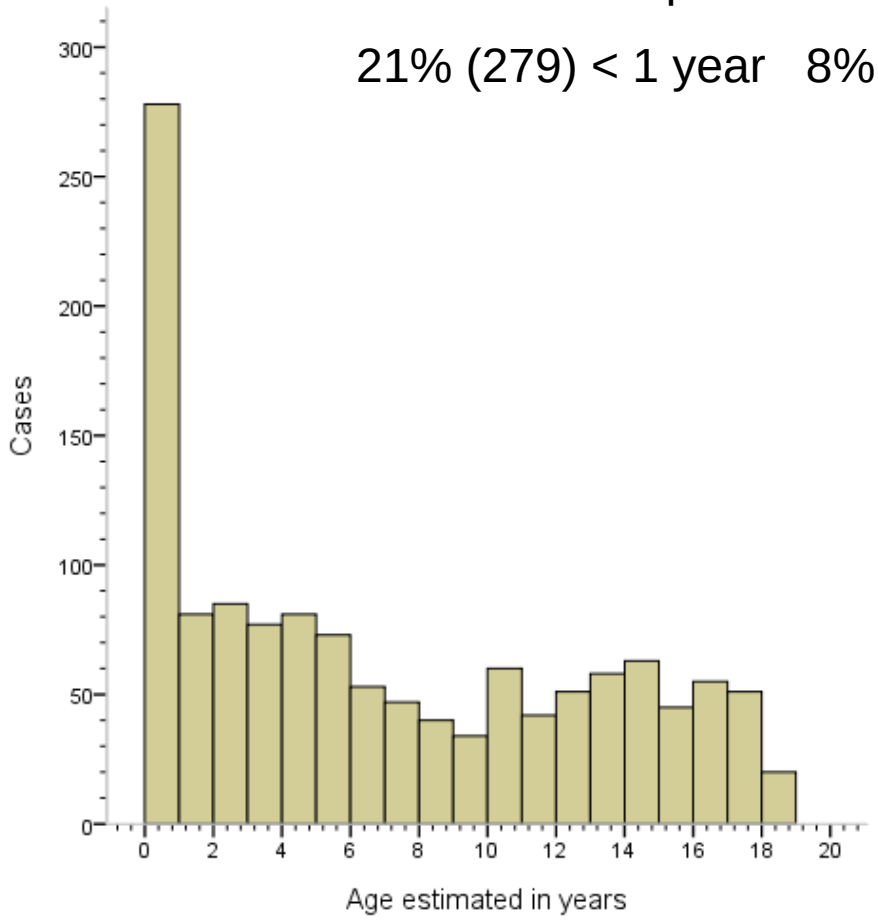
Risks vs benefits

- **Who is transfused?**
- **What are the risks?**
- **What blood is used for children?**
- **How decide when to transfuse?**
- **How to prescribe?**

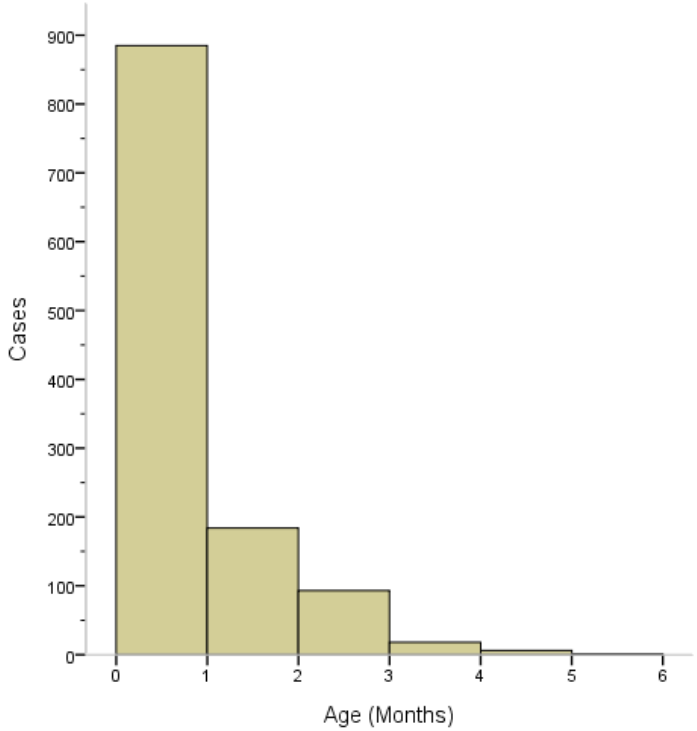
UK National Comparative Audit
Age of paediatric recipients

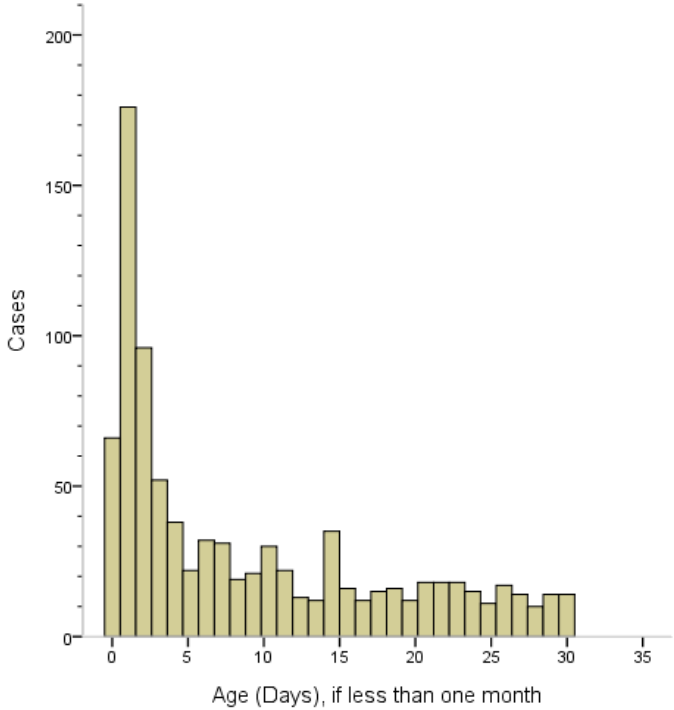
Median (IQR) age estimated at 5 (1-12) years for 1294/1302 patients.

21% (279) < 1 year 8% (102) < 1 month



Age of neonatal recipients

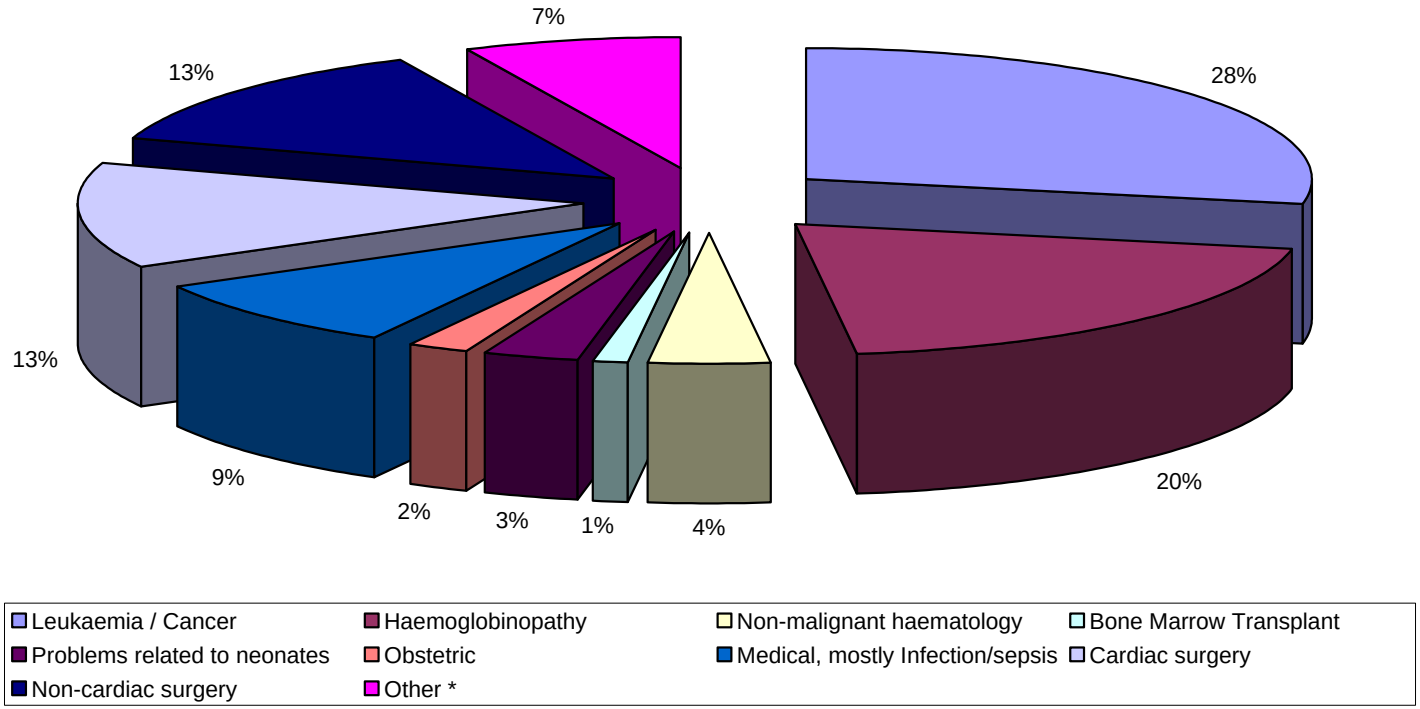




Comparative Audit of the use of Red Cells in Neonates and Children 2010.
http://hospital.blood.co.uk/library/pdf/NCA_red_cells_neonates_children.pdf

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?

Nopoulos et al, Arch Pediatr Adolesc Med. 2011;165:443-450

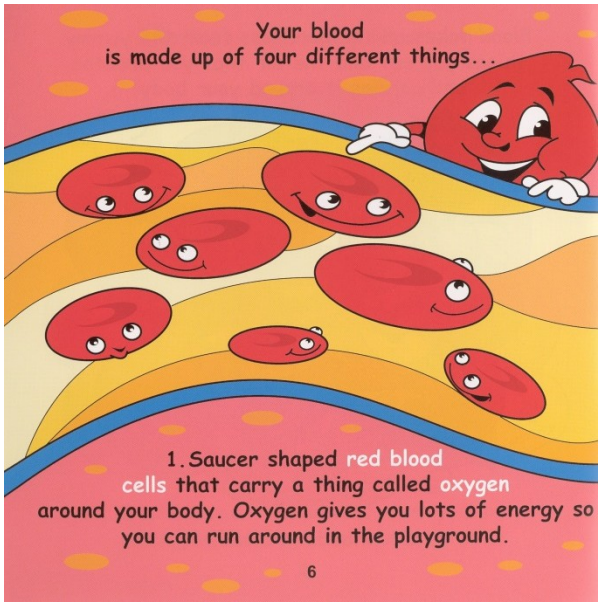
Age of blood?

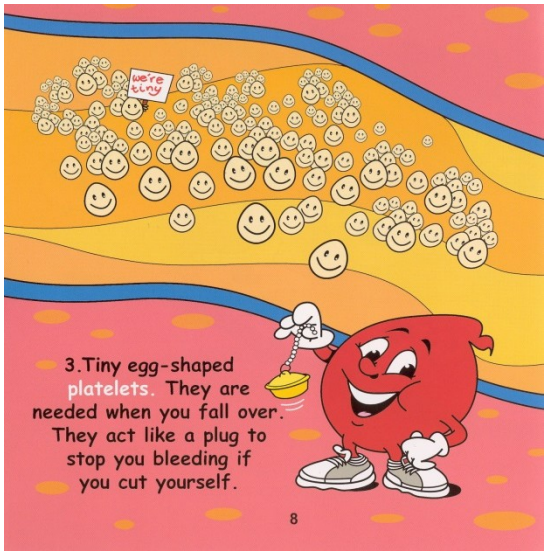
ARIPI trial Fergusson et al JAMA. 2012 10;308:1443-51

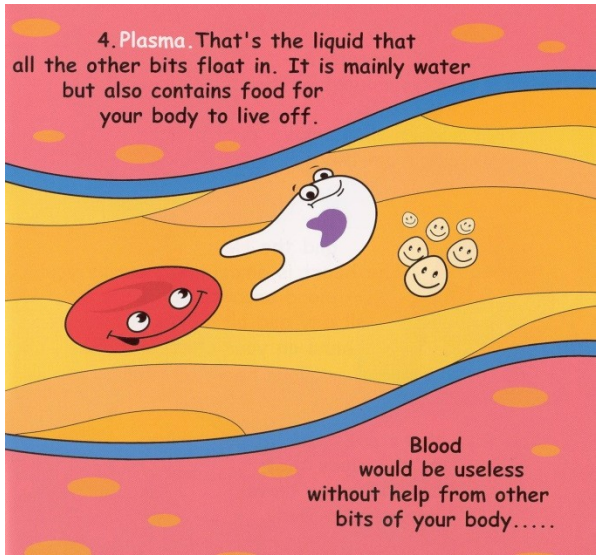
NEC - ?causal association

Haemovigliance: 'SHOT'

Indications for transfusion?







Neonatal Hb levels

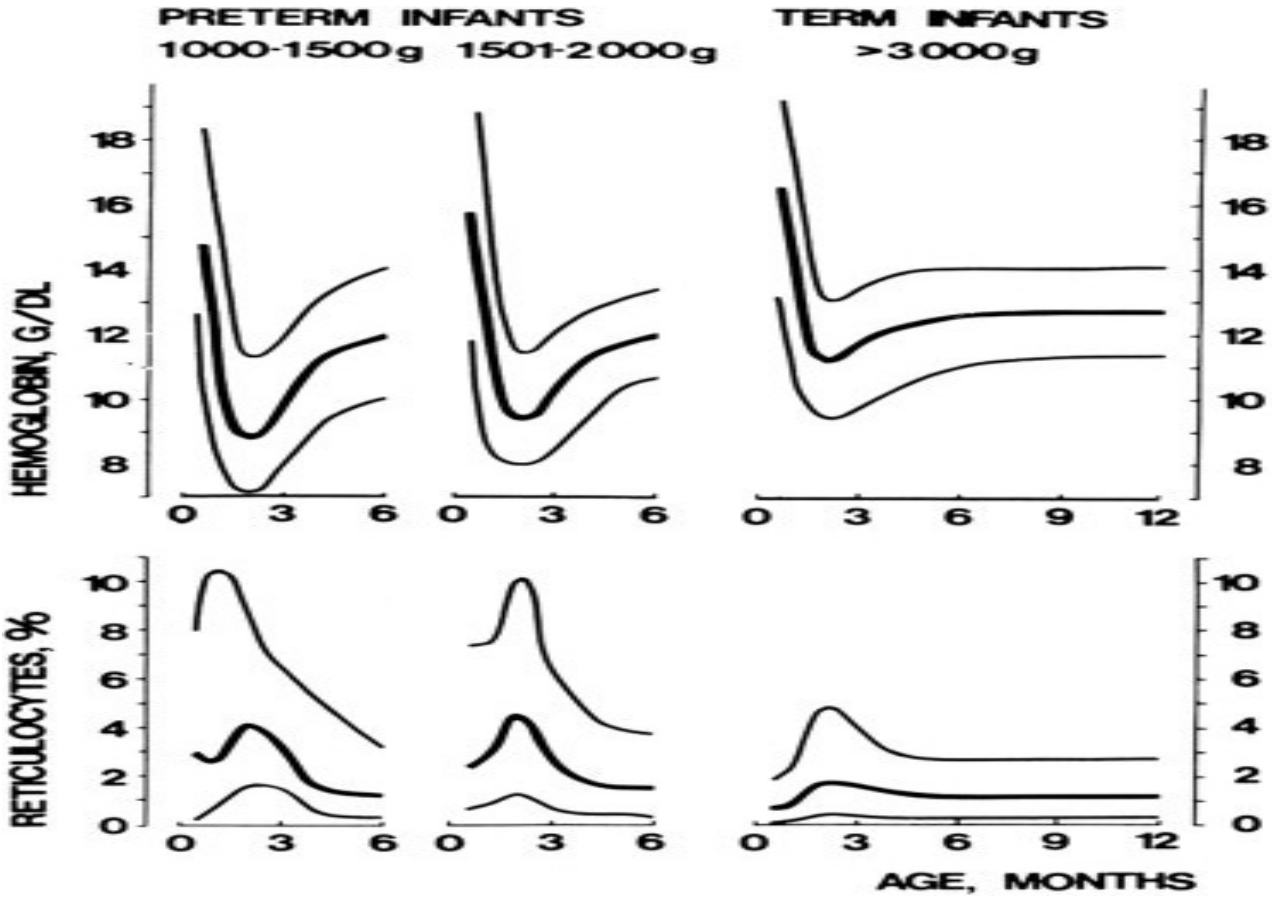


Figure 2 Hemoglobin concentrations and reticulocyte counts in preterm and term infants during the first 6 postnatal months. Median values and 95% confidence limits are indicated for each of 3 birth weight groups: >3000 g, 1501-2000 g, and 1000-1500 g. …

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

Outcomes

	Iowa (n=100)	PINT (n=451)
Mean Hb g/dl	8.3 vs 11.0	10.1 vs 11.2
No transfusion	10% vs 12%	5% vs 11%
Death/brain injury	16% vs 2%	31% vs 31%
Longer term	Approx 12 yr: Brain volumes in liberally transfused smaller than controls	18-21 mth - cognitive delay in restrictive group - post hoc

Whyte et al, Pediatrics 2009
Nopoulos et al, Arch Pedatr Adolesc Med 2011

Low versus high haemoglobin concentration threshold for blood transfusion for preventing morbidity and mortality in very low birth weight infants (Review)

Whyte R, Kirpalani H

Cochrane, 2011

Postnatal Age	Respiratory Support	No Respiratory Support
	Haemoglobin g/ l (Haematocrit %)	
Week 1	115 (35%)	100 (30%)
Week 2	100 (30%)	85 (25%)
Week 3	85 (25%)	75 (23%)

Also: Venkatesh *et al* The safety and efficacy of red cell transfusions in neonates: a systematic review of randomized controlled trials. *B J Haem*, 2012

ELSEVIER

SEMINARS IN PERINATOLOGY

International Survey of Transfusion Practices for Extremely Premature Infants

Úrsula Guillén, MD,* James J. Cummings, MD,† Edward F. Bell, MD,‡
Shigerharu Hosono, MD, PhD,§ Axel R. Frantz, MD,¶ Rolf F. Maier, MD,**
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John A. Widness, MD,‡ and Haresh Kirpalani, BM, MSc¶¶

Semin Perinatol 36:244-247 © 2012

- 1018 neonatologists,
- 11 countries

- scenarios for neonates < 1000g bw and/or < 28 wks gestational age

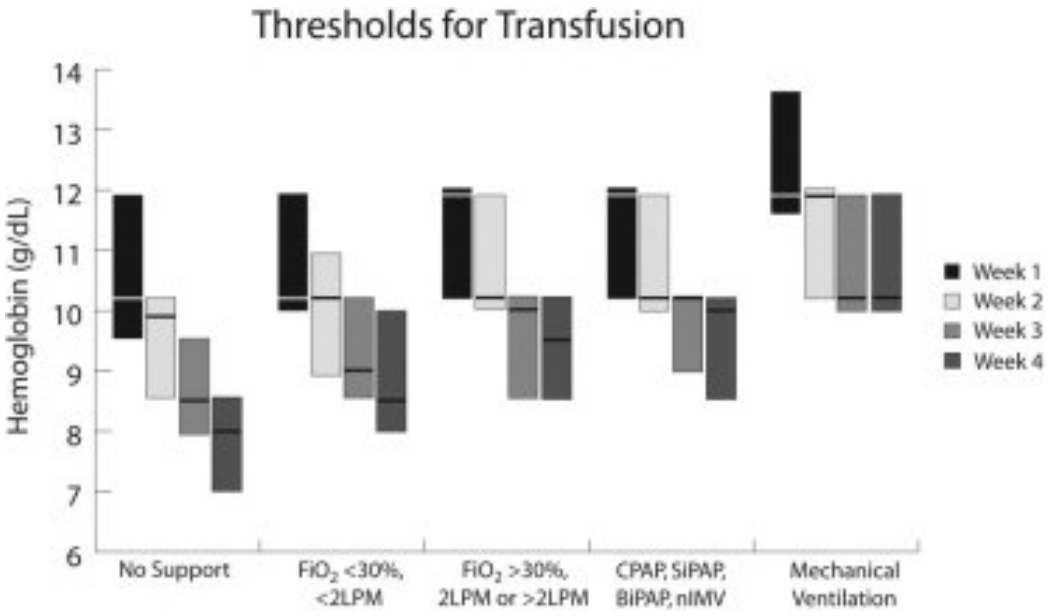


Figure 1 Thresholds for red cell transfusion for infants weighing <1000 g at birth and/or <28-week GA for each of the first 4 weeks of life given 5 different levels of respiratory support. Each box represents the interquartile range (25th-75th percentile). The median value intersects each box.

What do neonatologists do? UK NCA data

Audit findings by postnatal age & respiratory status

	Postnatal age 0-1 days		Postnatal age 2-7 days		Postnatal age 8-28 days		Postnatal age >28 days	
	N	Median (IQR) Hb	N	Median (IQR) Hb	N	Median (IQR) Hb	N	Median (IQR) Hb
• Mechanically ventilated	187/201	11.6 (10.3-12.6)	195/200	10.7 (9.9-11.6)	116/117	9.9 (9.1-10.7)	60/62	9.5 (8.2-10.5)
• On CPAP	17/18	11.2 (9.4-12.2)	54/55	10.3 (9.1-11.0)	148/148	9.3 (8.3-9.9)	86/87	8.4 (7.7-9.8)
• On supplementary O_2	9/9	5.6 (4.8-9.9)	1/1	8.9	33/33	8.4 (7.4-9.4)	85/86	8.0 (7.4-9.0)
ANY OF THE ABOVE	**213/228**	**11.5 (10.2-12.5)**	**250/257**	**10.6 (9.7-11.5)**	**297/298**	**9.5 (8.5-10.2)**	**231/235**	**8.5 (7.6-9.7)**
OFF OXYGEN	9/13	7.9 (5.9-11.1)	9/13	9.5 (7.7-10.6)	**45/45**	**7.6 (7.0-8.5)**	**76/76**	**7.5 (6.9-7.9)**

National Comparative Audit of the use of Red Cells in Neonates and Children 2010.
http://hospital.blood.co.uk/library/pdf/NCA_red_cells_neonates_children.pdf

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

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

Paediatric red cells

- **TRIPICU study 2007**
  - **Restrictive ≤ 7g/dl vs Liberal ≤ 9.5 g/dl**
  - **organ dysfunction scores**
  - **637 stable, critically ill children**
  - **mean age approx 38 mths**
  - **Restrictive: ↓ transfusions, no ↑ adverse outcomes**

- **Cardiac**
  - **Willems et al, TRIPICU 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

Annals of Internal Medicine | CLINICAL GUIDELINE

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. Tinmouth, MD; Marisa B. Marques, MD; Mark K. Fung, MD, PhD; John B. Holcomb, MD; Orieji Illoh, 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

Ann Intern Med. 2012;157:49-58.

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 x 10^9/l) not detrimental**
    - **Andrew et al, 1993 RCT**
  - **unclear < 50 x 10^9/l**

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

Stanworth et al *Pediatrics*, 2009

MRC Medical Research Council

NHS Blood and Transplant

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 $x10^9$/l
  Neonates with no bleeding (NAIT if no bleeding and no family history of ICH: 30 $x10^9$/l).

- Platelet count < 50 $x10^9$/l
  Neonates with bleeding, current coagulopathy, surgery or exchange transfusion, infants with NAIT if previously affected sibling with ICH

- Platelet count < 100 $x10^9$/l Neonates with major bleeding or requiring major surgery (e.g. neurosurgery)

FFP in paediatrics

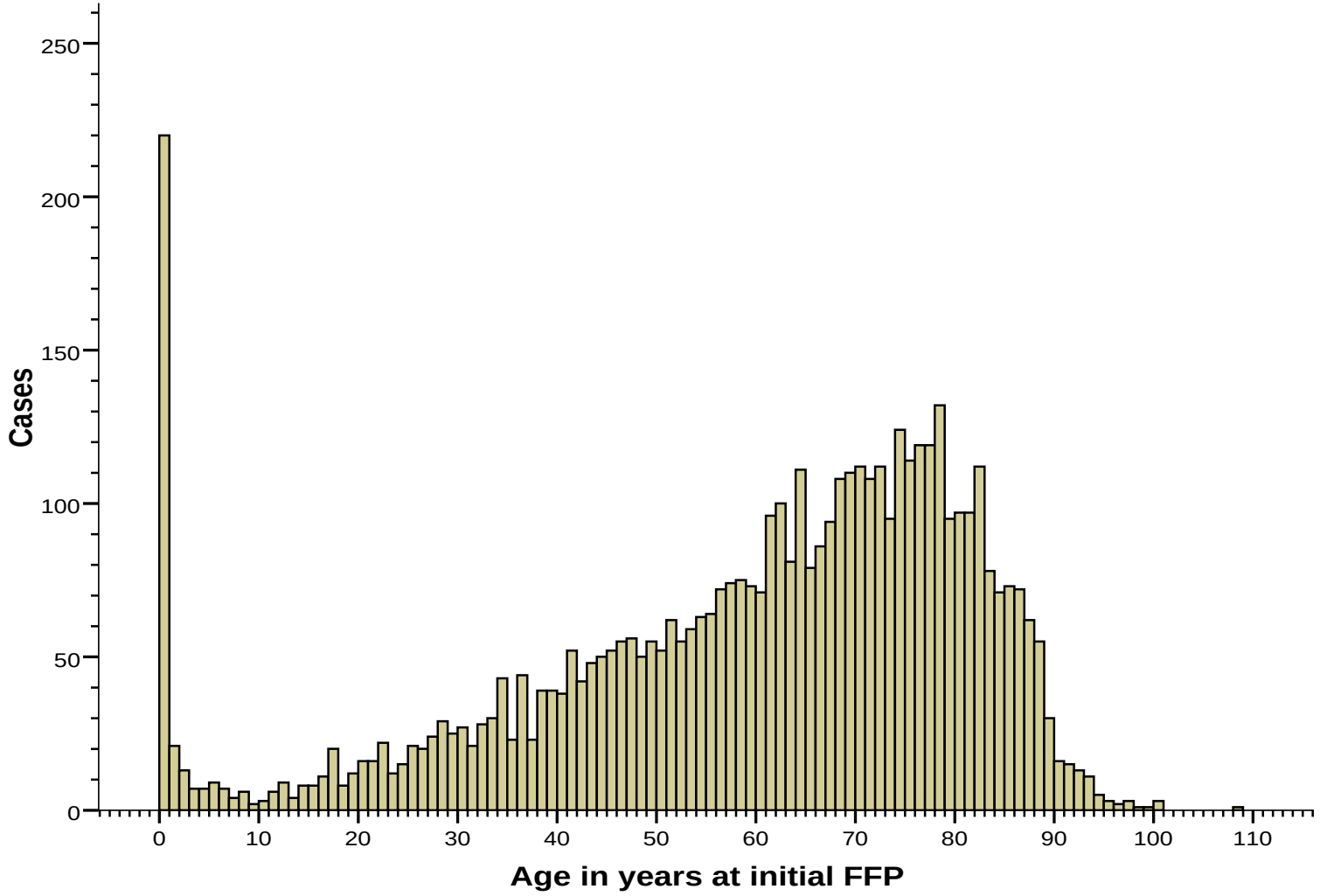
- **Lack of evidence for FFP use**
  - **Yang et al Transfusion 2012;52:1673-86**

- **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**

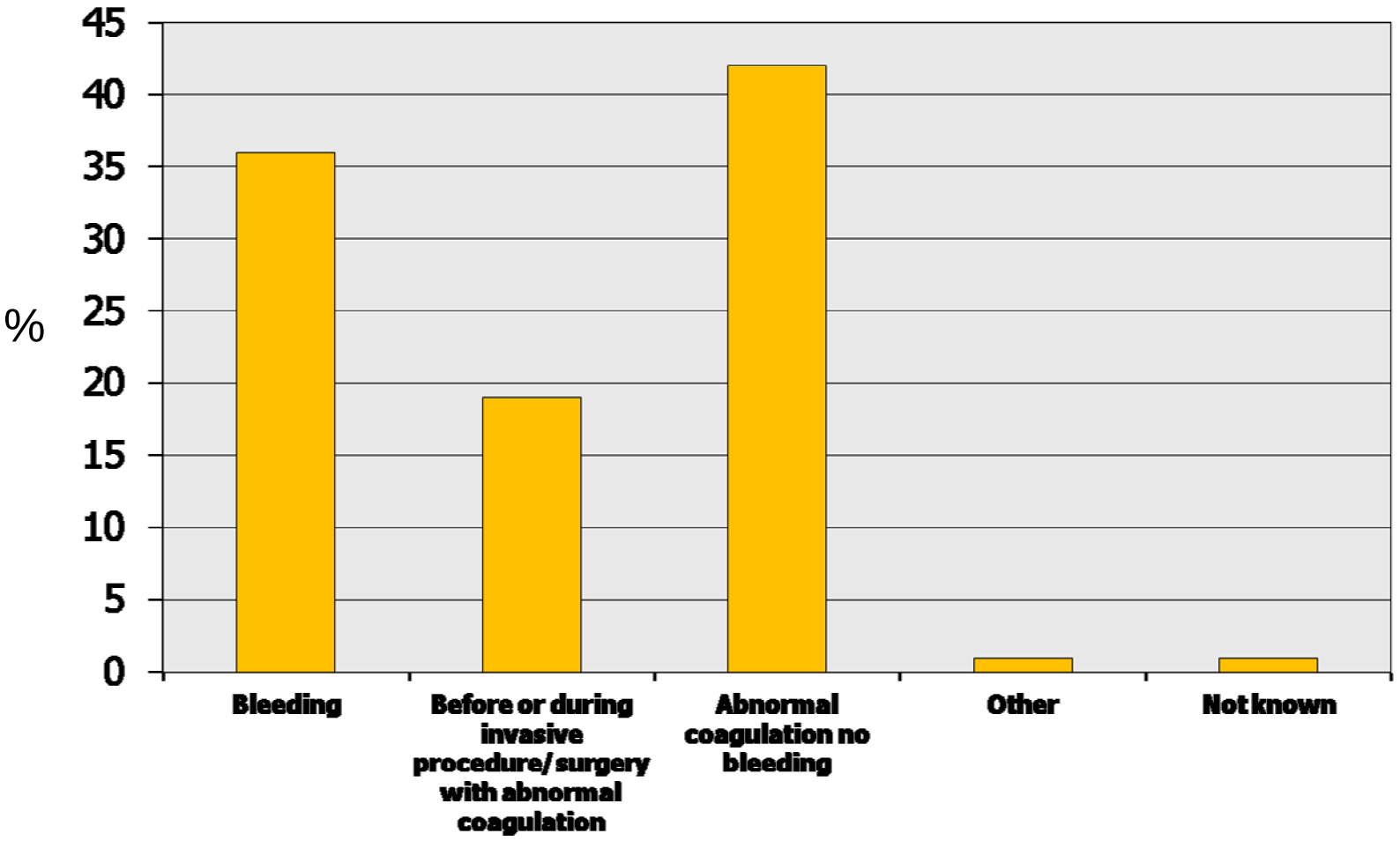
FFP National Comparative Audit

Age ranges: 4635 - 16+; 114 - 1-15 yrs; 220 < 1 yr



FFP National Comparative Audit 2009

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**

		Post natal age		
Test	**Day 1**	**Day 5**	**Day 30**	**Adult**
PT (secs)	13.0 (10.1-15.9)	12.4 (10.0-15.3)	11.8 (10.0-14.3)	12.4 (10.8-13.9)
APTT (secs)	42.9 (31.3-54.5)	42.6 (25.4-59.8)	40.4 (32.0-55.2)	33.5 (26.6-40.3)
Fibrinogen (g/l)	2.83 (1.67-3.99)	3.12 (1.62-4.62)	2.70 (1.62-3.78)	2.78 (1.56-4.00)

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

Draft new BCSH guidelines

- **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

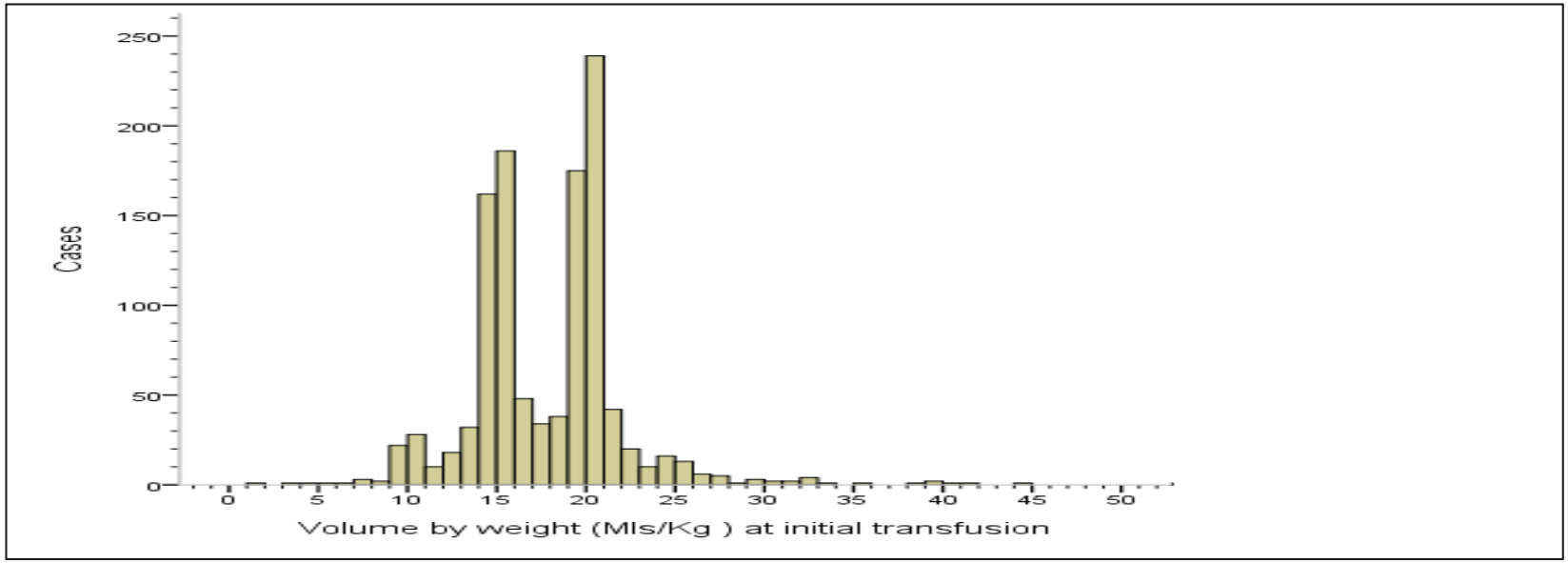
- **mL NOT 'Units'**
- **Neonates often 10-20ml/kg**
- **'Transfusion formula'**
  - **NB new Hb units (g/L – prev g/dL)**

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

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

$$\textit{Volume to transfuse} = \frac{90 - 60 \times 10 \times 4}{10} = 120 \text{ mL} \quad \textit{(ie 12 mL/kg)}$$

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

Option	Notes
1. Request urgent irradiated IUT red cells from blood service	• 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.
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.

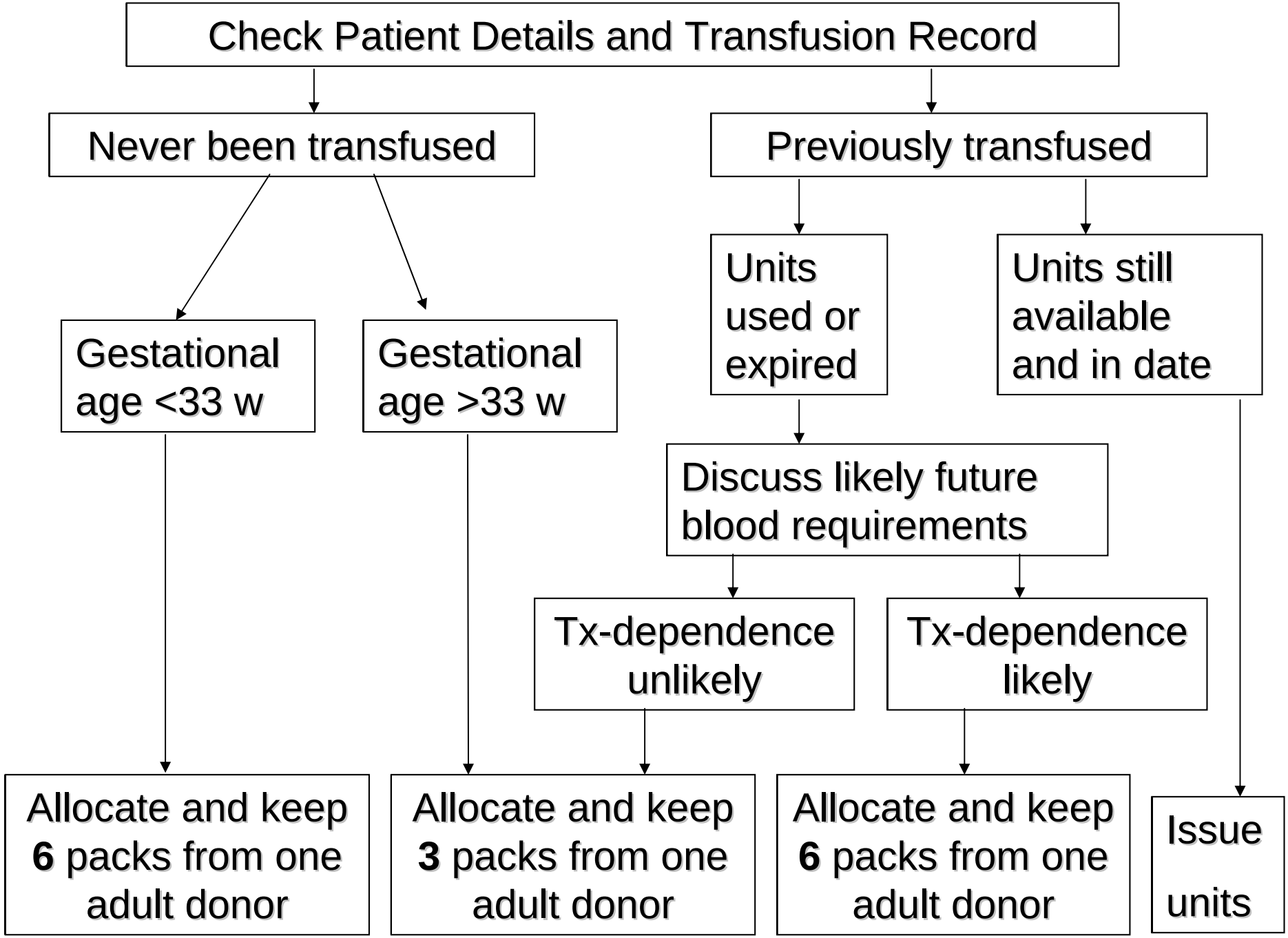
‘Emergency IUT’

- **Life threatening**
  - **no time to request blood from blood centre**
- **Not to use maternal blood**

Option	Notes
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
Previously transfused
Gestational age <33 w
Gestational age >33 w
Units used or expired
Units still available and in date
Discuss likely future blood requirements
Tx-dependence unlikely
Tx-dependence likely
Allocate and keep **6** packs from one adult donor
Allocate and keep **3** packs from one adult donor
Allocate and keep **6** packs from one adult donor
Issue units

Draft guidelines

- **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**