The Nitty Gritty of Neonatal Transfusion

Dr Satyam Arora
Associate Professor, Transfusion Medicine
Post Graduate Institute of Child Health (PGICH),
Noida, UP

Paediatric Transfusion Medicine

- Neonatal and Paediatric recipients are a *Special Group*
  - Immature immune and metabolic process (compared to Adults)
  - Undergoing rapid Neurodevelopment
  - Most Heterogeneous group with special requirements
  - Long life span post-transfusion

- *“Not about transfusing little adults or adjusting little volumes”*

Outline

- General Scenario
- RBC Transfusion
- Platelets Transfusion
- Plasma Transfusion
- Massive Transfusion
- Patient Blood Management in Paediatrics
- Adverse Transfusion Reactions- Hemovigilance

General Scenario

- Physiology
- Body Size/ Volume
- Blood Warming
- CMV Screening
- Compatibility Testing
- Donor Sparing/ Limiting Strategies
- Irradiation

Physiology

- Physiological Anemia (decline of Hb in first week of life)
  - Significant in preterm (rate of decline is function of gestational age)
    - Decreased erythropoietin production
    - Decreased survival of fetal red cells
    - Increase of blood volumes due to rapid growth
- Clotting Factors
  - Low levels of Vit K dependent factors (Factor II, VII, IX & X) and contact factors
  - Naturally occurring procoagulants are also low
- Platelets
  - Altered function in VLBW preterm
- Underdeveloped immune system

AABB 20th Edition

Body Size and Blood Volume

Blood volumes

- Full term newborn – 85 mL/kg
- Preterm – 100 mL/kg

Transfusion

- Volume based (10-15 ml/kg)
- Extra care with therapeutic procedures

Iatrogenic blood loss is not very well tolerated

- >10% of blood volume may lead to hypovolemia and anemia

AABB 20th Edition

Blood Warming

Hypothermia may trigger or exaggerate several responses

- Increased metabolic rate
- Hypoglycemia
- Metabolic acidosis
- Potential apneic events leading to hypoxia, hypotension and arrest

Indication for inline warmers

- Large volume transfusion (Exchange transfusion)

Even during giving phototherapy the tubing should be given minimum exposure to the UV light

CMV screening

- DNA containing herpes virus
- Transmission with blood may cause TA-CMV

Risk Factors for TA-CMV

- Premature infant born to a seronegative mother
- Blood transfusion of more than 50 mL from CMV seropositive donor
- Massive Transfusion

Differentiation is difficult in a scenario where mother is also seropositive

CMV screening

TA-CMV

- Fever, respiratory distress, hepatosplenomegaly
- CMV viremia
- Within 2 months of transfusion

Prevention strategies of TA-CMV

- Screening of donors for CMV status – *Not done in India*
- Leukoreduction
- Pathogen inactivation – *Not yet established*

Compatibility Testing

For Infants less than 4 months

- Only forward grouping (ABO and D typing as antibodies are not formed)
- Blood group confirmation at 5-6 months

Crossmatching or compatibility testing

- Using Maternal samples (Major crossmatch)
- Antibody screening of maternal samples
- Minor crossmatch for FFP and RDP (at some centers)

ABO of the unit issues is based on the

- ABOi between mother and the child
- RH based on the ruling out the Rh incompatibility

Donor Sparing/ limiting strategies

Strategies to minimize the multiple allogenic donor exposure

- Reducing the risk of TTI
- Reduction in risk of alloimmunization
- Reduced risk of immunomodulation
- Optimal utilization of resources
- Less wastage

Donor Sparing strategies

Strategies to minimize the multiple allogenic donor exposure

- Delayed cord clamping
- Small volume transfusions (“Penta bags” Vs “Aliquoting”)
- Use of rEPO
- Autologous donations
- Directed donations (risk of TTI/ TA-GVHD)
- Dedicated donor program (“only PRBC” Vs all components)
- Intraoperative hemodilution

Irradiation

- Primarily used to prevent TA-GVHD

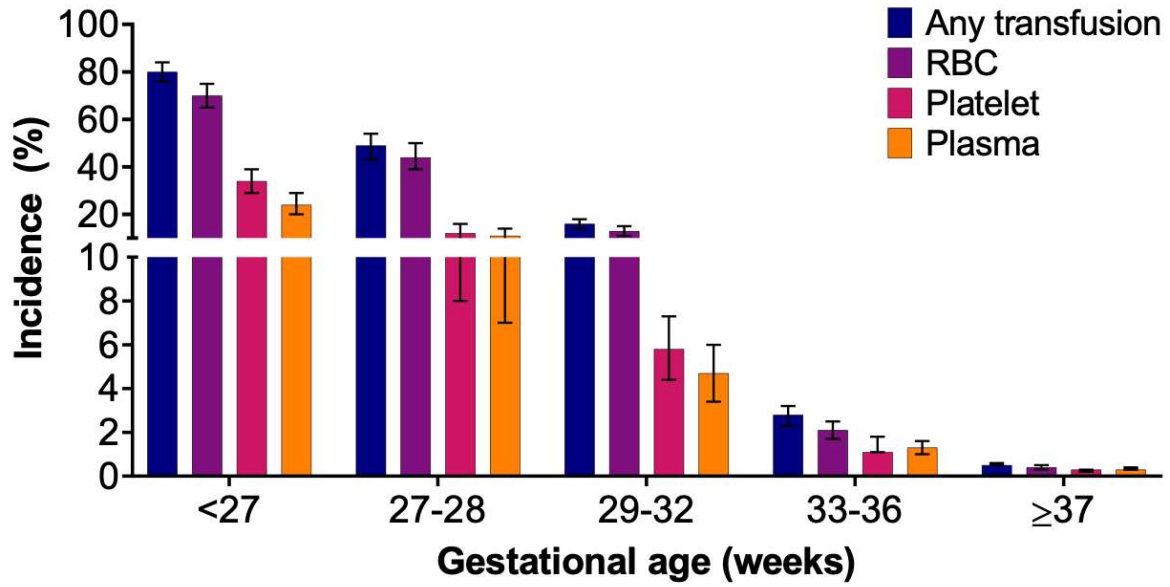
	Patient Group	Indications
Clear	Fetus/ Infant	• Intrauterine Transfusions • Premature infants • Congenital Immunodeficiency • Exchange Transfusion for erythroblastosis
	Child/ Adult	• Congenital Immunodeficiency, Hematopoietic malignancy, Hematopoietic transplant • Recipient of familial blood donation, Recipient of HLA matched components
Potential	• Term infant • Recipient and donor pair from a genetically homogenous population • Malignancy and solid organ tumors	

RBC Transfusion

- Indications
  - Maintain oxygen-carrying capacity
  - Increase red cell mass following significant hemorrhage
  - Chronic Anemia (when primary treatment have failed)
- Neonatal Age group
  - Majorly low birth weight (< 1.5 kg) will receive at least 1 unit
  - Mostly due to phlebotomy losses
- Up to 10-20% of critically ill children (PICU) receive a RBC transfusion
  - RBC transfusion in PICU are associated with 30-day mortality in up to 8% of admissions

Transfusion. 2014;54(2):365-375| J Intensive Care. 2016;4:2

Incidence of transfusion based on Gestational Age



Retrospective cohort study using data from 7 geographically diverse US academic and community hospitals that participated in the National Heart Lung and Blood Institute Recipient Epidemiology and Donor Evaluation Study-III (REDS-III) from 2013 to 2016.

Image source: Ravi M Patel | J Pediatr 2021;235:92-9

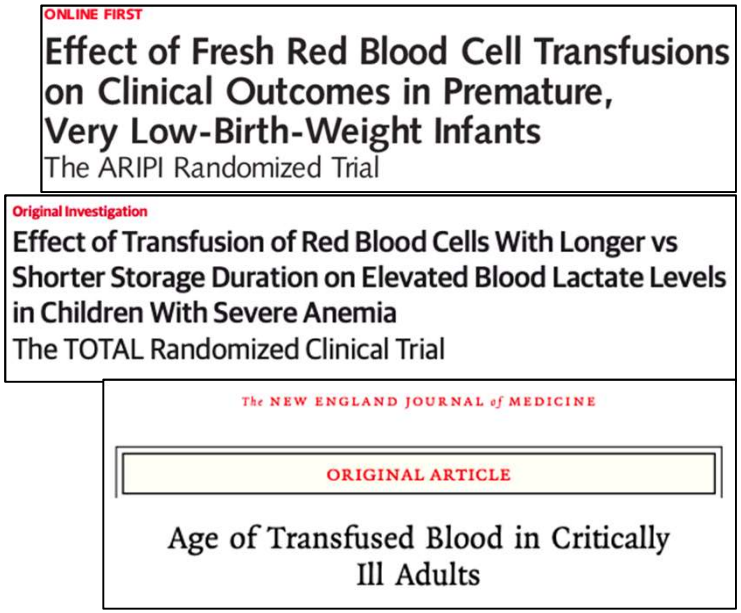
RBC Transfusion

- Fresh vs Old blood
- Use of Additive solution (AS; SAGM)
- Transfusion Thresholds- Liberal vs Restrictive policies
- When to transfuse a neonate ?
- Guidelines for transfusion

RBC Transfusion: Fresh Vs Old (Age of the unit)

- RBCs can be stored up to 42 days
  - Blood centers practice *"first in first out" (FIFO)*
  - In vitro and ex vivo studies suggest increased storage
    - Impair oxygen delivery
    - Affect immune, endothelial, hemostatic systems
- Many RCTs to evaluate the RBC storage
  - Premature Neonates
  - Sv. anemic children with malaria
  - Thalassemia
  - Hospitalized & critically ill adults

None of the above trial shows significant improvement with fresh units


ONLINE FIRST

Effect of Fresh Red Blood Cell Transfusions on Clinical Outcomes in Premature, Very Low-Birth-Weight Infants

The ARIPI Randomized Trial

Original Investigation

Effect of Transfusion of Red Blood Cells With Longer vs Shorter Storage Duration on Elevated Blood Lactate Levels in Children With Severe Anemia

The TOTAL Randomized Clinical Trial

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Age of Transfused Blood in Critically Ill Adults

JAMA. 2012; 308(14):1443-1451| JAMA. 2015;314(23): 2514-2523| N Engl J Med. 2015;372(15):1410-1418.

RBC Transfusion

RBC Transfusion: Fresh Vs Old (Age of the unit)

ONLINE FIRST

Effect of Fresh Red Blood Cell Transfusions on Clinical Outcomes in Premature, Very Low-Birth-Weight Infants

The ARIPI Randomized Trial

Limitation

- Standard-issue RBC was majorly < 14d

Objective To determine if RBCs stored for 7 days or less compared with usual standards decreased rates of major nosocomial infection and organ dysfunction in neonatal intensive care unit patients requiring at least 1 RBC transfusion.

Design, Setting, and Participants Double-blind, randomized controlled trial in 377 premature infants with birth weights less than 1250 g admitted to 6 Canadian tertiary neonatal intensive care units between May 2006 and June 2011.

Intervention Patients were randomly assigned to receive transfusion of RBCs stored 7 days or less (n=188) vs standard-issue RBCs in accordance with standard blood bank practice (n=189).

Main Outcome Measures The primary outcome was a composite measure of major neonatal morbidities, including necrotizing enterocolitis, retinopathy of prematurity, bronchopulmonary dysplasia, and intraventricular hemorrhage, as well as death. The primary outcome was measured within the entire period of neonatal intensive care unit stay up to 90 days after randomization. The rate of nosocomial infection was a secondary outcome.

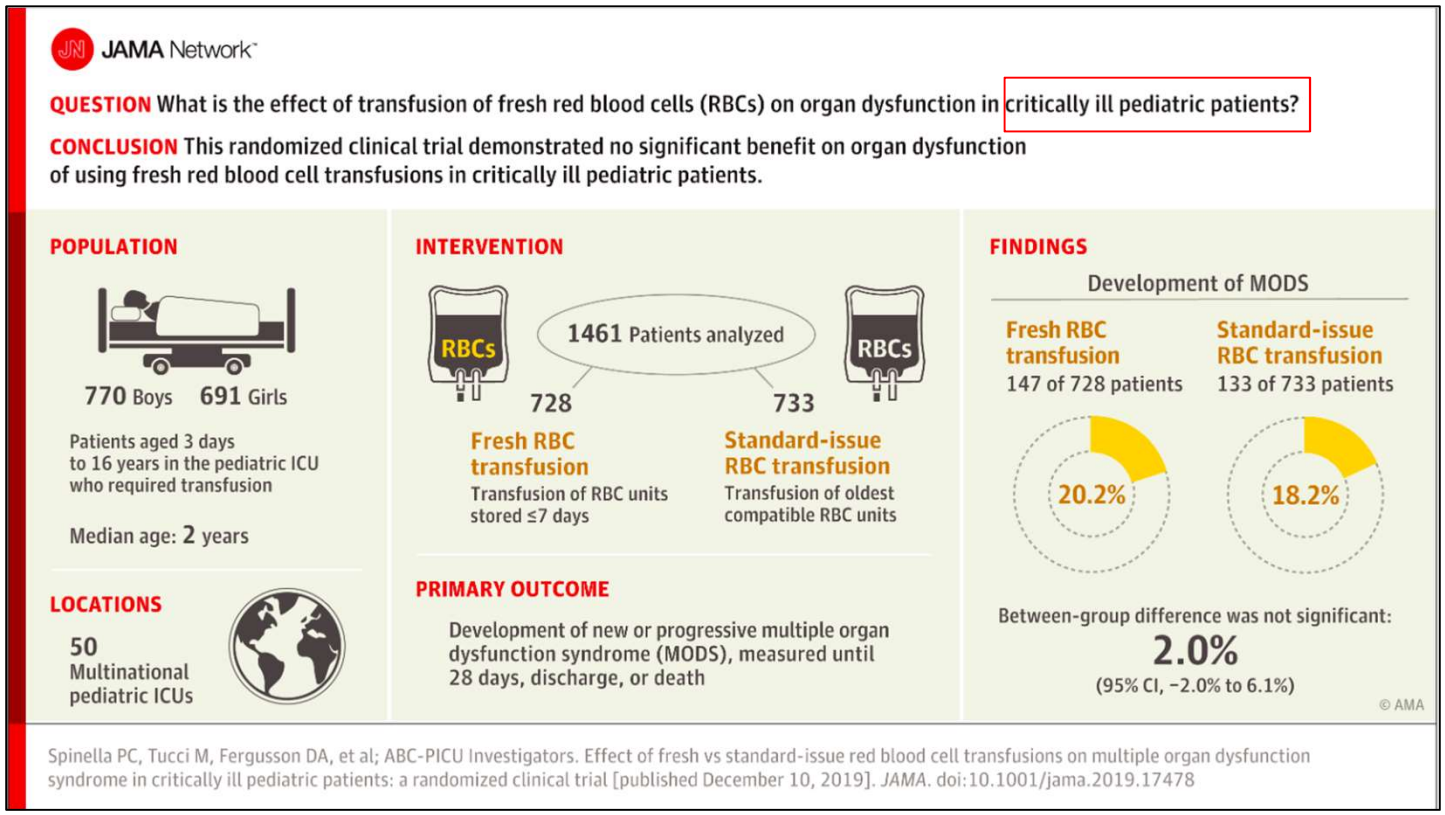
Results The mean age of transfused blood was 5.1 (SD, 2.0) days in the fresh RBC group and 14.6 (SD, 8.3) days in the standard group. Among neonates in the fresh RBC group, 99 (52.7%) had the primary outcome compared with 100 (52.9%) in the standard RBC group (relative risk, 1.00; 95% CI, 0.82-1.21). The rate of clinically suspected infection in the fresh RBC group was 77.7% (n=146) compared with 77.2% (n=146) in the standard RBC group (relative risk, 1.01; 95% CI, 0.90-1.12), and the rate of positive cultures was 67.5% (n=127) in the fresh RBC group compared with 64.0% (n=121) in the standard RBC group (relative risk, 1.06; 95% CI, 0.91-1.22).

Conclusion In this trial, the use of fresh RBCs compared with standard blood bank practice did not improve outcomes in premature, very low-birth-weight infants requiring a transfusion.

JAMA. 2012; 308(14):1443-1451|.

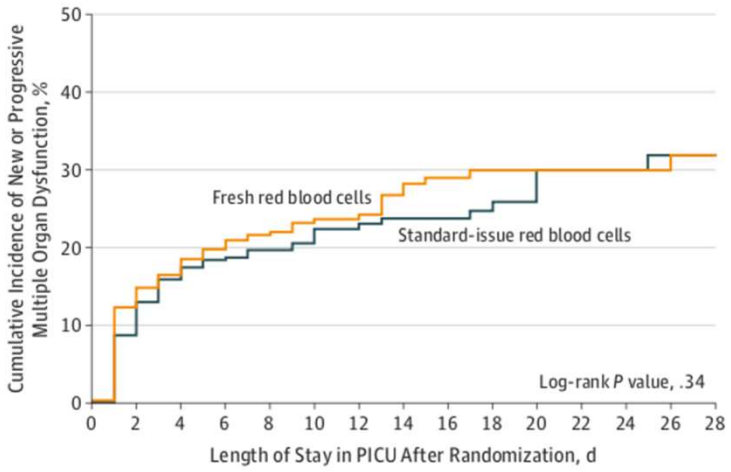
RBC Transfusion

RBC Transfusion: Fresh Vs Old (Age of the unit)



RBC Transfusion: Fresh Vs Old (Age of the unit)

Figure 2. Kaplan-Meier Analysis of Time to Development of New or Progressive Multiple Organ Dysfunction Syndrome



The primary analysis set of patients included 1460 patients. The hazard ratio in the fresh-blood group compared with the standard-issue group, was 1.12 (95% CI, 0.88 to 1.44; *P* = .34). For a definition of new and progressive multiple organ dysfunction syndrome and how it is categorized for this study, see the Methods section. PICU indicates pediatric intensive care unit. The median observation time until new or progressive multiple organ dysfunction was 5.0 days (95% CI, 2.0-10.0 days) in each study group.

- Median day of storage
  - 5d Vs 18d
- No significant diff in
  - Multiorgan dysfunction
  - Prevalence of sepsis
  - Prevalence of Acute respiratory distress syndrome
  - ICU mortality
- Limitations
  - Heterogeneity in cases
  - Multiple transfusions of diff age of PRBC
  - Day 35 to Day 42 not represented

RBC Transfusion: Potassium

- Not significant levels in 42 days stored unit
  - 2 ml supernatant plasma will deliver 0.1 mmol/L
  - Transfused at 10 ml/Kg
  - Amount of potassium infused will be less than the daily requirement of 2-3 mmol/L for patient weight 1 Kg.

- Some special scenarios
  - Post irradiation (washing is more than 24 hours)

RBC Transfusion: Additive Solutions

- Used to improve the shelf life of the RBC units
- Potential toxic effects *(majorly theoretical)* to neonates from some additives
  - Adenine (renal toxicity)
  - Mannitol (renal and neurological toxicity)
- Many studies have shown that use of AS-suspended PRBCs for *"Top up Transfusions"* does not result in toxic levels of additives in recipients
- Avoid during "Massive Transfusions"
  - Intra-Uterine Transfusions
  - Double Volume Exchange Transfusions
  - ECMO
- Variable practices of removing AS for conditions requiring massive transfusions

Transfusion 1991; **31**:229–235

RBC Transfusion

RBC Transfusion: Additive Solutions

ORIGINAL RESEARCH

In premature infants there is no decrease in 24-hour posttransfusion allogeneic red blood cell recovery after 42 days of storage

Demet Nalbant,[1] José A. Cancelas,[2] Donald M. Mock,[3] Svetlana V. Kyosseva,[3] Robert L. Schmidt,[1] Gretchen A. Cress,[1] M. Bridget Zimmerman,[4] Ronald G. Strauss,[1] and John A. Widness[1]

This conclusion supports the practice of transfusing RBCs *stored up to 42 days for small-volume neonatal* transfusions to limit donor exposure.

BACKGROUND: Critically ill preterm very-low-birthweight (VLBW) neonates (birthweight ≤ 1.5 kg) frequently develop anemia that is treated with red blood cell (RBC) transfusions. Although RBCs transfused to adults demonstrate progressive decreases in posttransfusion 24-hour RBC recovery (PTR_{24}) during storage—to a mean of approximately 85% of the Food and Drug Administration—allowed 42-day storage—limited data in infants indicate no decrease in PTR_{24} with storage.

STUDY DESIGN AND METHODS: We hypothesized that PTR_{24} of allogeneic RBCs transfused to anemic VLBW newborns: 1) will be greater than PTR_{24} of autologous RBCs transfused into healthy adults and 2) will not decrease with increasing storage duration. RBCs were stored at 4°C for not more than 42 days in AS-3 or AS-5. PTR_{24} was determined in 46 VLBW neonates using biotin-labeled RBCs and in 76 healthy adults using ^{51}Cr-labeled RBCs. Linear mixed-model analysis was used to estimate slopes and intercepts of PTR_{24} versus duration of RBC storage.

RESULTS: For VLBW newborns, the estimated slope of PTR_{24} versus storage did not decrease with the duration of storage ($p = 0.18$) while for adults it did ($p < 0.0001$). These estimated slopes differed significantly in adults compared to newborns ($p = 0.04$). At the allowed 42-day storage limit, projected mean neonatal PTR_{24} was 95.9%; for adults, it was 83.8% ($p = 0.0002$).

CONCLUSIONS: These data provide evidence that storage duration of allogeneic RBCs intended for neonates can be increased without affecting PTR_{24}. This conclusion supports the practice of transfusing RBCs stored up to 42 days for small-volume neonatal transfusions to limit donor exposure.

TRANSFUSION 2018 Feb;58(2):352-358

RBC transfusions: Thresholds

- Advantage of RBC Transfusion
  - Replacement of acute blood loss
  - Replacement of blood loss due to phlebotomy
  - In preterm
    - Prevention of apnoeas
    - Promotion of weight gain
- Threshold
  - No consensus
- Many RCT compared *"Restrictive" vs "Liberal" threshold policy* for transfusion but **NO** significant difference both on long term and short term outcomes

RBC Transfusion: When to Transfuse ?

- Threshold for Transfusion in Preterm Newborns

Postnatal Age	Suggested transfusion threshold Hb (g/L)		
	Ventilated	On Oxygen/ NIPPV	Off Oxygen
First 24 h	< 120	< 120	< 100
≤ Week 1 (d1-7)	< 120	< 100	< 100
Week 2 (d8-14)	< 100	< 95	< 75
≥ Week 3 (d15 onwards)	< 100	< 85	< 75

- Based on studies supporting restrictive transfusion thresholds
- Transfusion Volume 15 ml/kg for non bleeding neonates
- EPO is not recommended for preterm infants to reduce transfusions

British Journal of Haematology, 2016, 175, 784–828

RBC Transfusion

Threshold to Transfuse a Neonate

No Consensus in Guidelines

Clinical Status	BCSH Guideline	American Red Cross practice Guideline	Australian National Blood Authority Guideline	Canadian Blood Services Guideline
Anaemia in first 24 h	Hb <12 g/dl	-	No resp support- Hb 10-12 g/dl Resp support- Hb 11-13 g/dl	On ECMO and congenital cyanotic disease;Hb<15 g/dl
Intensive care Sv. Cardiopulmonary disease (FiO2>0.35)	Hb <12 g/dl	Hct 40-45%	Hb 11-13 g/dl	Hb < 12 g/dl
Chronic O2 dependency with Mod. Cardio pulmonary disease	Hb <11 g/dl	Hct 30-35%	Hb 8.5-11 g/dl	Hb < 10 g/dl
Late Anaemia, stable patient	Hb <7 g/dl	Hct 20-25%	Hb 7-10 g/dl	Hb < 7 g/dl

Neonatology 2018;114:7–16

Trial	Restrictive threshold	Liberal Threshold
Blank et al (1984)	Transfusion according to indication	Transfuse if Hb < 100 g/L
Ransome et al (1989)	Hb < 70 g/L or symptomatic	Transfuse if Hb < 100 g/L
Brooks et al (1999)	Transfusion according to indication	Transfuse if Hb < 133 g/L
Connelly et al (1998)	1st post natal wk 110 g/l; 2nd wk FiO2>40%, 110 g/L:FiO2<40%, 90 g/L; 3rd wk 80 g/L	1st post natal wk 130 g/l; 2nd wk FiO2>40%, 130 g/L:FiO2<40%, 100 g/L; 3rd wk 80 g/L
Mukhopadhyay et al (2004)	Hb ≤ 100 g/L or Hct ≤ 30%	Hb ≤ 133 g/L or Hct ≤ 40%
Bell et al (2005) *"Iowa Trial"*	Intubated:113g/L; CPAP: 93g/L; NRS: 67 g/L	Intubated: 153g/L; CPAP: 127g/; NPS: 73g/L
Kriplani et al (2006) *"PINT-study"*	*For infants requiring respiratory support:* Post-natal week 1: 115 g/L; Week 2: 100 g/L Week 3 till discharge: 85 g/L *For infants not requiring respiratory support:* Postnatal week 1: 100 g/L; Week 2: 85 g/L Week 3 till discharge: 75 g/L	*For infants requiring respiratory support:* Post-natal week 1: 135 g/L; Week 2: 120 g/L Week 3 till discharge: 100 g/L *For infants not requiring respiratory support:* Postnatal week 1: 120 g/L; Week 2: 100 g/L Week 3 till discharge: 85 g/L
Chen et al (2009)	Intubated: 116 g/L; CPAP:100 g/L,NRS:73 g/L	Intubated: 150g/L; CPAP: 133g/L, NRS: 100g/L

CPAP, continuous positive airway pressure; Hb, haemoglobin; Hct, haematocrit; RBC, red blood cell. a When capillary rather than central bloods were sampled the thresholds were 4% higher; NPS: No respiratory support

Hemoglobin levels as transfusion trigger

Table 1 Randomised trials published before 2020 comparing higher and lower haemoglobin transfusion thresholds for preterm infants

	Iowa trial[5]		PINT trial[6]		Taiwan trial[20]	
Transfusion threshold group	**Higher**	**Lower**	**Higher**	**Lower**	**Higher**	**Lower**
Highest haemoglobin threshold,* g/dL	15.3	11.3	13.5	11.5	15.0	11.7
Lowest haemoglobin threshold, g/dL	10.0	7.3	8.5	7.5	10.0	7.3
No of subjects	51	49	228	223	17	19
Mean gestational age, weeks	28	28	26	26	29	29
Mean haemoglobin,† g/dL	11.0	8.3	11.2	10.1	10.3	10.4
Mean no of transfusions	5.2	3.3‡	5.7	4.9	3.8	2.5
Mean no of RBC donor exposures	2.8	2.2	2.6	2.1‡	–	–
Infants never transfused, %	12	10	5	11‡	–	–
Died, %	2	4	18	19	6	11

*Thresholds varied with postnatal age and/or respiratory support; haematocrit thresholds converted to haemoglobin levels by dividing by 3.
†Mean haemoglobin levels at age 6 weeks in Iowa trial, at age 4 weeks in PINT trial and at day 30 in Taiwan trial.
‡Statistically significant difference, higher vs lower, $p<0.05$.

Arch Dis Child Fetal Neonatal Ed 2022;107:F126–F130

Outcome of “Iowa” and “PINT trials”

- Early outcomes of the Iowa and PINT trials
  - Found no clear difference between lower and higher Hb transfusion thresholds except; *“few transfusion in Iowa Trial and more apnea”*
  - Both the trials indicated towards

“Iowa trial” showed: • More sv cranial USG abnormalities (lower Hb group) but • Paradoxically Smaller brain volume and poorer performance on certain neurocognitive tests (higher Hb group) • Possibility of neurological effects from maintaining the Hb at different levels
“PINT trial” showed • Significant increase in the OR of the cognitive delay at 18 months (lower Hb group)

Arch Dis Child Fetal Neonatal Ed 2022;107:F126–F130

Need for further analysis and study

- In view of lacking evidence for
  - Appropriate transfusion thresholds for ELBW infants
  - Impact of early Hb levels (higher vs lower) on brain development

RBC Transfusion

Hypothesis

ELBW (<1000g) are high risk of transfusion due risk of anemia:

- Immaturity
- Impaired Erythropoiesis
- Frequent samplings

Two groups receiving Transfusion at different thresholds

- Lower Hb
- Higher Hb

TOP Trial
ETTNO Trial

Threshold for transfusion

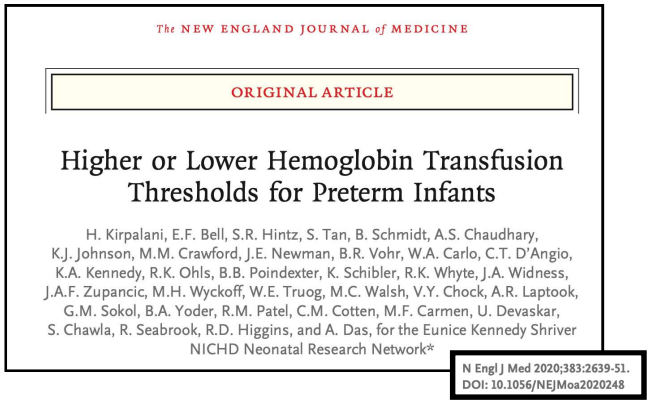
Effects of transfusion on Neuro Cognitive Development

Study Group → **Intervention** → **Trials** → **Outcome**

RBC Transfusion

Studies and Authors

TOP Trial



The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Higher or Lower Hemoglobin Transfusion Thresholds for Preterm Infants

H. Kirpalani, E.F. Bell, S.R. Hintz, S. Tan, B. Schmidt, A.S. Chaudhary, K.J. Johnson, M.M. Crawford, J.E. Newman, B.R. Vohr, W.A. Carlo, C.T. D'Angio, K.A. Kennedy, R.K. Ohls, B.B. Poindexter, K. Schibler, R.K. Whyte, J.A. Widness, J.A.F. Zupancic, M.H. Wyckoff, W.E. Truog, M.C. Walsh, V.Y. Chock, A.R. Laptook, G.M. Sokol, B.A. Yoder, R.M. Patel, C.M. Cotten, M.F. Carmen, U. Devaskar, S. Chawla, R. Seabrook, R.D. Higgins, and A. Das, for the Eunice Kennedy Shriver NICHD Neonatal Research Network*

N Engl J Med 2020;383:2639-51.
DOI: 10.1056/NEJMoa2020248

ETTNO Trial

Research

JAMA | Original Investigation

Effects of Liberal vs Restrictive Transfusion Thresholds on Survival and Neurocognitive Outcomes in Extremely Low-Birth-Weight Infants
The ETTNO Randomized Clinical Trial

Axel R. Franz, MD; Corinna Engel, PhD; Dirk Bassler, MD; Mario Rüdiger, MD; Ulrich H. Thome, MD; Rolf F. Maier, MD; Ingeborg Krägeloh-Mann, MD; Martina Kron, PhD; Jochen Essers, MD; Christoph Bührer, MD; Georg Rellensmann, MD; Rainer Rossi, MD; Hans-Jörg Bittrich, MD; Claudia Roll, MD; Thomas Höhn, MD; Harald Ehrhardt, MD; Stefan Avenarius, MD; Hans Thorsten Körner, MD; Anja Stein, MD; Horst Buxmann, MD; Matthias Vochem, MD; Christian F. Poets, MD; for the ETTNO Investigators

JAMA August 11, 2020 Volume 324, Number 6

Study/ Trial Design

	European group	American group
	Multi-centric, outcome assessor-blinded, parallel group randomised superiority trial (36 centers)	Open, Multi-centric, Randomised Controlled Trial (41 NICUs)
	Randomisation: 14th July 2011-14th Nov 2014 Follow up: 24 months	Randomisation: 31st Dec 2012-12th April 2017 Follow up: 3rd Feb 2020
	Written informed consent was obtained from parent or legal guardian	Written informed consent was obtained from parent or legal guardian

Arch Dis Child Fetal Neonatal Ed 2022;107:F126–F130

Methodology

Parameter	ETTNO Trial	TOP Trial
Inclusion Criteria	• Infants BW 400gm-999gm • Gestational age <29 wks 6 days	• Infants BW <1000gm • Gestational Age: 22wks - 28wk6d • Postnatal age =/<48 hours
Exclusion Criteria	• Lack of viability; or comfort care. • Major anomalies (eg, chromosomal anomalies, cyanotic heart defects, • Syndromes affecting long- term outcome) or malformations requiring surgical correction during the neonatal period; • For multiple pregnancies, only the eligible neonate who was delivered first was enrolled	• Considered to be nonviable, • Cyanotic congenital heart disease, • Parents refused to blood transfusion, • Parents with hemoglobinopathy or congenital anemia, • Received a transfusion in utero, • Twin-to-twin transfusion syndrome or isoimmune hemolytic disease, or • Received a previous red-cell transfusion after the first 6 hours of life
Randomisation	• Within 72 hours after birth, infants were randomly assigned to 1 of 2 parallel treatment groups. • Randomization was stratified by center and birth weight (400-750 g and 750 to 1000 g).	• Randomly assigned in a 1:1 ratio to the higher- or lower-threshold group • Randomisation was stratified according to birth weight (<750 g or 750 to 1000 g)

RBC Transfusion

Methodology

<table>
<tr><th>Parameter</th><th>ETTNO Trial</th><th>TOP Trial</th></tr>
<tr><td>Intervention</td><td>
• Algorithm based transfusion protocol
• Hemoglobin transfusion thresholds in both groups
  • Postnatal age and
  • Respiratory support
• A dose of 20 mL/kg of standard whole blood–derived, leukocyte-depleted erythrocyte concentrate was administered
• <u>Administration of erythropoietin was prohibited.</u>
• Standardization of delayed cord clamping/umbilical cord milking, and
• Iron, protein, vitamin B, and folic acid supplementation were recommended as described in the study protocol
</td><td>
• Algorithm based transfusion protocol
• Hemoglobin transfusion thresholds in both groups
  • Postnatal age and
  • Respiratory support
• The transfusion volume was 15 ml/kg of body weight.
• All transfusions received by the infants were from ABO-compatible and Rh- compatible donors.
• <u>Administration of erythropoietin was prohibited.</u>
<table>
<tr><th>Age</th><th colspan="2">High Threshold</th><th colspan="2">Low Threshold</th></tr>
<tr><td>Week of life</td><td>Resp. Support</td><td>No Support</td><td>Resp. Support</td><td>No Support</td></tr>
<tr><td>1</td><td>13.0</td><td>12.0</td><td>11.0</td><td>10.0</td></tr>
<tr><td>2</td><td>12.5</td><td>11.0</td><td>10.0</td><td>8.5</td></tr>
<tr><td>≥ 3</td><td>11.0</td><td>10.0</td><td>8.5</td><td>7.0</td></tr>
<tr><td colspan="5">Hemoglobin (g/dL)</td></tr>
</table>
</td></tr>
</table>

Methodology

Table 2 Haemoglobin transfusion thresholds and primary outcome for ETTNO and TOP trials

Study	ETTNO trial[24]				TOP trial[25]			
Transfusion threshold group	Higher		Lower		Higher		Lower	
Severity stratum	Critical	Non-critical	Critical	Non-critical	Respiratory support	No respiratory support	Respiratory support	No respiratory support
Haemoglobin threshold,* g/dL								
Week 1	13.7	11.7	11.3	9.3	13.0	12.0	11.0	10.0
Weeks 2–3 (ETTNO) or 2 (TOP)	12.3	10.3	10.0	8.0	12.5	11.0	10.0	8.5
Week >3 (ETTNO) or ≥3 (TOP)	11.3	9.3	9.0	7.0	11.0	10.0	8.5	7.0
Primary outcome	Neurodevelopmental impairment† at 2 years' corrected age or death before assessment				Neurodevelopmental impairment‡ at 2 years' corrected age or death before assessment			

Arch Dis Child Fetal Neonatal Ed 2022;107:F126–F130

Methodology

Parameter	ETTNO Trial	TOP Trial

Outcome	• **Primary Outcomes**
	  • Death or
	  • Neurodevelopmental impairment by 23 to 25 months of corrected age.
		• **Primary Outcomes**
		  • Death or
		  • Neurodevelopmental impairment in infants at 22 to 26 months of age, corrected for prematurity.

Methodology

Parameter	ETTNO Trial	TOP Trial

Outcome	• **Secondary Outcomes** (24 months of age)
	• Incidence of cognitive deficit (defined as an MDI score < 70), the MDI score, & PDI score.
	  • Measures of growth at discharge and follow-up, length of hospital stay, and
	  • Intervals from birth to final discontinuation of positive pressure respiratory support, respiratory stimulant (methylxanthine) therapy, and gavage feeding.
	  • Incidence of all major complications of prematurity (ie, bronchopulmonary dysplasia, retinopathy of prematurity, necrotizing enterocolitis, intestinal perforation, brain injury on cranial ultrasound, patent ductus arteriosus requiring therapy, and nosocomial infections)
		• **Secondary Outcomes** (22 to 26 mth of age)
		  • Neurodevelopmental impairment and its four components, and more detailed analyses of the composite cognitive, language, and motor scores on the Bayley Scales.
		  • Survival to initial hospital discharge without severe complications.
		  • Grade 3 or 4 intraventricular hemorrhage,
		  • Cystic periventricular leukomalacia,
		  • Stage 3 or greater retinopathy of prematurity
		  • Bronchopulmonary dysplasia
		  • Stage 2 or 3 necrotizing enterocolitis

Arch Dis Child Fetal Neonatal Ed 2022;107:F126–F130

Results

Table 3 Primary and main secondary outcomes in ETTNO and TOP trials

	n=1013		n=1692	
	ETTNO trial[24]		TOP trial[25]	
Transfusion threshold group	**Higher**	**Lower**	**Higher**	**Lower**
No of subjects randomised	492	521	911	913
Mean gestational age, weeks	26	26	26	26
Primary outcome, % – OR[24] or adjusted relative risk[25] (95% CI)	44.4 1.05 (0.80 to 1.39)	42.9	50.1 1.00 (0.92 to 1.10)	49.8
Death, % – OR[24] or adjusted relative risk[25] (95% CI)	8.3 0.91 (0.58 to 1.45)	9.0	16.2 1.07 (0.87 to 1.32)	15.0
Neurodevelomental impairment, % – OR[24] or adjusted relative risk[25] (95% CI)	37.6 1.12 (0.83 to 1.51)	35.9	39.6 1.00 (0.88 to 1.13)	40.3

Results

- Rarely two large, well-designed trials are published on similar topic showing identical results and conclusive following results
  - No additional advantage of using higher threshold for transfusion
  - No neurodevelopmental impairment in using lesser threshold

TABLE 82.1 Red Blood Cell Transfusion Thresholds for Preterm Infants in Randomized Trials[a]

		Iowa Trial (Bell et al., 2005)	PINT Trial (Kirpalani et al., 2006)	TOP Trial	ETTNO Trial
Liberal	Upper	15.3	13.5	13.0	13.7
	Lower	10.0	8.5	10.0	9.3
Restrictive	Upper	11.3	11.5	11.0	11.3
	Lower	7.3	7.5	7.0	7.0

Patel and Josephson. Neonatal Transfusion. Avery's Disease of Newborn. 10th ed

Results

Donors Exposure

- An advantage to using lower haemoglobin thresholds is
  - Reduction in the number of transfusions given to infants.

Table 3 Primary and main secondary outcomes in ETTNO and TOP trials

	ETTNO trial[24]		TOP trial[25]	
Transfusion threshold group	**Higher**	**Lower**	**Higher**	**Lower**
Mean no of transfusions	2.6	1.7†	6.2	4.4‡

- ETTNO Trial: 2.9 versus 1.7 (higher and lower threshold groups)
- TOP Trial: 6.2 versus 4.4 (higher and lower threshold groups)

Arch Dis Child Fetal Neonatal Ed 2022;107:F126–F130

Results

Transfusion Episodes

- Both the ETTNO and TOP trials found
  - More infants were never transfused in their lower threshold groups, but

Table 3 Primary and main secondary outcomes in ETTNO and TOP trials

	ETTNO trial[24]		TOP trial[25]	
Transfusion threshold group	**Higher**	**Lower**	**Higher**	**Lower**
Infants never transfused, %	21	40‡	3	12‡

- Overall, far more infants were able to avoid transfusion in the ETTNO trial
- No of patients never transfused in Higher and Lower threshold groups
  - ETTNO trial: 21% and 40%
  - TOP trial: 3% and 11%

Mean birth wt was similar in both trials (~750gm) still *why more transfusion in US group?*

Arch Dis Child Fetal Neonatal Ed 2022;107:F126–F130

Results

Transfusion Episodes

- This difference may be explained by an interesting observation/ differences in umbilical cord management at birth at both the regions:

Table 3 Primary and main secondary outcomes in ETTNO and TOP trials

	ETTNO trial[24]		TOP trial[25]	
Transfusion threshold group	**Higher**	**Lower**	**Higher**	**Lower**
Infants with delayed cord clamping or cord milking, %	63	61	27	24

- Delayed cord clamping at birth in both higher and lower threshold groups
  - ETTNO trial: 63% and 61%
  - TOP trial: 27% and 24%
- The numbers did not differ btw transfusion threshold groups in either trial

Arch Dis Child Fetal Neonatal Ed 2022;107:F126–F130

Results

Necrotising Enterocolitis (NEC)

- It is important to note that despite more frequent transfusions in the higher haemoglobin threshold groups in these trials, *No difference in the rates of necrotising enterocolitis (NEC).*

Table 3 Primary and main secondary outcomes in ETTNO and TOP trials

	ETTNO trial[24]		TOP trial[25]	
Transfusion threshold group	**Higher**	**Lower**	**Higher**	**Lower**
Necrotising enterocolitis§, %	5.3	6.2	10.0	10.5

- ETTNO Trial: Similar in the higher (5.3%) & lower (6.2%) threshold groups,
- TOP trial: Higher but equal between groups,10.0% and 10.5%

Arch Dis Child Fetal Neonatal Ed 2022;107:F126–F130

Results

Necrotising Enterocolitis (NEC)

- NEC not more frequent in more transfusions groups:
  - Transfusion thresholds, even in the lower threshold groups, were not low enough to precipitate the gut ischemia–reperfusion responses postulated by Patel *et al*

- It must be acknowledged, however, that neither trial was specifically powered to examine the impact of transfusion thresholds on the risk of NEC.

Patel et al *JAMA* 2016;315:889–97

Results

Other Secondary Adverse reactions

- There were also no differences between the higher and lower threshold groups in either study in

Table 3 Primary and main secondary outcomes in ETTNO and TOP trials

	ETTNO trial[24]		TOP trial[25]	
Transfusion threshold group	**Higher**	**Lower**	**Higher**	**Lower**
Patent ductus arteriosus§, %	41.5	37.8	44.5	47.8
Retinopathy of prematurity§, grade ≥3, %	15.9	13.0	19.7	17.2
Severe intraventricular haemorrhage or periventricular leucomalacia§¶	No significant difference		No significant difference	
Bronchopulmonary dysplasia**	28.4	26.0	59.0	56.3

- Rates of patent ductus arteriosus,
- Severe retinopathy of prematurity,
- Severe intraventricular haemorrhage or periventricular leucomalacia, or bronchopulmonary dysplasia

Arch Dis Child Fetal Neonatal Ed 2022;107:F126–F130

Results

Other Secondary Adverse reactions

- The mortality rates were higher in the TOP trial, suggesting that the subjects in this trial may have been sicker.

- Consequently, there may also have been differences in phlebotomy losses between the ETTNO and TOP trials, although phlebotomy losses were not reported for either trial.

- Erythropoiesis-stimulating agents were not allowed in either trial.

Arch Dis Child Fetal Neonatal Ed 2022;107:F126–F130

Discussion

Limitations

RCT may not be able rule out

- Advantage that may be with thresholds higher than discussed in the study,
- Advantage in brain development may not be apparent at 2 years but might be evident later
- Confounding factors: blood bank practices and age of the units used

Discussion

- Risk of doing at **higher thresholds**
  - Increase the risk of hyperviscosity after transfusion,
    - Compromise blood flow and oxygen delivery to the brain and other organs.
  - Adverse effects on brain size and neurocognitive function were found at school age [small cohort analysis of Iowa Trial (15.3 g/dl for ventilated infants)]

Arch Pediatr Adolesc Med 2011;165:443–50| Child Neuropsychology 2011;17:347–67| *JAMA* 2016;315:889–97

Discussion

- Risk of doing at **lower thresholds**
  - Risk tissue hypoxia in the brain
  - Increased risk of transfusion-associated NEC

Arch Pediatr Adolesc Med 2011;165:443–50| Child Neuropsychology 2011;17:347–67| *JAMA* 2016;315:889–97

Conclusion

- In both the **ETTNO and TOP trials**,
  - There was no difference in the rates of death between both the transfusion threshold groups,
  - No significant neurodevelopmental impairment at 2 years in both groups
- Unless information to the contrary emerges from the school-age examinations of the TOP trial infants, practitioners should be comfortable using transfusion thresholds within the ranges used in the ETTNO and TOP trials.

Conclusion

The haemoglobin transfusion thresholds

Parameter for Infants in the first week of life	Higher Threshold	Lower Threshold
Critically ill or require significant respiratory support	13g/ dL	11g/ dL
Stable, older infants who are not critically ill or require significant respiratory support	10g/ dL	7g/ dL

- Using the lower thresholds, 11g/dL for critically ill infants and 7g/dL for stable infants,
  - Reduce transfusions and donor exposure,
  - Reducing transfusion-associated risks.
  - Conserving blood

Arch Dis Child Fetal Neonatal Ed 2022;107:F126–F130

Platelets Transfusion

- Neonates
  - Indications
  - Threshold for transfusion in Neonates
  - Studies evaluating the threshold in Neonates
  - NAIT
  - Prophylactic platelets Transfusions
- Platelets Additive Solutions
- Pathogen Reduction

Platelets Transfusion: Neonates

- Indications
  - Thrombocytopenia
  - Thrombocytopathy - Abnormal Function
- Neonates admitted to NICU
  - 22% - 35% receive at least one transfusion
  - Incidence of thrombocytopenia is inversely proportional to gestational age (70% in neonates born less than 1000gms)
- 70% of pediatric transfusion recipients are long-term survivors and at risk for late transfusion-related adverse events.

J Pediatr 1987;110:457–64| J Perinatol 2006;26:348–53| Transfus Med 2016;26:111-7

Neonatal Platelets Transfusion- Threshold

Platelet Count	Clinical Situation to trigger transfusion
< 25 x10^3/L	Neonates with no bleeding (including neonates with NAIT if no bleeding and no family history of ICH)
<50 x10^3/L	Neonates with bleeding, current coagulopathy, before surgery, or infants with NAIT if previously affected sibling with ICH
<100 x10^3/L	Neonates with major bleeding or requiring major surgery (e.g. neurosurgery)

British Journal of Haematology, 2016, 175, 784–828

Neonatal Platelets Transfusions- Trigger

- Only platelet transfusion trigger trial in preterm infants (27 years ago)
- This trial assessed the effects of prophylactic platelet transfusions in
  - 152 (VLBW; <1.5 kg at birth) infants
  - Platelet counts 50-150 × 10^9/L in the first week of life,
  - Found that the incidence and severity of intraventricular hemorrhage (IVH) were no different when the platelet count was
    - *Maintained greater than 150 × 10^9/L vs allowed to fall to less than 60 × 10^9/L before transfusion (28% vs 26%, respectively)*

A randomized, controlled trial of platelet transfusions in thrombocytopenic premature infants

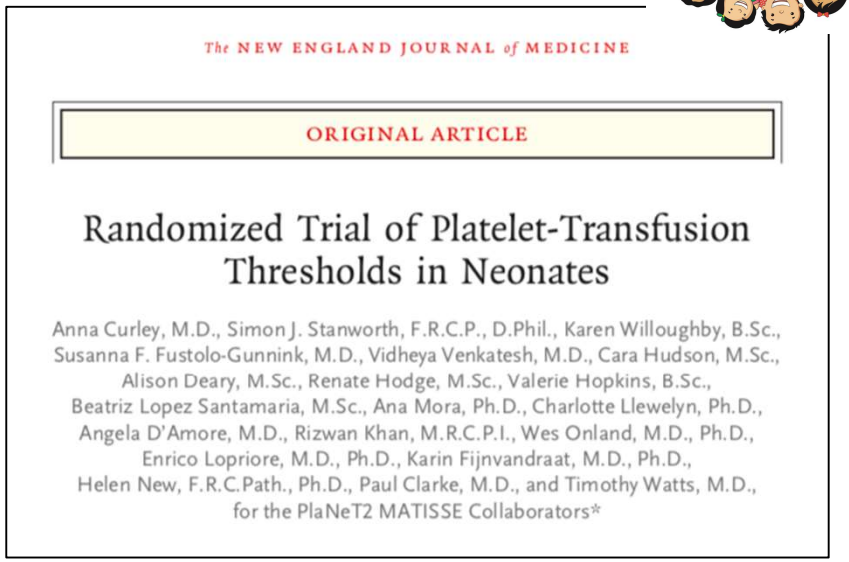
M. Andrew, MD, FRCPC, P. Vegh, C. Caco, MD, FRCPC, H. Kirpalani, MB, MRCP, A. Jefferies, MD, FRCPC, A. Ohlsson, MD, FRCPC, J. Watts, MB, BS, FRCP, FRCPC, S. Saigal, MD, FRCPC, R. Milner, MIS, and E. Wang, MD, FRCPC

From the Departments of Pediatrics, Pathology, Radiology, and Clinical Epidemiology and Biostatistics, McMaster University, Hamilton, Hospital for Sick Children, Toronto, Women's College Hospital, Toronto, and Mount Sinai Hospital, Toronto, Ontario, Canada

J PEDIATR1993;123:285-91

Neonatal Platelets Transfusion: Threshold

- Inclusion Criteria
  - Gestational age < 34 weeks
  - Platelets count < 50 x 10^9 /L
  - Cranial USG - No ICH (within 6 Hr)
- Exclusion Criteria
  - Congenital malformations
  - Maj Bleed in 72 hours
  - Fetal ICH
  - Immune thrombocytopenia
  - No parenteral Vit K
- Randomization
  - Low Threshold group - platelets count less than 25,000
  - High Threshold group - platelets count less than 50,000



The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Randomized Trial of Platelet-Transfusion Thresholds in Neonates

Anna Curley, M.D., Simon J. Stanworth, F.R.C.P., D.Phil., Karen Willoughby, B.Sc., Susanna F. Fustolo-Gunnink, M.D., Vidheya Venkatesh, M.D., Cara Hudson, M.Sc., Alison Deary, M.Sc., Renate Hodge, M.Sc., Valerie Hopkins, B.Sc., Beatriz Lopez Santamaria, M.Sc., Ana Mora, Ph.D., Charlotte Llewelyn, Ph.D., Angela D'Amore, M.D., Rizwan Khan, M.R.C.P.I., Wes Onland, M.D., Ph.D., Enrico Lopriore, M.D., Ph.D., Karin Fijnvandraat, M.D., Ph.D., Helen New, F.R.C.Path., Ph.D., Paul Clarke, M.D., and Timothy Watts, M.D., for the PlaNeT2 MATISSE Collaborators*

N Engl J Med 2019; 380:242-251

Platelets Transfusion

Neonatal Platelets Transfusion

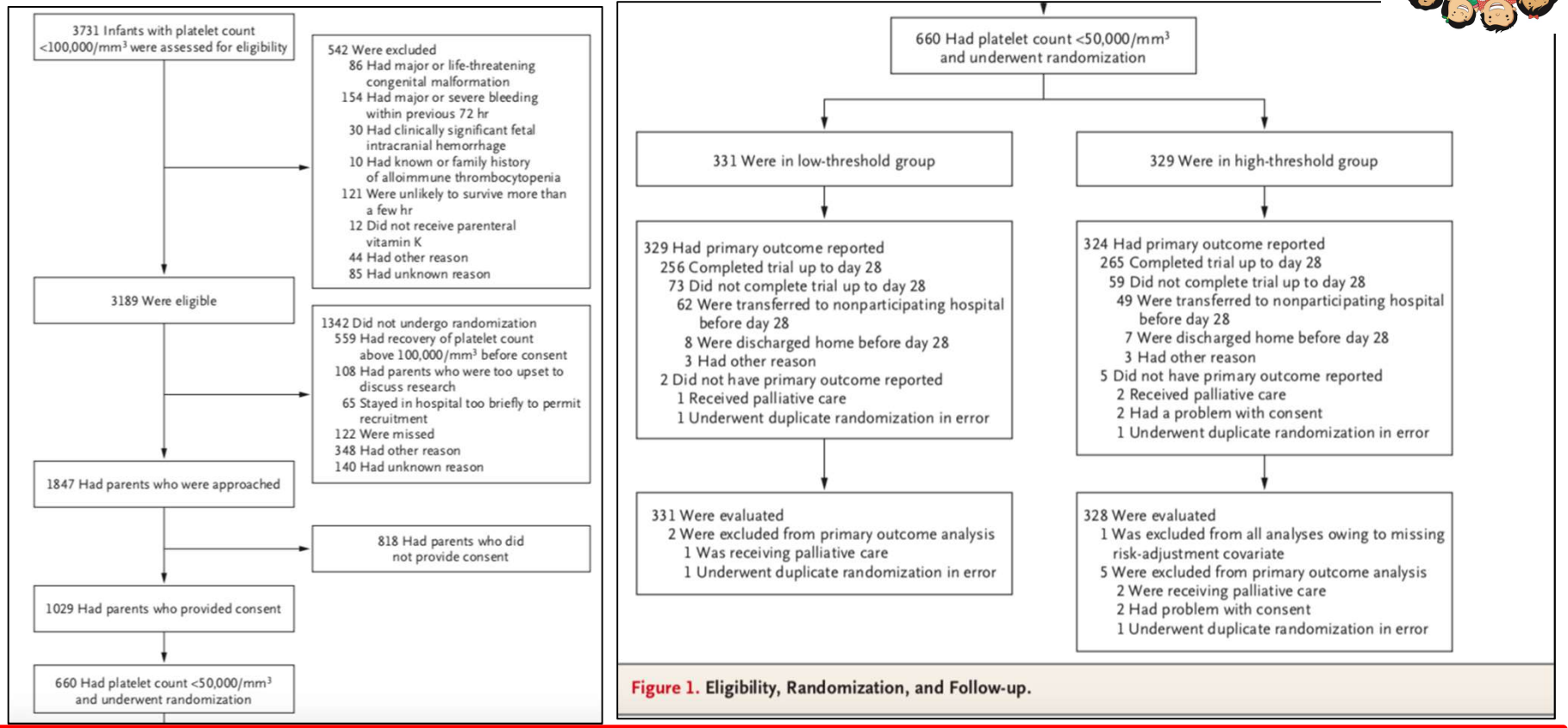


Figure 1. Eligibility, Randomization, and Follow-up.

Neonatal Platelets Transfusion: Threshold

- This large, multicenter, randomized trial involving preterm infants showed
  - *More deaths, major bleeding, or both occurred when a threshold of 50,000/μL was used.*
- Reducing the threshold may prevent
  - *Death or major bleeding in 7 out of 100 preterm neonates with Sv thrombocytopenia*

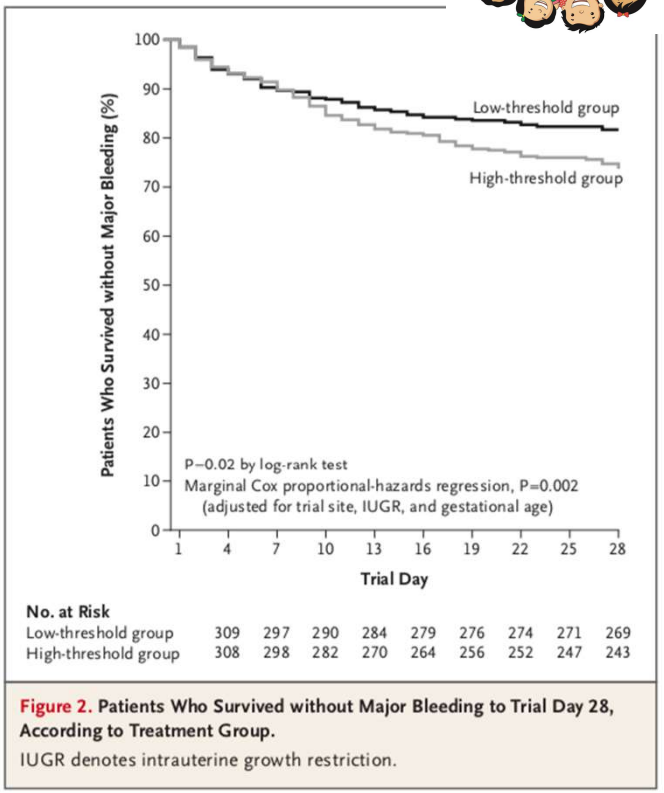


Figure 2. Patients Who Survived without Major Bleeding to Trial Day 28, According to Treatment Group.
IUGR denotes intrauterine growth restriction.

N Engl J Med 2019; 380:242-251

Neonatal alloimmune thrombocytopenia (NAIT)

- Maternally derived anti- HPA-1a or 5b platelet antibodies
  - Difficult to identify the specificity of the antibody
- Threshold for transfusion is 25 x 10^9/L in absences of bleeding
  - Close monitoring for ICH (cranial ultrasound)
  - Platelets should be maintained between 50-100 x 10^9/L
- Platelets product
  - HPA-1a, 5b Negative (90% cases)
  - When not available
    - Random donor platelets/ Maternal
    - IVIg may reduce the need of platelets
  - Spontaneous recovery in 1-6 weeks

British Journal of Haematology, 2016, 175, 784–828

Platelets Transfusion: ABO incompatibility

- Always considered necessary
- **Advantages ABOi transfusion policy**
  - Increase availability in resource limited setting
    - Emergencies and life threatening conditions
  - Reduce wastage of these products as they have short lifespan
- **Disadvantage ABOi transfusion policy**
  - Increased risk
    - Hemolysis
    - Fever
    - Alloimmunization
    - Reduced efficiency

Platelets Transfusion: ABO incompatibility

- *"Point Prevalence Study of Platelets Transfusion in Critically Ill Children" "P3T"*
- 82 centers; 16 countries; 6 rondom weeks- screened (AIIMS & PGIMER)
- Age group: 3 days to 16 years admitted in PICU
- Exclusion criteria
  - Gestational age < 37 weeks
  - Life expectancy < 24 hours
  - Received multiple pooled platelets of diff ABO compatibilities
- ABO Incompatibility
  - **Major:** A/B/AB to O; AB to A/B, Bidirectional (A to B, B to A)
  - **Minor:** O to A/B/AB or A/B to AB

Platelets Transfusion: ABO incompatibility

- 503 patients enrolled
  - 342 ABO compatible
  - 133 Major ABOi
  - 28 Minor ABOi

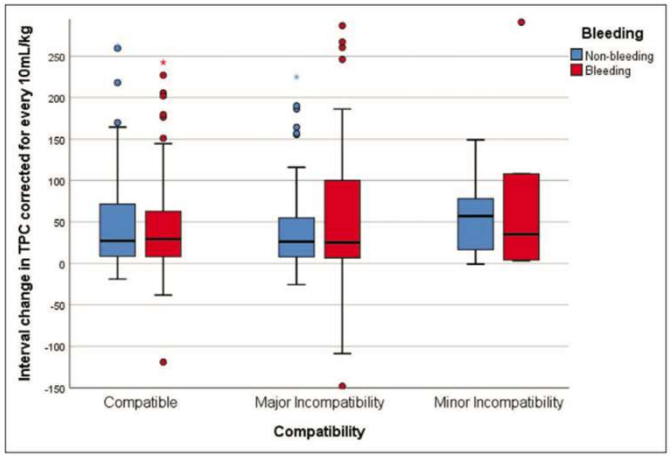


Figure 2. Interval change in total platelet count in bleeding versus nonbleeding subjects for each compatibility group.

TABLE 5. Transfusion Reactions

Reactions	Compatible ($n = 332$)	Incompatible ($n = 161$)	p
Any transfusion reaction, n (%)	25 (7)	5 (3)	0.07
New fever	9 (3)	2 (1)	0.36
Increase in temp by 1°C if already febrile	2 (0.6)	1 (0.6)	0.66
Urticaria	2 (0.6)	1 (0.6)	0.99
Bronchospasm	1 (0.3)	0 (0)	0.99
Hypotension	12 (4)	1 (0.6)	0.07
Transfusion stopped	2 (0.6)	1 (0.6)	0.99

There were no hemolytic reactions reported for any of the transfusions. p values calculated using χ^2 for large samples and Fisher exact for small samples.

Platelets Transfusions: ABO incompatibility

Effects of ABO Matching of Platelet Transfusions in Critically Ill Children*

Marianne E. Nellis, MD, MS[1]; Ruchika Goel, MD, MPH[2,3]; Oliver Karam, MD, PhD[4]; Melissa M. Cushing, MD[5]; Peter J. Davis, MBChB[6]; Marie E. Steiner, MD, MS[7]; Marisa Tucci, MD[8]; Simon J. Stanworth, MD, DPhil[9–11]; Philip C. Spinella, MD[12]; on behalf of the Pediatric Acute Lung Injury and Sepsis Investigators (PALISI) Network, Pediatric Critical Care Blood Research Network (BloodNet), and the P[3]T Investigators

In this large observational study in critically ill children, no differences were seen in incremental platelet count or transfusion reactions.

Limitations

- Type of product
- Type of Analyzer
- Bleeding as an Transfusion Rn
- ABO titre in the product
- Splenomegaly ?
- Variation in time of platelets count (both pre and post transfusion)

Pediatric Critical Care Medicine.Feb 2019 • Vol 20(2)

Fresh Frozen Plasma (FFP): Neonatal Transfusi

- **Indications for FFP transfusions**
  - Prophylactic transfusion prior to surgery *(unproven benefits)*
  - Bleeding *(including massive loss)*
  - Prior to invasive procedure *(with abnormal coagulation profile)*
  - Neonatal purpura fulminans (PF) due to
    - Severe protein C or protein S deficiency
- **Indication for cryoprecipitate transfusions**
  - Severe congenital hypofibrinogenemia
    - Acquired due to DIC or liver dysfunction
  - Neonatal cardiac surgery
  - Major Haemorrhage

British Journal of Haematology, 2016, 175, 784–828

Neonatal Exchange Transfusion

- Indication
  - Hyper bilirubinemia due to hemolytic disease of newborn
  - To eliminate toxic doses of drugs
  - To be performed before development of kernicterus
- Objectives
  - Removal of unconjugated bilirubin
  - Maximization of albumin binding of bilirubin
  - Removal of free and coated antibody
  - Replacing with Ag negative blood unit
- Types
  - Double volume exchange (two 85ml/kg for full term/ two 100 ml/Kg for preterm)
    - Removes approx. 70-90% of circulating cells and 50% of total bilirubin

Neonatal Exchange Transfusion

- Component Choice – *Reconstituted Whole Blood*
  - RBC
    - ABO and Rh compatible (Ag negative)
    - 5-7 days old
    - CPDA-1 suspended (avoid AS)
    - Hemoglobin s negative
    - CMV negative
    - Leukoreduced
    - Irradiated*
  - FFP (ABO compatible)
- Vascular Access
  - Umbilical venous catheters
  - Small saphenous catheters may also be used

Massive Transfusion:

- Massive Blood Loss
  - Loss of 80 ml/kg in 24 hours
  - 40 ml/kg in 3 hrs or 2-3 ml/kg/min
- Little evidence for management in children (mainly adapted from adults)
- *Key principles*
  - Early recognition
  - Active resuscitation and control of bleeding
  - Specialist assistance (paediatric specialist)
  - Rapid provision of O D-negative PRBCs
  - Transfuse components based on ml.kg not units
  - Anticipate Coagulopathy and treat it early
  - Avoid hypothermia, hypocalcaemia, acidosis and hyperkalemia
  - Use Tranexamic Acid in Trauma

British Journal of Haematology, 2016, 175, 784–828 |

Massive Transfusion

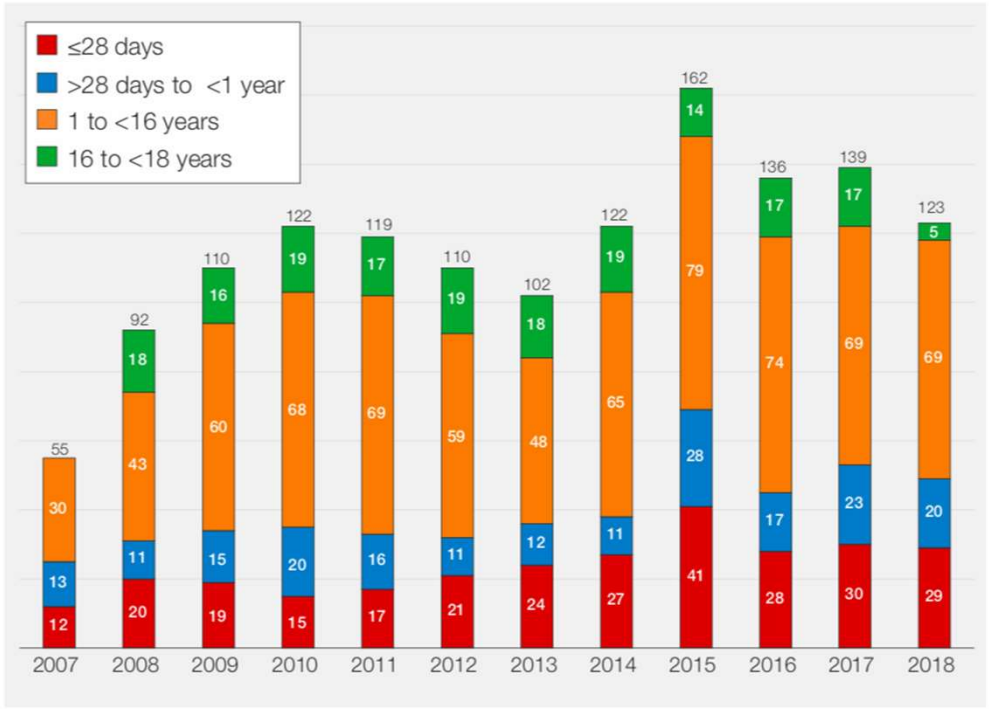
- Components should be given *based on volume* rather than as units
  - **RBC**: 20 ml/kg aliquots *(Ideally cross matched)*
  - **FFP:** 20 ml/kg aliquots *(upto max 4 adult units)*
  - **Platelets:** 15-20 ml/kg aliquots *(to be considered after every 40 ml/kg RBC)*
  - **Cryoprecipitate:** 10 ml/kg
- Ratio for component use
  - 1 FFP: 2 PRBC; early resuscitation of major haemorrhage
  - Ratio may be modified based on labs and status of bleeding
  - Therapeutic aim
    - Hb: 80 g/L
    - Fibrinogen: > 1.5 g/L; PT ratio < 1.5
    - Platelets count > 75 x 10^9/L
  - Early use of Tranexamic Acid

British Journal of Haematology, 2016, 175, 784–828

Adverse Reactions to Transfusions

a. Total paediatric reports subdivided by age

Figure 23.3: Trends in paediatric reports 2007-2018



In 2007 only cases <16 years were included

- 123/1659 (7.4%) of total cases were paediatric.
- If near miss (NM) and right blood right patient categories are included, 241/3326 (7.2%).

SHOT Data 2018

Adverse Reactions to Transfusions

January 2013 to April 2016

Table 1: Age-wise distribution of the patients

Age distribution	Number of patients
Adult	3470
Pediatric	337
Total	3807

May 2016 to December 2017

Table 1: Total number of males and females with age groups reported to HvPI 2016-2017

Age Category	Males		Females		Total
	2016	2017	2016	2017	
Pediatric (<=12 Years)	46	142	35	66	289
Adolescent (12-<=18)	35	69	40	65	209
Adult (>18)	463	1156	550	1270	3,439
Total	544	1,367	625	1,401	3,937

835 (10%) out of 7,744 Reports

Bisht et al. AJTS Dec 2020

Adverse Reactions to Transfusions

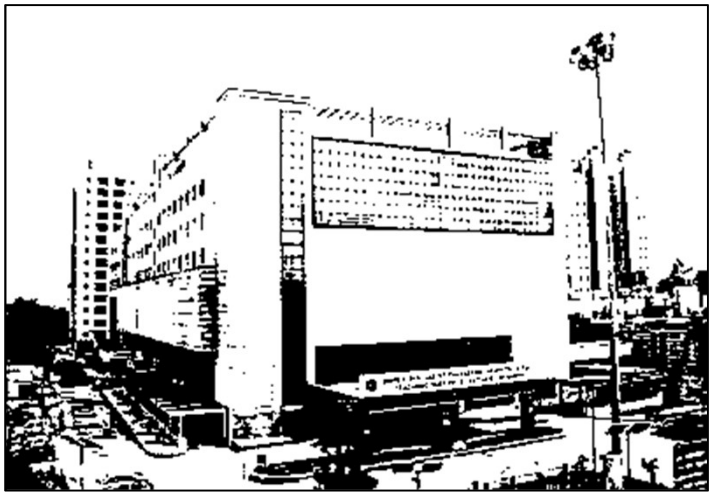
- *"Oxidative Stress"* due to elevated plasma "non-transferrin-bound iron" (NBTI)
  - RBC transfusion leads to overloading of liver with iron in VLBW infants
- Associations with
  - *Intraventricular Haemorrhage (IVH)*
  - *Bronchopulmonary dysplasia (BPD),*
  - *Chronic Lung Disease (CLD)*
  - *Retinopathy of prematurity (ROP)*
    - Association with PRBC volume transfused in infants with birth wt <1250 gms
- Still a possible effect due to confounding factors such as low birth wt, gestational age, a longer duration of oxygen therapy and state of tissue hypoxia

Eur J Pediatr 1997;156:465–470| Eur J Pediatr 1997;156:47–50| Early Hum Dev 2001;62:57–63

Conclusion

- Transfusion Medicine practices in Neonatology and Paediatrics **is evolving**
  - Not uniform practices
  - Still gathering data
  - Not many dedicated studied *(as guidelines are adapted from adults)*
  - Even after many studies appropriate “trigger” or “Threshold” not established
  - Not many long term outcome analysis of transfusion in Neonatal or paediatric group is published
- This is still a very important and ignored sub speciality of Transfusion Medicine which may gain a lot of importance in coming years.


00:00
ट्रांसफ्यूजन मेडिसिन और
ब्लड बैंक विभाग
Department of Transfusion
Medicine & Blood Bank
Edit profile
Peds Transfusion Medicine
@MedicinePeds
Tweets on Special Pediatric Apheresis and
Transfusion Medicine Needs| Health Care
New Delhi, India
Joined May 2018
162 Following
226 Followers



Thank You