

Neonatal Transfusion Medicine

2016 GHEST Transfusion Medicine Symposium

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Disclosure

- Canadian Blood Services Small Project Fund

Objectives

1. Why adults are **not** big babies
2. Blood product transfusion (in newborns)
3. Pre-transfusion testing (in newborns)
4. Risks and outcomes of neonatal transfusion



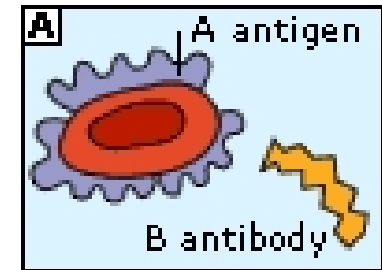
Why neonatal transfusion?

- Babies <1500 g
 - 50% transfused
- Babies <1000 g
 - 90% transfused
 - Avg 5 transfusions
- Potential life-years
 - complications
- Anemia of prematurity
- Transfused O blood
- Maternal antibodies (HDN)



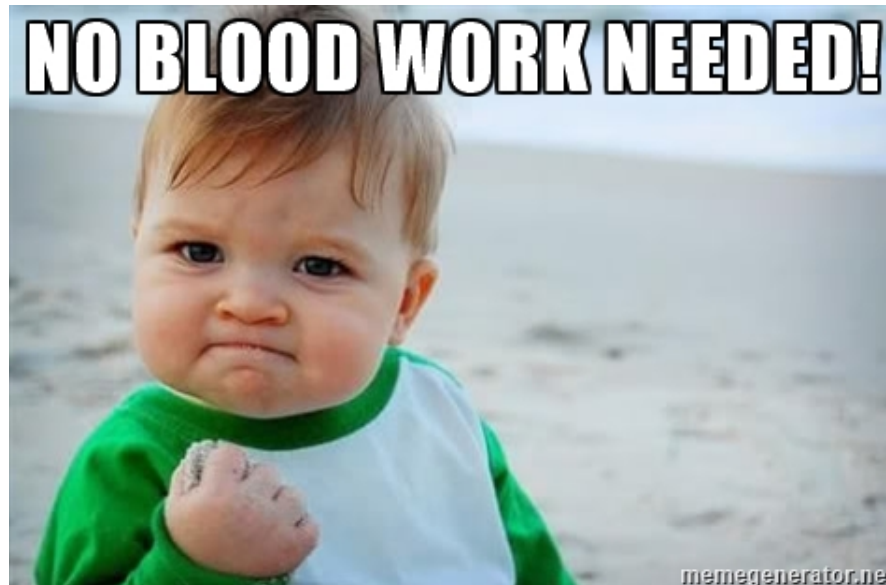
Pre-Transfusion Testing in Neonates

- ABO grouping
 - Red cell typing only
 - No plasma typing (ABO antibodies are maternal)
- Blood RhD must be compatible with mother & infant
 - No need for O neg red cells for all neonates
- Antibody screen
 - Neonatal or maternal



Pre-Transfusion Testing in Neonates

- Immature immune system
 - If initial **neg** screen → no repeat x 4 months
 - Electronic XM
 - No XM → decrease iatrogenic blood loss



Pre-Transfusion Testing in Neonates

- A, B, or AB neonate + group O mother
 - Test neonate for maternal anti-A or anti-B
 - Choice of blood: neonate's group + maternal antibodies
- **A bit complex!**
 - Use only group O RC
 - If all this testing is done → group-specific units

Anemia of prematurity: what is it?

- Physiological anemia of the newborn

and...

- Suppressed response to erythropoietin
- Short RBC life span
- Rapid increase in blood volume with growth
- Blood sampling!

Neonatal Red Cell (RC) Indications

1. Recurrent correction of anemia of prematurity
 - “Top up transfusion”
2. Acute hemorrhagic shock
 - Perinatal
 - Surgical

Premature Infants in Need of Transfusion (PINT) Study: Liberal vs. Restrictive

Postnatal age	Respiratory support*	No respiratory support
Week 1	115 (35)	100 (30)
Week 2	100 (30)	85 (25)
Week 3 and older	85 (25)	75 (23)

Data presented as hemoglobin, g/L (hematocrit, %).

*Respiratory support is defined as an inspired oxygen requirement in excess of 25% or the need for mechanical increase in airway pressure (Adapted from reference 6)

Hb → little benefit / harm

Prudent to avoid low Hb



Cochrane Database of Systematic Reviews



Kirpalani et al. J Pediatr 2006
Whyte & Kirpalani, Cochrane 2011
CBS Clinical Guide to Transfusion, 2014
Pediatr Child Health 2014

Age of Red Blood Cells in Premature Infants (ARIP) trial

- Fresh RC (5 days) vs. standard practice (14 days)
- No improvement in neonatal outcomes
 - ❑ Composite of:
 1. Necrotizing enterocolitis
 2. Retinopathy of prematurity
 3. Bronchopulmonary dysplasia
 4. Intraventricular haemorrhage
 5. Death

Intraventricular hemorrhage (IVH) in preterm infants

Early red cell transfusion →



Risks of neonatal transfusion

- IVH
- Hyperkalemia
- Circulatory overload (TACO)
 - Congenital heart
 - Renal failure
- Necrotizing enterocolitis (TA-NEC) ???
 - Transfusion-related acute gut injury (TRAGI)

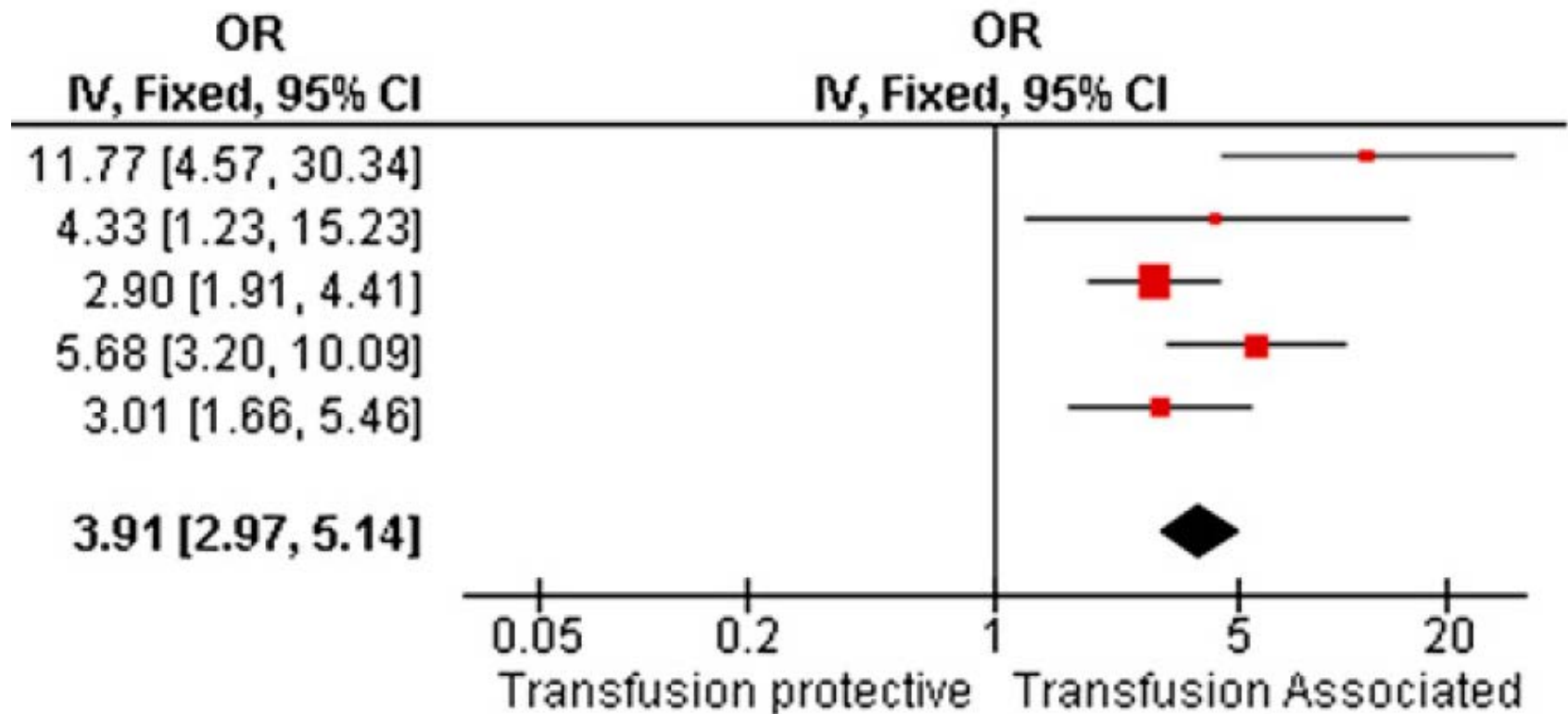
Neonatal transfusion reactions require further study

**2015 proceedings of the National Heart, Lung, and Blood
Institute's State of the Science in Transfusion Medicine symposium**

6. More studies on transfusion therapy for pediatric patients and, separately, on neonates are urgently required.

TA-NEC controversy: Meta-analysis of observational studies

Recent exposure: 48 hours



Original Investigation

Association of Red Blood Cell Transfusion, Anemia, and Necrotizing Enterocolitis in Very Low-Birth-Weight Infants

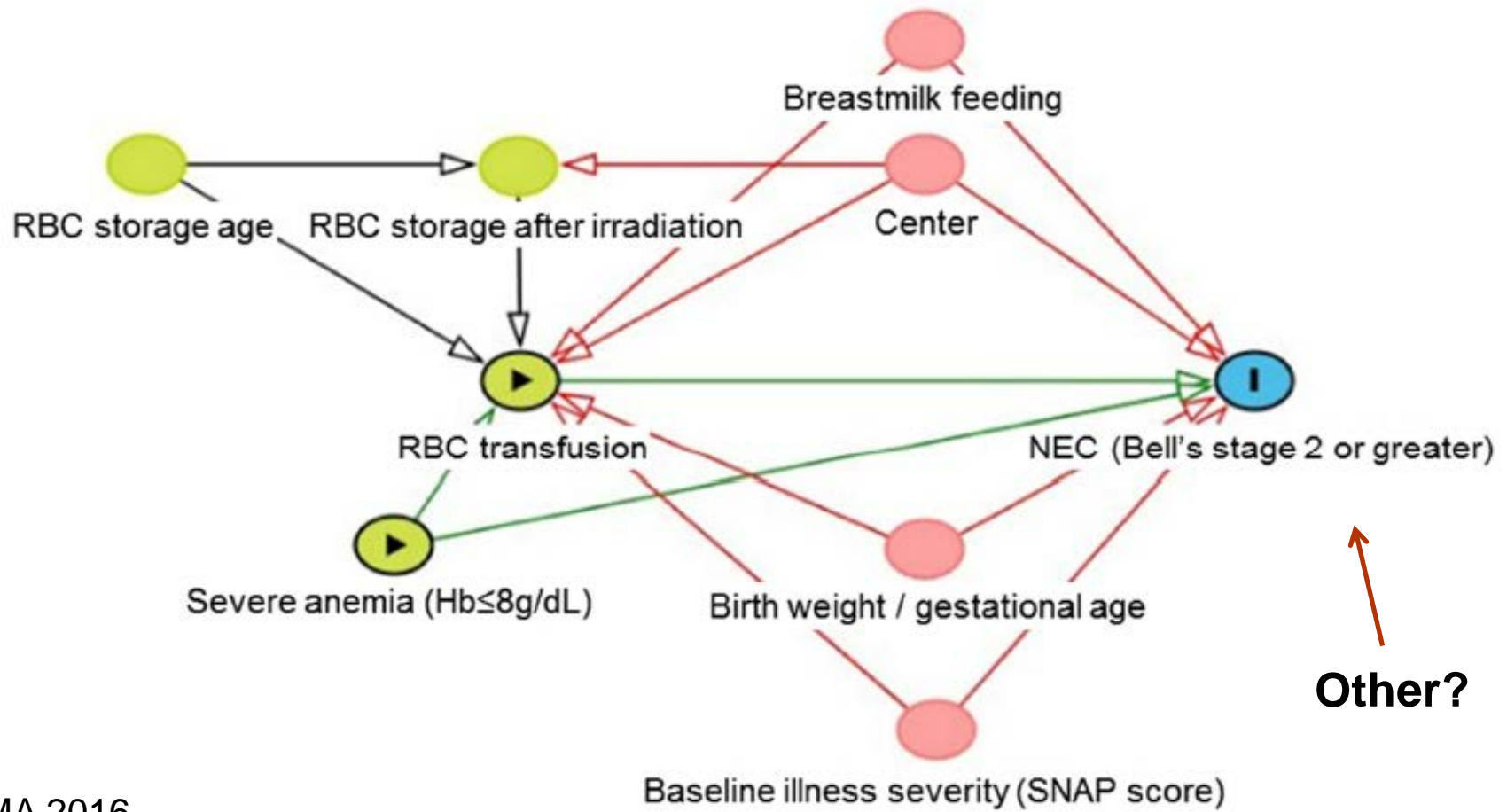
Ravi M. Patel, MD, MSc; Andrea Knezevic, MS; Neeta Shenvi, MS; Michael Hinkes, MD; Sarah Keene, MD; John D. Roback, MD, PhD; Kirk A. Easley, MApStat; Cassandra D. Josephson, MD

- 598 babies, prospective **observational** study
- NEC associated with severe anemia
 - Not transfusion



TA-NEC vs. AA-NEC

Figure key:



Other?

Intraventricular hemorrhage (IVH) in preterm infants

Early red cell transfusion →



Coagulopathy screening

Early FP use for prevention of IVH

NOT PREVENTIVE

NO BENEFIT

Baer et al. Transfusion 2011

Dani et al. Transfusion 2009

Tran et al. Blood Coag & Fibrinolysis 2012

Plasma in the NICU

- Routine coagulation screening in NICU
 - **Mild/moderate abnormalities \neq bleeding**



- Leads to increased FP use

Coag screen only if bleeding or sick

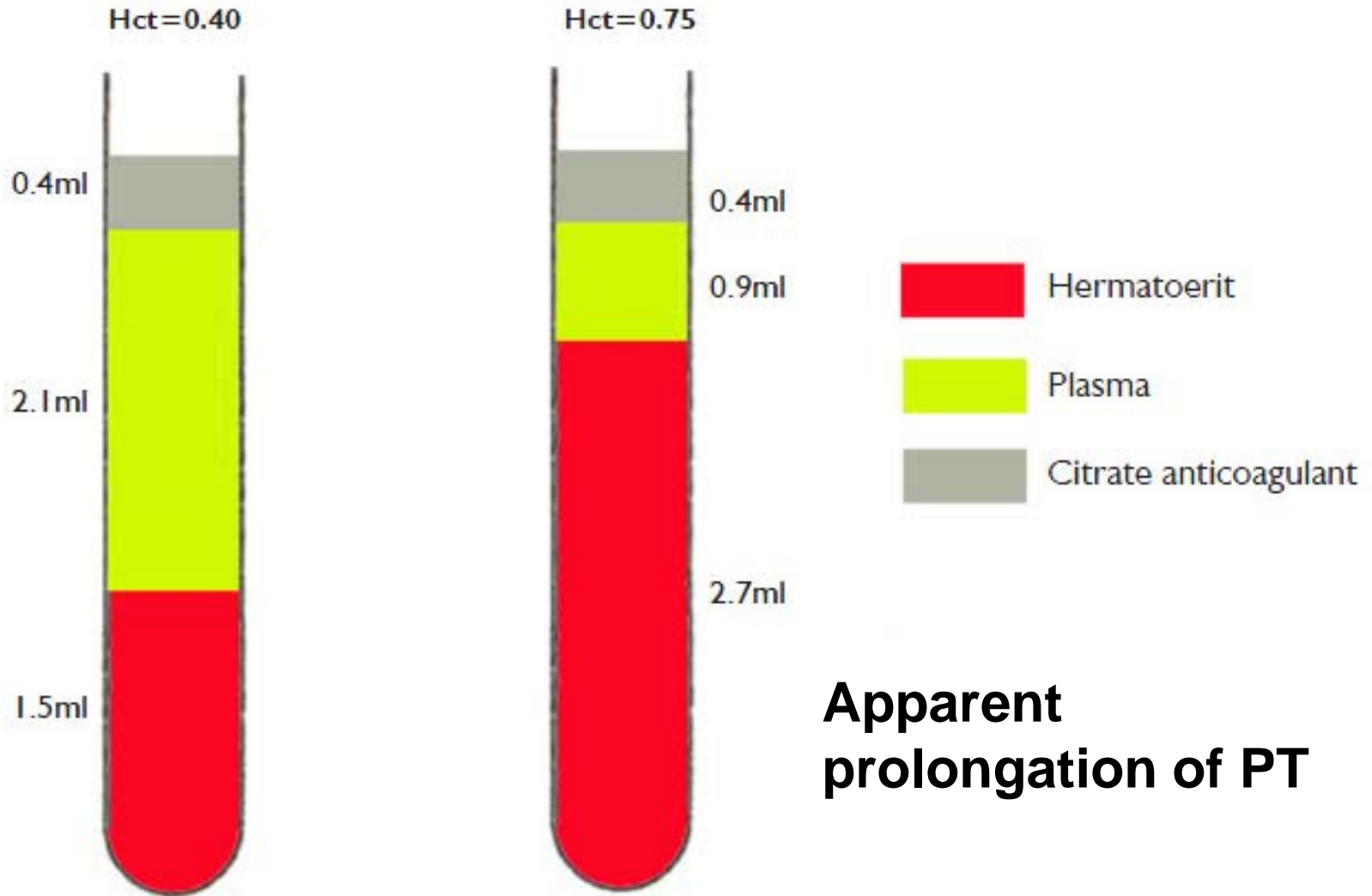
Neonatal coagulation

- Different procoagulant-anticoagulant balance
 - Both reduced
 - Normal thrombin generation
- Conventional tests
 - Don't account for low protein C
 - Age-based coagulation ranges
- Variation in reagents & analysers
 - Lab needs locally derived ranges
 - Old literature still widely quoted



Tripodi et al, Haematologica 2008
Andrew et al, Blood 1987, 1988
Monagle et al, JTH 2006

Polycythemia in neonates



Hemorrhagic Disease of the Newborn (HDNB) Vitamin K deficiency bleeding (VKDB)

	Onset	Cause	Prevention
Early-onset	1 st 24 hours	Maternal meds (phenytoin, rifampin)	Maternal vit K in last 2-4 weeks
Classic	24h - 1 week (up to 1 month)	No vit K at birth	Vit K at birth
Late-onset	2 - 12 weeks (up to 6 months)	Nutritional (breastfed)	Diet

- Vitamin K recommended for every newborn
- PCC is preferable to FP

Use of PCC in Neonates

- 16 patients: age 3 weeks - 16 years
- 2 neonates received 2-5 mL Beriplex
- Complications
 - 1 DVT in a 4 year old
 - 1 death in a 16 year old

CMV Neg Blood

- No indications
- But can order for intra-uterine transfusion
 - due to insufficient evidence
- Leukoreduced (CMV-safe) for all patients
 - Equivalent to CMV neg
 - USA vs. Canada

Blood Transfusion and Breast Milk Transmission of Cytomegalovirus in Very Low-Birth-Weight Infants

A Prospective Cohort Study

Cassandra D. Josephson, MD; Angela M. Caliendo, MD, PhD; Kirk A. Easley, MS, MAppStat;
Andrea Knezevic, MS; Neeta Shenvi, MS; Michael T. Hinkes, MD; Ravi M. Patel, MD, MSc;
Christopher D. Hillyer, MD; John D. Roback, MD, PhD

- 539 babies (462 mothers), 2061 transfusions
- 29 babies with CMV disease
 - None linked to transfusion
- Primary source of post-natal CMV
 - **Maternal breast milk**

Irradiation: Indications & precautions

- Suspected immunodef
• DiGeorge (cardiac)
- IUT
- Family donation
- HLA matched cells
- Hodgkin's Lymphoma
- Fludarabine
- < 1500 g (case reports)
- Expiration 14 days after irradiation
 - Irradiate immediately before transfusion
- Don't have irradiator?
 - Kidney function
 - Central line in atrium

Directed Donation: why not?

1. Transfusion-associated GvHD
2. Need to irradiate (affects quality)
3. Future eligibility to donate stem cells
4. TRALI from maternal plasma (Dunbar et al. Spine 2010)
5. First-time donors
 - Higher pathogen detection (Wales et al. J Pediatr Surg 2001)
 - If not first-time, no safety advantage
6. Perceive undue pressure
 - May conceal risk

Neonatal Alloimmune Thrombocytopenia (NAIT)

- New ICTMG guidelines @ AABB Oct 2016
- Patient handout + Medical app
- Video + Podcast



Thank you!

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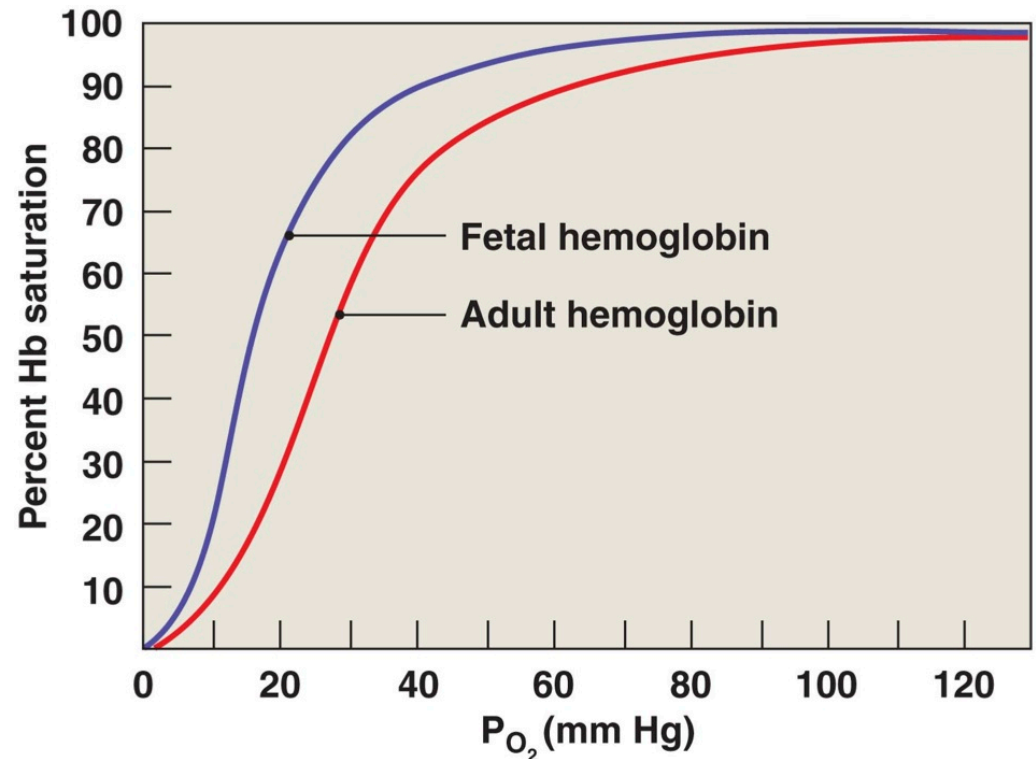
Canadian Blood Services
Société canadienne du sang



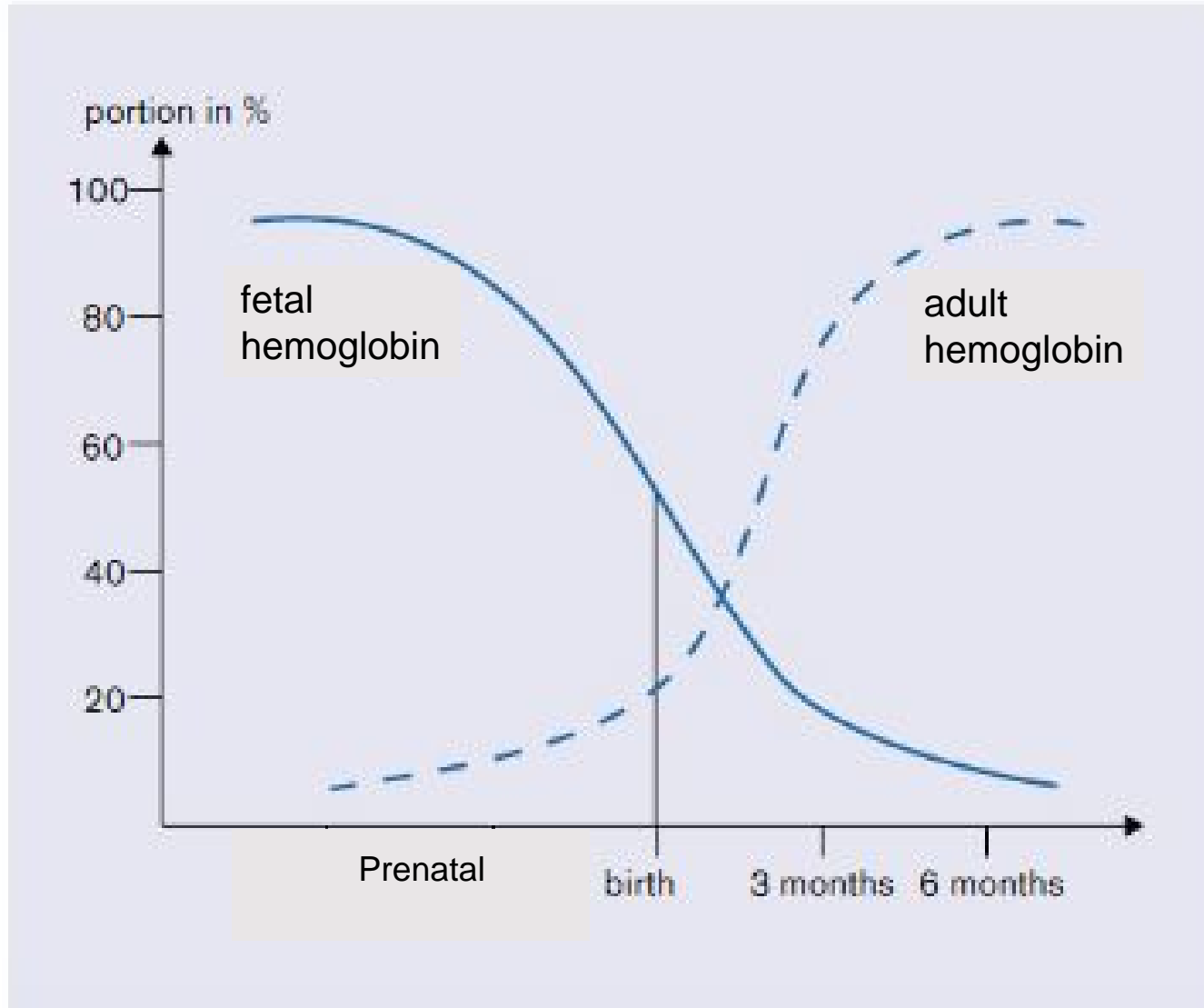
McMaster Centre for
Transfusion Research

TA-NEC: Pathophysiology

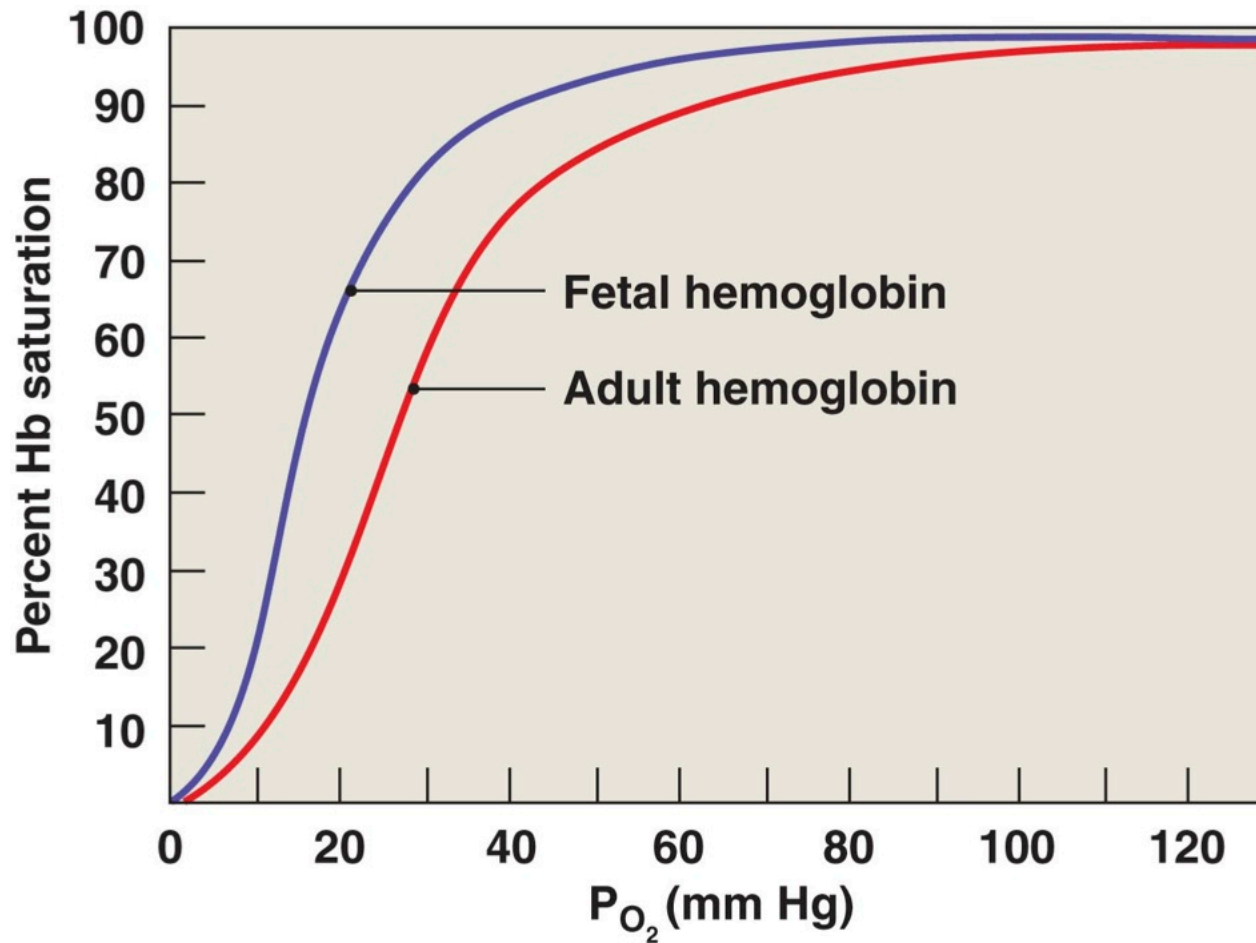
- O₂ related neovascularization
- 2,3 DPG and O₂ delivery
- Cytokines
- HbA vs. HbF



Hemoglobin & Development



Oxygen affinity of HbF and HbA



Hyperbili: exchange transfusion

- Whole blood
 - combine O blood with AB neg plasma
- Double volume: ~ 160 mL/kg (1 unit)

