Chapter 15: Hematology

Pamela Kling, MD & Henry Zapata Galarza MD

Anemia

- Anemia-Blood Loss
  - Obstetrical-abruption, placenta previa, umbilical cord trauma
  - Immediate (vs. delayed) umbilical cord clamping
  - Feto-maternal hemorrhage
  - Twin-twin transfusion syndrome
  - Internal hemorrhage-IVH, subgaleal hemorrhage, cephalohematoma, adrenal hemorrhage, subcapsular hematoma of liver
  - Iatrogenic-lab tests
- Anemia-Increased RBC destruction
  - Hereditary RBC disorders-G6PD, hereditary spherocytosis, thalassemia
  - Immune hemolysis-Rh/ABO incompatibility
  - Acquired hemolysis-infection, drugs
- Anemia-Decreased RBC production
  - Anemia of prematurity
  - Aplastic or hypoplastic anemia
  - Bone marrow suppression-parvovirus, rubella
  - Nutritional anemia-iron deficiency
- Anemia-Physiologic
  - Normal nadir at 6-8 weeks in term infant
  - Delayed clamping or cord milking can minimize the Hgb at the nadir
  - Earlier for preterm infant (4-6 weeks)
  - Preterm infant nadir is lower than term infant (Hgb of 9 versus 11).

Anemia Initial Work-up

- Must be completed before transfusion
- CBC with platelets
- Reticulocyte count
- Peripheral smear (spherocytes, ABO incompatibility; nRBC, Rh disease)
- Type/Coombs on mother and infant
- Kleihauer-Betke on mother (looking for fetal RBCs)

Additional Tests

- RBC enzyme studies: G6PD and pyruvate kinase
  - G6PD-may be falsely negative during acute process due to increased enzyme activity in reticulocytes
- Hemoglobin electrophoresis (newborn screen)
- Head or abdominal ultrasound

Management

- Consider transfusion guidelines from Iowa Study: Low Threshold vs. (High Threshold): Less IVH in High group, better long-term outcome in girls in Low.

Hematocrit	Other Clinical/Lab data
<7-10 (<21-30)	Stable child > 1 wk old, asymptomatic, RA or NC, NCPAP with FiO2<40%, Room air, & retic <4%
<28 (<38)	Mild lung disease, NC/CPAP/NPSIMV with FiO2>40%, or major surgery >21%
<11-13 Hb (<33-39 Hct)	Critically ill, severe lung disease in first week or major surgery
Any Hct	Acute blood loss & signs of shock

- Draw first newborn screen prior to transfusion
- Neonatal Transfusion workup (NTW; aka-Type and screen) only needs to be completed once during the admission, up to 4 months of age
- Transfuse with 15-20 ml/kg of CMV negative, irradiated, type specific pRBCs.
  - Irradiation inactivates donor lymphocytes reducing GVHD, but increases potassium concentration of packed cells and reduces the half-life of stored blood.
  - Some centers used leukocyte-reduced/filtered blood in place of CMV negative blood. This also reduces CMV transmission.
  - Transfusion of 15-20 ml/kg will raise the Hct about 10%
  - Transfusion of pRBCs causes bone marrow suppression
  - Hold feedings, before & during transfusion per guidelines in the feeding protocol chapter
  - Note: At UW AFCH pRBCs are not type-specific and have higher Hct., so transfuse up to 15 ml/kg/d in one installation.

Special Transfusions

Double-Volume Exchange Transfusion

- Indications-hemolytic disease of the newborn

Volume to be exchanged = 2[infant's blood volume (ml/kg) x weight (kg)]

Blood volume estimates: term = 80 ml/kg; preemie = 90-100 ml/kg

Partial Exchange Transfusion

- Indications

Polycythemia, Significant anemia with normal blood volume

- Volume to be exchanged if wanting to lower

$$\frac{\text{Hct} = [(\text{Blood volume x wt}) \times (\text{observed Hct} - \text{desired Hct})]}{\text{Observed Hct}}$$

- Volume to be exchanged to increase Hct =

$$\frac{(\text{Blood volume x wt}) \times (\text{desired Hct} - \text{observed Hct})\ \text{Hct}}{\text{of pRBCs}}$$

Anemia of Prematurity Etiology

Reduced erythrocyte half-life

Iatrogenic losses from phlebotomy

Hemo-dilution due to increasing body mass

Relative deficiency of erythropoietin

- Site of Epo production shifts from liver to kidney
- Liver less sensitive to hypoxia, thus protection from polycythemia in fetus

Prevention

Delayed umbilical cord clamping is indicated to prevent anemia/iron deficiency

Possible Exceptions: abruption, cord avulsion, monochorionic twins, or extremely poorly controlled diabetes

Management

Minimize phlebotomy losses (obtain only relevant lab tests that can change clinical care, use ABL point of care if possible).

IV Iron Sucrose (*do not use IV Iron Dextran*) to prevent Anemia of Prematurity

Use with premature/SGA patients with prolonged NPO status (usu. surgical)
Start at 14 days of life (3 mg/kg IV iron sucrose over 4 hrs once weekly)
Monitor vital signs during transfusion, tachycardia, tachypnea, BP may fall
If not tolerating, stop infusion & consider premedicating for next dose
Monitor CBC, plus Ferritin or reticulocyte Hb after 2 wks
Switch to oral iron 6 mg/kd/d when feeds are tolerated
Target Ferritin 70-100 ng/mL (µg/L) or target reticulocyte Hb 29-35 pg
If Ferritin <100: dose IV iron weekly. If 101-199: IV iron every other week
If Ferritin 200-249: dose IV iron every 4 weeks. If >250: stop IV iron sucrose

SA (rEpo and Darbepoietin) to Prevent Transfusions

RBC-stimulating doses are neuroprotective in retrospective studies
rEpo: 250-300 U/kg SQ or IV, 3 times weekly until 34-35 wks gestation or later if Hct <28 and on respiratory support
Consider with premature/small surgical infants with prolonged NPO
Begin either rEpo or Darbepoietin at approx. 2 weeks of life
Consider dosing in some ELBW micropremie infants, esp. <850 g BW
Begin either rEpo or Darbepoietin within 24-48 hours of life
Darbepoietin: 10 mcg/kg SQ or IV once weekly until 34-35 wks gestation
If Hb does not rise by 1 g/dL after 4 weeks, increase dose by 25%
If Hb rises >1 g/dL after 4 wks, consider decreasing dose by 25%
Stop ESA if Hb >15 g/dL or Hct >45%
Do not stop ESA for transfusion or with infection work up
Must give iron with ESA
Start oral Iron 6 mg/kg/d if tolerating 60 mL/kg/day enteral feeding
If NPO/unable to take oral iron in 1st wk, IV iron sucrose 3 mg/kg/wk
Consider stopping oral or IV iron X 1-2 wks post transfusion.
Target Ferritin 70-100 ng/mL (µg/L) or target reticulocyte Hb 29-35 pg

- If Ferritin <100: dose weekly. If 101-199: every other week
- If Ferritin 200-249: dose every 4 weeks. If >250: stop IV iron sucrose–Term infants (unless SGA, late preterm, or < 2500 g)

No need for routine iron dosing until later in life

- Iron fortified formulas (@150 ml/kg/day) provide ~2 mg/kg/day
- Standard concentration of iron for inpatients = 3 mg/0.2 mL

Give 3 mg dose 1-3 times per day based on patient need

- Multivitamin drops with iron provide 10 mg iron/1 mL
- Continue iron until 12 months of age.
- Hold oral iron for 2 wks after transfusion, unless on ESA (hold for 1 wk)

Blood transfusion (PRBC) may be needed (see Transfusion Guidelines).
Check Ferritin at 28 days before immunizations: Should be ≥70 ng/mL
See IV Iron/Erythrocyte Stimulating Agents Clinical Guidelines

Thrombocytope
nia
tiology

Increased Platelet Destruction
–Autoimmune – maternal ITP, maternal autoimmune disease (SLE)
–Neonatal Alloimmune – due to human platelet antigen 1, 3, or 5
–Placental insufficiency – ex. Preeclampsia or chronic hypertension
–Sepsis/NEC/Perinatal asphyxia – DIC
–Drug-induced – heparin, antibiotics
Decreased Platelet Production
–TORCH

Platelet transfusions

Clinical Characteristics	Platelet Count
Stable term infant or premature >7 days	<25,000
<28 wks, <7 days, risk for IVH	<50,000

Prior significant hemorrhage/surgery	<50,000
Hemorrhage	Transfuse

Transfuse at any level in presence of active bleeding
Platelets short shelf life, may need to put on hold for some, delays up to 4-6 hrs.
Transfuse 10-20 ml/kg of CMV negative, irradiated platelets over 2-3 hrs.

Other Blood Products

FFP transfusion:

- Indications – bleeding, DIC, vitamin K deficiency, Factor IX deficiency
- Components – All clotting factors, fibronectin, gamma-globulins, albumin, plasma proteins

Cryoprecipitate

- Indications – Factor VIII deficiency, von Willebrand disease
- Components – Factor VIII, vWF, fibrinogen, factor XIII, fibronectin

Statistics about Safety of Blood Supply; ARC 2004

HIV 1:2,000,000	HBV 1:250,000–500,000
HCV 1:2,000,000	HTLV 1:640,000
WNV 1.5/1000, 3/100,000	HAV 1:1,000,000
Malaria 1:1,000,000	Bacterial RBC–1:1:500,000; Platelet–1:1000-2000

Reference:

1. Curley A, et al. PlaNeT2 MATISSE Collaborators. Randomized Trial of Platelet-Transfusion Thresholds in Neonates. *N Engl J Med*. 2019 Jan 17;380(3):242-251
2. Widness JA. Pathophysiology of Anemia During the Neonatal Period, Including Anemia of Prematurity. *Neoreviews.* 2008;9;e520
3. Committee on Obstetric Practice, Timing of Umbilical Cord Clamping After Birth. *Obstetrics & Gynecology.* 2012;120;1522-1526.
4. Bell EF. *Arch Dis Child.* 2021doi:10.1136/archdischild-2020-320495.