Hematological Disorders In Neonates

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How do blood cells develop?

- Hematopoiesis
- Formation, production, maintenance from Stem Cells
- All blood cells are made from these cells Starts in the yolk sac during 3rd week of gestation
- Liver vs. Bone

  Liver early in pregnancy during the 1st 12 weeks

  Bone mirror

  Predominates from 22 weeks gestation forward Hypoxia, bacterial infection, physiologic stress influence the rate of differentiation of stem cells

How do blood cells develop?

- Hemoglobin Normal 14-20 g/dL
- Carries oxygen from the lungs to the tissue cells
- HbF – fetal Hgb, begins ~14 days of life
- RBCs contain 70%-90% HbF at birth Has higher affinity for oxygen
- HbA – adult Hb, begins at end of fetal life

How do blood cells develop?

- Hematocrit (Hct)% of RBCs in a 100ml volume of blood
- Reticulocyte

  At birth, the neonatal reticulocyte count is 4% -7%, dropping to 2-3% by 7 days of age.

  The ↓ gestation the ↑ the count

  ↑ count indicative of chronic blood loss or hemolysis

Anemia

Definition

- Decrease in the Hb level below the mean for age and sex

- Oxygen carrying capacity & level of oxygen available to the tissues reduced by Low Hb concentration

Etiology of anemia

- physiological anemia of neonates
- Hemorrhage
- Hemolysis
- Iatrogenic frequent blood sampling
- Decrease RBC production in BM

physiological anemia (Anemia of Prematurity)

- Considered physiologic
- Erythropoietin falls to minimal level due to improved relative oxygenation after birth
- higher oxygen supplementation to preterm infants decrease erythropoietin production
- Hb falls by 1 g/dL/week in preterm infants reach 7-9 g/dL at 6 to 8 weeks of life
- shortened RBC life span
- Transfusions result in a greater fall in Hb due to active suppress of erythropoiesis in BM
- Frequent blood sampling

Anemia of Prematurity

- Baby manifest by Poor feeding, poor weight gain, dyspnea, tachypnea, tachycardia, diminished activity, pallor, increased apnea/bradycardia events
- Retic count decreased
- How to treat…

  Minimizing blood losses

  Iron supplementation 2mg/kg/day as prophylaxis and 6mg/kg/day as therapy

  Transfusion if Hb fall below 7gm/dl in asymptomatic preterm and less than 10 gm/dl in manifest babies

  Recombinant Human Erythropoietin (EPO) 400u/kg/dose 3-5 dose/week

Etiology of anemia Hemorrhage

- Twin two twin transfusion (Monozygotic twin, 15%-30% of twin pregnancies, Hb difference between twins > 5 g/dL, one anemic and other polycythemic.
- Placental/Cord as placenta previa
- Intracranial hemorrhage
- Organ rupture (liver, spleen, Pulmonary Hge
- Hemorrhagic disease of newborn
- Iatrogenic frequent blood sampling

Anemia – Causes of Hemolysis

- Immue hemolytic anemia as Rh and ABO incompitability
- Enzymatic Defect as G6PDn pyrovite kinases def.
- alpha thalasemia, spherocytosis
- Infection as sepsis, torch infections

Anemia – Causes of decrease BM production

- Infections
- Aplastic anemia
- Congential leukemia
- Osteopetrosis
- maternal chloramphenicol intake

Treatment

- How to treat…

  Minimizing blood losses

  Treatments of the causes

  Transfusion if Hb fall below 7gm/dl in asymptomatic neonates and less than 10 gm/dl in manifest babies.

  Start iron preparation as early as possible even during the 1st month

Polycythemia

Too much of a good thing!

Polycythemia

- Definition Hemoglobin > 22 g/dL or Hematocrit > 65% in the 1st week of life

- Hyperviscosity, Blood viscosity increases with hematocrits > 60% Leads to a reduction in organ blood flow
- Baby at risk of hyperbilirubinemia and kernictrus

Causes of polycythemia

- Intrauterine hypoxia, placental insufficiency as Hypoxia stimulates erythropoiesis lead to increased RBC production
- Preeclampsia, eclampsia, placenta previa,
- postmaturity syndrome, IUGR
- Twin-to-twin transfusion
- Placental hypertransfusion
- Maternal diabetes
- Congenital adrenal hyperplasia, Beckwith-Wiedemann syndrome

How to treat…Polycythemia

- Hemoglobin…>22 g/dL, Hematocrit…> 65%, Bilirubin…often elevated, Retic count…may be elevated
- treatment with Good hydration, May need normal saline boluses
- Partial exchange transfusion
  - Controversial when asymptomatic
  - Goal is to reduce hematocrit to < 60%

Neonatal thrombocytopenia

Neonatal thrombocytopenia

- Thrombocytopenia (platelet count <150 thousand/dl
- occurs in 1-4% of term newborns,
- 40% of sick preterms

Causes of neonatal thrombocytopenia in sick neonates

- Bacterial sepsis
- Congenital viral infections (torch infections)
- Disseminated intravascular coagulation
- Hypoxia and/or acidosis after birth trauma
- Chronic hypoxia from placental insufficiency, Pre-eclampsia
- Respiratory distress syndrome
- Persistent pulmonary hypertension
- Necrotizing enterocolitis
- post exchange transfusions
- Bone marrow disorders (congenital leukemia, neuroblastoma,)

Thrompocytopenia with Dysmorphic Features

- Thrombocytopenia with absent radius (TAR) syndrome
- Fanconi anemia
- Chromosomal disorders due to trisomy 13, 18, or 21 and Turner syndrome
- Kasabach-Merritt syndrome (Hemangiomas and thrombocytopenia).
- Wiskott-Aldrich syndrome is a rare X-linked disorder characterized by immunodeficiency, eczema, and thrombocytopenia.

Thrompocytopenia with Health-appearing neonates

- **Occult infection**
- **Due to maternal autoimmune thrombocytopenia (Maternal ITP)**
- Neonatal alloimmune thrombocytopenia
- congential amegakaryocytic thrombocytopenia
- Wiskott-Aldrich syndrome

Neonatal alloimmune thrombocytopenia (NAIT)

- NAIT is the platelet equivalent of hemolytic disease of the newborn due to red blood cell Rh D incompatibility.
- It occurs when a mother lacks a platelet antigen that her fetus has inherited from the father.
- Maternal immunoglobulin G antibodies form against the “foreign” antigen on fetal platelets, cross the placenta, and destroy fetal platelets.
- NAIT can result in severe thrombocytopenia, Unlike Rh hemolytic disease, 50% of NAIT cases occur in the first pregnancy of an at-risk couple.
- The most commonly identified antibody in sensitized women is antihuman platelet antigen-1a (HPA-1a)

DIAGNOSTIC EVALUATION OF ABNORMAL BLEEDING

1. History:

- •Family history of bleeding disorders
- •Maternal history of bleeding disorders, medication intake, previous neonatal deaths, auto-immune disease
- •Perinatal: Toxemia of pregnancy, IUGR, infections, antepartum bleeding
- •Neonatal: History of asphyxia, birth trauma, administration of Vitamin K, gender (X-linked disorders)

2. Neonatal physical examination:

- **•Signs of bleeding •Signs of infection (hepatosplenomegaly)**
- •Signs of hypovolemia •Hemangiomas, vascular malformations
- •Other malformations •Other illness (*e.g., NEC, hemolytic disease)*

3. Laboratory investigation:

A. Initial screen

- •CBC, differential, smear •Platelet count
- •Prothrombin time (PT) •Partial Thromboplastin Time (PTT)

B. If Neonatal Allo-Immune Thrombocytopenia (NAIT) is suspected, send mother's and infant's blood for platelet count and typing.

MANAGEMENT

- **For secondary bleeding disorders, treat underlying disease.**
- **Severe, life threatening bleeding:** Maintain adequate circulating blood volume with whole blood transfusion in severe anemia
- Vitamin K 2-5 mg IV **slowly over 1 min**
- Fresh Frozen Plasma 10 mL/kg over 5-10 min if coagulation profile impaired.
- Platelets 1 unit transfusion only needed when platelet reach < 50 thousand/Dl in manifest baby and <20 thousand in asymptomatic one

Hemorrhagic disease of newborn
Vitamin k deficiency bleeding

History

- Townsend in Boston (1864) described 50 cases of "hemorrhagic disease of the newborn" during first 2 weeks of life
- In 1929, Vitamin K isolated by Dam and Doisy (Nobel Prize, 1942), and conducted clinical trials showing Vitamin K protects against HDN
- 1961, Am Acad Pediatrics and Am College Obstetrics and Gynecology recommended routine prophylaxis with Vit K for all newborns
- Controversy in Britain in 1990s resolved to satisfaction of AAP, ACOG, Canada, Australia, New Zealand and others

early HDN

- Often fatal condition
- Diffuse hemorrhage in otherwise healthy infant
- During the first week of life
- Particularly in low birth weight babies
- Results of low levels of prothrombin and other vitamin K dependent clotting factors, (Factors II, VII, IX and X)
- An exaggerated of physiologic deficiency of clotting factors normal in the first few days of life
- Incidence between 2.5 to 17.0 per thousand newborns not given vitamin K prophylactic

Late HDN

- Between 2-12 weeks of life,
- Especially in breast-fed babies.
- Immaturity of liver affects production of clotting factors
- Late HDN primarily in breast fed infants without or inadequate vitamin K rates of 5/100,000 live births

Treatment

- **Treatment:**
  - Resuscitation & supportive care
  - Therapeutic IV vitamin K 2-5mg daily for 3-5day and until PT and concentration normal
  - Fresh frozen plasma 10ml/kg over one hour
  - In severe pallor we give blood transfusion

- **Prevention**
  - IM vitamin K (1mg) within 6 hours after labor.
  - Vitamin K can also be given orally with repeated doses

Disseminated intravascular coagulation

Thank you