Newborn Blood Disorders: Recognition and Management

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Objectives

- List common blood disorders found in newborns
- Recognize signs and symptoms of common blood disorders in newborns
- Newborns who need additional screening tests for blood disorders

Review: Blood

Blood Cell Production

www.wikipedia.com

Newborn Normal Values

- Blood volume 80-100 ml/kg
- Hemoglobin 16-18 g/L
- Hematocrit 53-58%
- MCV 98-108
- RDW - elevated
- Reticulocytes 3-7%, 1-3%
- Platelets 150-350
- WBC - wide range of normal
  - 3,500/uL – 18,000/uL
  - Peaks 8-12 hours after delivery
Peripheral Smear

- Macrocytic normochromic RBCs with nucleated RBCs
- Macroovalocytes, stomatocytes, red cell fragments
- Large lymphocyte with abundant cytoplasm

Physiologic Anemia of Infancy

- Increase in blood oxygen content and tissue oxygen delivery down regulates red blood cell production.
- Hemoglobin decreases as aged red blood cells are removed from circulation.
- Hemoglobin reaches nadir of 9.5-11 g/100 mL at 6-12 weeks of life.
- Relative hypoxemia triggers release of erythropoietin and increased red blood cell production.
- Exaggerated in premature infants.

Your office phone rings.....

- A family is calling you at the hospital requesting circumcision.
- 3 day old born at home
- Baby is doing great, is breastfeeding well, and seems to be very healthy.
- No vitamin K or erythromycin eye ointment.
- Do you want to circumcise this baby?

Vitamin K Deficiency

- Vitamin K required for the gamma carboxylation of clotting factors 2, 7, 9, 10.
- Newborns inherently vitamin K deficient.
- Poor placental transfer of vitamin K.
- Low concentration of vitamin K in breast milk (<5ug/L).
- Lack of GI flora.
- Vitamin K deficiency may lead to Vitamin K Deficient Bleeding (VKDB).

Early VKDB

- First 24 hours of life.
- Caused by placental transfer of compounds that interfere with vitamin K metabolism.
- Anticonvulsants (carbamazepine, phenytoin, barbiturates).
- Antibiotics (Cephalosporin).
- Anti-TB medications (rifampin, isoniazid).
- Warfarin.
- Incidence low – only 5% of at risk births.
- Presentation: cephalohematoma, umbilical stump bleeding, intracranial hemorrhage.

Classical VKDB

- First week of life.
- Physiologic deficiency combined with lack of vitamin K in breast milk and poor feeding.
- Without prophylactic vitamin K incidence as high as 1.5%.
- Extremely rare with prophylaxis.
- Presentation: bleeding from GI tract, umbilical stump, circumcision site.
- Intracranial bleeding infrequent but possible.
Late Onset VKDB

- After 2 weeks up to 6 months
- Inadequate Vitamin K in breast milk
- Additional risk factors that reduce vitamin K intake and absorption
  - Liver or pancreatic disease
  - GI disorders
  - Ingestion of vitamin K antagonists
- Incidence 4.4-10.5/100,000 babies
- Presentation: Intracranial bleeding

Evaluation of Infant

- In deciding whether to circumcise this baby you start with history and physical exam
  - Mom is not on any medications
  - No signs of bleeding in baby
  - Laboratory evaluation
    - Prolonged PT (INR > 3.5)
    - Normal fibrinogen
    - Normal platelet count

Counseling Parents

- Prophylactic Vitamin K at birth reduces incidence of VKDB
- Single IM dose of 1 mg vitamin K prevents classic and late VKDB
  - Concerns may include local trauma and higher cost
  - No significant link between vitamin K and childhood cancer
  - Oral dosing regimens prevent classic VKDB but have not been shown to decrease late VKDB

Case Conclusion

- Parents decide that they really want their baby circumcised and are concerned about the lab findings indicating vitamin K deficiency. They wonder if it is too late to give the shot?
  - No. Vitamin K prophylaxis can be given anytime.
  - SQ injection if actively bleeding
  - IV Vitamin K can cause anaphylaxis if given too quickly
  - Baby is given 1mg of IM vitamin K. You circumcise the baby the next day in the nursery without complication.

Your pager goes off....

- You are asked to come look at a baby’s head. Mom is worried about the way her baby’s head looks! This baby is about 4 hours old and was born earlier that morning by NSVD to an otherwise healthy 28 year old G1P0-1 mom. Mom is O+, serologies are all negative. Pregnancy has been uncomplicated. Baby had great Apgar scores of 9 and 9, weighed 8 pounds, and is otherwise doing well.
What is your next step?

- Forget about it!
  - Cone heads are a dime a dozen and lots of babies have red spots
- Watch and wait...
  - you aren’t really sure if there is anything here out of the ordinary and you don’t want to wake anyone up
- Worry!
  - There is evidence of bruising and/or bleeding on this baby’s head and maybe these red spots are petechia on a different part of the baby’s body… Would a CBC be a good idea?

Worry!

- Evidence of bleeding and bruising in multiple sites...
  - CBC returns with:
    - WBC = 20
    - HGB = 16
    - HCT = 48
    - Platelets = 15
  - Of course you repeat this lab...
    - Same results

Thrombocytopenia

- Platelets < 150
- Presentation
  - Mucocutaneous bleeding
    - Bruising, Petechia
    - Internal hemorrhage
    - Platelet levels <30
  - Incidental finding
    - CBC performed for another reason
    - Platelet levels <50

Common Causes

- Infection
  - Sepsis, NEC, TORCH, parvovirus
- Asphyxia
  - DIC caused by tissue damage
- PIH and Preeclampsia
  - Rarely severe, normalizes by 7-10 days
- Hemangiomas
- Consumptive coagulopathy
- Immune mediated thrombocytopenia
  - NAIT and ITP

Approach to Thrombocytopenia

**Congenital Thrombocytopenia**

- Wiskott-Aldrich Syndrome
- TAR Syndrome
- GAMT
- Trisomies
- Bernard-Soulier Syndrome
- X-linked macrothrombocytopenia

**Acquired Thrombocytopenia**

**Mucocutaneous Bleeding or Incidental finding**

- Well infant
  - Maternal ITP
  - Hereditary NAIT
  - Pre-eclampsia
- Sick infant
  - Asphyxia
  - Infections
  - IUGR/SGA
  - Hemangioma
NAIT
• Maternal alloantibodies against paternal antigens on infant’s platelets
• Mother has normal platelet counts
• Can occur in first pregnancy
• Presents as severe isolated thrombocytopenia in a healthy full term baby
  • Petechia, GI tract hemorrhage, hematuria, hemoptysis
  • Intracranial hemorrhage in 15-25% of infants
• Treat with washed and irradiated maternal platelets and IgG

Autoimmune Thrombocytopenia
• Maternal ITP
  • 15-45% of infants will have thrombocytopenia
  • 5-15% of infants will have severe thrombocytopenia
  • Nadir occurs 2-4 days after birth
  • Monitor infant platelets for first week of life
  • Presents with petechia or no findings
  • Rarely requires treatment
  • IgG, steroids, transfusion

Evaluation of Baby
• History
  • Clinical condition
  • Family history
  • Age of onset
  • Abnormal physical findings
• Lab Evaluation
  • CBC, peripheral smear, platelet count
  • Maternal platelet count

Case Conclusion
• On reviewing maternal history, you discover that mom has been followed during this pregnancy for ITP. Baby receives a dose of IgG and is followed clinically with resolution of thrombocytopenia and no further bleeding problems.

You get a call from the hospital lab......
• A baby in your care just had a routine screening bilirubin level that came back at 3.5! A critical lab value in your hospital!
• As you relay this information to parents and organize the phototherapy treatments what are some other things you may want to think about?

History and Physical Exam
• A lot of things can cause neonatal jaundice....
  • Exclusive breastfeeding?
  • Well appearing baby?
  • Does baby have bruising or birth injury?
  • Family history of neonatal jaundice?
  • Risk for hemolysis?
    • Immune mediated hemolysis
    • RBC membrane defects – spherocytosis or eliptocytosis
    • G6PD deficiency
**Additional History**
- Mom is a 28 year old first-time mother. She is healthy and her pregnancy was uncomplicated. Her blood type is O-. She received Rhogam during pregnancy.
- No family history of red blood cell disorders
- Lab work for baby:
  - Baby is A+, direct coombs test positive
  - Elevated reticulocyte count
  - Normal hemoglobin and hematocrit

**Hemolytic Anemia**
- Increased red blood cell destruction
- Isoimmune: Rh and ABO incompatibility
- Maternal immune disease
- Acquired RBC disorders
  - Infection: CMV, toxoplasmosis, sepsis
  - Hereditary RBC disorders
  - Spherocytosis and elliptocytosis
  - G6PD deficiency
  - Hemoglobinopathies: thalassemias

**Rh Hemolytic Disease**
- Rh - mom, Rh + baby
- Exposure and sensitization of maternal immune system to D antigen
  - Rare in first pregnancy
  - Placental transfer of maternal antibodies against D antigen on fetal RBCs
  - Destruction of antibody coated fetal RBCs

**Spectrum of Rh Disease**
- Mild hemolytic disease
  - + Coombs test
  - Little or no anemia
  - Minimal hyperbilirubinemia
  - Risk for severe late anemia at 3-6 weeks of age
- Moderate hemolytic disease
  - + coombs test
  - Moderate anemia
  - Hyperbilirubinemia requiring phototherapy/exchange transfusion
  - Hepatosplenomegaly
- Severe hemolytic disease
  - Risk for stillbirth, hydrops fetalis

**ABO Incompatibility**
- Type O moms produce anti A and anti B IgG
  - IgG crosses placenta
  - Does not require sensitization
  - Coombs test positive or negative
  - ABO incompatibility present in 12% of pregnancies
    - Less than 1% of births will have significant hemolysis
    - Less severe than Rh disease because A and B antigens present on many tissues throughout body

**Coombs Test**

<table>
<thead>
<tr>
<th>DIRECT COOMB’S TEST</th>
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<tbody>
<tr>
<td>Patient Sample</td>
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<tr>
<td>Anti-Hu IgG Reagent</td>
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Example: The RBCs in the dilution of the patient’s blood are agglutinated by the anti-A, anti-B reagent.
Treatment

- Important to monitor for jaundice after hospital discharge
- Phototherapy
- Exchange transfusion
- Follow up hemoglobin at 2-3 weeks to evaluate for anemia

Non-Immune Acquired Hemolysis

- Infection
  - CMV
  - Toxoplasmosis
  - Syphilis
  - Bacterial Sepsis
- Typically will also see thrombocytopenia
- Mechanism of hemolysis unknown

Hereditary RBC Disorders

- Hereditary Spherocytosis
  - 70-80% of cases autosomal dominant
  - Mutations in RBC membrane cytoskeleton
  - RBCs become more spherical
  - Spherical RBCs entrapped in spleen and hemolyze
  - Hemolysis in half of affected infants
  - Spherocytes common in newborn and with ABO incompatibility
  - Test family members
  - Wait until infant is 3 months old to diagnose

- Glucose-6-Phosphate Dehydrogenase Disorder
  - X linked inheritance pattern
  - Mediterranean, African and Chinese ancestry
  - Provides protection against Malaria
  - Episodic hemolysis and anemia
  - Following exposure to oxidants (some medications and fava beans) and infection
  - Diagnosis: coombs negative anemia
  - Heinz bodies and red blood cells with a bite out of them on peripheral smear

Case Conclusion

- Baby was diagnosed with ABO incompatibility. Received phototherapy for first 4 days of life with resolution of hyperbilirubinemia and no anemia.

A mother asks you....

- Why does my baby look so red?
- Full term LGA infant born vaginally to a 28 year old mother with gestational diabetes. Mother is healthy and pregnancy had no other complication. Baby has been doing well since delivery.
Don’t all babies look red?

- Hemoglobin levels > 60-65%
- Blood viscosity increases exponentially
- Impairs blood flow and oxygen delivery
- Most babies asymptomatic

Symptoms:
- Poor perfusion: plethora, cyanosis, lethargy, hypotonic, poor feeding, tremors
- Hypoglycemia
- Hypocalcaemia
- Hyperbilirubinemia

Causes of Polycythemia

- Increased red blood cell production
- Intrauterine hypoxia
- Maternal diabetes
- Neonatal hyper or hypothyroidism
- Chromosomal abnormalities: Tri 21
- Erythrocyte transfusions
- Delayed cord clamping
- Materno-fetal transfusion
- Twin-twin transfusion

Delayed cord clamping

Benefits to infants include:
- Increased blood volume
- Reduced need for transfusion
- Decreased incidence of intracranial hemorrhage in preterm infants
- Lower frequency of iron deficiency anemia in term infants
- Delaying cord clamping until 30-60 seconds after birth
- Optimal length of delay has not been established
- Clear evidence of benefit in preterm babies
- No clear evidence of benefit in term infants

Risks:
- Interference with resuscitation efforts
- Polycythemia

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Treatment of Polycythemia

- Reduce red blood cell mass without increasing intravascular volume
- Isovolumetric partial exchange transfusion with normal saline

Case Conclusion

- Infant was found to have a hematocrit of 60%
- Continued to be asymptomatic
- Was observed clinically with a hematocrit checked 1 week later and found to have fallen into a lower range
- No further concerns

I got a call from my sister…….

- My sister is about to have a baby boy.
- Family history of Von Willebrand’s Disease vWD
- She is first person in our family to have a baby boy
- She asked me if it is safe to circumcise him?
Hereditary Hemorrhagic Disorders
• Hemophilia A and B
• Von Willebrand Disease (vWD)

Hemophilia A and B
• 1/5000 male births
• X linked recessive trait
• 20-30% spontaneous mutations
• Types
  • Hemophilia A = Clotting Factor 8 deficiency
  • Hemophilia B = Clotting Factor 9 deficiency
• Severity
  • Severe - <1% of normal levels
  • Most common to manifest in newborns
  • Moderate ~ 1-5% of normal levels
  • Mild >5 <40% of normal levels

Clinical Presentation
• 40-70% diagnosed in newborn period
• Majority present with bleeding
  • Intracranial hemorrhage
  • Cephalohematoma
  • Umbilical stump bleeding
  • Bleeding following venipuncture, heel prick or circumcision
• Diagnose by measuring factor levels

Perinatal Management
• Vaginal or cesarean delivery
• Avoid vacuum extraction
• Minimize heel stick and venipuncture
• Give IM Vitamin K
• Do not circumcise
• Consult hematology and neonatology
• Treat with purified or recombinant Factor 8 or Factor 9

vWD
• Deficiency of von Willebrand Factor, required for platelet adhesion
• Most common hereditary bleeding disorder
  • 1% of general population
  • Autosomal dominant, occasionally recessive
• Rarely manifests in newborn period
  • Levels of vW Factor naturally elevated after birth
  • Rare reports of intracranial hemorrhage, thrombocytopenia and soft tissue bleeding
• Newborn care should not be different:
  • Circumcision not contraindicated.

Thank You!

References
• Avery’s Diseases of the Newborn 8th Edition
• Lange Neonatology 6th Edition