Hematology

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Overview

- Blood cell development
- Normal values
- Diagnostic tests
- Common hematologic problems and therapies

Blood Cell Development

- Stem cells – from which all blood cells derive - are present at 16 days in the yolk sac
- Circulation begins on day 22
- Liver hematopoiesis begins by 9 weeks gestation; peaks by 4-5 months and then regresses
- Hematopoiesis in the bone marrow begins ~ 22 weeks gestation
Types of cells

- Red blood cells
  - ~5,000 at term
- White blood cells
  - 10,000-26,000 at term at birth; 5,000-19,000 preterm at birth
- Platelets
  - 150,000 to 400,000
- Blood volume
  - Term – 80-100 ml/kg
  - Preterm – 90-105 ml/kg

Red Blood Cells

- Life span is 35-50 days (preterm); 60-70 days (term); 100-120 days (adult)
- Nucleated RBC’s are immature RBC’s
- Indices – measure size and hemoglobin content
- MCV (mean corpuscular volume) – size and volume of RBC
- MCH (mean corpuscular hemoglobin) – average amount of Hgb in the RBC
- MCHC (mean corpuscular hemoglobin concentration) – average concentration of Hgb in each RBC
Types of White Blood Cells

- **Granulocytes**
  - Basophils (0.5-1%)
  - Allergic and inflammatory responses
- Neutrophils
  - Include segmented neutrophil (mature) and bands, metas, myelos (immature forms)
  - Function as phagocytes – ingest and destroy bacteria, protozoa, cellular debris
  - Physiologic stress increases production
- Eosinophils (1-3%)
  - Similar function to neutrophil, but less effective
  - Allergic and anaphylactic responses, most effective granulocyte for parasite destruction

Types of White Blood Cells

- **Lymphocytes**
  - Thymus derived (T lymphocytes) – important in graft vs host disease and delayed hypersensitivity reactions
  - Bone marrow (B lymphocytes) – production and secretion of immunoglobulins and antibodies
- Monocytes
  - Immature macrophages
  - Clear old blood cells, debris

Retic count

- Inversely proportional to gestational age
  - 5-10% at 28 weeks
  - 3-10% at 34 weeks
- Falls rapidly to <2% by 7 days
- Persistent reticulocytosis – chronic blood loss or anemia
Coagulation

- Cascade of events
  - Extrinsic system is triggered by tissue injury
  - Intrinsic system is triggered by vascular endothelial injury
- Coag tests
  - PT – prothrombin time – checks extrinsic and common portions of the coag cascade
  - PTT – partial thromboplastin time – checks intrinsic and parts of the coag cascade
  - Fibrinogen – assess fibrinogen substrate which is required for clot formation

Anemia at birth

- Low Hgb concentration and/or decreased RBCs
  - Venous Hgb <13 g/dl in babies 34 weeks and > and in the first week of life is not normal
  - Decreased oxygen carrying capacity of the blood and amount of oxygen available to the tissues

Causes of Anemia at Birth

- Blood loss
  - Fetal maternal – spontaneous, traumatic amniocentesis, external version
  - Twin to twin – single placenta, hgb difference >5g/dl
  - Placental/Cord – cord rupture, anomalous insertion, accidental incision of placenta or cord, previa, abruption
  - Internal – intracranial, organ rupture, pulmonary
  - External - phlebotomy
Causes of Anemia at Birth

- Hemolysis
  - Blood group incompatibilities
  - Rh – sequence of events
    - Fetal cells with Rh antigen enter mom’s circulation
    - Maternal immune system makes antibodies
    - Maternal antibodies enter fetal circulation in subsequent pregnancies and destroy fetal red blood cells
    - Present with anemia, CHF, hydrops, ascites, pleural effusion, petechiae, hypoglycemia
    - Treatment: Rhogam – Anti-D antibodies
  - ABO
    - Occurs more often than Rh, but is less severe
    - Mom with O positive blood type, baby is A or B

- G6PD
  - Sex linked (mostly males) inherited disorder of red cells

- Infection
  - Intrauterine (viral, protozoal)
  - Postnatal (bacterial)

- Underproduction of erythrocytes

Anemia of Prematurity

- Hemoglobin falls during the first 2-3 months – to lowest value in neonatal period
- Some infants develop hypoxemia – poor feeding and weight gain, dyspnea, tachypnea, tachycardia, decreased activity, pallor – and require a transfusion
- Preterm infants require frequent blood sampling – iatrogenic anemia
Anemia of Prematurity

Diagnosis
- Hemoglobin concentration
- Retic count (reflects new erythrocyte activity)
- Peripheral blood smear – size, shape and structure
- Blood type
- Coombs
  - (+) direct Coombs – maternal IgG antibodies are present
  - (+) indirect Coombs – antibodies against the infant’s RBC’s are present in maternal serum
  - Kliehauer-Betke test – fetal hemoglobin in maternal blood

Anemia of Prematurity

Management - Transfusion
- Emergent – O, Rh negative
  - 10-20 ml/kg
  - Can give FFP, albumin or NS if blood is not available
- Non emergent – for preterm baby with low Hct
  - Protocols to determine need for exchange
  - Retic count – measures new erythrocyte activity
  - Exchange transfusion – jaundice or severe hydrops

Anemia of Prematurity

Management – Erythropoietin
- Consider if baby may require a transfusion the next week
  - Hct < 29
  - Retic count < 5
- Used in conjunction with iron supplementation
**Physiologic Anemia**
- High levels of RBCs at birth
- Gradually drop to a normal low ~2 months of age
- Stay low, and then increase
- Treatment – none (unless symptomatic)

**Hemorrhagic Disease of the Newborn**
- Caused by Vitamin K deficiency and decreased activity of factors II, VII, IX, and X
- Bleeding is noted at 24-72 hours – may be local or diffuse and is rarely life threatening
  - Or, late onset bleeding at 2-3 weeks
- Ecchymosis, petechiae, oozing puncture sites, bleeding circ
- PT and PTT are prolonged

**Differential diagnosis**
- Decreased Vitamin K absorption
  - Biliary atresia
  - Cystic fibrosis
- Pharmacologic
  - Anticonvulsants and anticoagulants
  - Heparin should be replaced with coumadin during pregnancy
- Complications
  - Anemia, IVH
- Treatment
  - Vitamin K at delivery
  - Transfusion
- Outcome
  - Vitamin K at delivery has mostly eliminated this disease

DIC
- Acquired hemorrhagic disorder
- Common precipitating factors:
  - Fetal distress
  - Infection
  - Hypoxia, shock, acidosis
  - Severe Rh incompatibility
  - Thrombocytopenia
  - Tissue injury (birth trauma)
Predominant symptom: hemorrhage

Diagnostic studies
- Platelet count – low
- PT and PTT prolonged
- Fibrinogen – low

Care
- Transfusion for bleeding
- Replace clotting factors

Outcome – related to cause

Thrombocytopenia

Significant decrease in platelet count (<100,000)

Causes:
- Platelet destruction
  - Idiopathic thrombocytopenia – maternal antibodies bind to platelet surface antigens
  - Neonatal conditions
  - Alloimmune thrombocytopenia (like Rh incompatibility)
  - Infection (bacterial or TORCH)
  - Thrombotic disorders
  - Impaired production
    - Trisomy 13, 18
    - Fanconi anemia

Care and treatment of underlying disease

Platelet transfusion
- < 30,000 in the first 48 hours
- < 50,000 if surgery is needed

IVIG – 80% effective in increasing platelet count

Exchange transfusion
Steroids
**Polycythemia**
- Hct > 65%
- Blood viscosity increases with Hcts >60% and causes decreased blood flow to the organs
- Presentation: plethora, cyanosis, tachypnea, poor feeding, hypoglycemia
- Treatment: partial exchange transfusion
  - Controversial if baby asymptomatic

**Inherited Bleeding Disorders**
- Only the most severely affected are identified in the neonatal period
  - Hemophilia
  - Von Willebrand disease
  - Factor XIII deficiency (most likely in neonatal period)
- Symptoms: delayed bleeding (cord, circ)
- Diagnosis: coags
- Give FFP, cryo if needed

**Transfusions**
- PRBC’s
  - 10-15 ml/kg; 20ml/kg
- Platelets
- FFP – replaces coagulation proteins
- Cryo – factor VIII and XIII
- Albumin – major contributor to oncotic pressure
- Granulocytes – rarely used
Transfusions

- Informed consent includes:
  - Risk of infection
    - Pre-donation questions self-eliminate donors with high-risk behaviors
    - Screened for HIV, HBV, CMV
  - Risk of transfusion reaction
    - Febrile reactions (most common)
    - Allergic reactions
    - Hemolytic reactions
  - Risk of Graft-vs-host disease
    - Preterm immune system may not reject foreign lymphocytes and damage the host

Transfusions

- Benefits
  - PRBCs
    - Improved oxygen carrying capacity
    - Relief of anemia symptoms
    - Minimal fluid administration
  - Platelets
    - Improve coagulation
  - FFP
    - Replace clotting factor deficiency

Transfusions

- Alternatives
  - Direct donation
    - Family and friends, if compatible
    - Blood must be irradiated
    - No evidence of increased safety
  - Erythropoietin
Partial exchange

- With NS – treat polycythemia
  - Calculate amount to be given:
    - Blood volume x (measured Hct – desired Hct) / measured Hct
- With PRBCs – treat hydrops (reduce Hct without reducing blood volume)
  - Calculate amount:
    - Blood volume x (desired Hct – measured Hct) / PRBC Hct – measured Hct

Exchange Transfusions

- For treating hyperbilirubinemia, DIC, autoimmune thrombocytopenia
- Preservatives contain glucose – expect hypoglycemia
- Preservatives contain citrate – hypocalcemia and magnesemia may occur
- Potassium level rises as blood ages

CBC Interpretation

- Altered results:
  - Interreader differences
  - Crying for more than 4 minutes – increased WBC
  - Stress – increased WBC, left shift
  - Birth asphyxia, maternal hypertension, tocolytics – neutropenia
  - Hemolytic disease, steroids – neutrophilia (in the first 72 hours)
**CBC with Infection**

- Elevated WBC
- Neutrophil response – immature cells are released with depletion of pool
- ANC – multiply total neutrophils by WBC count
  - Normal is 1750-5400 (term) and 1200 – 5400 (preterm)
- I/T ratio
  - Total immature forms / total neutrophils
  - >2 – probable sepsis

**Increased I/T ratio without sepsis**

- Maternal fever
- Maternal oxytocin administration
- Stressful labor
- Asphyxia
- Pneumothorax
- IVH
- Seizures
- Prolonged crying (>4 min)
- Hypoglycemia
- Surgery

**RBC indices**

- Anisocytosis – variation in the size of the cells (severe anemia)
- Macrocytosis – diameter >9mm (vitamin B12 or folic acid deficiency)
- Microcytosis – <9mm (iron deficiency, anemia)
- Spherocytosis – increased thickness and rounding (congenital spherocytosis, hemolytic anemias)
- Burr cells – long spinous processes (hemolytic anemia, DIC, liver disease)
- Howell-Jolly bodies – spherical bodies on cells (pernicious anemia)
- NRBCs
**Case study**

- 20 year old g1 mom delivered at 27 weeks; ROM at delivery.
- Baby was 1016 grams; Apgars 9/9. Foul smelling at delivery.
- Intubated and given surfactant x1; extubated to CPAP in ~ 8 hours.
- Treated with antibiotics (amp/gent) for 48 hours.
- GI priming feedings started on day of birth; increased to trophic feeds day 2. Trophic feeds gradually increased and TPN dc’d on day 8.

Baby had a streak of blood in his stool on day 10 (feeds at 139ml/kg). KUB with increased bowel gas, normal pattern. Fortifier was started on day 8; vitamins on day 9. Both stopped. Feeds continued.

- CBC non shifted. CRP < 5. Stool culture sent – Klebsiella identified.
- Baby had a sepsis work-up on day 12 due to increased spells and required intubation. CBC not shifted, but WBC down to 5.4. Started on amp/gent.
- KUB with nonspecific bowel gas pattern on day 13, placed NPO. Bowel gas then decreased on subsequent KUBs.

- CBC shifted on day 13 (60 segs, 24 bands). WBC 43.1. Platelet count decreasing (126,000).
- Blood culture from day 13 – gram negative rods.
- CRP on day 14 – 32, day 15 – 8.8.
- Cefotaxime added on day 14 to broaden coverage (high CRP, lower platelet count, identification of blood culture – Klebsiella).
References

- Up to Date.