Neonatal Lab Interpretation

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“Lab called... your CBC clotted”
Objectives

- Interpret lab values
- Discuss jaundice of the newborn
- Understand specific hematologic problems
CBC-Hematopoiesis
Erythrocytes-RBCs

- Main protein is hemoglobin (Hgb)
- RBC function is to protect Hgb
- Hgb function is oxygen/CO2 transport

Reticulocytes

- Inversely proportional to GA at birth
- Falls quickly to less than 2% by 7 days
- Elevated early Retic Ct may indicate bleeding, hemolysis or chronic blood loss

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Components of CBC

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- RBC function is to protect Hgb
- Hgb function is oxygen/CO2 transport

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RBC Indices

- Mean corpuscular volume (MCV): size and volume
- Mean corpuscular hemoglobin (MCH): average amount (weight) of hemoglobin
- Mean corpuscular hemoglobin concentration (MCHC): average concentration
- Nucleated RBC: circulating pre- reticulocyte

Anemia

- **Differential**
  - ↓ Erythrocyte production
    - infection, nutritional deficiencies, leukemia, bone marrow failure, anemia of prematurity
  - ↑ Erythrocyte destruction
    - hemolytic anemia, blood incompatibility, infection, other rare diseases
- **Blood loss**
  - iatrogenic, obstetric accidents, cord/placenta malformation, TTTS, abruption, DIC
Anemia of prematurity

All infants experience a progressive Hg decline in the 8-10 weeks following birth

• Not necessarily symptomatic

• Anemia possibly r/t rapid body growth, shortened RBC lifespan, and low blood erythropoietin (EPO) levels
  – Term infants nadir at 11-12 g/dL
  – Preterm may be as low as 7-8 g/dL

Anemia of Prematurity may be exaggerated physiologic response or pathologic
Erythropoiesis

What stimulates increased RBC production?

- Medications
  - Iron
  - Multivitamin
  - Erythropoietin
A 32-week 1700 gram infant has a UAC in place. 15 minutes after an xray, the nurse notices a large pool of blood under the infant. Estimated blood loss is 45mL.

Which set of s/s is most likely to reflect the infant’s condition in the first 30-60 minutes following this acute loss of blood?

<table>
<thead>
<tr>
<th></th>
<th>Hematocrit</th>
<th>Blood Pressure</th>
<th>Heart Rate</th>
<th>Multisystem</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Decreased</td>
<td>Hypotension</td>
<td>Tachy</td>
<td>Tachypnea, Pallor</td>
</tr>
<tr>
<td>B</td>
<td>Same as before incident</td>
<td>Hypotension</td>
<td>Tachy</td>
<td>Pallor, cap ref 3 sec, resp distress</td>
</tr>
<tr>
<td>C</td>
<td>Same</td>
<td>Hypotension</td>
<td>Brady</td>
<td>Apnea, cyanosis</td>
</tr>
<tr>
<td>D</td>
<td>Decreased</td>
<td>Same as</td>
<td>Same</td>
<td>Hepatosplenomegaly</td>
</tr>
</tbody>
</table>
Clinical Findings

Varies with the volume of blood loss and the time period over which blood is lost

**Acute**
- Pallor, then cyanosis and desats
- Shallow, rapid, irregular respirations
- Weak or absent peripheral pulses
- Low or absent blood pressure
- Hemoglobin may be normal initially, with rapid decline over 4-12 hours with hemodilution

**Chronic**
- Pallor without signs of distress
- Possible CHF with hepatomegaly
- Normal BP
- Low hemoglobin concentration
Diagnosis

- **History**
  - Family history: anemia, blood incompatibilities, jaundice
  - Maternal history: blood type, third trimester bleeding

- **Lab findings**
  - Hemoglobin concentration/CBC
  - Reticulocyte count
  - Blood smear- evaluate size, shape, structure
  - Blood type
  - Coombs test
  - Kleihauer-Betke test- identifies fetal hemoglobin in maternal blood
Management

- **Prenatal**
  - Diagnose early
  - Delayed cord clamping

- **Postnatal**
  - Anemia of Prematurity
    - Limit blood draws
    - EPO course
    - Transfusion PRBCs
  - Acute blood loss
    - Rapid replacement whole blood or PRBCs 10-20 mL/kg
    - If blood unavailable, saline 10-15 mL/kg
Platelets

- Etiologic Factors:
  - Platelet destruction: Maternal autoimmune (ITP, Lupus)
  - Neonatal conditions: Neonatal alloimmune thrombocytopenia, Infection, thrombotic disorders, DIC, Birth asphyxia, giant hemangiomas
  - Impaired platelet production (rare): Trisomy syndromes, TARS, Fanconi’s anemia
  - Platelet interference: maternal drug ingestion (Demerol, Phenergan, sulfonimides, thiazides)
Platelets Clinical Presentation

- Petechiae, purpura, epistaxis
- Ecchymosis over presenting part
- Cephalohematoma
- Bleeding (mucous membranes, GI, GU, umbilical cord, puncture sites)

Platelets Clinical Assessment

- Family, birth, medication history
- Blood smear, platelet count
- Physical exam (jaundice, congenital anomalies)
- Rule out DIC & Vitamin K deficiency
Thrombocytopenia management

- Supportive care and treatment
- Cesarean if maternal symptoms severe or previous child severely affected
- Platelet transfusion: keep greater than 30,000 in first 2 days, greater than 50,000 if surgery needed, or infant premature or at risk for IVH
- Steroids may be useful for counts less than 25,000 and active bleeding, or initial treatment for hemangioma
CBC-White Blood Cells with differential

- Protect against infective organisms and foreign substances
- Leukocytosis and leukopenia can be problematic
- 5 main types of WBCs
  - **Neutrophils** (31-57%)
  - Lymphocytes (35-61%)
  - Monocytes (4-7%)
  - Eosinophils (2-4%)
  - Basophils (0-1%)
CBC-WBC with differential

- Neutrophils are primarily responsible for killing & digesting bacteria
- Levels peak about 6-8 hours after birth (normal depends on age and gestation)
- With infection immature neutrophils are released
  - Bone marrow attempt to maximize neutrophils
- Immature to total ratio (I/T ratio)
- “Left shift”
“Left Shift”
CBC-Hematopoiesis
Absolute Neutrophil Count ANC

- Concentration of neutrophils in blood
- Low levels are especially concerning
- Considerations: Infants of hypertensive mothers, Trisomy 13, 18, 21

<table>
<thead>
<tr>
<th>Gestational Age range</th>
<th>&gt;36 weeks</th>
<th>28 to 36 weeks</th>
<th>&lt; 28 weeks</th>
</tr>
</thead>
<tbody>
<tr>
<td>At birth neutropenia defined as:</td>
<td>ANC &lt; 3500</td>
<td>ANC &lt; 1000</td>
<td>ANC &lt; 500</td>
</tr>
<tr>
<td>Time of peak ANC and value that defines neutropenia at time of peak</td>
<td>8 hours: ANC &lt; 7500</td>
<td>6 hours: ANC &lt; 3500</td>
<td>24 hours: ANC &lt; 1500</td>
</tr>
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</table>


## ANC calculation practice

<table>
<thead>
<tr>
<th>White Blood Cell count WBC</th>
<th>15,000</th>
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<tbody>
<tr>
<td>Segmented neutrophils (segs)</td>
<td>35%</td>
</tr>
<tr>
<td>Band neutrophils (bands)</td>
<td>15%</td>
</tr>
<tr>
<td>Metamyelocytes (metas)</td>
<td>3%</td>
</tr>
<tr>
<td>Lymphocytes</td>
<td>42%</td>
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<tr>
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<td>4%</td>
</tr>
<tr>
<td>Eosinophils</td>
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\[
\text{ANC} = \frac{\left(\%\;\text{segs} + \%\;\text{bands} + \%\;\text{metas}\right) \times \text{(WBC)}}{100}
\]

\[
\left(35\;\%\;\text{segs} + 15\;\%\;\text{bands} + 3\;\%\;\text{metas}\right) \times (15,000) \quad \frac{1}{100}
\]

\[
\frac{(35 \times 15,000) + (15 \times 15,000) + (3 \times 15,000)}{100} = 7,950
\]

**ANC is 7950**

Within normal range for gestation and age
I/T Ratio ➔ Immature to Total Ratio

- I/T ratio is most sensitive for estimating the risk that infection is present
  - Majority of neutrophils should be mature cells (segmented)
  - Elevated immature neutrophils raises suspicion

\[
\text{Immature (I)} = \frac{I}{T} \quad \text{ratio}
\]

\[
\text{Total (T)}
\]
Calculating I/T ratio

<table>
<thead>
<tr>
<th>White Blood Cell count WBC</th>
<th>15,000</th>
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\[
\text{Immature (I)} = \text{I/T ratio} \\
\text{Total (T)}
\]

15 bands + 3 metas = 18 immature
15 bands + 3 metas + 35 segs = 53 total

\[
= \frac{18}{53} = 0.34 \text{ I/T ratio}
\]

I/T ratio > 0.2 raises index of suspicion for infection
I/T ratio > 0.8 correlated with higher risk of death from sepsis
C-Reactive Protein (CRP)

- Non-specific marker for inflammation
  - trauma, surgery, infection, acute inflammation
- Useful when trended
- Generally elevates within 4-8 hours of event
- CRP levels remain high as long as the inflammation or tissue damage persists and then decrease rapidly
  - Possibly useful to monitor response to antibiotics

Definition of Neonatal Sepsis

- The presence of signs/symptoms of infection and/or isolation of a pathogen from the bloodstream

- Most commonly presents as bacteremia and/or meningitis

- Early onset sepsis: <72 HOL-7days, caused by maternal intrapartum transmission

- Late onset sepsis: >72 HOL, >7 days pathogens acquired postnatally
Bacteria on the move…

- Airborne- RSV
- Body fluid
- Transplacental- Listeria, Syphillis
- Ascending- chorioamnionitis
- Transcervical/intrauterine/birth canal- GBS, E Coli, gonorrhea, herpes
- Fecal/oral
- Contact- Staph, candida
- Nosocomial- CONS
- Pathogen dependent

Prophylaxis & Prevention!!
- GBS screening
- Eye prophylaxis for Chlamydia, Gonorrhea
- Hand hygiene
- NICU infection control practices
Maternal and Neonatal Risk Factors for Sepsis

- **Major risk factors**
  - Maternal GBS colonization
  - Preterm labor
  - Membrane rupture > 18 hours
  - Maternal s/s of intra-amniotic infection (chorioamnionitis)
- **Other risk factors:** recent maternal illness or infection, any maternal GU infection, procedures, instrumentation with delivery
- **Other variables that contribute to incidence include:** ethnicity, low socioeconomic status, male sex, and low Apgar score
Neonatal Risk Factors

- Prematurity
- Low birth weight
- Difficult delivery
- Birth asphyxia
- Meconium
- Resuscitation/Low apgars
- Male gender
- Congenital anomalies
- Multiple birth
Clinical Presentation of Sepsis

▪ Central Nervous System
  • Temperature instability
  • Lethargy/irritability
  • Hypo or hypertonia
  • Seizures

▪ Respiratory System
  • Cyanosis
  • Grunting, flaring or retracting
  • Tachypnea
  • Apnea
  • Increased oxygen requirement

▪ Gastrointestinal
  • Poor feeding
  • Emesis (may be bile-stained)
  • Increased residuals (may be bile-stained)
  • Abdominal distention
  • Edema/erythema of abdominal wall
  • Diarrhea/decreased stools
  • Hepatomegaly, jaundice
Clinical Presentation of Sepsis

- **Cardiovascular**
  - Pallor, cyanosis, or mottling
  - Bradycardia/tachycardia
  - Hypotension
  - Decreased perfusion
  - Edema

- **Skin**
  - Rashes
  - Pustules
  - Erythema
  - Omphalitis
  - Edema
Clinical Presentation of Sepsis

▪ Hematopoietic
  • Jaundice
  • Bleeding
  • Purpura/ecchymosis
  • Splenomegaly
  • Thrombocytopenia

▪ Metabolic
  • Glucose instability
  • Metabolic acidosis
Bacterial Organisms

- **Gram positive**
  - Coagulase-negative Staph
  - Staphylococcus Aureus
  - Listeria monocytogenes
  - Streptococcus pneumonia
  - GBS
  - Group A Strep

- **Gram negative**
  - E Coli
  - Neisseria meningitides
  - Haemophilus influenza
  - Klebsiella pneumoniae
  - Pseudomonas aeruginosa
  - Acinetobacter
  - Citrobactoer
  - Enterobacter
  - Serratia marcescens
  - Proteus
Lab Studies & Sepsis

- CBC with differential
- Platelet count
- Blood Culture
- Time to detection
- CRP
- Urine Culture
- Gram stain
- CSF studies
- CXR
- Coagulation studies
- Tracheal Aspirate
Blood Culture Volumes

- 0.5 ml of blood is NOT an adequate specimen
- One quarter of neonatal bacteremia are LOW COLONY COUNT (4 CFU/ml or less)
- At a minimum obtain at least ONE ml of blood

- Time to detection is a sensitive tool to detect true infection
- At 36 hours 99% of EOS are detected in term infants
Cerebrospinal Fluid CSF

- Up to 50% of neonates with meningitis may have negative blood cultures!!
- Lumbar puncture
  - Tube 1: CSF glucose, protein
  - Tube 2: CSF culture/gram stain
  - Tube 3: CSF cell count/diff
  - Tube 4: if needed for other studies

**CSF labs (generally)...**

\[ \uparrow \text{WBC} \quad \uparrow \text{Protein} \quad \downarrow \text{Glucose} \]
Treatment

- Broad spectrum
- Sensitivity
- Antibiotic choice
  - History in the NICU
  - Suspected organism
  - Degree of illness
  - Age
  - EOS vs LOS
    - LOS are primarily Gram + organisms (CONS, S epi)

- Patient Considerations…
<table>
<thead>
<tr>
<th></th>
<th>Meningitis</th>
<th>Pneumonia</th>
<th>Urinary Tract</th>
<th>Candida</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Incidence</strong></td>
<td>0.4-1/1000</td>
<td>&gt;10% in preemies/ill infants</td>
<td>Less common newborn period 1% term, 3% preterm</td>
<td>Varies w/increase High m/m (25-33%</td>
</tr>
<tr>
<td><strong>Common organism</strong></td>
<td>E. Coli, GBS, Listeria</td>
<td>GBS, pseudomonas</td>
<td>Enterococcus, E. coli, GBS</td>
<td>Infection with fungi (Candida)</td>
</tr>
<tr>
<td><strong>Acquisition</strong></td>
<td>Direct invasion, contamination from blood, skin or CSF</td>
<td>Airway</td>
<td>CAUTI</td>
<td>Skin, mouth, vagina, GI tract, catheter associated, “fungal balls”</td>
</tr>
<tr>
<td><strong>Risk factors</strong></td>
<td>Prematurity, CNS abnormalities, L&amp;D complications</td>
<td>Intubation, VAP</td>
<td>Males, premies, urinary malformations, maternal UTI, neurogenic bladder</td>
<td>Prematurity, Intubation, surgery, NEC, low WBC, steroids, abx, TPN/lipids, hyperglycemia, histamine blockers</td>
</tr>
<tr>
<td><strong>Treatment</strong></td>
<td>Longer course 14-21 days Cephalosporins</td>
<td>Organism dependent</td>
<td>7-10 days, r/o malformations with multiple UTI</td>
<td>Prophylaxis for VLBW, abx, central line-Fluconazole Oral-Fluc/Nystatin Systemic- Fluc, Ampho B</td>
</tr>
</tbody>
</table>
Rules of the R/O

▪ All preterm infants with the possible exception of a delivery after an induction for maternal reasons

▪ All infants with any respiratory symptoms, feeding intolerance or changes in neurologic status

▪ Any baby that just “doesn’t look quite right”

▪ Early, rapid and thorough evaluation is essential

▪ **Asymptomatic** newborn with even one risk factors needs evaluation

▪ Treatment should not be delayed with a **symptomatic** newborn with “normal” labs
Neonatal Response to Sepsis

- Decreased phagocytosis & chemotaxis
- Neutrophil deficiency
- Impaired migration
- Impaired diapedesis
- Inability to localize infection
- Decreased killing ability of neutrophils
  - 75% response in term infants
  - 50% response in preterm infants
Cascading Complications of Sepsis

- Pulmonary edema, secondary surfactant deficiency, PPHN
- Endocrine: adrenal insufficiency (hypotension), altered thyroid function
- Lymphocyte loss secondary to thymic involution, splenocyte apoptosis

Major Complications

- Septic Shock
- DIC
- Meningitis
Sepsis Cascade

- Bacterial cascade triggers the release of cytokine mediators
- Coagulation complement activation, neutrophil activation, immune activation, acidosis pathway
- Vasodilation leads to vascular leak and edema, decreased oxygen delivery, tissue injury and cell death

- SHOCK- A state in which the body can not meet the tissues demands for oxygen and substrate
  - Hypovolemic
  - Septic / Maldistributive
  - Cardiogenic
Early Septic Shock – compensated phase

- Baby looks “okay”
- Hyperdynamic
  - tachycardia
  - blood pressure WNL, pulse pressure widened
  - bounding peripheral pulses
  - tachypnea
  - flushed skin

Late Septic Shock – uncompensated phase

- Baby looks BAD
- Respiratory failure, PPHN
- Hypodynamic
  - decreased cardiac output
  - hypotension
  - diminished peripheral pulses, delayed CFT, cool skin
  - progressive metabolic acidosis DIC
Disseminated Intravascular Coagulation (DIC)

- Hemorrhagic disorder associated with underlying disease with uncontrolled activation of coagulation and fibrinolysis
- Fibrin deposited in blood vessels > microvascular thromboses
- Consumption of coagulation factors and platelets > hemorrhage = Consumptive coagulopathy
Disseminated Intravascular Coagulation (DIC)

- Important concepts:
  - Clotting factors don’t cross placenta
  - Most clotting factors produced in liver and require vitamin K
  - Neonatal levels of PT/PTT, coagulation inhibitors (ATIII, protein C), and fibrinolysis factors are < adult levels
  - Fibrinogen & platelets are similar levels to adult
  - Secondary to other disease processes
- Maternal factors: PIH, eclampsia, abruption, placental abnormalities
- Intrapartum factors: fetal distress, death of multiple, traumatic delivery
DIC-Lab Diagnosis

- Thrombocytopenia-consumed by clot, decreased production
- ↑ PT – deficiency in Vitamin K dependent factors
- ↑ PTT – clotting factor deficiency, heparin contamination
- ↓ Fibrinogen (consumed to form fibrin)
- ↑ FSP & D-dimer (fibrinolytic activity)
- RBC smear – presence of schistocytes ~ RBCs destroyed by fibrin strands
# Blood component therapy

<table>
<thead>
<tr>
<th>Product</th>
<th>Contents</th>
<th>Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Packed Red Blood Cells</td>
<td>RBC, WBC, plasma</td>
<td>↑ hematocrit</td>
</tr>
<tr>
<td>Platelets</td>
<td>Platelets, RBC, WBC, plasma</td>
<td>↑ platelet count</td>
</tr>
<tr>
<td>Fresh Frozen Plasma</td>
<td>Fibrinogen, antithrombin III, factors V &amp; VIII*</td>
<td>↑ fibrinogen</td>
</tr>
<tr>
<td>Cryoprecipitate</td>
<td>Fibrinogen, factors VIII &amp; XIII and Von Willebrand</td>
<td>↑ fibrinogen</td>
</tr>
</tbody>
</table>
DIC-Treatment

- Treat underlying condition
- Supportive care
- Replace coagulation factors, platelets
  - Vitamin K
  - Fresh Frozen Plasma
  - Cryoprecipitate
  - Platelets
  - Blood
  - Clotting factor concentrates
Management of Sepsis

▪ Report changes in the clinical exam immediately
▪ Consider all the risk factors
▪ Obtain lab work if not already done
▪ Administer IV antibiotics
▪ Monitor for signs of shock – compensated vs. uncompensated shock
  • Support the A, B, Cs
  • Volume resuscitation and inotropes
Nosocomial Infections

- Prevention is key!
- Hand hygiene
- Skin prep
- Vascular access
- Risk factors
Hyperbilirubinemia
### Unconjugated (Indirect) Bilirubin
- Fat-soluble
- Not yet metabolized by the liver
- Is not easily excreted
- Is the biggest concern for newborn jaundice
- Causes the yellowing of skin
- Can lead to Kernicterus

### Conjugated (Direct) Bilirubin
- Water soluble, non-toxic
- It is mostly excreted in stool and some in the urine
- “Cholestatic jaundice”
- Management
- No suntanning!!

Hyperbilirubinemia is defined as an elevated serum total bilirubin (TB) level

- > 10-12 mg/dl in term
- > 4-5 mg/dl in preterm infants
  - Usually peaks around 5-7 days
    - Later peak in preterm infants
Hyperbilirubinemia - Etiology

- Increased formation / synthesis of bilirubin
- Hemolysis
- Sepsis
- Sequestered blood
- Decreased/altered conjugation
- Delayed passage of meconium
- Dehydration
The role of phototherapy in the treatment of hyperbilirubinemia is:

1. Increase the amount of ligand at the liver wall, thus facilitating uptake
2. Cause oxidation and isomerization of bilirubin into a water-soluble, excretable form
3. Increase the amount of glucuronyl transferase so that bilirubin can be more easily conjugated
4. Cause movement of extravascular bilirubin into the vascular space, thus facilitating albumin binding
Phototherapy

[Image of a cartoon light bulb shining light on a baby with the caption: "Let me cut that for you."
Treatment Options

- Hydration
  - Optimize breastfeeding, formula supplementation
  - IV support
- Phototherapy
  - Light, wavelength and dose dependent
- Exchange transfusion
- Medications
  - Phenobarb-increases bilirubin conjugation
  - IVIG