Neonatal Sepsis and Lab Work Interpretation

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“Lab called… your CBC clotted”
The Astute Nurse’s Recognition of Sepsis in the Newborn...

“Something is just not right”
Case Study

- Baby Boy G was born to a G3-P2 with hx of 2 prior c-sections at 38 3/7 weeks at 11 am
- Mom was GBS + but did not receive abx because she was a scheduled c/s and not ruptured prior to delivery
- Baby was born with Apgars of 9 and 9 and no resuscitative measures required at delivery
- Birth took place at a hospital with a level II NICU
Case Study

- At 1 pm (2 HOL) during bath, baby “turned blue”, had emesis clear fluid and required BB O2
- A 2nd episode 10 minutes later prompted transfer to the special nursery
- Blood cx and cbc was ordered
- During blood draw baby had 2 more episodes
- Pediatrician to bedside, ECHO ordered
- ECHO was done and was “clear”
- Pediatrician went home with orders to get labs and call with results
- RR 88; baby irritable
Case Study

- At 2 pm (3 HOL) Lab and NICU staff still unable to get lab draws
- PIV placed
- Bruising noted at tourniquet sites
- MD called back in to assist/place line
- Baby now on 60% nasal cannula
- Intermittent emesis; described as “very fussy”
- VS at 3:15 pm (4 HOL): HR 168; RR 143; intermittent grunting; Temp 101.3, RN adjusted RW
Case Study

• At 6 pm UAC placed; blood cultures drawn and Amp and Gent ordered
• Amp started at 7:15; nursing note states that “Amp infusing, IV infiltrated” IV d/c’d
• Gent given via UAC
• The long story short…
Group Beta Strep “GBS”

- Normal vaginal flora in many women (10-30%)
- Ascending infection
- A major cause of morbidity & mortality in neonates
  - Stillbirth, sepsis, pneumonia
- **Risk factors:**
  - GBS bacteruria
  - Previous infant with GBS disease
  - < 37 weeks
  - ROM > 18 hours
  - Fever in labor > 38.0 C
Clinical Presentation...

- Respiratory signs
- Unstable Temperature, usually hypothermic
- Change in baseline color (pale, mottling, cyanotic and/or evidence of petechiae)
- Change in tone-lethargic or irritable
- Glucose instability

The Key is Noting a Change From Normal
Objectives

At the end of this presentation, the learner will be able to:

• Define early-onset and late-onset neonatal sepsis

• Discuss the management of the neonate with risk for early-onset neonatal sepsis

• Identify risk factors and calculate the probability of early-onset neonatal sepsis utilizing the sepsis calculator

• Gain an enhanced knowledge of laboratory tests for sepsis evaluation

• Name and discuss at least four components of the blood gas interpretation lab test, and the nursing implications of the test.
Definitions

▪ Bacteremia: Blood culture positive sepsis

▪ Sepsis / Septicemia: Blood culture positive AND systemic response

▪ Septic Shock: Blood culture positive, systemic response, AND cardiovascular compromise
Sepsis

- Common sites of neonatal infection:
  - Blood
  - CSF
  - Lungs
  - Urinary tract

- Incidence:
  - 1-8/1000 term infants
  - 1-250 preterm infants

- Associated with 20-50% mortality rate with substantial morbidity for survivors

- >30% of all neonatal deaths are attributable to infection

- 50% of all neonatal deaths in the first day of life are attributable to infection.
Maternal and Neonatal Risk Factors for Sepsis

• Major risk factors
  • Preterm birth
  • Maternal GBS colonization
  • 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
Chorioamnionitis

- Dysfunctional labor
- Foul smelling vaginal discharge
- Maternal fever
- Uterine tetany
- Uterine irritability
- Hemorrhage
- Endometritis
- Sepsis
Potential Fetal Effects

- Fetal tachycardia
- Fetal intolerance to labor
- **Poor neurologic outcome**
- Frequency highest in preterm deliveries with PROM
  - <27 weeks (41%)
  - 28-36 weeks (15%)
  - Term (2%)
Potential Fetal Effects Associated with Chorioamnionitis

- Sepsis
- Pneumonia
- Meningitis
Environmental Risk Factors for Sepsis

- Hospital admission
- Length of stay
- Invasive procedures
- Antibiotic therapy
Early Onset Sepsis

• ≤72 hours
  – Usually due to vertical transmission
  – Source may be ascending contaminated amniotic fluid or contact with colonizing or infectious bacteria in lower genital tract
Late Onset Sepsis

• >72 hours

• Occurring after the first 3-5 days of life, typically nosocomial microorganisms
  • Maternal vertical transmission colonizing and later infecting neonate
  • Iatrogenic reasons: contaminated hands; disruptions in skin; invasive monitoring, devices
What About Viruses?

- Viral infections can severely alter fetal growth and organ development – including visual, hearing, brain, cardiac and/or liver damage

- Common viral pathogens include:
  - Herpes simplex virus (HSV), Human immunodeficiency virus (HIV), Hepatitis, Cytomegalovirus (CMV), Parvovirus, and Rubella, Zika

- When obtaining a maternal history, considering including questions related to family illness, especially siblings or family members in the home, and sexual history and activity including partner history

(Karlson, K. 2013)
What do Neonatal Nurses need to know about Zika?

▪ First human reported case 1954

▪ World Health Organization has declared a public health emergency of international concern as of February 2016

▪ Spread through bodily fluid transfer
  • Includes vertical transmission

▪ Clinical signs may range from transient infection to severe illness and death in those affected

▪ Mother’s stage of pregnancy affects fetal outcomes!
  • May include birth defects, pregnancy loss
What do Neonatal Nurses need to know about Zika? (Williams, 2016)

- Full spectrum of outcomes not fully understood
  - Microcephaly
  - Eye calcifications
  - Microphthalmia
- Greatest risks are when mother is exposed in first trimester
- Diagnosed clinically
- Other abnormalities & infections should be ruled out
All Roads Lead to Sepsis

▪ Non-specific signs and symptoms
▪ You must rule it in until it can be ruled out
▪ Infants with mild illness become asymptomatic over the first 6 hours and can be observed without treatment, unless signs worsen or fail to improve (Benitz, Wynn, Polin. 2015)
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”
- Everyone admitted in between…
  - What do R/O sepsis look like in your unit?
Clinical Presentation of Sepsis

- Central Nervous System
  - Temperature instability
  - Lethargy/irritability
  - Hypo or hypertonia
  - Seizures
Clinical Presentation of Sepsis

▪ Respiratory System
  • Cyanosis
  • Grunting, flaring or retracting
  • Tachypnea
  • Apnea
  • Increased oxygen requirement
Clinical Presentation of Sepsis

- 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 (weak pulses, cool hands & feet)
  - Edema
Clinical Presentation of Sepsis

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

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

▪ Metabolic
  • Glucose instability
  • Metabolic acidosis
Neonatal Response to Sepsis

- Decreased response to chemotaxis
- Difficulty in cell surface adhesions
- Impaired migration
- Impaired diapedesis
- Abnormalities in oxidative glucose metabolism
- 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 cannot meet the tissues' demands for oxygen and substrate

Types
- 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)

- Very ill infant with generalized bleeding/oozing from puncture sites, catheter insertion sites, etc.
- Fibrin deposited in blood vessels > microvascular thromboses
- Consumption of coagulation factors and platelets > hemorrhage
DIC

- Underlying disorder
- Activates coagulation cascade
  - Blood clot formation
  - Coagulation factors become depleted
  - Results in uncontrolled bleeding
    - Death
Lab Diagnosis of DIC

- All of the routine screening tests of coagulation yield grossly abnormal results

<table>
<thead>
<tr>
<th>Laboratory Test</th>
<th>Value</th>
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<tbody>
<tr>
<td>Platelets</td>
<td>Decreased</td>
</tr>
<tr>
<td>Fibrinogen</td>
<td>Less than 200</td>
</tr>
<tr>
<td>Fibrin Split</td>
<td>Increased</td>
</tr>
<tr>
<td>PT &amp; aPTT</td>
<td>Initially</td>
</tr>
<tr>
<td></td>
<td>increased</td>
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</table>
# Blood component therapy

<table>
<thead>
<tr>
<th>Product</th>
<th>Contents</th>
<th>Effect</th>
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</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>
Meningitis - Signs and Symptoms

- Generalized signs/symptoms sepsis
- Increased irritability, high-pitched cry
- Increased intracranial pressure
  - bulging fontanel
  - emesis
  - decreased tone, lethargy
- Seizures
Meningitis-Long Term Outcome

▪ Overall mortality: 20-40%
▪ Morbidity of survivors: 20-50%
  • mental and motor problems
  • seizure disorders
  • hydrocephalus
  • hearing loss
  • blindness
  • abnormal speech patterns
Urinary Tract Infections

- Gram negative or gram positive bacteria
  - 70% E coli
  - GBS, Klebsiella, Pseudomonas, Proteus
- Obstructive congenital anomaly
- Neurogenic bladder (spina bifida)
- Vague, generalized symptoms or asymptomatic
- If UTI, also draw blood culture
- VCUG prior to discharge to evaluate for reflux, which increases the risk for recurrent infections
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
Case Study

- Male infant 36w3d, born to a 35 y/o G1P1
  - Spontaneous vag delivery, ROM 22 hours, afebrile, GBS unk, Amp given
  - Prenatals significant for O POS, otherwise unremarkable
- APGAR 8/9, 2660 g
- Slight bruising down the upper back, likely from delivery
- Discharge note at DOL 2
  - Jaundice to umbilicus. Lost 5% bw.
  - Given d/c instructions and had f/u appt the next day
Case Study

▪ DOL 3
  • F/u jaundice “under medium risk”, pt to return tomorrow for jaundice & weight check.

▪ DOL 4
  • Weight down again to 7% BW, Bili rising still to 14.7, cutoff for GA is 17. F/u tomorrow.

▪ DOL 5
  • No weight change, jaundice to groin. Tbili 15.7. Sent for labs

▪ DOL 6
  • “Tbili coming down” follow up in one week

▪ DOL 14
  • Weight improved, Normal checkup
Case Study

- DOL 17
  - Per mother “crying inconsolably” 6 hours, refused to eat, vomit x1

- DOL 21
  - Milk supply decreasing, supplementing, some reflux

- DOL 23
  - Presents to ED with labored breathing, lethargic and pale since this morning “Had similar episode once”
    Inconsolable for 12 hours, decreased tone, decreased intake, pale

- VS: BP: 72/41, Heart Rate: (!) 212, Temp: (!) 35.9 °C (96.7 °F), *Resp: 50, SpO2: 100 %
Case Study

- “Lethargic, weak cry, distressed”
- Cap refill 3-5 seconds with mottling, pallor
- Glucose 22, D10 bolus given. CBC, blood culture, CRP, ammonia, VBG, CXR, EKG ordered.
  - Sepsis treatment started (amp/gent, acyclovir, IVF)
- Intubated for multiple apneas, blood gas results

### Recent Labs

<table>
<thead>
<tr>
<th>blood gas</th>
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<tbody>
<tr>
<td>PH37</td>
<td>7.36</td>
</tr>
<tr>
<td>PCO2</td>
<td>30</td>
</tr>
<tr>
<td>PO2</td>
<td>95</td>
</tr>
<tr>
<td>HCO3</td>
<td>17*</td>
</tr>
<tr>
<td>BEX</td>
<td>Neg 8.0</td>
</tr>
</tbody>
</table>
Case Study

- Upon arrival to ICN (DOL 23)
  - All 4 extremities extended c/f seizures
    - Neuro consulted
      - EEG, multiple brief seizures from left hemisphere and encephalopathy.
  - Purple non blanching lesions noted, which slough off later in the day
  - Later that day culture is positive.
    - Group B Streptococcus

<table>
<thead>
<tr>
<th>Recent Labs</th>
<th></th>
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<tbody>
<tr>
<td>WBC</td>
<td>4.2*</td>
</tr>
<tr>
<td>HGB</td>
<td>11.0*</td>
</tr>
<tr>
<td>HCT</td>
<td>30.8*</td>
</tr>
<tr>
<td>PLT</td>
<td>465*</td>
</tr>
<tr>
<td>NEUTA</td>
<td>0.92*</td>
</tr>
<tr>
<td>LYMA</td>
<td>2.94</td>
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</table>
Case Study

- DOL 24
  - Sepsis
  - Status Epilepticus

### Blood Gas

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
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<tbody>
<tr>
<td>PH37</td>
<td>7.05*</td>
</tr>
<tr>
<td>PCO2</td>
<td>72*</td>
</tr>
<tr>
<td>PO2</td>
<td>104*</td>
</tr>
<tr>
<td>HCO3</td>
<td>19*</td>
</tr>
</tbody>
</table>

### Recent Labs

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>WBC</td>
<td>1.6*</td>
</tr>
<tr>
<td>HGB</td>
<td>14.8</td>
</tr>
<tr>
<td>HCT</td>
<td>40.7</td>
</tr>
<tr>
<td>PLT</td>
<td>122*</td>
</tr>
<tr>
<td>NEUTA</td>
<td>0.80*</td>
</tr>
<tr>
<td>LYMA</td>
<td>0.61*</td>
</tr>
<tr>
<td>BANDA</td>
<td>0.06</td>
</tr>
</tbody>
</table>
Case Study

▪ DOL 26
  • MRI showed injury to cortex, white matter, and deep gray matter associated with leptomeningeal enhancement consistent with infection. Injury to the occipital and temporal lobes consistent with effects of hypoglycemia

▪ DOL 29
  • Passed in parents arms
Where Are We Now?

▪ The current incidence of EOS ranges from 0.5 to 1.2 cases per 1000 live births

▪ This is a threefold to fivefold decrease over the past 20 years!

▪ In 2010, GBS sepsis was reported at 0.25 cases per 1000 live births, a decrease from 1.8 cases per 1000 live births in 1990 (Escobar, Puopolo, et al, 2014)
Prevention Strategies: What are we doing?

- Maternal prenatal GBS screening
- The only intervention proven to decrease the incidence of early-onset neonatal sepsis is maternal treatment with intrapartum intravenous antimicrobial agents for the prevention of GBS infections
- In other words...maternal antibiotics in labor, specifically penicillin
- Ampicillin or cefazolin are acceptable if given greater than 4 hours prior to delivery
- Erythromycin is no longer recommended (high resistance rates)

http://www.cdc.gov/mmwr/preview/mmwrhtml/figures/r5910a1f5.gif
Intrapartum Antibiotic Indications

- Positive GBS culture or molecular test
- Unknown colonization with gestation less than 37 weeks, rupture for greater than 18 hours, or temperature greater than 100.4 degrees F
- GBS bacteriuria during the current pregnancy
- Previous infant with invasive GBS disease
The Challenges

- #1: Define chorioamnionitis consistently
- #2: Identifying infants with clinical signs or symptoms consistent with sepsis with a "high likelihood" of early-onset sepsis who require antibiotics soon after birth
- #3: Identifying infants that are well-appearing with a "high likelihood" of early-onset sepsis who require antibiotics soon after birth
Current method

Maternal Risk Factors
- GA
- GBS
- ROM
- Abx
- Fever

Infant
- Clinically Ill
- Well-Appearin

Labs
- Blood culture (at birth)
- CBC, CRP, LP (6-12 hours)

Minimun of 48 hours
Abx
Are We Over Treating?

- The incidence has fallen, but our evaluation and treatment remain substantial (Escobar, Puopolo, et al, 2014)
- Treating the well-appearing, at risk newborn
- What are some of the problems with over treating?
  - Breastfeeding rates
  - Microbiome
Are We Under Treating?

- Do you know a case of a previously well newborn presenting to the ED at less than a week of age?
How Soon Can You Rule Out Sepsis?

- Is there an early exit route?
- What are some of the negative effects of the r/o sepsis process?
  - Sensitivity and specificity of CBC
- Is there a place for the actual patient assessment?
Early Identification… A New Approach: The Probability of Neonatal Early Onset Infection

▪ Based on the work by Drs Gabriel Escobar and Karen Puopolo, et al. (2014)

▪ Goal: To define a quantitative stratification algorithm for the risk of EOS in newborns greater than or equal to 34 weeks gestation

▪ The question: Is there a way to use maternal OBJECTIVE data with OBJECTIVE neonatal clinical findings to define more efficient strategies for the evaluation and treatment of EOS in term and late preterm infants?

▪ The potential result: Decreased antibiotic treatment in newborns
How?

- Escobar, Puopolo, et al. looked at over 600,000 live births with a gestational age greater than or equal to 34 weeks at 14 hospitals between the years of 1993 and 2007

- Identified ALL 350 EOS cases that occurred at less than 72 hours of age

- These cases were matched by birth year and birth hospital to 1063 controls
Probability of Sepsis

- Using the information gathered from the 350 cases of proven EOS and their matched controls, the probability of sepsis was predicted using only objective clinical data available at the time of birth.
- Based on 350 cases of 608,014 births, the sepsis rate for the population was 0.58 per thousand live births.
- The model uses 5 predictors to compute a potential risk of sepsis at birth.
- The risk is then adjusted based on infant-specific data to guide evaluation and treatment decision (Bayesian approach).
“The Calculator” – Let’s try it!


- **CASE:** 39 1/7 week G3P1 presents with c/o labor. Contractions every 3 - 5 minutes. Cervical exam at 1.5 cm. BOW intact. Labors to complete in 1.5 hours. Ruptures 20 min prior to delivery. GBS negative, no antibiotics administered. Last temperature prior to delivery 98.9 degrees F.

- Based on the calculator, what is the baseline risk of EOS?

- What if the gestational is 35 1/7 weeks?
Equivocal Signs

- In the first 12 hours of life, the baby experiences either:
  - Two (2) of the following abnormalities that persist for 2 hours, or
  - One (1) abnormality that persists for 4 hours

- Heart rate ≥ 160
- Respiratory rate ≥ 60
- Temperature ≥ 100.4F or < 97.5F
- Respiratory distress (grunting, flaring or retracting)

(Escobar, et al. 2014)
Which baby gets antibiotics?

- 39 1/7 week
  - 98.9 F
  - BOW intact
  - GBS neg

- 35 1/7 week
  - 98.9 F
  - ROM 1 hour
  - GBS neg

- 35 1/7 week
  - 100.5 F
  - ROM 4 hour
  - GBS neg

- 35 1/7 week
  - 101.6 F
  - ROM 14 hour
  - GBS pos w/abx

- 35 1/7 week
  - 102.1 F
  - ROM 19 hours
  - GBS pos w/abx
Which baby gets antibiotics?

<table>
<thead>
<tr>
<th>Risk per 1000/births</th>
<th>EOS Risk @ Birth</th>
<th>0.30</th>
</tr>
</thead>
<tbody>
<tr>
<td>EOS Risk after Clinical Exam</td>
<td>Risk per 1000/births</td>
<td>Clinical Recommendation</td>
</tr>
<tr>
<td>Well Appearing</td>
<td>0.12</td>
<td>No culture, no antibiotics</td>
</tr>
<tr>
<td>Equivocal</td>
<td>1.49</td>
<td>Blood culture</td>
</tr>
<tr>
<td>Clinical Illness</td>
<td>6.29</td>
<td>Empiric antibiotics</td>
</tr>
</tbody>
</table>
You Got a Number, Now What?

- Labs – timing is clearly an issue
  - Blood Culture (at birth or prior to starting antibiotics)
  - CBC with WBC differential and platelet count
  - CRP
  - Blood Gas
  - Blood Glucose
  - LP
- Are the lab results enough to start or stop antibiotics?
- There is still value in RN assessment!
Obtaining a “Good” Blood Culture

- Sterile technique for the draw and the transfer into the culture bottle
- Obtain **at least** 1 mL of blood per culture bottle
- What do you do if you only get 1 mL of blood? **AEROBIC BOTTLE ONLY**!
- Obtain a culture prior to starting antibiotics
Blood Cultures

- What did we learn from the earlier case study?
  - How long do we wait for antibiotics?
  - What is reasonable?

- TRUE or FALSE…
  - The lid of a blood culture bottle is sterile? **FALSE!!**
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-Hematopoiesis

Hematopoiesis in humans

Bone marrow

Common myeloid progenitor

Multipotent hematopoietic stem cell (Hemocytoblast)

Common lymphoid progenitor

Lymphoid progenitor

Thrombopoiesis

Thrombocytes (Platelets)

Erythropoiesis

Erythrocyte [2] (Red blood cell)

Granulopoiesis

Neutrophil

Monocyte

Natural killer cell (Large granular lymphocyte)

Lymphoid dendritic cell [3]

Mast cell

Myeloid dendritic cell [3]

Macrophage

Plasma cell

B lymphocyte

T lymphocyte

Small lymphocyte [4]

Lymphopoiesis

By A. Rad - Own work, CC BY-SA 3.0, https://commons.wikimedia.org/w/index.php?curid=1042490

Notes

- The morphological characteristics of the hematopoietic cells are shown as seen in a Wright's stain, May-Giemsa stain or May-Grünwald-Giemsa stain. Alternative names of certain cells are indicated between parentheses.
- Certain cells may have more than one characteristic appearance. In these cases, more than one representation of the same cell has been included.
- Together, the monocyte and the lymphocytes comprise the agranulocytes, as opposed to the granulocytes (basophil, neutrophil and eosinophil) that are produced during granulopoiesis.
- B, N, and E. stand for B-lymphoid, Neutrophilic and Eosinophilic, respectively— as in Basophilic promyelocyte. For lymphocytes, the T and B are actual designations.

[1] The polychromatic erythrocyte (reticulocyte) at the right shows its characteristic appearance when stained with methylene blue or Azure B.
[2] The erythrocyte at the right is a more accurate representation of its appearance in reality when viewed through a microscope.
[3] Other cells that arise from the monocyte: osteoclast, microglia (central nervous system), Langhans cells (epididymides), Kupffer cell (liver).
[4] For clarity, the T and B lymphocytes are split to better indicate that the plasma cell arises from the B-cell. Note that there is no difference in the appearance of B- and T-cells unless specific staining is applied.
CBC-White Blood Cells with differential
CBC-WBC with differential

- Neutrophils are primarily responsible for killing & digesting bacteria
- Levels peak about 6-8 hours after birth
- With infection immature neutrophils are released
  - Bone marrow attempt to maximize neutrophils
- Immature to total ratio (I/T ratio)
- “Left shift”
“Left Shift”
## 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>
</tbody>
</table>


### ANC calculation practice

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<thead>
<tr>
<th>White Blood Cell count WBC</th>
<th>15,000</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Segmented neutrophils (segs)</strong></td>
<td>35%</td>
</tr>
<tr>
<td><strong>Band neutrophils (bands)</strong></td>
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</tr>
<tr>
<td><strong>Metamyelocytes (metas)</strong></td>
<td>3%</td>
</tr>
<tr>
<td><strong>Lymphocytes</strong></td>
<td>42%</td>
</tr>
<tr>
<td><strong>Basophils</strong></td>
<td>4%</td>
</tr>
<tr>
<td><strong>Eosinophils</strong></td>
<td>1%</td>
</tr>
</tbody>
</table>

\[
(\% \text{ segs} + \% \text{ bands} + \% \text{ metas}) \times (\text{WBC}) \quad \frac{(100)}{}
\]

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

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

\[
\text{Immature (I)} = \frac{I}{T} \text{ ratio}
\]
\[
\text{Total (T)}
\]
### Calculating I/T ratio

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#### Immature (I) = I / T ratio

**Total (T)**

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

**I/T ratio**

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

- 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
- CRP levels remain high as long as the inflammation or tissue damage persists and then decrease rapidly
  - Possibly useful to monitor response to antibiotics

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

Cerebrospinal Fluid CSF

↑ WBC
↑ Protein
↓ Glucose

Culture is most critical for diagnosis

# Blood Gases

<table>
<thead>
<tr>
<th></th>
<th>Arterial</th>
<th>Capillary</th>
</tr>
</thead>
<tbody>
<tr>
<td>pH*</td>
<td>7.30 - 7.45</td>
<td>Same</td>
</tr>
<tr>
<td>PCO₂ *</td>
<td>35 - 45 mmHg</td>
<td>35 - 50 mmHg</td>
</tr>
<tr>
<td>PO₂ (on room air)</td>
<td>60 – 80 mmHg</td>
<td>--- (not useful)</td>
</tr>
<tr>
<td>HCO₃ Bicarb</td>
<td>19 – 26 mEq/L</td>
<td>19 – 26 mEq/L</td>
</tr>
<tr>
<td>Base Excess</td>
<td>-4 to +4</td>
<td>-4 to +4</td>
</tr>
</tbody>
</table>

*preterm infants have lower acceptable pH, and higher CO₂*
$\text{CO}_2 = \text{ACID}$

$\uparrow H^+$

$\text{HCO}_3^- = \text{BASE}$

$\downarrow H^+$

**Blood pH Levels**

- **Death**: pH 6
- **Acidosis**: pH 7
- **Normal pH**: pH 7.35
- **Alkalosis**: pH 7.45
- **Death**: pH 7.8

UCSF Benioff Children’s Hospitals
ACIDOSIS
pH < 7.35
↑ CO₂ Respiratory
↓ HCO₃⁻ Metabolic

ALKALOSIS
pH > 7.45
↑ HCO₃⁻ Metabolic
↓ CO₂ Respiratory
Blood Gases

1. Where did the gas come from?
2. Is the pH: low, normal or high?
3. If pH low: ↑ CO₂, ↓ HCO₃, or mixed
4. If pH high: ↑ HCO₃, ↓ CO₂, or mixed
Respiratory Acidosis

$pCO_2 >= 45mmHg, \hspace{1em} pH < 7.35$

Causes...

Loss of tidal volume
- Lung disease
- Pneumothorax
- Airway obstruction
- “Mechanical” interference

Loss of respiratory drive
- Poor effort
- Neurologic injury
- Apnea
Respiratory Acidosis

\[ pCO_2 \geq 45\text{mmHg}, \quad pH < 7.35 \]

Treatment-

- Renal compensation
- CPAP
- Positive Pressure Ventilation
- Intubation
  - ↑ tidal volume and/or rate

Chronic Respiratory acidosis will see a rise in \( \text{HCO}_3^- \)
Metabolic Acidosis

HCO₃ <= 18 mEq/L, pH < 7.35

Causes…

• ↑ Lactic acid production
  • Shock
  • Sepsis
  • Cardiac disease
  • Hypothermia
  • Hypoglycemia
• Excessive loss of HCO₃
• Inborn error of metabolism
Metabolic Acidosis

HCO₃≤18 mmol/L, pH <7.35

Identify and treat underlying causes!

• Hypoxia
• Hypotension
• Infection
• Hypoglycemia
• Hypothermia

Medications…
• NS bolus, Bicarb
Sodium Bicarbonate... useless therapy?

- Efficacy and safety of sodium bicarbonate replacement therapy unproven
- Still used in severe acidosis
- Not recommended in resuscitation
  - Lack of efficacy
  - Potential for harm
- Not recommended for preterm infants
  - Increased mortality
  - Increased IVH

Never to be given if patient not ventilating well
Case 1:

- Term baby
- Delivered by emergent c/s due to fetal distress
- RR 26, HR 124, weak respiratory effort
- SpO₂ 90% on 0.50 FiO₂ via NC
- Hypotonic
- Capillary blood gas
  - pH 7.16, PCO₂ 70, HCO₃ 21, BE -7
Case 1: Baby N

- Had an asphyxial insult
- Inadequate respirations → high $\text{PCO}_2$ (respiratory acidosis)
- Tissue hypoxia → metabolic acidosis
- What to do now?
Case 2: Baby M

- 28 weeks’ gestation
- Developed RDS
- Now intubated and ventilated
- Blood gas:
  - pH 7.47, PCO2 28, HCO3 22, BD 4
- What does Mia have?
Case 2: Baby M

- Respiratory alkalosis
- Excessive ventilation
- Correct by
  - Decreasing ventilator rate
  - Decreasing tidal volume or
  - Decreasing inspiratory pressure
Implications for all patients…

• Know if your patients are at risk
• Always review lab work
• Don’t normalize abnormal results
• Trust your instincts!
References


Questions?

Thank you!!

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