Laboratory Interpretation: A Focus on WBC’s, RBC’s, and LFT’s

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Objectives

• Upon completion of this lecture, the participant will be able to:
  – Identify a step approach to the interpretation of a cbc – rbc’s and wbc’s; hepatic function tests
  – Discuss various laboratory abnormalities identified on an individual throughout the lifespan
  – Systematically interpret laboratory findings using case studies

Red Blood Cell Formation

• Formed in bone marrow (erythropoiesis)
• When mature, the rbc is released into circulation
• Mature rbc has a life span of approximately 120 days
  – Many factors trigger an increase in the production of rbc’s by the bone marrow, but a decrease in O2 is the most common.
  – Low tissue oxygen levels trigger the endothelial cells in the kidneys to secrete erythropoietin – which in turn, stimulates bone marrow red cell production


Anemia: Defined

• Anemia – comes from the Greek word “Anaimia” – meaning “without blood”
• A decrease in the number of red blood cells, hemoglobin, or hematocrit
  OR
• A decrease in the oxygen carrying capacity of the blood

Step Approach is Essential

Relevant Financial Relationship Disclosure Statement

Title of talk

• I will not discuss off label use and/or investigational use of any drugs/devices.
• I don’t have the following relevant financial relationships to report in relationship to this presentation.
The CBC - A Blessing or a Curse

- RBC
  - 4.1-5.1 m/mm³
- Hemoglobin
  - 12-16 g/dl
- Hematocrit
  - 36-46%

**1 hemoglobin : every 3 hematocrit

The Indices - Your Most Important Tools

- MCV - Mean Corpuscular Volume
  - 80 - 100: Normocytic
  - <80: Microcytic: defect in hgb synthesis
  - >100: Macrocytic

The MCV allows you to classify the type of anemia to further determine the etiology

MCHC - Mean Corpuscular Hemoglobin Concentration

- Average concentration of hemoglobin in red blood cells
  - Much more helpful than the MCH
  - Provides you with information regarding the color of the cells
- Normal:
  - 32-37: Normochromic
  - <32: Hypochromic

Classifications/Causes of Anemia

- Macrocytic, Normochromic
  (↑ MCV, Normal MCHC)
- Vitamin B12 Deficiency
- Folate Deficiency
- Myelodysplastic process
- Hypothyroidism

- Normocytic, Normochromic
  (Normal MCV and Normal MCHC)
- Anemia of Chronic Disease
- Acute Blood Loss
- Early Iron Deficiency

Classifications/Causes of Anemia

- Microcytic, Hypochromic
  (↓ MCV and ↓ MCHC)
- Iron deficiency Anemia
- Thalassemia
- Lead Poisoning
- Sideroblastic Anemia
- Aluminum Toxicity
- G6PD

(Occasionally: Anemia of Chronic Disease)
RDW

• Red Cell Distribution Width
  – Normally all red cells are about equal in size
  – RDW is the degree of anisocytosis or the variability of the red cell size
  – Helps to differentiate between various causes of microcytic, hypochromic anemia
    • IDA, Thalassemia, and Anemia of Chronic Disease
      – Increased RDW - IDA
      – Normal RDW-Anemia of Chronic Disease
      – Normal or slightly increased RDW- Thalassemia

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Reticulocyte Count

• The number of new, young, red blood cells found in 100 rbc’s in circulation
  – It is expressed as a percentage with normal being approximately 1-2 %
  – It is an index of the bone marrow’s health and response to the anemia

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What Does an Elevated Reticulocyte Count Indicate?

ELEVATED RETICULOCYTE COUNT MEANS THAT THE BONE MARROW IS HEALTHY and/or YOUR TREATMENT IS WORKING BUT…Blood loss or destruction is likely occurring

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Case Study - 1

18 year old female presents with fatigue and sob while cheerleading. +Increase in ice consumption. PE-pallor, pale conjunctiva, systolic murmur, and tachycardia.
What type of anemia does she have?
What would you order?

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Iron Deficiency Anemia

Blood loss is the number ONE cause for IDA in individuals > 4

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Iron Deficiency Anemia

• Most prevalent anemia worldwide
• Causes
  – Increased iron loss
    – Dietary inadequacy
    – Malabsorption
    – Increased iron needs

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Important History

• Medications?
• Any Blood Loss?
  – Menorrhagia
  – Black or Blood Stools
  – Hematuria
  – Hemoptysis
  – Blood Donation
• Family History of Anemia?
  – Celiac disease (sprue)

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However…

• Signs and symptoms of iron deficiency anemia are determined by...
  – Degree of anemia
  – Acuteness of the anemia
  – Presence of underlying disease states

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Diagnosis of Iron Deficiency Anemia

• Ferritin
  – Measurement of iron stores
  – Level < 16 is diagnostic of IDA
  – Normal: 10 - 210
  – Keep in mind that this can be falsely elevated in the individual with febrile illness, malignancy, liver disease, inflammatory diseases
• Iron
  – Normal: 50 - 160
  – Amount of circulating iron
  – Low level coupled with an elevated TIBC is suggestive if IDA

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Diagnosis of Iron Deficiency Anemia

• TIBC
  – Normal: 250 - 350
  – Number of cells not bound with iron
  – Higher the iron, lower the TIBC
  – Lower the iron, higher the TIBC
• Peripheral Blood Smear
  – Anisocytosis
  – Poikilocytosis
  – Microcytosis, hypochromia

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Red Cell Morphology

- Spherocyte – hereditary condition; hemolytic anemia
- Schistocyte – prosthetic heart valve
- Elliptocyte or ovalocyte – iron deficiency anemia
- Teardrop cells – Iron deficiency anemia
- Sickle cells – sickle cell disease
- Target cells – thalassemia
- Basophilic stippling – Thalassemia, lead toxicity
- Bite cells – G6PD deficiency

Most Important Take Away Message!

- Find out why
  - Colonoscopy
  - UGI/Endoscopy
  - Chest X-ray
  - Urinalysis
  - Endometrial biopsy

Treatment of IDA

- Increase Iron Rich Food Intake
  - liver, beef, lamb, pork, veal, chicken, eggs, fish, beans, prunes, green leafy vegetables
- Iron Supplements
  - Ferrous Sulfate 325mg: 1 po tid
  - Ferrous Sequel: 1 po tid

- Chromagen Forte
  - Capsules
  - 1 capsule daily
  - Iron, plus folic acid

- If the bone marrow is healthy
  - Within 5 days, the reticulocyte count will increase
- With adequate treatment
  - The hematocrit should rise 1 point each week
    - For instance, if someone’s hematocrit is 28
      - Goal is 36-40
      - It will take 8-12 weeks to correct

- Once hematocrit has normalized, it takes 3-6 months to replenish iron stores
  - This is provided that the bleeding or dietary issue is corrected
  - Many providers stop the iron too quickly
Treatment of IDA

• Intravenous Iron Dextran may be necessary if the individual is unable to absorb the iron or when the rate of blood loss exceeds absorption
  – Increased risk of anaphylaxis
• Should be performed in setting capable of handling this potentially life-threatening emergency

Case Study-2

26 year old male presents for a complete physical. He is asymptomatic. Routine labs reveal the following:

CBC: wbc 7.78, rbc 5.84, hgb 11.5, hct 38.5, MCV 68.2, MCHC 28.1, RDW 14.9; Normal diff.
Peripheral Smear: 1+microcytes, ovalocytes, target cells, and basophilic stippling. Remainder of labs normal.

What type of anemia does he have?
What would you order next?

Macrocytic, Normochromic Anemia

Macrocystic Anemia

Vitamin B12 Deficiency

Megaloblastic Anemia

• Vitamin B12 (cobalamin) is essential for the production of DNA
• Deficiency in Vitamin B12 results in the alteration in the production of DNA
  – Decreased rate of production
  – Enlarged red cell
### General Causes of Vitamin B12 Deficiency
- Inadequate intake
- Decreased absorption
- Inadequate utilization
- Most common cause:  
  - Inadequate absorption

### Other Potential Causes
- Inadequate absorption or utilization  
  - Crohn’s disease
  - Celiac disease
  - S/p Gastrectomy or Bariatric surgery
- Medications  
  - Methotrexate or Fluorouracil
- Altered gastric acid production  
  - PPI’s

### Pernicious Anemia
- Most common cause of a vitamin B12 deficiency
- Autoimmune disease characterized by the presence of autoantibodies to the parietal cells in the stomach and their secretory product called intrinsic factor  
  - Remember – intrinsic factor is essential for the absorption of vitamin B12 in the terminal ileum of the bowel

### Important History Questions
- Dietary intake
- Alcohol consumption
- Medication history  
  - Chemotherapeutics
  - PPI’s
- PMH  
  - Surgeries
  - Conditions affecting ileum/stomach

### Pernicious Anemia
- onset is usually insidious
- begins in the 5th – 6th decade of life
- Women > men

### Pernicious Anemia
- Very commonly seen in the setting of other autoimmune conditions such as:  
  - Hashimoto’s thyroiditis
  - Vitiligo
### Neurologic Manifestations

- Neurologic manifestations are related to the inability to maintain myelin integrity
- Paresthesias
  - Pins and needles – stocking/glove distribution
  - Weakness in extremities
- Delirium/psychosis may occur
- Decreased position and vibratory sense
- Incoordination
- Depression

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### Treatment of Vitamin B12 Deficiency

- **Vitamin B12 Deficiency**
  - Cyanocobalamin: 1000 iu/day x 5 days
  - Weekly until hemoglobin normal
  - 1000 µg/month for life
  - Reticulocytosis within 1 week
  - Increase in hemoglobin and hematocrit with 1 week
  - Normalization of h/h within 2 months
  - Rapid improvement in symptoms; however may take 12 – 18 months for all neurologic symptoms to improve

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### Words of Warning

- Patients who are severely vitamin B12 deficient can develop severe hypokalemia
- Monitor potassium levels as vitamin B12 is administered

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### Treatment of Vitamin B12 Deficiency

- **Vitamin B12 Deficiency**
  - Nascobal (cyanocobalamin)
    - 500 micrograms/0.1ml nasal gel
    - Maintenance of Vitamin B12 deficiency
    - Used after IM B12 has resolved the anemia
    - 1 spray into 1 nostril each week

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### Folate Deficiency

- Most often results from an inadequate intake of folic acid
  - Poor dietary intake such as the elderly, chronically ill, alcoholics, fad diets
- Occasionally
  - Increased need
  - Impaired absorption
  - Inadequate utilization

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Reasons for Folate Deficiency

- Body has very little folate in storage
  - Very different from vitamin B12 where 3 – 5 years of B12 is held in storage
- Impaired absorption
  - Celiac disease
  - Giardia infection
  - Phenytoin

Reasons for Folate Deficiency

- Increased need
  - Pregnancy
  - Hyperthyroidism
  - Malignancy
  - Chronic inflammatory disorders – Crohn’s
- Impaired utilization
  - Methotrexate
  - Metformin
  - Trimethoprim

Diagnosis

- Serum folate level
- Additional tests
  - MMA (methylmalonic acid)
  - Homocysteine (Hcy)
  - Both will be elevated in vitamin B12 deficiency
  - Only homocysteine will be elevated in folate deficiency

Treatment of Folic Acid Deficiency

- Folic Acid Deficiency
  - 1mg po qd
  - May increase to 5 mg/day
  - Review cause with patient – i.e. dietary sources
  - Reticulocytosis within 1 week
  - Hematocrit and hemoglobin should improve within 1 week
  - Hematocrit should normalize in 2 months

Monday, September 25

32 year old male presents with a 3 week history of fatigue, nasal discharge-clear; seen by MD 1 week prior and started on Augmentin. Not feeling any better.

PE: pallor, tachycardia, diaphoretic; Lungs clear, HEENT-normal; CBC: wbc: 8.9; rbc: 1.54; hgb: 5.5, hct: 17.2, MCV: 112, MCHC: 32; platelet: 32; Bands: 0; Segs: 5 (L) Monocytes: 21, Abnormal lymphocytes: 33.

Case - 1

86 year old woman in for a complete physical.

Labs: wbc 7.1, rbc 4.64, hgb 8.8, hct 28.1, MCV 84, MCHC 32.8, RDW 13.0, normal diff.

What type of anemia?
What would you order?
**Normocytic Anemia**

- Acute Bleeding
- Normocytic Anemia
- Schistocytes
- Sickle Cell
- Elliptocytes
- Hemolysis
- ARC > 100,000/ml
- Iron
- TIBC
- Ferritin
- Iron Deficiency Anemia
- Renal disease
- Liver disease
- Hypothyroidism
- Malignancy
- Anemia of Chronic Disease
- ARC < 100,000/ml

**Chronic Disease**

- Frequently accompanies chronic disorders
  - Acute and chronic infections
  - Malignancy
  - Inflammatory disorders
  - HIV disease
- Hypoproliferative state
- Commonly confused with iron deficiency

**Pathophysiology**

- Usually caused when there is a trapping of iron by macrophages
- Renders iron unavailable for erythropoesis
- Inflammatory processes also suppress erythropoesis leading to diminished production of rbc's

**Laboratory Diagnosis**

- Anemia – Normal MCV, normal MCHC
- Rarely will the hematocrit go below 25% with an ACD
- Serum iron is often low
- TIBC is also often low – differentiates it from IDA
- Ferritin will be normal or even increased – very helpful to differentiate ACD from early IDA

**Treatment of Normocytic Anemia**

- Renal disease
  - Erythropoietin, Procrit, Aranesp
- Malignancies
  - Chemotherapy
- Inflammatory disease
  - Optimal control
- Hypothyroidism
  - Goal: TSH = 1.5

**Epoetin Alfa**

- Dosing
  - CKD: 50-100 units/kg 1x/week – every two weeks
  - Cancer: 150 units/kg 1x/week
  - HIV: 50-100 units/kg 1x/week
- Administered IV or subcutaneously
- Less frequent dosing if often performed
- No known drug interactions
Darbepoetin alfa (Aranesp)

- Indications
  - Anemia: related to CRF
  - Chemotherapy induced anemia
- Advantages
  - 3 fold longer half life than Epoetin alfa
  - Early and sustained effect
  - Less frequent dosing

Recent Warnings

- Caution regarding increasing hemoglobin > 12 in individuals using any of these products
- Goal: hemoglobin at 10 - 12
- Increased risk of MI

Treatment of Vitamin B12 or Folic Acid Deficiency

- If anemia fails to resolve, remember IDA coexists in 1/3 of patients with these types of anemia

Liver Function Tests

Function of the Liver

- Numerous functions
  - Production of plasma proteins
  - Glucose homeostasis
    - Production occurs significantly at night
  - Lipoprotein synthesis
    - Necessary for sex hormones
  - Bile acid production
    - LDL production
  - Vitamin B12, A, D, E, K storage

Additional Functions

- Detoxification of medications and endogenous substances
  - Primarily through the CY P450 enzyme
  - Purpose: take fat soluble medication and convert to water soluble for purposes of renal excretion
- Production of clotting factors
**Bilirubin**

- Results from the enzymatic breakdown of heme in the body
- Unconjugated (indirect) and conjugated (Direct) = total bilirubin
  - If total bilirubin is elevated – ask for breakdown

**Bilirubin**

- Conjugated (Direct) levels do not become elevated until the liver has lost at least ½ of its excretory capacity
  - Conjugated bilirubin is rarely present in the blood in healthy individuals
  - Thus – when conjugated bilirubin is elevated – there is a marked decrease in secretion into the bile
    - Increase in bilirubin in serum and urine
    - Hepatobiliary disease is very common

**Causes of Elevated Bilirubin**

- Common to see slight elevation in bilirubin after fasting
  - 12 – 24 hours
- Elevated bilirubin –
  - Elevated unconjugated (indirect) with normal CBC
    - Gilbert's syndrome
    - Neonatal jaundice
  - Elevated conjugated (direct)
    - Hepatobiliary disease is almost always seen
    - Cholestasis/hepatocellular diseases of all types

**Causes of Increased AST or ALT in Asymptomatic Patients**

- A - Autoimmune Hepatitis
- B – Hepatitis B
- C – Hepatitis C
- D – Drugs or Toxins
- E - Ethanol
- F – Fatty Liver
- G – Growth (tumor)
- H – Hemodynamic disorders (CHF)
- I – Iron
- Copper
- M – Muscle injury

**Narrowing It Down**

- ¾ of all elevated AST and ALT values are caused by:
  - Alcohol
  - Hepatitis B
  - Hepatitis C
  - I would add – fatty liver (NASH)

**AST (Formerly SGOT)**

- Enzyme found within the liver cell
- Rises rapidly with hepatic injury
- Resolves very quickly
  - Half life – 17 hours
- Not as specific to the liver as ALT
  - Found also in heart muscle, skeletal muscle, pancreas, kidney, brain, lung, white and red blood cells
- Alcohol
- Statin medications
- Tylenol

Adapted from http://www.aafp.org/afp/990415ap/2223.html accessed February 9, 2006

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ALT (Formerly SGPT)

- More specific than AST to liver
- Half life - 47 hours
- Avandia or Actos
- Liver infection or diseases
- Toxic agents

www.fhea.com

Approach to Patient with Asymptomatic Elevation

- Person asymptomatic and picked up on screening or monitoring for various medications
  - Repeat enzymes in next 2 weeks
  - Avoid alcohol, acetaminophen, ibuprofen
  - 50% of individuals will have normal LFT’s upon repeat
  - Remember —
    - Hepatitis C patients do have fluctuating LFT’s and you may be falsely assured

Degree of Elevation

- Degree of Transaminase elevation provides significant clues as to the etiology of the liver problem
  - < 5 times – mild
  - 5 – 10 times ULN – moderate
  - > 10 times ULN – marked/severe
- For instance:
  - > 1000 units/L: hepatitis, drugs or toxins, acute biliary obstruction
  - Another way to look at this: moderate – marked increase – acute hepatic injury

Gary

- 48 year-old male who presents for routine annual examination (new patient to practice)
- Complaining of increased abdominal bloating and on further questioning – breast enlargement
- Social history: 8 – 16 beers daily; Cigarette abuse – 1 ppd x 30 years
- PMH: Asthma - childhood

Laboratory Evaluation

- CBC with differential
  - Hgb: 13.2
  - Hct: 40.0
  - MCV: 108
  - MCHC: 33
  - RDW: 16%

Gary’s Lipid Panel

- Total cholesterol: 208
- HDL: 62
- LDL: 110
- Triglycerides: 284
Liver Function Tests

- AST: 178
  - (normal 0 – 40)
- ALT: 86
  - (normal 0 – 40)
- AST/ALT > 1
  - If AST/ALT is > 1
  - Consider: AST

AST/ALT > 1

- Highly suggestive of alcoholic liver disease
- If ratio is > 2: VERY suggestive of alcoholic liver disease
  - One study showed that 90% of individuals who presented with an AST/ALT ratio > 2 had alcoholic liver disease on biopsy
  - This percentage is 96% when AST/ALT ratio is > 3

Gary’s Ratio: > 2  (178/86)

The Good News

- With sobriety
  - AST – normalize within 3 months
  - GGT – normalize within 1 – 2 weeks
  - Triglycerides – normalize in 1 month
  - MCV – normalize within 4 months
  - But remember…these are not liver function tests, they are liver injury tests
  - Normalization does not mean that there is NO damage

CW

- CW is a 52-year-old woman who presents to discuss her recent cholesterol profile
  - Lab results are as follows:
    - Total cholesterol: 286
    - HDL: 46
    - LDL: 199
    - Triglycerides: 154
    - Risk ratio: 6.22
    - LFT’s: normal

6 Months Later

- CW calls complaining of cramping in her feet only at night
- It is occurring every night
- This is new; she has never had anything like this before and because of our discussion regarding potential side effects of the statin class, she decided to call
- She was advised to stop atorvastatin and come into the office for an evaluation and a few additional laboratory tests

Treatment

- CW has been on a diet and exercise plan for the last 3 months attempting to lower her cholesterol without pharmacotherapy
- At today’s visit, atorvastatin therapy initiated
- Dosage: 20 mg qhs
### Labs
- Physical examination: normal; no evidence of tender or edematous muscles
- AST: 102
- ALT: 75
- Ratio: AST/ALT - > 1
- CPK: 3305 (normal level: 20-170)
- Remainder of Chemistry panel: normal
- Urinalysis: normal
- CBC with differential: normal

### Rhabdomyolysis
- Laboratory Features:
  - Elevated CK-MM\(^*\) Most sensitive test
  - With rhabdo, range is often: 500 - >100,000 units/L
  - Degree of elevation roughly correlates with the risk of renal failure
  - BUN/Creatinine ratio <5
  - Normally, this ratio is 10
  - With rhabdomyolysis, creatine phosphate is released from damaged muscle and is converted into creatinine
  - Increased serum uric acid
    - Often times, the uric acid levels are markedly elevated
    - Can be > 40 mg/dL

### What Changed?
- Why did this happen?
- CW went to a walk-in center
- Diagnosed with “walking pneumonia”
- Given a prescription for clarithromycin

### Remember CY P450 3A4
- Atorvastatin is a substrate
- Clarithromycin is an inhibitor
- Blocks 3A4 enzyme causing atorvastatin levels to increase significantly (50%)

### AST/ ALT < 1
- This is the most commonly encountered abnormality
  - Consider Avandia/Actos
  - Liver infection or disease (NASH)
  - Toxic agents

### NASH
- Fatty liver is thought to be present in up to 23% of Americans
- Typical Picture: Obese, hyperlipidemia, hypertension, diabetes
  - AST/ALT ratio < 1 is most common initially
    - Ratio can shift — AST/ALT > 1
    - Indicative of advanced fibrosis — 61% of patients with advanced fibrosis will have this ratio
  - Increased GGT — up to 3x ULN
Other Differentials: AST/ALT < 1

- Hepatitis A IgM
- Hepatitis B sAg
- Anti Hep C
  - Hepatitis C RNA
- Hepatitis D IgM
- Alpha1 Antitrypsin

Other Differential AST/ALT < 1:

Hemochromatosis

- Autosomal recessive condition
- Abnormal deposition of iron in the liver, heart and pancreas
- Labs:
  - AST/ALT < 1 – often seen
  - Elevated ferritin (> 300+)
  - Transferrin saturation index
    - > 45% is highly suggestive of this condition

White Blood Cells

Earl

66 year old man employed by the town presents with a 6-day history of a cough, worsening sob, fever, chills, pain in back with inspiration, and yellow-brown sputum.

- PMH: Nonsmoker, Hx: MI age 51, Type 2 Diabetes
- PE: T: 103.8; P: 148; R: 32; BP: 138/90; HEENT: unremarkable; Tired appearing; Lethargic; Crackles in right lower lobe; Do not clear with coughing
- Finger stick: 188
- Xray: Consolidation-RLL
- Sputum Gram Stain: Pending

Leukocytes or WBC's

- Heterogeneous group of cells
- Arise from single stem cell
- Differentiation occurs during stem cell maturation
White Blood Cells
- WBC's or leukocytes are divided into 2 groups
  - granulocytes and agranulocytes
- Granulocytes: receive their name from the granules that are present in the cytoplasm of the cell
- Agranulocytes – absence of granules

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Leukocyte Forms
- Granulocytes
  - Also known as polys or segs
  - Neutrophils
  - Eosinophils
  - Basophils

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Agranulocytes
- Do not have the granules in the cytoplasm
  - Lymphocytes
  - Monocytes

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Action of Leukocytes
- Leukocytes fight infection and defend body by a process called phagocytosis
  - Leukocytes encapsulate the foreign organism and destroy it
- Leukocytes: produce, transport and distribute antibodies in response to the foreign organism

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Interpreting the WBC Count
- Useful guide as to severity of the infection, however, can be fooled by this as well
- Normal Leukocyte count:
  - Adult: 4,500 – 10,500/mm³
  - Children: 6 – 18 years
  - 4,800 – 10,800/mm³

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Leukocytosis
- Often occurs in response to acute infections
- Degree of response is determined by the severity, patient’s resistance, patient’s age and marrow efficiency and reserve

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But...Not Always Related to Infections

- Leukemia
- Trauma
- Bronchogenic carcinomas
- Uremia
- Drugs (quinine, epinephrine)
- Acute hemolysis
- Hemorrhage
- S/P splenectomy
- Polycythemia Vera
- Pregnancy

Earl

- 66 year old man employed by the town presents with a 6 day history of a cough, worsening sob, fever, chills, pain in back with inspiration, and yellow-brown sputum.
  - PMH: Nonsmoker, Mi-age 51; Type 2 Diabetes
  - PE: Crackles in right lower lobe; Do not clear with coughing. RR - 32
  - Xray: Consolidation-RLL
  - Sputum Gram Stain: Pending
  - CBC: wbc 16,500; Bands 7%, Neuts: 83%
  - Blood cultures pending

Differential: Functions of Circulating WBC's

- Neutrophils: bacterial infections
- Eosinophils: allergic disorders and parasitic infections
- Basophils: parasitic infections, some allergic disorders (store histamine); inflammation
- Lymphocytes: viral infections
- Monocytes: Share vacuum cleaner function with neutrophils, severe infections
- Bands/stabs: severe bacterial infections

Normals

<table>
<thead>
<tr>
<th>WBC Type</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neutrophils</td>
<td>30% - 70%</td>
</tr>
<tr>
<td>Lymphs</td>
<td>15% - 40%</td>
</tr>
<tr>
<td>Monocytes</td>
<td>2% – 8%</td>
</tr>
<tr>
<td>Eosinophils</td>
<td>0% - 8%</td>
</tr>
<tr>
<td>Bands</td>
<td>0% - 4%</td>
</tr>
<tr>
<td>Basophils</td>
<td>0% - 3%</td>
</tr>
</tbody>
</table>

Earl

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Neutrophils

- Most numerous and most important leukocytes in the body
- Polys/segs often used interchangeably
- Constitute our body's primary defense against infection through the process of phagocytosis
  - Immature neutrophils: stabs or bands
Neutrophils

- First responders to a bacterial infection
- Life span
  - 10-hours in circulation
  - 4-5 days in tissue
- Highly mobile
- Death of neutrophils in large numbers forms pus

Neutrophilia

- Causes of Neutrophilia
- Bacterial Infection
- Inflammatory causes
  - RA, Pancreatitis, Gout
- Burns
- Acute hemorrhage
- Uremia, DKA
- Tumor necrosis
  - Significant elevation

Earl

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  - Blood cultures pending

Bands

- Bands (0% - 4%)
  - Immature neutrophils
  - Neutrophil form with banded nucleus, and distinctive granules
  - Termed band because of the appearance of the nucleus.
  - It has not developed into the lobed shape that is present in a mature neutrophil

Order of Leukocyte Migration and Elevation in a Bacterial Infection

- Increased neutrophils
- Elevated WBC count
- Elevated bands
- Further increase in WBC count

Earl

- 66 year old man employed by the town presents with a 6 day history of a cough, worsening sob, fever, chills, pain in back with inspiration, and yellow-brown sputum.
  - PMH: Nonsmoker, Type 2 Diabetes
  - PE: Crackles in right lower lobe; Do not clear with coughing. RR - 32
  - Xray: Consolidation-RLL
  - Sputum Gram Stain: Pending
  - CBC: wbc 16,500; Bands 7%, Neuts: 83%
  - BUN - 42
  - Blood cultures pending
**What Does Earl Have?**

- Respiratory rate 
- Urea > 7 mmol/L (BUN > 19 mg/dL)
- Systolic blood pressure < 90 mm and Diastolic blood pressure ≤ 60 mm Hg
- Age > 65 years of age

**“Left Shift”**

- Pulling up of less mature granulocyte forms from various pools in response to overwhelming infection
- Sign of a significant bacterial infection
- What do you need present in order to have a left shift?

**What Do We Do With Earl?**

- Hospitalization based on CURB-65 criteria
- IV Antibiotics
- IV Fluids
- Awaiting Sputum

**Most Important Decision!!!**

- Decision to hospitalize or not
- Single most important decision in the course of the illness
  - Can determine life or death
  - Average mortality for hospitalized patients: 14% compared with non-hospitalized: <1%
- Average cost of treatment for CAP in the hospitalized patient vs. non-hospitalized
  - $7500 (20x more than non-hospitalized)

**CURB-65 Score**

- Confusion
- Urea > 7 mmol/L (BUN > 19 mg/dL)
- Respiratory rate > 30/min
- Systolic blood pressure < 90 mm and Diastolic blood pressure ≤ 60 mm Hg
- Age > 65 years of age

**Remember Earl...**

- Age: 66
- Confusion: 0
- Urea: 1
- Respiratory rate: 1
- Blood pressure: 0
- Age: 1
- CURB Score: 3
### CURB-65 Score
- **CURB ≥ 4** – ICU management
  - (27.8% 30-day mortality)
- **CURB = 3** – Hospital admission (consider ICU)
  - (14% 30-day mortality)
- **CURB = 2**: Hospital admission or outpatient management with very close follow-up
  - (6.8% 30-day mortality)
- **CURB = 0 – 1**: Outpatient management
  - (2.7% 30-day mortality)


### Next Day:
Repeat CBC with Differential
- Earh seems to be worsening
  - Temp still 102-103;
  - RR: 34 labored
- More lethargic; seems confused
- Moved to intensive care unit

Something you never want to see...

### CBC with differential
- **WBC count**: 12,100/mm³ (↓)
- **Neuts**: 58% (↓)
- **Bands**: 20% (↑)
- **Now we see the presence of:**
  - Metas: 3% (↑)
  - Metamyelocytes: 2% (↑)

### Cells typically found in bone marrow
- **Metamyelocyte**
  - Crescent-shaped nucleus
- **Myelocyte**
  - Round nucleus, small number of granules
- **These cells are typically recruited when circulating wbc's i.e. neutrophils and bands have been exhausted**

### Granulopoiesis
- **Process of differentiation from earliest form to mature neutrophil**
  - 7 - 11 days in health
- **When demand is increased, maturation period will shorten**
  - 48 - 72 hours in illness

### Degenerative Left Shift
- **When available and more mature neutrophils forms are exhausted**
  - Less mature forms accessed
  - Total number of wbc's begin to fall
  - General supply is less
The sign of….

- A desperate attempt to control infection.....
- Often associated with a very poor prognosis

Earl: CBC with differential

- WBC count: 12,100 (↓): Was 16,500
- Neuts: 58% (↓): Was 83%
- Bands: 20% (↑): Was 7%
- Metas: 3% (↑)
- Metamyelocytes: 2% (↑)

Unfortunately, Earl...

- Continued to worsen
- Grew out: DRSP and despite multiple antibiotics/ventilator assistance etc, he did not survive the pneumonia and died within 48 hours of presentation

Had Earl Recovered…This is What We Would Have Seen!

Sean

- 14 month-old w/ 5-day hx fever, irritability, no wet diaper in >6 h
  - H/ H= 11g / 37%
  - WBC= 2,600 mm3
  - Neuts= 35%
  - Bands= 48%
  - Metas= 2%

  Degenerative Shift

Sean

- After initiation of antimicrobial therapy and rehydration
  - WBC= 7,200 mm3
  - Neuts= 59%
  - Bands= 10%
  - Monos= 10% (>5%)
Regenerative Left Shift
- Rise in total WBC
- Drop in immature forms
- Rise in monocytes
  - Predictor of recovery

MA
- 19 year-old male who presents with a sore throat, low-grade fever, achiness, fatigue x 5 days
- Decreased appetite
- No other family members ill
- Has missed 3 days of school
- Denies medications

Physical examination
- VSS: T:99.2; RR – 18; Pulse - 104
- Skin: p/w/d; no jaundice
- Ears: Canals/TM's normal
- Nose: Turb/mucosa pink; no discharge
- Mouth: Tonsils erythem; +exudate; no petecchiae

Physical examination
- Nodes: .5 cm tonsilar, occipital, posterior cervical nodes
- Lungs: clear bilaterally; no c/w/r
- Heart: S1S2: RRR; no murmurs
- Abdomen: +BS; +hsm; R&L UQ tenderness; no masses, rebound, guarding
- Eyes: no icterus

Michael
- WBC = 3,900 (4,500- 10,500/mm³)
- Neuts = 25% (40% - 70%)
- Bands = 3% (0 - 4%)
- Lymphs = 64% (20% - 42%)
- Downey cells

Labs
- Mono: +
- CMP:
  - AST: 48 (0-40)
  - ALT: 89 (0-40)
  - Otherwise normal
Diagnosis: Mononucleosis
Leukopenia

- Leukopenia: WBC < 4500
  - Viral infections, some bacterial infections, (overwhelming bacterial infections)
  - Primary bone marrow disorders
    - Leukemia, aplastic anemia, pernicious anemia
  - Pernicious anemia
  - Mononucleosis
  - Medications (antibiotics, anticonvulsants, chemotherapy, diuretics)

Lymphocyte

- 2nd most numerous WBC in circulation
- 15% - 40% of total WBC count

Lymphocytosis

- >4000 mm³ in adult
- >7200 mm³ in child
- 1st cell to enter viral infected tissue
  - Increases common in viral infection
- May be seen with leukocytosis, normal WBC count or leukopenia

Lymphocytes

- Small, mononuclear cells without granules
- Very motile cells
- Migrate to areas of inflammation in early and late stages of the process
- Manufactured in the bone marrow
  - B Lymphocytes: mature in the bone marrow
  - T Lymphocytes: mature in the thymus

Other Differentials: Lymphocytosis

- Lymphatic leukemia
  - Acute and chronic
- Inflammatory bowel disease
  - Crohn's and Colitis
- Addison's disease
- Thyrotoxicosis

Atypical Lymphocytes or Downey Cells...

- Atypical/ reactive lymphs = 14%
- Atypical lymphs: also called Downey cells, Reactive lymphs
- Large, deeply indented with deep blue cytoplasm
Downey Cells

- Commonly seen with:
  - Mononucleosis
  - Viral hepatitis
  - Tuberculosis
  - Drug reactions

Monday, September 25

17 year old male presents with a 3 week history of fatigue, nasal discharge-clear; seen by MD 1 week prior and started on Augmentin. Not feeling any better. PE: pallor, tachycardia, diaphoretic; Lungs clear, HEENT-normal; CBC: wbc: 8.9; rbc: 1.54; hgb: 5.5, hct: 17.2, MCV: 112, MCHC: 32; platelet: 32; Bands: 0; Segs: 5 (L) Monocytes: 21, Abnormal lymphocytes: 33.

Important References


Thank You!!

I Would Be Happy to Answer Any Questions You May Have

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