

Laboratory Evaluation: A Focus on Red Blood Cells and White Blood Cell Abnormalities

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Objectives

Upon completion of this lecture, the health care provider will be able to:

1. Discuss the various causes of commonly encountered red and white cell abnormalities.
2. Review the laboratory tests needed to identify the various causes
3. Review treatments for the various red and white cell abnormalities

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Disclosures

- None

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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

Goodnough LT, Skikne B, Brugnara C. Erythropoietin, iron, and erythropoiesis. *Blood*. 2000;96:823-833. Wright, 2025

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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

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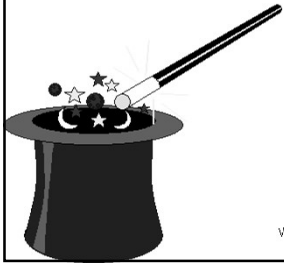
Statistics

- Approximately 3.5 million Americans have some form of anemia
- Approximately 17.5/1000 individuals in primary care practice have anemia
- Approximately 20% of all women have anemia
 - Iron deficiency anemia is by far the most common anemia, particularly in the women
 - Most common anemia in the older adult:
 - Anemia of Chronic Disease

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Step Approach is Essential



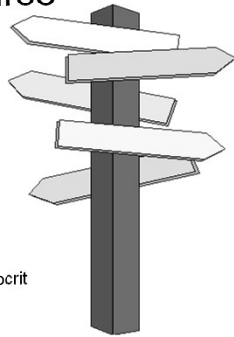
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The CBC - A Blessing or a Curse

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

**1 hemoglobin:every 3 hematocrit



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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

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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

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Classifications/Causes of Anemia

Macrocytic, Normochromic
(↑MCV, Normal MCHC)
Vitamin B12 Deficiency
Folate Deficiency

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Classifications/Causes of Anemia

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

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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)

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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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Anemia is not a diagnosis; it is a sign of an underlying problem.



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Krepzek Study

- Pathology was found in 50% of individuals diagnosed with iron deficiency anemia.

Diagnoses included:

- | | |
|-------------------------|--------------------------|
| • Cancer | Adenomas |
| • Gastritis | Vas Malformations |
| • Esophagitis | Hemorrhoids |
| • Gastric Ulcer | |
| • Duodenal Ulcer | |
| • Crohn's | |

(Journal of Digestive Diseases, June 1995)

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Macrocytic, Normochromic Anemia



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Powerpoint image

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Macrocytic Anemia

Macrocytic Anemia

MCV > 100

Vitamin B12 Deficiency	Folate Deficiency	Elevated APC (rbc x Reto %) >100,000/ml	Decreased APC (rbc x Reto %) <100,000/ml	Other Causes Hypothyroidism Myelodysplastic Syn
Vitamin B12 level Schilling's Test Peripheral smear (hypersegment polymorph leuk)	Folate	Acute Bleeding Hemolysis	Defect-RBC Prod	TSH Bone marrow aspiration
Reduced gastric production of intrinsic factor Gastrectomy Dietary disease	Inadequate dietary ingestion usually due to alcohol Increased demand Pregnancy, malignancy	Coombs Test	Alcohol Liver disease	

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Vitamin B12 Deficiency

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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

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General Causes of Vitamin B12 Deficiency

- Inadequate intake
- Decreased absorption
- Inadequate utilization
- Most common cause:
 - Inadequate absorption

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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

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Vitamin B12

- Food sources: animal products
- Amount provided in average diet'
 - 5 – 15 ug/day (RDA – 2ug/day)
- Storage amount
 - 2 – 5 mg is stored mainly in the liver
 - Takes 2 – 5 years to develop a deficiency even in the setting of severe malabsorption

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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

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Pernicious Anemia

- Very commonly seen in the setting of other autoimmune conditions such as:
 - Hashimoto's thyroiditis
 - Vitiligo
 - Celiac
 - RA, SLE

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Pernicious Anemia

- Onset is usually insidious
- Begins in the 5th – 6th decade of life
- Women > men

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Important History Questions

- Dietary intake
- Alcohol consumption
- Medication history
 - Chemotherapeutics
 - PPI's
- PMH
 - Surgeries
 - Conditions affecting ileum/stomach

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Signs and Symptoms of Pernicious Anemia

- Anemia with elevated MCV
- Smooth and beefy red tongue
 - Tongue is frequently very sore
- Diarrhea
- Anorexia

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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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Diagnosis of Pernicious Anemia

- CBC
- Peripheral smear
- Vitamin B12 level

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Treatment of Vitamin B12 Deficiency

- Vitamin B12 Deficiency
 - Cyanocobalamin: 1000 iu/day x 5 days
 - Weekly until hemoglobin normal
 - 1000 ug/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

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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, alcohol use disorder, 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

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Reasons for Folate Deficiency

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

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Important Information

- Source
 - Green, leafy vegetables, beans, grains, liver, wheat
- RDA: 100 ug/day
- Amount in diet: 200 – 300 ug/day
- Storage amount: 5 – 10 mg

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Clinical Presentation

- May be asymptomatic
- Glossitis
- Similar presentation to vitamin B12, when severe

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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

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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

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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

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Microcytic Anemia

Microcytic Anemia

MCV < 80

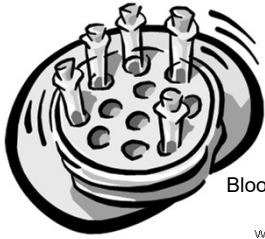
Iron Def Anemia Iron TIBC Ferritin	Thalassemia Hgb Electrophoresis Peripheral Smear	Plumbism Lead level	Sideroblastic Anemia Ringed sideroblasts (Peripheral)	Aluminum Toxicity	G6PD
Bleeding Diet Pregnancy Poor absorption	Beta Thal (Elevated A2 or F) Alpha Thal (Normal A2 or F)	Lead exposure Home Work	Bone Marrow Aspiration Ringed sideroblasts (Bone marrow) (Drugs or chemicals)	Aluminum level	Peripheral Smear Spleen cells G6PD Enzyme Assay (X linked disorder)

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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

- | | |
|---|---|
| <ul style="list-style-type: none"> • Medications? • Any Blood Loss? <ul style="list-style-type: none"> – Menorrhagia – Black or Blood Stools – Hematuria – Hemoptysis – Blood Donation • Family History of Anemia? <ul style="list-style-type: none"> – Celiac disease (sprue) | <ul style="list-style-type: none"> Dietary Intake? Alcohol Intake? Any Chronic Disease? Any Surgeries? <ul style="list-style-type: none"> •Gastric bypass |
|---|---|

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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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Transferrin Saturation

- Although evidence is limited, TSAT <20% generally indicates absolute iron deficiency.¹ However, TSAT >20% does not exclude this condition.

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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
- Sick cells – sickle cell disease
- Target cells – thalassemia
- Basophilic stippling – Thalassemia, lead toxicity
- Bite cells – G6PD deficiency

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Most Important Take Away Message!

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

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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

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Treatment of IDA

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

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Treatment of IDA

- 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

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Treatment of IDA

- 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

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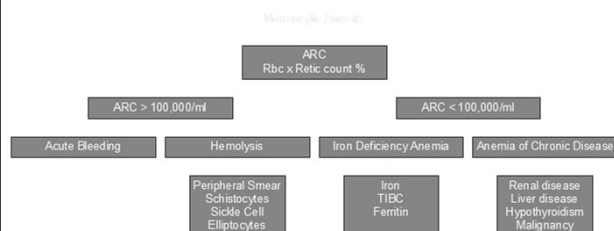
Treatment of IDA

- 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

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Normocytic Anemia



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Chronic Disease

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

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Pathophysiology

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

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The Burden of Anemia in CKD

- Anemia in CKD results primarily from reduced erythropoietin secretion
- As CKD progresses, the risk for anemia increases
- Reduced quality of life⁴
 - Fatigue
 - Reduced exercise capacity
- Greater risk of comorbidities and adverse outcomes²
 - Increased ventricular mass
 - Higher risk of kidney events and major cardiovascular events
 - Increased hospitalizations

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Anemia of CKD: Role of the Kidney

- Hepcidin is a small peptide produced by the liver, is increased during inflammatory states and blocks iron absorption
 - **CKD is an inflammatory state**
- Low Fe iron levels, low transferrin saturation (TSAT) yet, high ferritin levels
- EPO is produced by the kidney; which is failing....

Weiss G et al. *Blood*. 2019 Jan 3;133(1):40-50.

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Anemia of CKD: Role of the Kidney

- Lifespan of RBCs is shortened by:
 - Chronic disease status (RBC lifespan about 60 days in CKD)
 - Inflammation
 - Blood loss; increased blood draws to monitor, GI bleeds, dialysis, hospitalizations
- With lower levels of EPO and/or iron, anemia of CKD occurs
- Bleeding common with many medications, including blood thinners
 - 20% of CKD patients have atrial fibrillation

Weiss G et al. *Blood*. 2019 Jan 3;133(1):40-50.

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Clinical Presentation

- Asymptomatic
- Fatigue
- Tachycardia
- Pallor
- Similar presentation to an IDA

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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

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White Blood Cells

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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

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Community Acquired Pneumonia

- Acute infection of the pulmonary parenchyma that is associated with symptoms of an infection such as fever, chills, shortness of breath and physical examination findings
 - Found in a person not hospitalized or residing in a long-term care facility for $\geq$ 14 days before the onset of symptoms

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Streptococcus Pneumoniae

- Gram positive diplococci
- Most common cause of Community Acquired Pneumonia
 - Most common in individuals 50 years of age and older
 - Also the most common bacterial cause of OM and sinusitis
- 70% of children and 30% of adults have nasopharyngeal colonization
- Disease results from a microaspiration

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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.
 - CBC: WBC 16,500; Bands 7%, Neuts: 83%
 - What does this mean to you?
 - What is the likely etiology?

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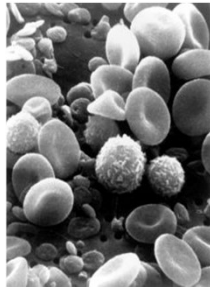
Let's Talk About White Blood Cells and the Differential: What Do Each of the Components Mean?

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Leukocytes or WBC's

- Heterogeneous group of cells
 - Arise from single stem cell
 - Differentiation occurs during stem cell maturation



Fischbach, F.T. 2004. A Manual of Laboratory ~~Wright, 2025~~ Diagnostic Tests. Ed 7. Philadelphia, PA: Lippincott Williams & Wilkins.

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Leukocytosis

- Elevated white blood cell count
 - Generally $> 10,500/\text{mm}^3$
- Very commonly encountered abnormality
- Words of warning
 - Must look at the cells that are present in excess in the differential to determine relevancy and importance of this elevated wbc count!!

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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
 - Neutrophils
 - Also known as polys or segs
 - Eosinophils
 - Basophils

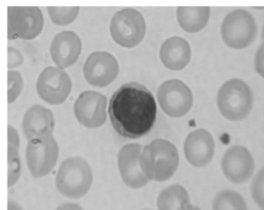


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Agranulocytes

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



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Endocrine System

- Important regulator of the number of leukocytes in the blood
- Hormones affect the production of leukocytes in the blood-forming organs, their storage, release from tissue, and their destruction

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Infection/Inflammatory Response

- Inflammatory process occurs in response to exposure to an infection and/or an acute inflammatory process
 - Results in the release of inflammatory mediators
- Causes the mobilization of leukocytes
- Leukocyte released and lives for 13 – 20 days
- Destroyed by the lymphatic system
- Excreted from the body in fecal matter

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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

- Elevated WBC count: > 10,500/mm³
- Usually elevated by one type of leukocyte and it is the type that shows the biggest increase that will give the condition its name
 - For instance:
 - Neutrophilic leukocytosis: neutrophilia
 - Lymphocytic leukocytosis: lymphocytosis
 - Monocytic leukocytosis: monocytosis
 - Basophilic leukocytosis: basophilia
 - Eosinophilic leukocytosis: eosinophilia

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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

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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

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Physiologic Leukocytosis

- | | |
|--|---|
| <ul style="list-style-type: none">• Leukocytosis with a normal differential<ul style="list-style-type: none">– Stress response– Labor– Menstruation– Exercise | <ul style="list-style-type: none">• Healthy 30 year old• Just exercised x 1 hour vigorously• TWBC-16,100<ul style="list-style-type: none">– Neuts-50%– Bands-1%– Lymphs-40% |
|--|---|

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Differential

- Differential: expressed as a percentage of the total number of leukocytes
- The distribution of cells in the differential along with the degree of increase and decrease are very significant and can help the clinician diagnostically
- Absolute count: obtained mathematically by multiplying percentage by the total wbc count
 - $\% \times \text{WBC count} = \text{Absolute count}$

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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

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Normals

WBC Type	Percentage
Neutrophils	30% - 70%
Lymphs	15% - 40%
Monocytes	2% – 8%
Eosinophils	0% - 5%
Bands	0% – 4%
Basophils	0% - 3%

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Earl

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 - Xray: Consolidation-RLL
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Neutrophils

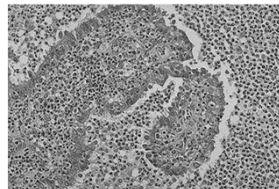
- Most numerous and most important leukocytes in the body
- Polys/segs often used interchangeably
- Constitute our body's primary defense against infection through the process of phagocytosis
 - Immature neutrophils: stabs or bands

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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

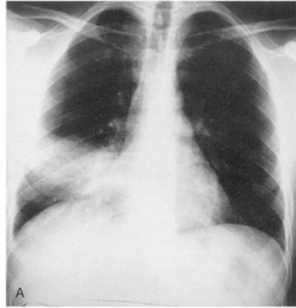


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Neutrophilia

- Normal:
30% – 70%
- Neutrophilia:
> 70%



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Neutrophilia

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



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Neutrophil Morphology: Additional Information

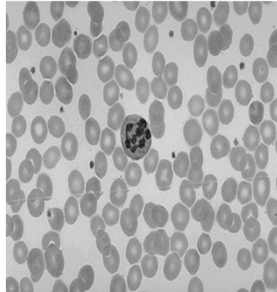
- Seen in inflammation and infections
 - Toxic granulation
 - Coarse black or purple granules found in the cytoplasm
 - Dohle bodies
 - Small blue cytoplasmic inclusions
 - Infections, inflammation, burns

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Neutrophil Morphology: Additional Information

- Hypersegmented neutrophils
 - Mature neutrophil
 - > 5 distinct lobes
 - IDA - severe
 - Megaloblastic anemia
 - Long-term chronic infections



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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%
 - Blood cultures pending

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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

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Order of Leukocyte Migration and Elevation in a Bacterial Infection

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

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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

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What Does Earl Have?



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“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?

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Left Shift

- Elevated wbc count
- Elevated neutrophil count
- Elevated band count

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What Do We Do With Earl?

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

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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)

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CURB-65 Score

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

<http://www.mdcalc.com/curb-65-severity-score-community-acquired-pneumonia> accessed 01-28-2010
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Remember Earl...

- | | |
|--------------------|-----|
| • Age: | 66 |
| • Confusion | 0 |
| • Urea | 1 |
| • Respiratory rate | 1 |
| • Blood pressure | 0 |
| • Age | 1 |
| • CURB Score | 3 - |

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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)

<http://www.mdcalc.com/curb-65-severity-score-community-acquired-pneumonia>
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accessed 01-28-2010

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Next Day: Repeat CBC with Differential

- Earl 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...
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CBC with differential

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

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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

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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

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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

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The sign of....



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

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Earl: CBC with differential

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

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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

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

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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

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Sean

- After initiation of antimicrobial therapy and rehydration
 - WBC= 7,200 mm3
 - Neuts= 59%
 - Bands= 10%
 - Monos= 10% (>5%)

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Regenerative Left Shift

- Rise in total WBC
- Drop in immature forms
- Rise in monocytes
 - Predictor of recovery

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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

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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 petechiae

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Physical examination

- Nodes: .5 cm tonsillar, 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

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Michael

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

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Labs

- Mono: +
- CMP:
 - AST: 48 (0-40)
 - ALT: 89 (0-40)
 - Otherwise normal

Diagnosis: Mononucleosis

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Leukopenia

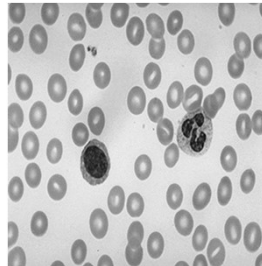
- Leukopenia: WBC < 4500
 - Viral infections, some bacterial infections, (overwhelming bacterial infections)
 - Primary bone marrow disorders
 - Leukemia, aplastic anemia, pernicious anemia
 - Pernicious anemia
 - Mononucleosis
 - Medications (antibiotics, anticonvulsants, chemotherapy, diuretics)

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Lymphocyte

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



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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

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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

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Other Differentials: Lymphocytosis

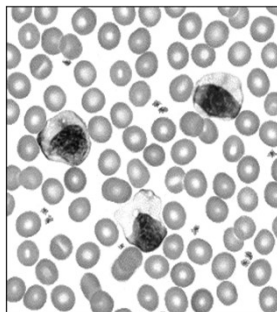
- Lymphatic leukemia
 - Acute and chronic
- Inflammatory bowel disease
 - Crohn's and Colitis
- Addison's disease
- Thyrotoxicosis

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Atypical Lymphocytes or Downey Cells...

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



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Downey Cells

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

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Eosinophils

- Eosinophils
 - Increase in response to worms, wheezes and weird diseases
 - Variability in the eosinophil count
 - Highest between 12:00am – 4:00am
 - It decreases as the day progresses

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Most Common Causes of Eosinophilia

- Allergic Rhinitis
- Asthma
- Parasitic infection
- Atopic disorders
- Acute eosinophilic leukemias

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Basophils

- Responsible for antigen response and allergic response
- Release histamine causing inflammation

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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?

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IL – 69 year old male

- Presents with complaints of numbness of fingers /toes and fatigue. No additional neuro symptoms

– Labs: Vitamin B12: 182 (211-911)
Folate: 6.0 (2.5 – 10.0)

– Treatment initiated: Now – 489
– Resolution of symptoms

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63 year old male

- 63-year-old, nonsmoker
- Type 2 diabetes, well controlled
- HTN, Hyperlipidemia
- Labs:
 - CBC – rbc 2.86, hgb 8.4, hct 25.5
 - RDW: 16.4%
 - Total protein: 10.4 (H) and Globulin: 6.2 (H)
 - What would you order and why?

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Case Study - 3

18 year old female presents with fatigue and SOB while cheerleading. +Increase in ice consumption. PE-pallor, pale conjunctiva, systolic murmur, and tachycardia.
CBC: wbc 7.58, rbc-3.02, hgb 5.4, hct 18.7, MCV 61.9, MCHC 28.9, RDW 18.7, Normal diff. Peripheral Smear: aniso, microcytes, hypochromia, teardrop cells, few ovalocytes, elliptocytes.

What type of anemia does she have?
What would you order?

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Case Study-4

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 she have?
What would you order next?

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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.

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General References

- Fischbach, F.T., Fischbach, M.A., & Stout, K. (2021). *Fischbach's A Manual of Laboratory and Diagnostic Tests*. Philadelphia: Lippincott Williams &Wilkins.\
- Turner J, Parsi M, Badireddy M. Anemia. [Updated 2023 Aug 8]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 Jan-. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK499994/>

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Thank You!!

I Would Be Happy to
Answer Any Questions
You May Have

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