Anemia In the Insurance Applicant … What do the numbers mean?

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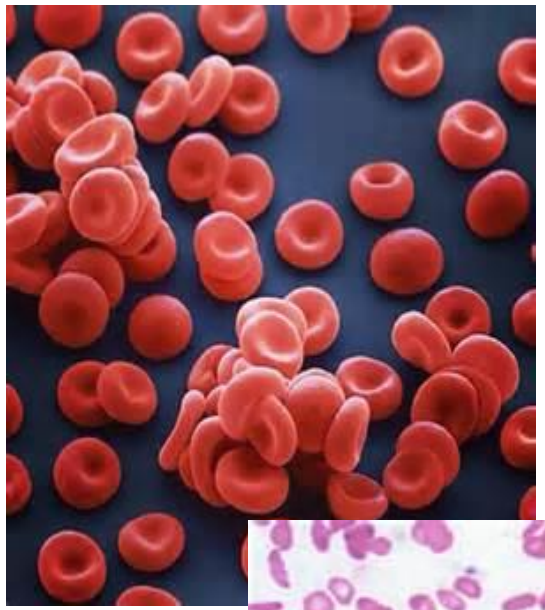
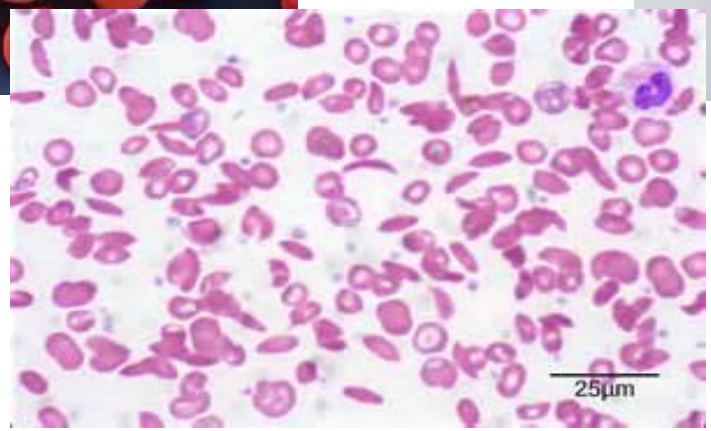
Goals of the presentation

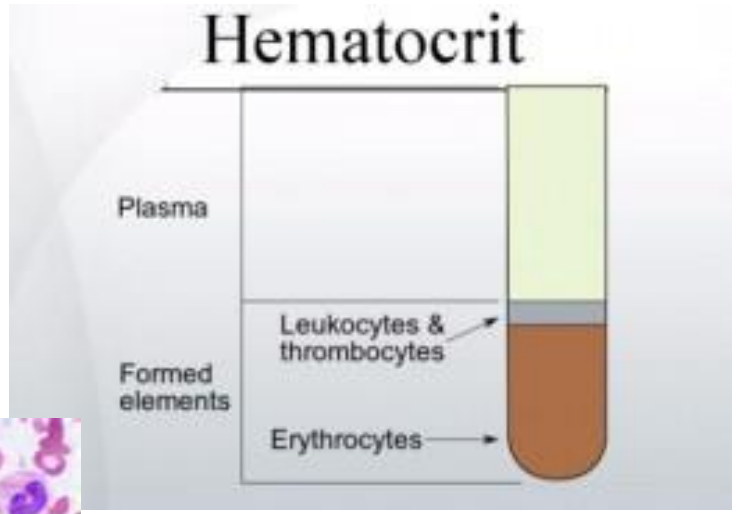
- Develop a consistent way to analyze Complete Blood Count (CBC) in an APS
  - How to use RBC (red blood cell) indices to determine type of anemia
    - Iron deficiency anemia
    - Anemia of chronic disease
    - Macrocytic anemia
    - Hemolytic anemia
- Determine how the anemia is related to the entire medical history
  - Use the anemia rating table or go to another impairment where anemia may be a sign of disease severity

Blood Basics

Whole blood is a mixture of plasma ~ 55% and blood cells ~ 45%







Blood Basics

- Blood is a specialized body fluid – largest organ in the body!
- Components of blood
  - Plasma is the unformed element of the blood – proteins circulate here
  - Red blood cells (erythrocytes)
  - White blood cells (leukocytes)
  - Platelets (thrombocytes)
- Functions of the blood
  - Transport oxygen and nutrients to organs
  - Formation of blood clots to prevent blood loss
  - Carry cells and antibodies to areas of infection
  - Transport waste products from the liver and kidneys

American Society of Hematology. Blood Basics/Homepage Accessed 5/18/16

RGA

Basic Hematology

Components of the complete blood count (CBC)

- WBC = White blood cells/infection-fighting cells
- RBCs
  - Hemoglobin – major oxygen carrying molecule of the blood
  - Hematocrit – intact RBCs in volume of plasma
    - Expressed as a percentage of volume of blood
- Platelets = involved with hemostasis (clotting)

Underwriting Anemia

Building Blocks

- Anemia is a pathologic state – it is never normal
  - Menstrual related blood loss exception
- Anemia increases mortality risk
  - Chronic kidney disease with decreased erythropoietin production
    - **Normochromic, normocytic and mild usually = anemia of chronic disease**
  - Anemia related to cancer suggests worse prognosis
    - Poorer drug delivery, less oxygen delivery for reparative processes, BM involvement?
      - Breast, Hodgkins lymphoma, and lung cancer
  - Anemia and chronic inflammation go hand in hand – anemia of chronic disease
    - Active inflammation effects utilization of iron through inflammatory mediators
    - Inflammatory bowel disease and RA: **Anemia is one of the criteria for disease severity**

Price, Elizabeth, MD, Schrier, Stanley. UpToDate.com. Anemia in the older adult. Accessed Feb 2,2017.

Underwriting Anemia

Building Blocks

- Anemia in the elderly – 10% of individuals over 65 were anemic!
  - National Health and Nutrition Examination Survey (NAHANES III)
  - Causes for anemia
    - 1/3 related to nutritional deficiencies
    - 1/3 related to chronic diseases: diabetes, renal disease
    - 1/3 Unexplained – however 17 % had elements of myelodysplastic syndrome
- Elderly individuals are commonly anemic!
  - Associated comorbidity or is this a stand alone problem?

Price, Elizabeth, MD, Schrier, Stanley. UpToDate.com. Anemia in the older adult. Accessed Feb 2,2017.

Underwriting Anemia

Building Blocks

- Hemoglobin is the most reliable index for anemia
  - Many cases it's all we get on insurance lab
  - Look at indices if present to determine type of anemia
- Age is important
  - Menopausal vs. post-menopausal
    - Anemia is common in menstruating females and related to menstrual blood loss
    - Anemia is pathologic in a post-menopausal woman
- Trends are critically important
  - Male vs. female

Red Blood Cell Indices

- Mean Corpuscular Volume (MCV) 80- 96 fl
  - Average volume / size of the RBCs
  - Helps to identify type of anemia
    - **Low = Iron deficiency or Thalassemias (microcytic anemia)**
      - < 80 fl, if iron studies present low Fe, low FERRITIN- tip off
    - **Normal = anemia of chronic disease (normocytic anemia)**
      - 80- 96fl, if iron studies present low Fe, normal to high ferritin
    - **Elevated = B12 or folate deficiency (macrocytic anemia)**
      - > 100 fl
      - Elderly individual : Anemia, Neutropenia, Thrombocytopenia/Myelodysplastic Sydrome – More than one cell line effected = Bone Marrow problem

Price, Elizabeth, MD, Schrier, Stanley. UpToDate.com. Anemia in the older adult. Accessed Feb 2,2017.

Red Blood Cell Indices

- MCV (mean corpuscular volume) – normal values 80 to 96 fL
  - Average volume or size of the RBCs
- Low MCV
  - Low MCV < 80 fL = iron deficiency anemia, thalassemia, chronic disease
- Normal MCV
  - 80 to 96 fL= hemolysis, renal insufficiency, diabetes, chronic diseases
- High MCV
  - > 100 fL = B12 or folate deficiency, liver disease, hypothyroidism, drugs

Schrier, S. Approach to the adult patient with anemia. Last updated: Dec 19, 2016. Up to Date. Accessed January 19. 2017.

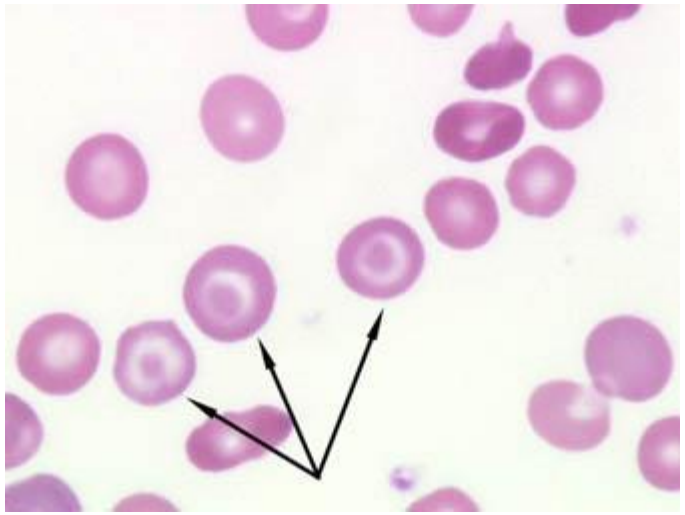
Red Blood Cell Indices

Consistent Assessment of the CBC

- Mean Corpuscular Hemoglobin Concentration (MCHC)
  - **Average hemoglobin content in a RBC**
  - Hypochromia (pale = low iron content) in the peripheral smear
    - Iron deficiency anemia and thalassemias = decreased MCHC
    - Hereditary spherocytosis = increased MCHC
- Red Cell Distribution Width (RDW)
  - Measure of the variation of size of the RBCs
    - Young, immature RBCs are large
  - A high RDW suggests a variety of different cell sizes
    - Iron deficiency anemia
    - Myelodysplastic syndrome, Alpha and Beta Thalassemias, Sickle Cell trait and Disease
    - Transfusion recipients

Target Cell - Peripheral Smear

- Sign of decreased hemoglobin content relative “membrane excess”
- Seen in thalassemias, liver disease, sickle cell, iron deficiency anemia



Anemia

- Depend on red blood cell mass and volume
  - Normal to high in pregnancy but with expanded plasma volume in 3rd trimester

    RBC mass and plasma volume are expanded up to 25-50% of normal – dilutional anemia
  - High if volume is depleted (dehydration)- hemoconcentration
  - Low if the red cells are decreased due to decreased production/ defective cells, increased loss
- Mild Anemia
  - Men less than 13 grams of Hgb
  - Women less than 12 grams of Hgb
  - Different labs have different cut off points

Iron Deficiency Anemia : 3 Major categories

Dietary Deficiency	• Infants • Elderly/malnourished
Malabsorption	• Inflammatory bowel disease • Gastric disease • Bariatric surgery
Loss	• Pregnancy • Menstruation • Chronic blood loss of any cause (colon cancer, peptic ulcer disease, AVM)

Practical Application

- Anemia in a 46 year old male : Nonsmoker/ 2-3 drinks/ week
- 5 million face amount
  - Past history: Low thyroid on replacement and Acid reflux
  - Insurance Lab: Creatinine is 1.0mg/DL, Cholesterol 121 MG/ DL
  - Hgb 10.2 G/DL (Reference range :13.0-16.0 G/DL) – lab dated 12-22-16
  - Medications listed: Synthroid, Omeprazole
    - APS review:
      - Records date back to 2010
      - Hypothyroid and GERD date back to 2013- asymptomatic
        - Has endoscopy every 2 years because of history of Barrett's
        - 2013 exam : external hemorrhoid – Preparation H given

Practical Application

Cont'd

- 06/2016 Office notes: notes frequent bright red blood per rectum – no weight loss
  - Further review of the APS shows CBCs dating back to 2010
    - Hgb/ Hct 05/2010 = 13.9/ 38.6 % MCV 85fl
    - Hgb/Hct 12/29/14 = 15.7/42.8 % MCV 87fl
    - Hgb/Hct 01/04/17= 9.7/ 30.6% MCV 63.99(l), MCHC 21.3(l)RDW 17.2 (h)
      - 2+ microcytes noted on the peripheral smear
      - Iron studies : serum iron: low at 24 ug/dl, ferritin low 6 ug/L (normal 22-322 ug/L)

Practical Application

Decision Making

- What type of anemia is this ?
- Would you offer on the anemia ?
- If not why not and if so at what rating would you assess?

Practical Application

- 63 year old female / nonsmoker. 5'6" #214
  - MAJOR DIAGNOSES: Cad with multiple stents
    - APS comment from office visit recently admitted to the hospital for CP
    - Anemia: Hemoglobin is 9.9mg/dl. Following with GI for possible bleeding
      - Takes ferrous sulfate 325 mg po q week
      - ASA, atorvastatin, Clopidogrel, Lisinopril, and Nitroglycerin, Omeprazole
  - Further review of the APS demonstrates
    - 09/14/2015 CBC Hgb/ Hct 12.4/ 39.6 MCV 78.6
    - 07/06/2016 CBC Hgb/ Hct 9.9/ 31.9/ MCV 76.9/ MCHC 37 (low), MCH 23.9 (low), RDW 15.5
- NO GI aps available
- Since she is wnl for our basic anemia rating table – would you offer ?

Anemia of Chronic Disease

- Also called anemia of inflammation
  - Associated with a number of different impairments
    - Thought to be related to bone marrow's inability to use iron appropriately
    - Marrow production of RBCs is decreased despite increased erythropoetin (EPO)
- What does it look like?
  - Variable severity of anemia
  - Mild anemia 10-11 mg Hgb with low normal indices
    - MCV is normal to low – rarely less than 70 fl
    - MCHC is normal
    - RDW is normal to increased

Useful table for CBC Interpretation

Laboratory findings in iron deficiency anemia, thalassemia, and anemia of chronic disease/inflammation			
Test	**Iron deficiency anemia**	**Alpha or beta thalassemia**	**Anemia of chronic desease/inflammation**
Complete blood count			
Hemoglobin	Decreased	Decreased	Decreased
Mean Corpuscular volume (MCV)	Decreased or normal	Decreased	Normal to decreased
Red cell distribution width (RDW)	Increased	Increased	Normal to increased
Red blood cell count	Decreased	Increased or normal	Decreased
Iron studies			
Serum iron	Decreased	Normal or increased	Decreased
Total iron-binding capacity (TIBC); transferrin	Increased	Normal	Decreased
Transferrin Saturation	Decreased	Normal	Decreased
Serum ferritin	Decreased	Normal	Increased
Erythrocyte protoporphyrin*	Increased	Normal or increased	Increased
Soluble transferrin receptor*	Increased	Increased	Normal

Refer to UpToDate topics on anemia for further details of the evaluation and interpretation.
*Not used in the routine evaluation of anemia.

What do you think?

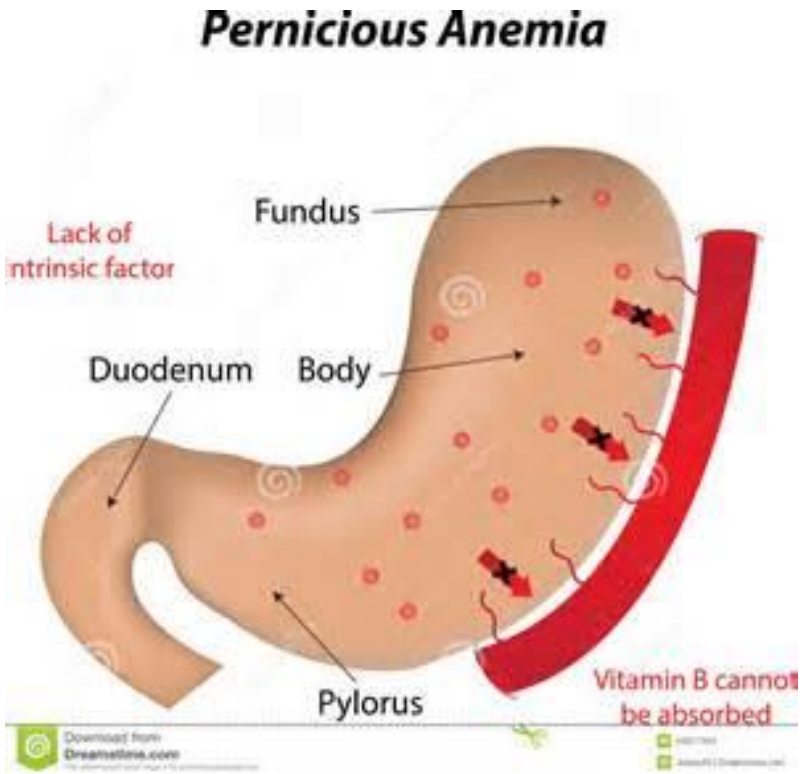
- 62 yo male / nonsmoker / 5'8" - #140 BMI 21 kg/m2
  - Drinks nightly - one glass of ?
  - Protein is low at 6.2 G/DL with albumin 3.9 G/DL (3.8-5.5)
  - HDL 53 mg/dl with total cholesterol of 182 mg/dl
    - **Past history significant for esophageal cancer 1999 with surgical treatment**
      - No chemotherapy
      - GERD with EGDs every 3 years- inflamed squamous and columnar mucosa- 2013 upper endoscopy (egd)
      - EGD 2016 – Squamous mucosa with active inflammation and ulceration
      - Cardiac type mucosa with moderately active chronic inflammation
        - No Dysplasia

What Do You Think ?

- Anemia noted as well:
  - 2012 CBC: Hgb/ HCT : 13.9/ 40.5
  - 2013 CBC: Hgb/ HCT : 14.1/ 41.6
  - 2015 CBC : Hgb/ HCT : 12.9/ 40.8 MCHC 31.5 (Low) and RDW 15.4 (High)
  - 2016 CBC : Hgb/ HCT : 12.7 / 39.5 MCHC 32.2 (nl) and RDW 16.0 (High)
- Assessment on the anemia?
  - What type of anemia
  - would you rate for the anemia?
  - If not, why not ?

B12 Deficiency MCV elevated > 100 fL

- Pernicious anemia – antibodies to parietal cells in duodenum responsible for B12 absorption
  - Can in very rare cases lead to spinal cord dysfunction, neuropathy and dementia
  - Alcoholism/ Liver disease
  - Post-gastric bypass- malabsorption
    - Iron deficiency is common as well
  - Gastric sleeve
  - Inflammatory bowel disease
    - Can see iron deficiency anemia
    - Can also see macrocytic anemias from nutritional depletion/ malabsorption



Megaloblastic Anemias = Macrocytic Anemias

- Folate deficiency – “The big three”
  - Alcoholics------ Nutritional deficiencies : commonly both iron deficiency and folate deficiency
  - Pregnancy ------Inadequate intake for increased demand by fetus
  - Medications - Interfere with DNA synthesis
    - Hydroxyurea, Methotrexate, Azathioprine or 6- Mercaptopurine
    - Zidovudine – Retrovir or Combivir

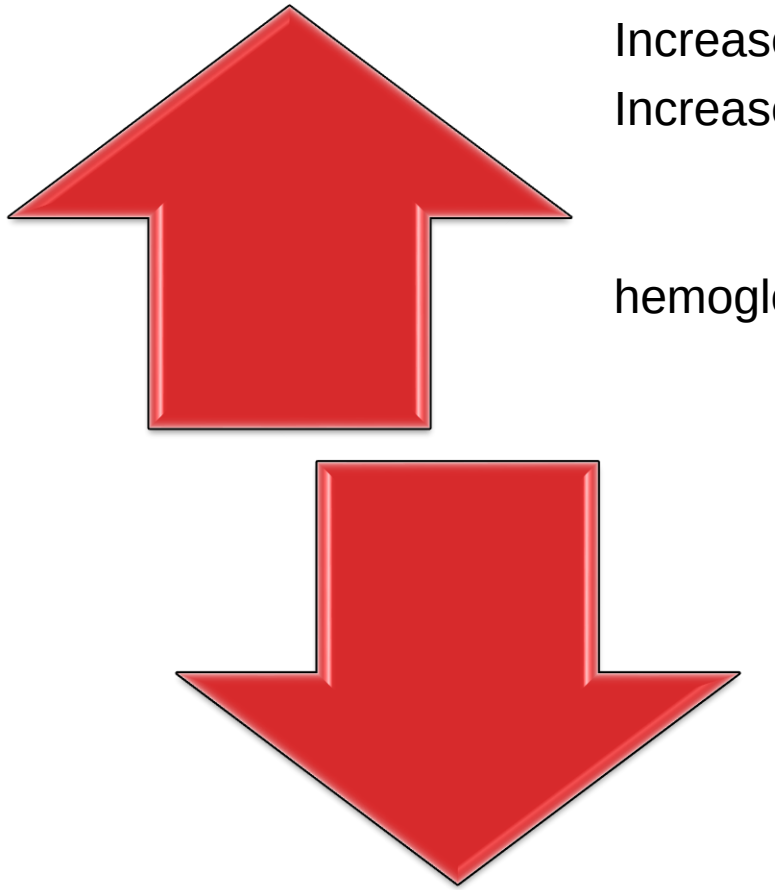
Megaloblastic Anemias = Macrocytic Anemias

- Other causes for macrocytosis
  - Multiple myeloma
  - Liver disease and hypothyroidism
  - Aplastic anemia
  - Reticulocytosis
    - Hemolytic anemia
    - Bone marrow recovery after chemotherapy or bone marrow transplant

Schrier, S., MD. Macrocytosis/Macrocytic anemia. UpToDaate.com. Accessed on Feb 5, 2017.

Anemia

Causes of anemia



Increased blood loss: iron deficiency

Increased blood destruction (hemolysis)

1. Increased bilirubin, increased LDH

Causes include: medications, hemoglobinopathies, and hematologic malignancies

Decreased blood production (hematopoeisis)

1. Anemia of chronic disease : 2nd most common anemia

- Related to the underlying disease process: RA, Malignancies, IBD, CHF, Diabetes, Renal insufficiency, COPD, older age applicant

Recognizing Hemolytic Anemia

Building Blocks

- Hemolytic anemia = premature destruction of RBCs
  - Average life span of a RBC is 120 days ~ 4 months
  - Hemolysis can be caused by inherited or acquired conditions
    - RBC membrane is deformed and not able to maintain shape going through the reticuloendothelial system (RES)
      - Splenic sequestration occurs and hemolysis follows
    - Hemolysis stimulates the bone marrow to produce RBCs = Reticulocytes (immature RBCs) seen on peripheral smear
      - Lab suggestive of CBC destruction: Increased LDH, increased bilirubin, and …
        - What would you expect the CBC indices to look like?

Recognizing Hemolytic Anemia

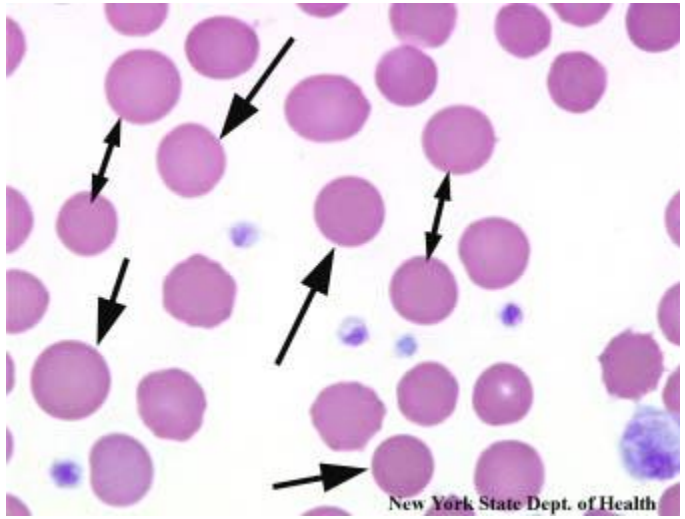
Building Blocks

- RBC indices in hemolytic anemia:
  - Mild to moderate anemia
  - MCV normal to slightly low : hemolysis with anemia is offset by reticulocyte counts
  - MCHC is elevated and the RDW is elevated as well!
    - High reticulocyte count –Bone marrow producing increased numbers of RBCs

Blood Destruction/Hemolysis

Spherocytosis

- Autosomal dominant
- RBCs are normally concave
- In this disorder they are spherical, which makes them subject to destruction (especially in the spleen) > splenomegaly
- Hemolytic crises worse with cold, infections
- Other signs of hemolysis
  - Elevated bilirubin
  - Jaundice
  - Gallbladder disease
- Spherocytes on peripheral smear



Blood Destruction/Hemolysis

Spherocytosis

- Treatment – splenectomy – not curative but reduces many of the complications
- More at risk for infections
- Still can have a hemolytic crisis
- Other hereditary causes:
  - Elliptocytosis
  - Congenital hemolytic anemia
  - Hereditary pyropoikilocytosis
  - Hereditary stomatocytosis

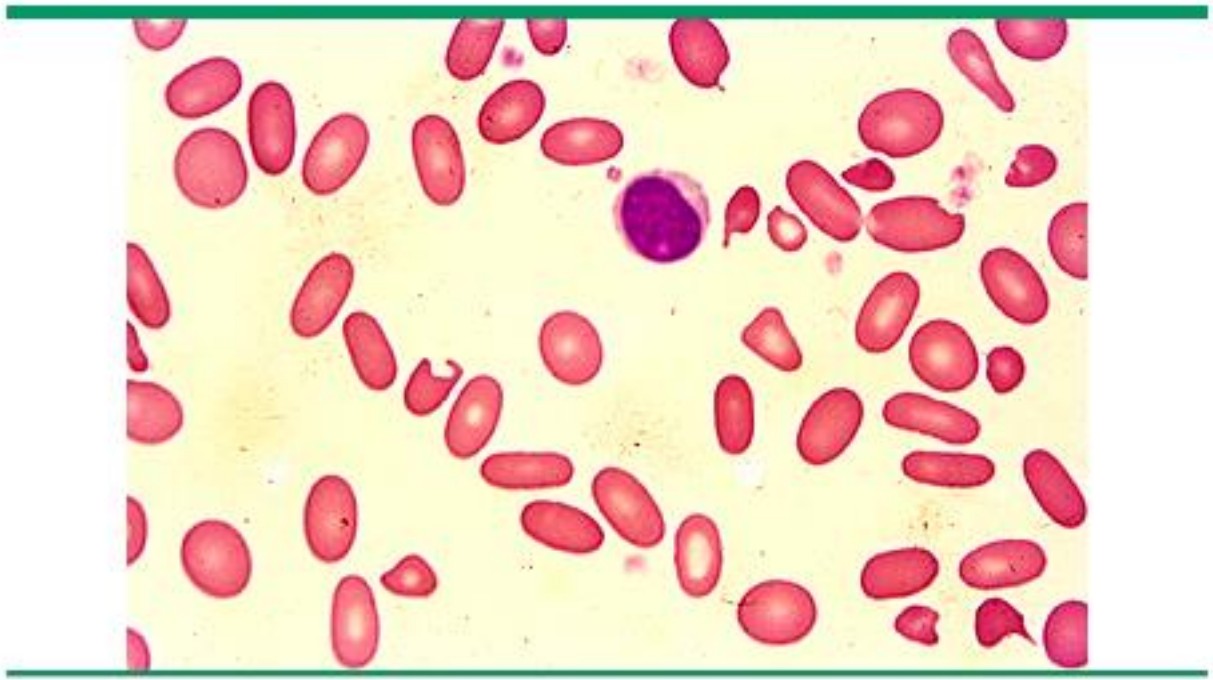
Schrier, S., MD. Diagnosis of hemolytic anemia in the adult. UpToDate.com Accessed Feb. 7, 2017.

Blood Destruction/Hemolysis

Elliptocytosis

- Hereditary hemolysis
  - Elliptocytosis- uncommon in USA
    - Much more common in Africa, and southeast ASIA where elliptocytosis confers immunity to malaria

Elliptical red cells in hereditary elliptocytosis



Peripheral blood smear from a patient with hereditary elliptocytosis shows multiple elliptocytes.

Courtesy of Carola von Kapff, SH (ASCP).

UpToDate®

Menzer., W. ,MD UpTodate.com accessed Feb 6, 2017,

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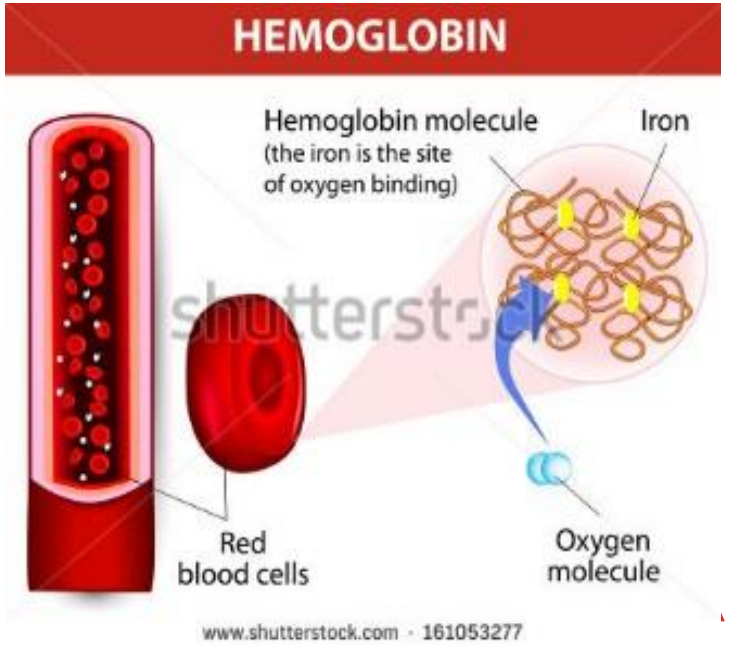
Acquired Hemolytic Anemias

Splenomegaly	• Myeloproliferative diseases • Lymphomas • Gaucher's
Immune Causes	• Lupus • Drug reactions • Post-viral infections • Cold agglutinins • Paroxysmal cold hemoglobinuria
Toxins and Trauma	• Drugs • DIC

Thalassemias

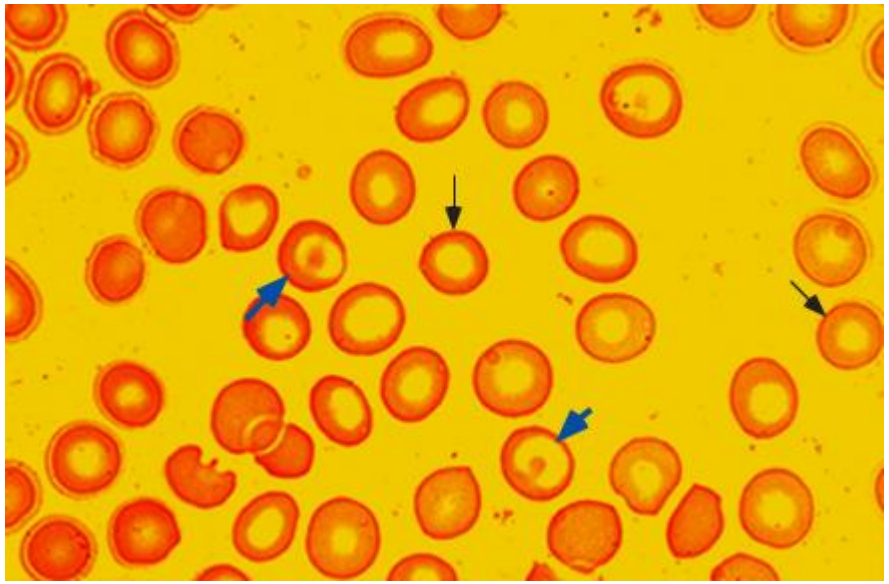
- The major form of hemoglobin circulating in the blood is hemoglobin A
  - 4 chains of proteins bound together with iron bound to each chain
    - Thalassemias have reduced or absent production of either the alpha or beta chains that create the hemoglobin molecule
      - Alpha thalassemia minor- reduced production of alpha globin- unstable and precipitate within the cell
      - Beta thalassemia minor **– heterozygous for the gene leading to reduced beta globin production**

- Thalassemia intermedia
  - Compound heterozygotes of 2 thalassemic variants
    - More symptomatic than the minors
    - Later onset of disease and not transfusion dependent
      - Iron overload is problematic



Beta Thalassemia Trait

Hypochromic, microcytic indices

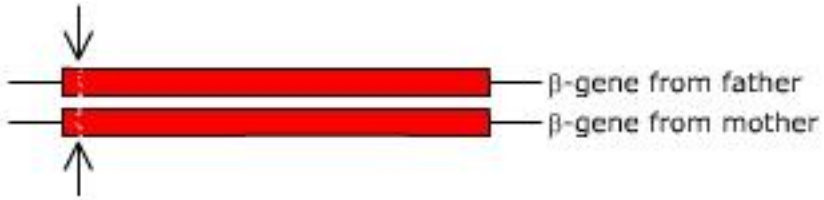


Thalassemia Major

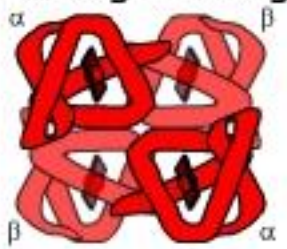
- Produce variable amounts of the beta globin chain
  - Relative excess of alpha chains and distortion of the normal configuration of the hemoglobin molecule
    - The degree of alpha globin chain excess determines severity of disease
    - Severely limited or no effective production of beta globin chains
      - Originally described by Cooley – Cooley's anemia
      - Profound and life long transfusion dependent anemia

Genetic Explanation for Thalassemia

With a mutation on one of the two ß-globin genes, a carrier is formed with lower protein production, but enough hemoglobin



Without a mutation enough Hemoglobin



No thalassemia carrier

With one mutation less Hemoglobin

β-thalassemia carrier without illness, but less hemoglobin (slight aneamia)

With two mutations no β-globin

β-thalassemia major patient with severe aneamia

Summary

- Blood disorders are complex so a process to evaluate will help with consistency in underwriting decisions
- Two major components of the blood
  - Formed elements: RBCs, WBCs, platelets
  - Plasma: proteins /immunoglobulins
- RBCs carry oxygen to the tissues and WBCs are involved with immunity against infections as well as neoplasms
  - Neutrophils are the infection-fighting cells (most commonly bacterial infections)
  - Lymphocytes comprise the immune system: antibodies and T cells involved with protection against infections and neoplasms
    - Leukemias most commonly involve lymphocytes

Summary

- Always be on the lookout for blood malignancies
  - Many blood diseases are insurable but some are not
  - Look at trends: if something is consistently going in the wrong direction > take action
- Develop a systematized approach so you don’t miss something abnormal

Questions?