Common Hematologic Abnormalities

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Objectives

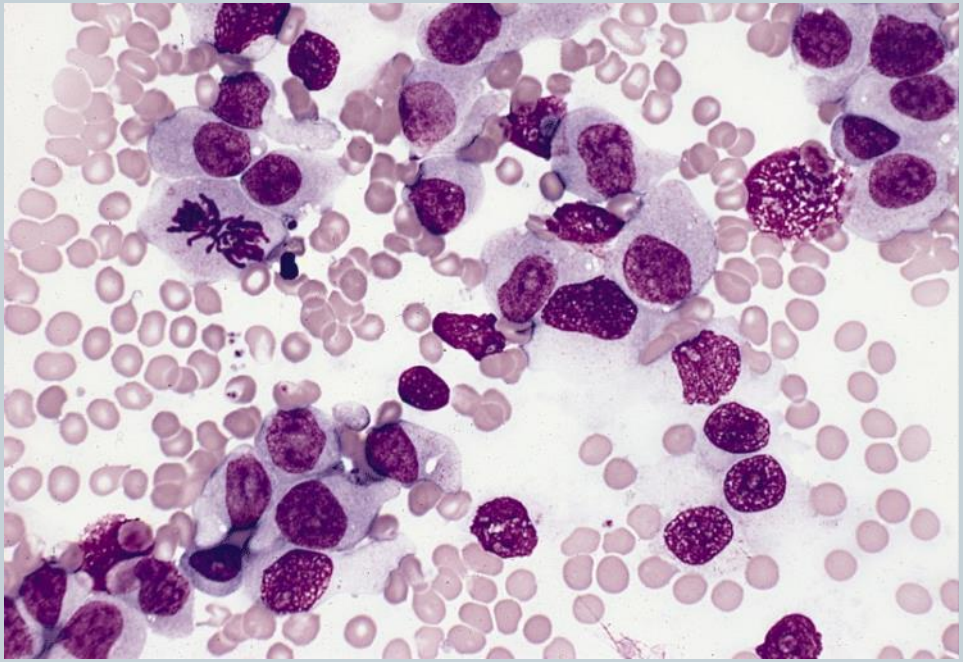
- To be familiar with different causes of anemia
- Identify patterns suggestive of iron deficiency versus anemia of chronic inflammation
- To recognize erythrocytosis, identify potential causes, and be aware of indications for phlebotomy
- To be able to provide a differential diagnosis for leukopenia and leukocytosis based on the differential count.
- To be familiar with the recommendations for treatment of DVT

Overview

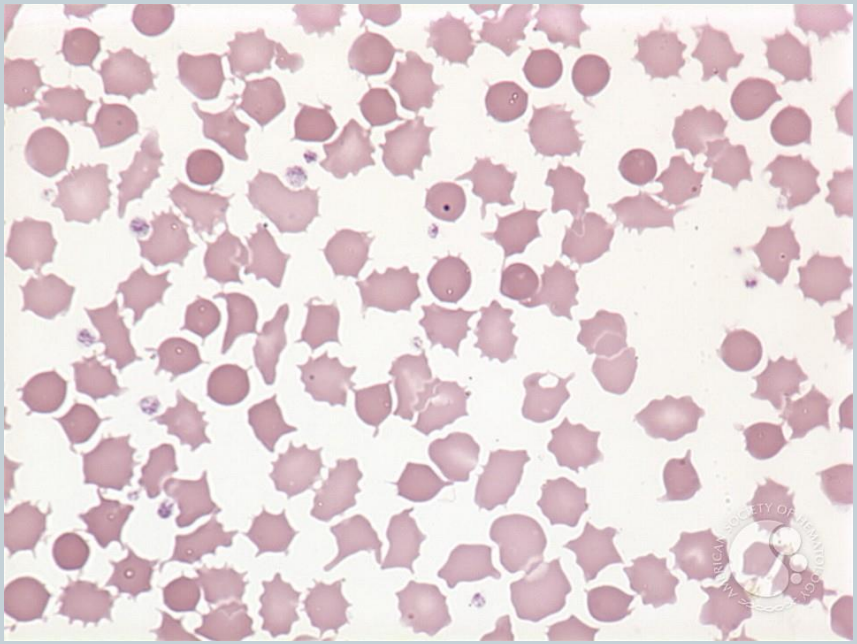
- Red Cell Abnormalities
  - Interpreting abnormal red cell indices
  - Anemia- Microcytic, Normocytic or Macrocytic
- White Cell Abnormalities
  - An Abnormal Differential count
  - Leukocytosis
  - Leukocytopenia
- Platelet Abnormalities
  - Thrombocytopenia
  - Thrombocytosis

Abnormal CBC

- WBC 42,000 x 10^3 /µL
- Hgb 8.2 g/dL
- Hct 24.6 %
- MCV 87 fL
- Platelets 18 x 10^3 /µL
- Granulocytes 11%
- Lymphocytes 23%
- Monocytes 5%
- Blasts 61%



Red Cell Abnormalities



- Abnormal red cell indices
  - Size- Mean Corpuscular Volume (MCV)
  - Variation in size- Red cell distribution width (RDW)
  - Morphology- Poikilocytosis, Ansiocytosis, Acanthocytes, Spherocytes Nucleated red cells

Acquired Underproduction Anemias

- Vitamin/Nutrients:
  - Iron deficiency
  - Iron dysregulation (Anemia of Chronic Disease)
  - Megaloblastic Anemias:
    - Cobalamin deficiency
    - Folate deficiency
    - Copper Deficiency
- Organ Dysfunction
  - Renal Disease
  - Endocrine deficiency (thyroid, pituitary, adrenal, testis)
  - Liver disease
- Marrow Failure
  - Immune, Infection, Drug
- Marrow Microenvironment
  - Infiltration (Malignant, Storage Diseases, Hemaphagocytic syndrome)
- Multifactorial
  - Pregnancy
  - Aging
  - Cancer
  - HIV

Case

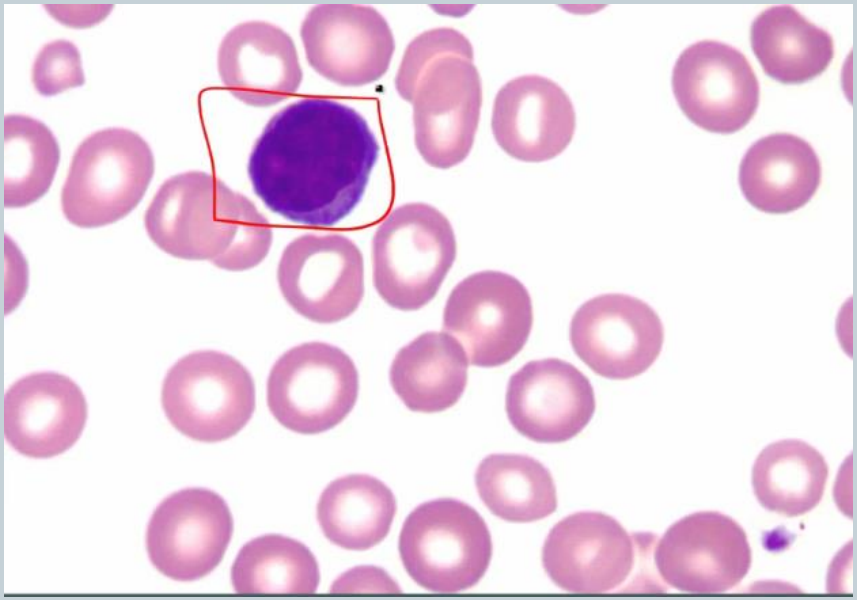
- 42 year old female with microcytic anemia presents for evaluation. She has not had a primary physician, but was recently evaluated in the ED for severe fatigue, dizziness, and shortness of breath. She reports a craving for ice, and restless legs at night. She has very heavy menses that last 5-6 days, and occur every 28 days.
- She was noted to have the following findings on CBC:
- Hgb 6.5 g/dL MCV 72 fL Plt 535 x 10^3 /µL

Iron Studies

- Ferritin 3
- TIBC 452
- Iron Saturation 5%

She has been started on Provera, and her bleeding has decreased in severity.

Microcytic Anemias



- Iron Deficiency
- Anemia of Chronic Disease
- Thalassemia
- Other hemoglobinopathies
- Microspherocytes

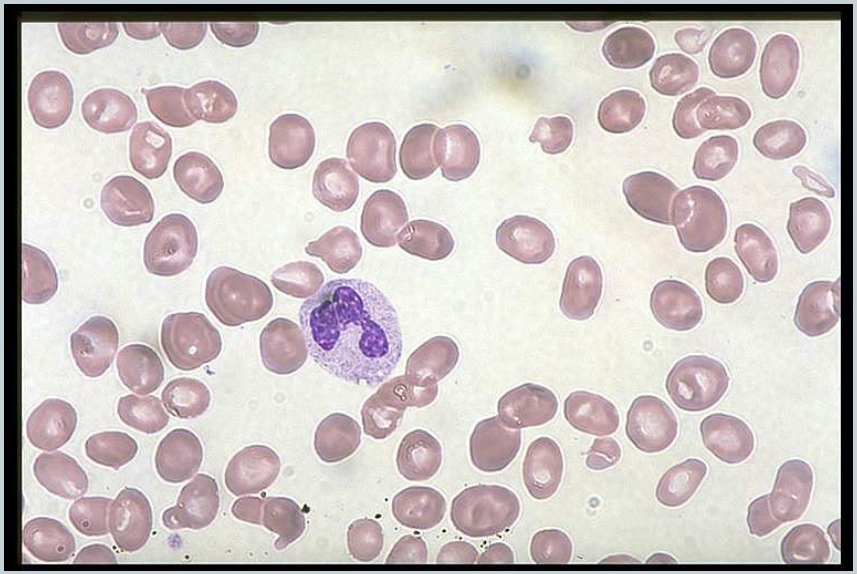
Iron Deficiency vs. Anemia of Chronic Inflammation

Iron Deficiency	AOCI
• Serum Fe ↓ to normal	• Serum Fe ↓ to normal
• TIBC high Nl to ↑	• TIBC ↓ to low Nl
• Iron Sat ↓↓	• Iron Sat ↓
• Serum Ferritin ↓↓	• Serum Ferritin Nl to ↑↑
• MCV ↓ to ↓↓	• MCV ↓ to Nl
• RDW ↑	• RDW Nl to ↑

Iron Deficiency- Why?

- Increased Iron Requirements
  - Blood Loss
    - GI disorders- varices, hemorrhoids
    - Menstrual losses
    - Chronic blood donation
    - Dialysis
  - Intravascular Hemolysis/Hgburia
    - PNH
    - Metallic Valve/Valve dysfunction
  - Pregnancy/Lactation
- Inadequate Iron Supply
  - Poor PO Intake
  - Malabsorption
    - Celiac disease
    - Gastric Bypass Surgery
    - Achlorhydria
    - Crohn's disease
  - Abnormal Transferrin Function

Macrocytic Anemias



- Cyanocobalamin Deficiency
- Folate Deficiency
- Paraproteinemia
- Alcohol use
- Medications:
  - 5-fu
  - Methotrexate
  - Azathioprine
  - AZT
  - Hydroxyurea
  - Anticonvulsants
  - PPIs
- Myelodysplastic conditions
- Reticulocytosis

Indications for transfusion

- ●Hgb <6 g/dL – Transfusion recommended except in exceptional circumstances
- ●Hgb 6 to 7 g/dL – Transfusion generally likely to be indicated
- ●Hgb 7 to 8 g/dL – Transfusion should be considered in postoperative surgical patients, including those with stable cardiovascular disease, after evaluating the patient's clinical status
- ●Hgb 8 to 10 g/dL – Transfusion generally not indicated, but should be considered for some populations (eg, those with symptomatic anemia, ongoing bleeding, acute coronary syndrome with ischemia)
- ●Hgb >10 g/dL – Transfusion generally not indicated except in exceptional circumstances

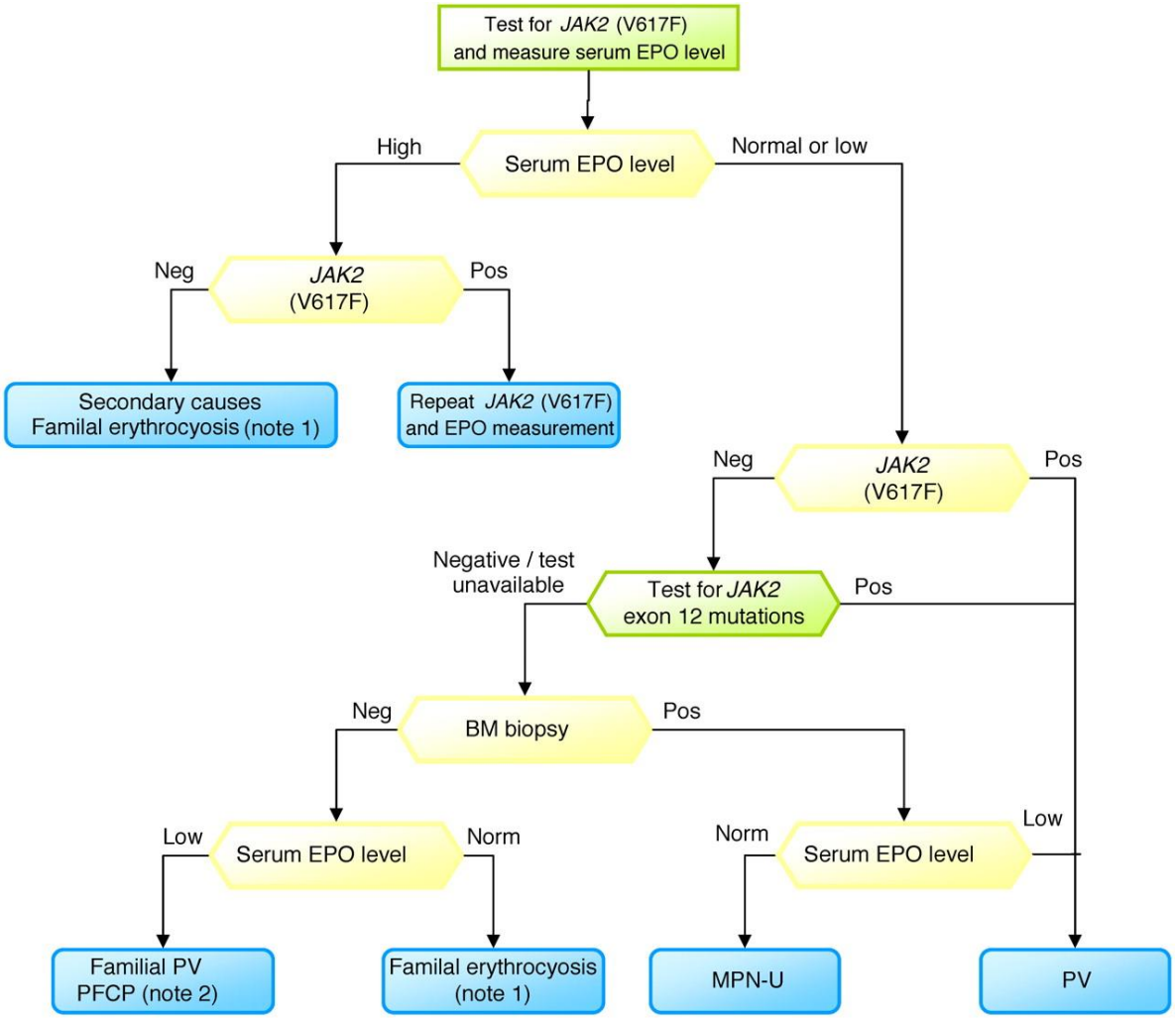
Erythrocytosis

- **Hematocrit** – The hematocrit (HCT) is expressed as the percent of a blood sample occupied by intact RBC. Polycythemia in the adult patient is considered to be present when the HCT is >48 or >52 percent in women and men, respectively.
- **Hemoglobin concentration** – The hemoglobin concentration (HGB) is expressed in grams per 100 mL of whole blood. Polycythemia in the adult is considered to be present when the HGB is >16.5 or >18.5 g/dL in women and men, respectively

Causes of Erythrocytosis

- Primary
  - Polycythemia Vera
- Secondary
  - Congenital
  - Hypoxemia/Impaired Tissue Oxygenation
    - High Altitude
    - COPD
    - Smoking
    - Carbon Monoxide Poisoning
  - Renal Lesions
    - Tumors
    - Cysts
    - Diffuse Parenchymal disease
    - Hydronephrosis
    - Renal Artery Stenosis
    - Renal Transplant
  - Tumors
    - Parotid, Uterine fibroids, Cerebellar Hemangiomas, Lymphomas, Ovarian tumors, Meningiomas, Pheochromocytoma, Hepatoma
  - Drugs/Chemicals
    - Androgens

Diagnostic approach to erythrocytosis.



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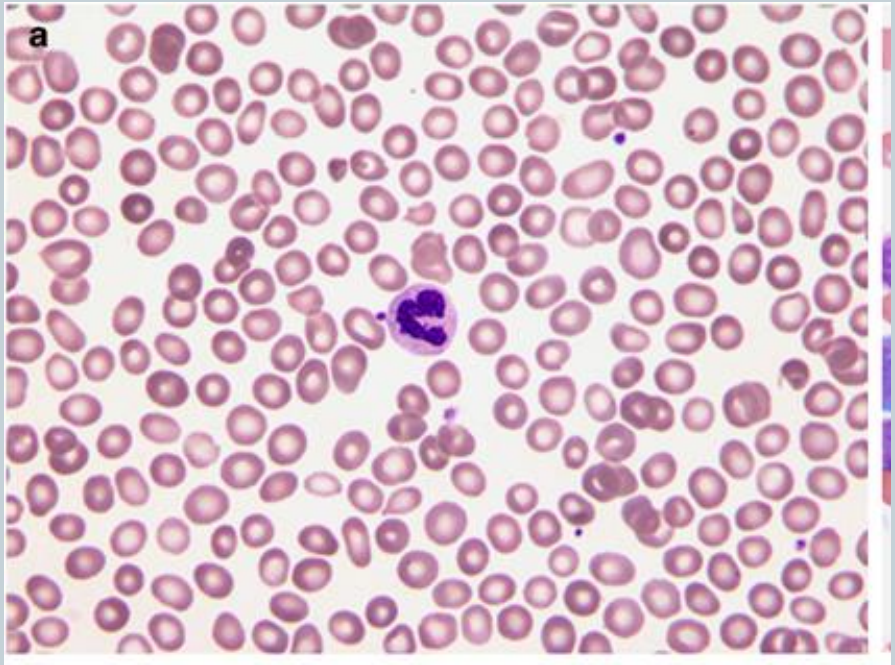
Indications for Phlebotomy

- Primary Polycythemia
  - **Hematocrit control** – If no active thrombosis and in those not at risk for thrombosis (ie, age <60, no prior thrombosis), hematocrit should be kept within the normal range via serial phlebotomy
    - A standard one unit phlebotomy (500 mL) should reduce the hematocrit by 3 percentage points in a normal-sized adult (eg, from 46 to 43 percent).
    - Optimal control is to keep the hematocrit continuously below 45 percent in men and 42 percent in women. Secondary Polycythemia
  - Control of the underlying cause, if possible (eg, removal of an Epo-secreting tumor, cessation of exposure to carbon monoxide)
  - Limited phlebotomy, as tolerated, if symptoms are present and the total blood volume is increased. Such patients may achieve relief following a modest reduction in their hematocrit, but may become more symptomatic if the hematocrit is reduced to the normal range.

Leukopenia



- Total WBC below the normal range
  - Racial and Gender differences
  - Infection
- Neutropenia vs. Lymphopenia

Primary Neutropenia

- Congenital/Inherited
  - Cyclic Neutropenia
  - Diamond-Blackfan
  - Schwachman-Diamond
  - Kostmann Syndrome
- Acquired
  - Acute Leukemia
  - Myelodysplastic Syndrome
  - CLL
  - Lymphomas
  - Aplastic Anemia
  - Chronic Idiopathic Neutropenia
  - Copper, B12, Folate Deficiency

Secondary Neutropenia

- Immune Neutropenias
  - Autoimmune Neutropenia
  - Neutropenia with Autoimmune disease
    - SLE
    - RA
    - Felty Syndrome
    - Sjogren Syndrome
  - Large Granular Lymphocytosis
  - Infection
    - Viral
    - Sepsis
    - Rickettsial
  - Drugs

Lymphopenia

- Congenital Immune Deficiency Syndromes
- Infection
  - Bacterial- TB, Typhoid Fever, Brucellosis
  - Viral- HIV, SARS, measles, hepatitis, CMV
  - Fungal
- Medications
  - Steroids, Rituximab, Alemtuzumab
  - Chemotherapy
  - Radiation therapy
- Chronic Renal Failure
- Alcohol Abuse
- Elderly Age
- SLE
- RA
- Sarcoidosis

Leukocytosis

- Inflammation
- Infection
- Malignancy
- Trauma
- Medications
- Congenital/Familial

Approach to the Patient with Leukocytosis

- Neutrophilia? Monocytosis? Lymphocytosis? Eosinophilia?
- History and Physical Exam is Key!
  - Fevers, Rashes, splenomegaly, arthopathy…
  - Family history of elevated white blood cells?
  - Fatigue, bruising, lymphadenopathy, gum bleeding/swelling?

Case 2

- A 69 year old female is referred for evaluation of leukocytosis. She reports some fatigue, but otherwise feels well. Denies any recent infections or inflammation. She has not noticed any swollen lymph nodes. She has not had night sweats, or early satiety.
- WBC 15.3 x $10^3/\mu L$ Hgb 11.2 g/dL Plt 175 x $10^3/\mu L$

  Neutro 30% Lymphs 60% Monos 7% Eos 2% Basos 1%

Case 2 (Continued)

- Peripheral Smear:
  - Small, mature lymphocytes. Smudge cells noted. Mild, normocytic anemia
- Flow Cytometry:
  - CD20+ CD5+ CD 23- Clonal population of B-Lymphocytes, consistent with CLL

Neutrophilia	Monocytosis	Eosinophila	Lymphocytosis
Elevated Cortisol/Corticosteroids	Pregnancy	Allergic Rhinitis/ Asthma	Mononucleosis
Inflammatory Bowel Dz	Tuberculosis	Parasitic Infxn	EBV
Rheumatologic Dz	Syphillis	Aspergillosis	CMV
Granulomatous Infection	Endocarditis	Coccidiodal infxn	HIV
Occult Malignancy	Sarcoidosis	HIV	Viral Illness
Smoking	SLE	Immunodeficiency	Pertussis
Beta Agonists	Asplenia	Vasculitidies	Bartonella Henslae
Asplenia	Corticosteroids	Drug Reaction	Toxoplasmosis
Stress	CMML	Adrenal Insuffiency	Drug Reaction
Thyrotoxicosis		Occult Malignancy	Reactive LGL
Hereditary Neutrophilia		Hypereospinphilic Syndromes	Lymphoma/CLL

Common Causes of Thrombocytopenia

- Pseudothrombocytopenia – clumping, giant platelets
- HIT
- ITP
- DIC
- Infection
- Autoimmune disease
- Infection
- Medications- HIV, Hepatitis C, Malaria
- Vitamin deficencies-B12, Folate, Copper
- Alcohol- Marrox toxic; Cirrhosis/Hypersplenism
- Bone Marrow Infiltration
- Myelodysplastic Syndrome
- RA/SLE
- TTP, HUS

Thrombocyotpenia

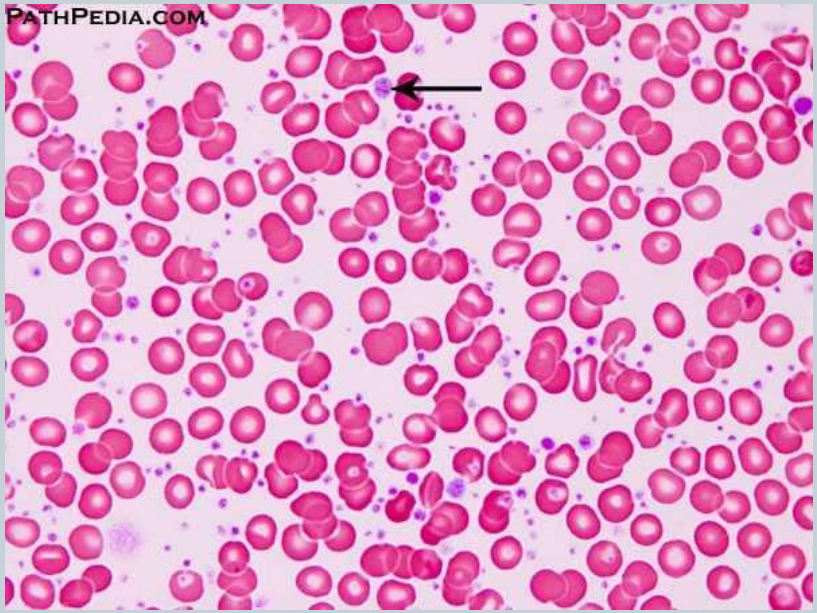
- New or Chronic? Review of old results is important!
  - Chronic:
    - Splenomegaly/Portal Hypertension
    - Autoimmune diseases
    - Inherited disorders
  - New:
    - ITP
    - Infection
    - Malignancy
    - Medications
- Review the smear
  - Clumping, Large platelets, Other abnormal cells/morphology
  - Schistocytes? Could be DIC, TTP or other microangiopathic processes.

Thrombocytosis

- Reactive:
  - Infection
  - Inflamation
  - Post-surgical Status
  - Trauma
  - Malignancy
  - Asplenia
  - Iron Deficiency/Acute Blood Loss
- Autonomous Thrombocytosis:
  - Myeloproliferative Disorders
  - Myelodysplastic Syndrome with 5q-

Case 3

- A 59 year old gentleman presents with elevated platelets:
- WBC 4.8 x 10^3 /µL
- Hgb 13.5 g/dL
- Hct 41%
- Plt 886 x 10^3 /µL
- Differential count normal



DVT

- ACCP 2012 Guidelines
  - Provoked or Unprovoked?
  - Provoking Events:
    - Surgery
    - Trauma
    - Medical Illness
    - Prolonged Immobility
    - Oral Contraceptive or Hormonal Therapy
    - Intravenous Catheters

Duration of Anticoagulation

- Provoked: Reversible risk factor- Three Months
- Unprovoked: Long term- consider risk/benefit ratio; cost, patient choice, any identified thrombophilia.

"Oh waiter! Will you pass me the anticoagulant please?"

Choice of Long-Term Anticoagulant

- Warfarin
  - Monitoring, Dietary Restrictions, Medication interactions.
  - Reversible with Plasma, Vitamin K
- Anti-Xa agents (Rivaroxaban)
  - No monitoring
  - Short half life
  - Caution with renal or hepatic Dysfunction
  - Not reversible
- LMWH
  - Better efficacy than Warfarin in patients with active malignancy
- Fondaparinux

Immediate Treatment

- LMWH vs. Unfractionated IV Heparin?
  - ACCP guidelines recommend AGAINST Unfractionated Heparin in patients for whom LMWH can be used.
  - Recommendation is NOT different for patients with PE- LMWH is still better.
- Immobilize or Early Mobility
  - Early mobility is recommended
  - Compression Stockings can be used early

Hypercoagulable Workup

- Universally Ordered, but Controversial
- Many abnormalities are not clearly associated with recurrent thrombosis
- May be useful in making decisions regarding discontinuation of therapy, bridging therapy

How much did you learn?

CASES

Challenge Case #1

- A 30 year old female presents with fatigue, and generalized malaise. She does have heavy bleeding with her menses. She has a vegan diet. She does have joint pain and stiffness in the morning, and has a rash on her nose and cheeks after sun exposure.

CBC	Iron Studies/Other
WBC 2.6 x $10^3/\mu L$	Iron 20
Hgb 10.2 g/dL	Iron Saturation 6%
Hct 31%	TIBC 207
MCV 87 fL	Ferritin 10
RDW 19.9%	B12 197
Plt 489 x $10^3/\mu L$	Folate >20

Question

- What type of anemia does she have?
  - A. Iron Deficiency
  - B. Vitamin B12 Deficiency
  - C. Anemia of Chronic Inflammation
  - D. A & B
  - E. A, B, & C

Answer

- What type of anemia does she have?
  - A. Iron Deficiency
  - B. Vitamin B12 Deficiency
  - C. Anemia of Chronic Inflammation
  - D. A & B
  - **E. A, B, & C**

Challenge Case #2

- A 70 year old male presents for evaluation of anemia. He has recently noted some fatigue, shortness of breath on exertion, and some bone pain, which he has attributed to arthritis.

CBC	Chemistry Panle
WBC 5.4 x $10^3/\mu L$	BUN 44
Hgb 8.9 g/dL	Cr 2.1
Hct 26%	Alb 2.3
MCV 106 fL	Total Protein 8.1
RDW 19.9%	Calcium 10.1
Plt 163 x $10^3/\mu L$	

Question #2

- Which is the most likely cause of the anemia:
  - A. B12 Deficiency
  - B. Hemolytic Anemia
  - C. Paraprotein/Myeloma
  - D. Renal Insufficiency
  - E. C & D

Answer

- Which is the most likely cause of the anemia:
  - A. B12 Deficiency
  - B. Hemolytic Anemia
  - **C. Paraprotein/Myeloma**
  - D. Renal Insufficiency
  - E. C & D

Challenge Case #3

- A patient presents for evaluation of Erythrocytosis. He is a 40 year old non-smoker. He is very active and is an avid body builder who lives in Denver, CO. He has previous labwork with him that shows normal red blood cell counts. He denies any symptoms of blurred vision, headaches, shortness of breath, erythromelalgia, or early satiety.

CBC
WBC 9.9 x 10^3 /µL
Hgb 19.3 g/dL
Hct 58%
Plt 363 x 10^3 /µL

Question

- Which of the following are likely causes of his elevated Hgb?
  - A. Iagtrogenic (Anabolic Steroid use)
  - B. High Altitude
  - C. Polycythemia Vera
  - A & B

Answer

- Which of the following are likely causes of his elevated Hgb?
  - A. Iagtrogenic (Anabolic Steroid use)
  - B. High Altitude
  - C. Polycythemia Vera
  - **D. A & B**

Challenge Case #4

- A 29 year old female presents after recent diagnosis of RLE DVT. She is currently taking oral contraceptives. On questioning, she admits to smoking a pack of cigarettes daily. She has no family history of thrombosis, but notes that she was told in the hospital that she has a heterozygous Factor V Leiden Mutation.

Question

- You are asked to decide the duration of anticoagulation. Should she take an anticoagulant for:
  - A. 3 months
  - B. 6 months
  - C. Indefinitely
  - D. None of the above

Answer

- You are asked to decide the duration of anticoagulation. Should she take an anticoagulant for:
  - **A. 3 months**
  - B. 6 months
  - C. Indefinitely
  - D. None of the above

Questions?

THANK YOU FOR YOUR ATTENTION!

References

- ASH- Self Assessment Program 3rd Edition
- ASH Image Bank
- UpToDate (www.uptodate.com)
- 2012 ACCP Guidelines on Anti-Thrombotic therapy
- AABB Guidelines for Transfusion