LAB 1: THE HEMATOPOIETIC SYSTEM – CLINICAL CASES

The focus of this week's lab will be pathology of the hematopoietic system. Diseases of the blood can be organized into disorders that mainly affect red blood cells (erythrocytes), white blood cells (leukocytes), or the hemostatic system (including platelets and clotting factors).

Disorders of red bloods cells usually result in a deficiency of red blood cells called *anemia*. In contrast, disorders of white blood cells usually result in excess white blood cells called *leukocytosis*. Disorders affecting the hemostatic system can result in *hemorrhagic diatheses* (bleeding disorders).

Red cell disorders most often result in anemia. Anemia can be caused by 1) loss of blood, 2) increased red cell destruction, or 3) decreased red cell production. Red blood cells are approximately 45% of blood volume; this is expressed clinically as a hematocrit of 45. The red blood cell is a soft, elastic, biconcave disc with a diameter of approximately 7.5 μm in a blood film and about 8.5 μm in vivo. Specific features of the red blood cell can be examined and correlated with pathological changes including cell size (*normocytic, microcytic, macrocytic*), extent of hemoglobinization observed by cell color (*normochromic, hypochromic*), and shape of cells. The presence of darkly staining ribosomal RNA in a red blood cell may indicate an immature red blood cell called a *reticulocyte*, which should comprise approximately 1% of red blood cells. Reticulocytes can increase (reticulocytosis) with increased regeneration of red blood cells following anemia.

Diseases of white blood cells may involve deficiencies (*leukopenias*) or, more often, proliferation of white blood cells (*leukocytosis*). Proliferation may be reactive in response to microbial disease or neoplastic. White blood cells include monocytes, lymphocytes, neutrophils, eosinophils, and basophils. Neutrophils are the most prevalent (55-60%) of all white blood cells and are 10-12 μm in diameter and have a segmented nucleus (referred to as "segs" clinically); immature neutrophils have a band shaped nucleus (referred to as "bands") and can be increased with infection or inflammation. Lymphocytes make up 30% of leukocytes and although they look alike in blood smears, lymphocytes are composed of different types, including B and T cells. Monocytes are larger cells (12-19 μm in diameter) and are the precursors of macrophages. Proliferation of leukocytes can occur in response to infection or as part of a neoplastic process.

Platelets are small pieces of a large cell found in bone marrow called a megakaryocyte. Platelets are important for blood clotting and disorders that reduce platelets numbers can result in hemorrhage and increasing platelet number can increase the risk of *thrombosis*.

The cases we will cover are:

A. Hereditary Spherocytosis
B. Iron Deficiency Anemia
C. Pernicious Anemia

A. HEREDITARY SPHEROCYTOSIS

CC/HPI: A 9-month-old infant is brought to the pediatrician because of jaundice, lethargy, and easy fatigability. The parents of the child are immigrants of northern European origin. The child's mother suffers from a blood disorder.

What proteins are most frequently mutated in hereditary spherocytosis? Does the patient's mother likely have this disease too?

PE: Physical exam reveals fever, pallor, and jaundice. The child also has splenomegaly.

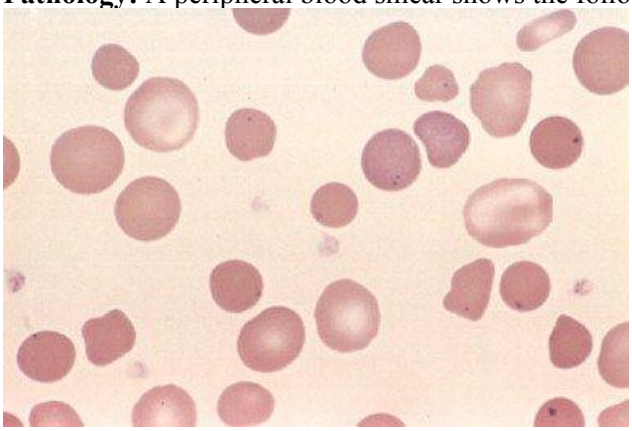
What does the spleen do? Why is a splenectomy helpful to these patients?

Labs: Microcytic anemia; hematocrit (15); small, dark, rounded RBCs lacking central pallor (spherocytes). Elevated indirect serum bilirubin; increased reticulocytes; increased mean corpuscular hemoglobin concentration; decreased mean corpuscular volume; abnormal RBC osmotic lysis test.

Is this patient's hematocrit normal? What is normal?

What is the function of the proteins that are mutated in this disease?

Pathology: A peripheral blood smear shows the following:



(From Robbins and Cotran, Pathological Basis of Disease, 8th Ed.)

Do these RBCs look normal? Why or why not?

B. IRON DEFICIENCY ANEMIA

CC/HPI: A 20-year-old vegetarian female presents to her physician complaining of weakness, listlessness, and fatigue. She also complains of cravings to eat non-food items (pica) particularly dirt and clay. She has a history of peptic ulcer disease and heavy menstrual periods.

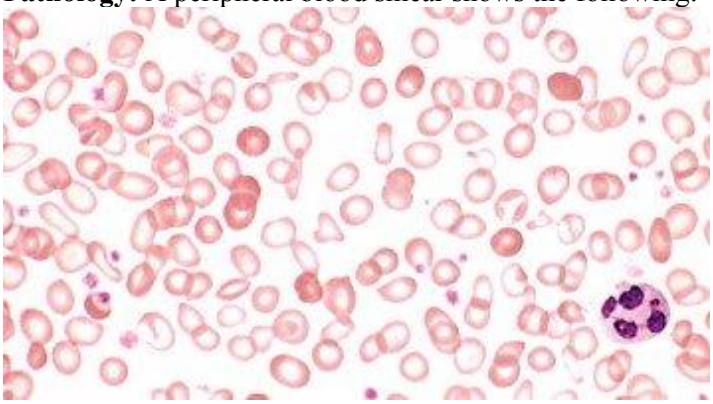
PE: Physical exam reveals pallor of skin and mucous membranes. Thin, flat, "spooned" fingernails.

Labs: Hematocrit is low; low serum ferritin and iron. Low transferrin saturation, but increased binding capacity; increased serum erythropoietin. Microcytic and hypochromic RBCs present. Stool guaiac test reveals fecal occult blood.

Why does a decrease in iron availability result in anemia?

What are the contributing factors to this patient's anemia and what is their relevance?

Pathology: A peripheral blood smear shows the following:



Do these RBCs look normal? Why or why not?

C. PERNICIOUS ANEMIA

CC/HPI: A 55-year-old woman presents to her physician complaining of weakness, dizziness, fatigue, dyspnea (shortness of breath), and nausea over the past three months. She also reports tingling and burning sensations in her feet and hands and has felt unsteady during walking. Patient has a history of Addison's disease.

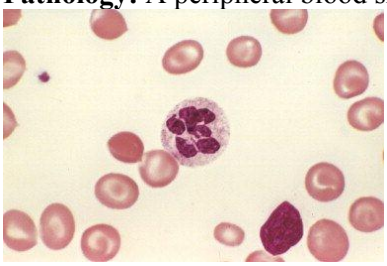
PE: Physical exam reveals decreased sensation and reflexes in extremities. Pallor and mild jaundice are present, as well as hepatosplenomegaly, mild icterus (jaundice). Patient has beefy red tongue (glossitis). "Glove and stocking" distribution of parathesias; loss of balance, vibratory and positional sense in both lower extremities.

Labs: Macrocytic, hypochromic anemia, leukopenia. Hematocrit is low; serum B_{12} is low, folate is normal, serum antibodies to intrinsic factor are present. Hypersegmented neutrophils and macro-ovalocytes present.

This patient has an autoimmune disorder that affects B_{12} absorption (by immune destruction of intrinsic factor). What is the significance of B_{12} deficiency for myeloid maturation and division?

Deficiency in what other vitamin produces megaloblastic anemia due to its role in DNA synthesis?

Pathology: A peripheral blood smear shows the following:



Do these RBCs look normal? Why or why not?

Do these WBCs look normal? Which WBC type is seen here and what looks unusual?

What happens to myeloid precursor cells in the bone marrow? How does this result in the cells seen in the peripheral blood smear?