Hematology Pathology

Dr. Gary Mumaugh – Campbellsville University

Anemia

- Reduction in the total number of erythrocytes in the circulating blood or in the quality or quantity of hemoglobin
    - Impaired erythrocyte production
    - Acute or chronic blood loss
    - Increased erythrocyte destruction
    - Combination of the above
- Classifications:
    - Etiology
    - Morphology
        - Size
            - Identified by terms that end in -cytic
            - Macrocytic, microcytic, normocytic
        - Hemoglobin content
            - Identified by terms that end in -chromic
            - Normochromic and hypochromic
- Physiologic manifestation
    - Reduced oxygen-carrying capacity-hypoxemia
- Variable symptoms based on severity and the ability for the body to compensate
- Classic anemia symptoms:
    - Fatigue
    - Weakness
    - Dyspnea
    - Pallor

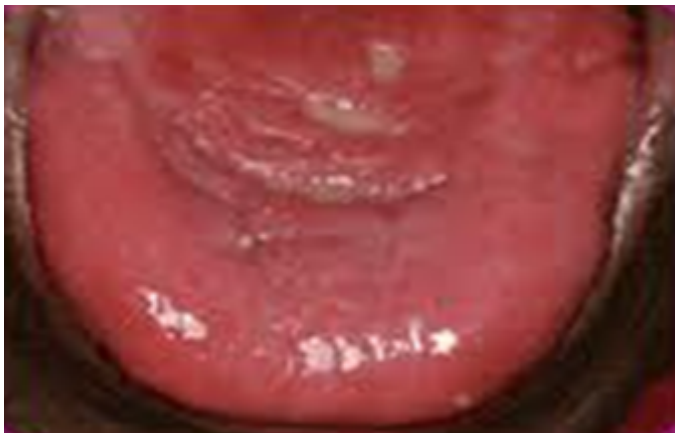
Megaloblastic Anemia

- Macrocytic-Normochromic Anemia
- Characterized by defective DNA synthesis
    - Caused by deficiencies in vitamin B_{12} or folate
        - Coenzymes for nuclear maturation and the DNA synthesis pathway
- Ribonucleic acid (RNA) processes occur at a normal rate
    - Results in the unequal growth of the nucleus and cytoplasm

Pernicious Anemia

- Macrocytic-Normochromic Anemia
- Caused by a lack of intrinsic factor from the gastric parietal cells
- Required for vitamin B_{12} absorption
- Results in vitamin B_{12} deficiency
- Typical anemia symptoms
- Neurologic manifestations:
    - Nerve demyelination
    - Absence of intrinsic factor

Pernicious Anemia (cont'd)



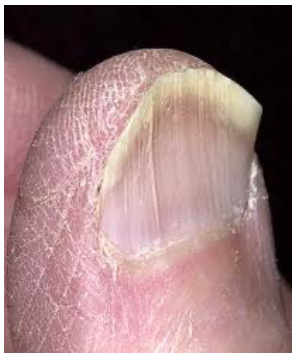
- Other Symptoms:
    - Loss of appetite
    - Abdominal pain
    - Beefy red tongue (atrophic glossitis)
    - Icterus
    - Splenic enlargement
- Treatment
    - Parenteral or high oral doses of vitamin B_{12}

Folate Deficiency Anemia

- Macrocytic-Normochromic Anemia
- Absorption of folate occurs in the upper small intestine
- Similar symptoms to pernicious anemia except neurologic manifestations generally not seen
- Treatment requires daily oral administration of folate

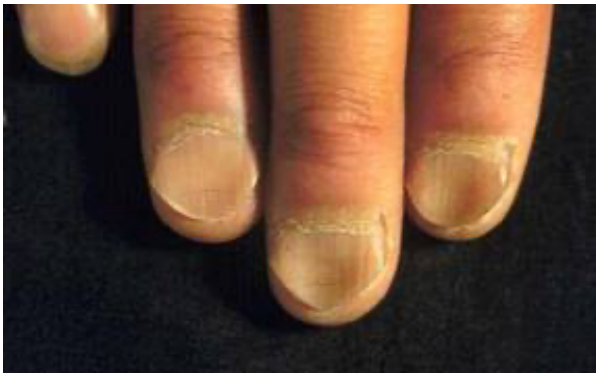
Microcytic-Hypochromic Anemias

- Characterized by red cells that are abnormally small and contain reduced amounts of hemoglobin
- Related to:
    - Disorders of iron metabolism
    - Disorders of porphyrin and heme synthesis
    - Disorders of globin synthesis



Iron deficiency anemia

- Most common type of anemia worldwide
- Nutritional iron deficiency
- Metabolic or functional deficiency
- Manifestations when serum Hgb decreased to 7 or 8 gm/dl
    - Early: fatigue; weakness; shortness of breath; pale ear lobes, palms, conjunctiva
    - Progression of iron deficiency causes:
        - Brittle, thin, coarsely ridged, and spoon-shaped nails (koilonychia)
        - A red, sore, and painful tongue
        - Dry, sore corners of mouth (angular stomatitis)



Hemolytic Anemia

- Normocytic-Normochromic Anemia
- Accelerated destruction of red blood cells
- Autoimmune hemolytic anemias
- Immunohemolytic anemia
- Warm antibody immunohemolytic anemia
- Drug-induced hemolytic anemia
- Cold agglutinin immunohemolytic anemia
- Cold hemolysin hemolytic anemia
- Sickle cell anemia

Anemia of chronic inflammation

- Mild to moderate anemia seen in:
    - AIDS
    - Rheumatoid arthritis
    - Lupus erythematosus
    - Hepatitis
    - Renal failure
    - Malignancies
- Pathologic mechanisms:
    - Decreased erythrocyte life span
    - Ineffective bone marrow response to erythropoietin
    - Altered iron metabolism

Myeloproliferative RBC Disorders

- Polycythemia
    - Overproduction of red blood cells
- Relative polycythemia

    - Result of dehydration
    - Fluid loss results in relative increases of red cell counts and Hgb and Hct values
- Absolute polycythemia
    - Primary absolute
        - Abnormality of stem cells in the bone marrow
        - Polycythemia vera (PV)
    - Secondary absolute
        - Increase in erythropoietin as a normal response to chronic hypoxia or an inappropriate response to erythropoietin-secreting tumors

Alterations of Leukocyte Function

- Quantitative disorders:
    - Increases or decreases in cell numbers
    - Bone marrow disorders or premature destruction of cells
    - Response to infectious microorganism invasion
- Qualitative disorders:
    - Disruption of cellular function

Quantitative Alterations of Leukocytes

- Leukocytosis
    - Leukocytosis is a normal protective physiologic response to physiologic stressors
- Leukopenia
    - Leukopenia is not normal and not beneficial
    - A low white count predisposes a patient to infections
- Granulocytosis (Neutrophilia)
    - Neutrophilia is evident in the first stages of an infection or inflammation
    - If the need for neutrophils increases beyond the supply, immature neutrophils are released into the blood
    - This premature release is detected in the manual WBC differential and is termed a shift to the left
    - When the population returns to normal, it is termed a shift to the right
- Neutropenia
    - Reduction in circulating neutrophils
    - Causes:
        - Prolonged severe infection
        - Decreased production
        - Reduced survival
        - Abnormal neutrophil distribution and sequestration
- Eosinophilia
    - Hypersensitivity reactions trigger the release of eosinophilic chemotactic factor of anaphylaxis from mast cells
    - Increased in allergic disorders
    - Increased in parasitic invasions
- Eosinopenia
    - Decrease in circulation numbers of eosinophils

    - Usually caused by migration of cells to inflammatory sites
    - Other causes:
        - Surgery
        - Shock
        - Trauma
        - Burns
        - Mental distress
- Basophils
    - Basophils account for only 0% to 1% of the circulating WBCs
    - Basophilia
        - Response to inflammation and hypersensitivity reactions
    - Basopenia
        - Occurs in acute infections, hyperthyroidism, and long-term steroid therapy
- Monocytes
    - Monocytosis
        - Usually occurs with neutropenia in later stages of infections
        - Monocytes are needed to phagocytize organisms and debris
- Lymphocytes
    - Lymphocytosis
        - Acute viral infections - Epstein-Barr virus
- Lymphocytopenia
    - Immune deficiencies
    - Drug destruction
    - Viral destruction

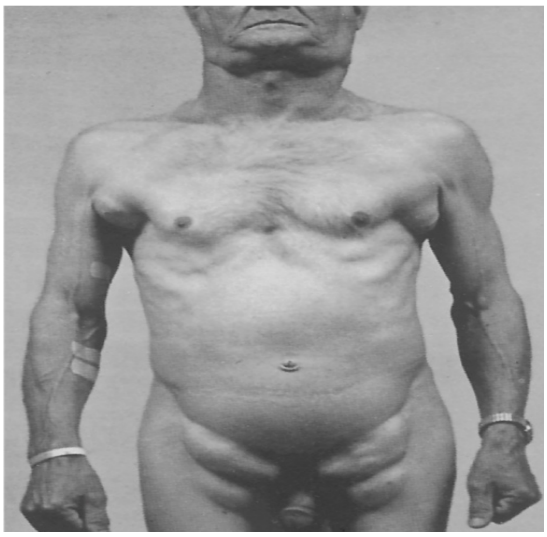
Infectious Mononucleosis

- Acute, self-limiting infection of B lymphocytes transmitted by saliva through personal contact
- Commonly caused by the Epstein-Barr virus (EBV)—85%
    - B cells have an EBV receptor site
    - Others viral agents resembling IM:
        - Cytomegalovirus (CMV)
        - Hepatitis
        - Influenza
        - HIV
- Symptoms:
    - Fever
    - Sore throat
    - Swollen cervical lymph nodes
    - Increased lymphocyte count
    - Atypical (activated) lymphocytes
- Serious complications are infrequent (<5%)
    - Splenic rupture is the most common cause of death
- >50% lymphocytes and at least 10% atypical lymphocytes
- Diagnostic test

    - Monospot qualitative test for heterophilic antibodies
- Treatment: symptomatic

Leukemias
- Malignant disorder of the blood and blood-forming organs
- Excessive accumulation of leukemic cells
- Pancytopenia if cells crowd bone marrow
- Acute leukemia
    - Presence of undifferentiated or immature cells, usually blast cells
- Chronic leukemia
    - Predominant cell is mature but does not function normally
- Leukemia Types
    - Acute lymphocytic leukemia (ALL)
    - Acute myelogenous leukemia (AML)
    - Chronic myelogenous leukemia (CML)
    - Chronic lymphocytic leukemia (CLL)

- Signs and symptoms of leukemia
    - Anemia
    - Bleeding purpura B-lymphocytes
    - Petechiae
    - Ecchymosis
    - Thrombosis
    - Hemorrhage
    - DIC
    - Infection
    - Weight loss
    - Bone pain
    - Elevated uric acid
    - Liver, spleen, and lymph node enlargement



Lymphadenopathy
- Enlarged lymph nodes that become palpable and tender
- Local lymphadenopathy
    - Drainage of an inflammatory lesion located near the enlarged node
- General lymphadenopathy
    - Occurs in the presence of malignant or nonmalignant disease

Malignant Lymphomas
- Malignant transformation of a lymphocyte and proliferation of lymphocytes, histiocytes, their precursors, and derivatives in lymphoid tissues
- Two major categories:

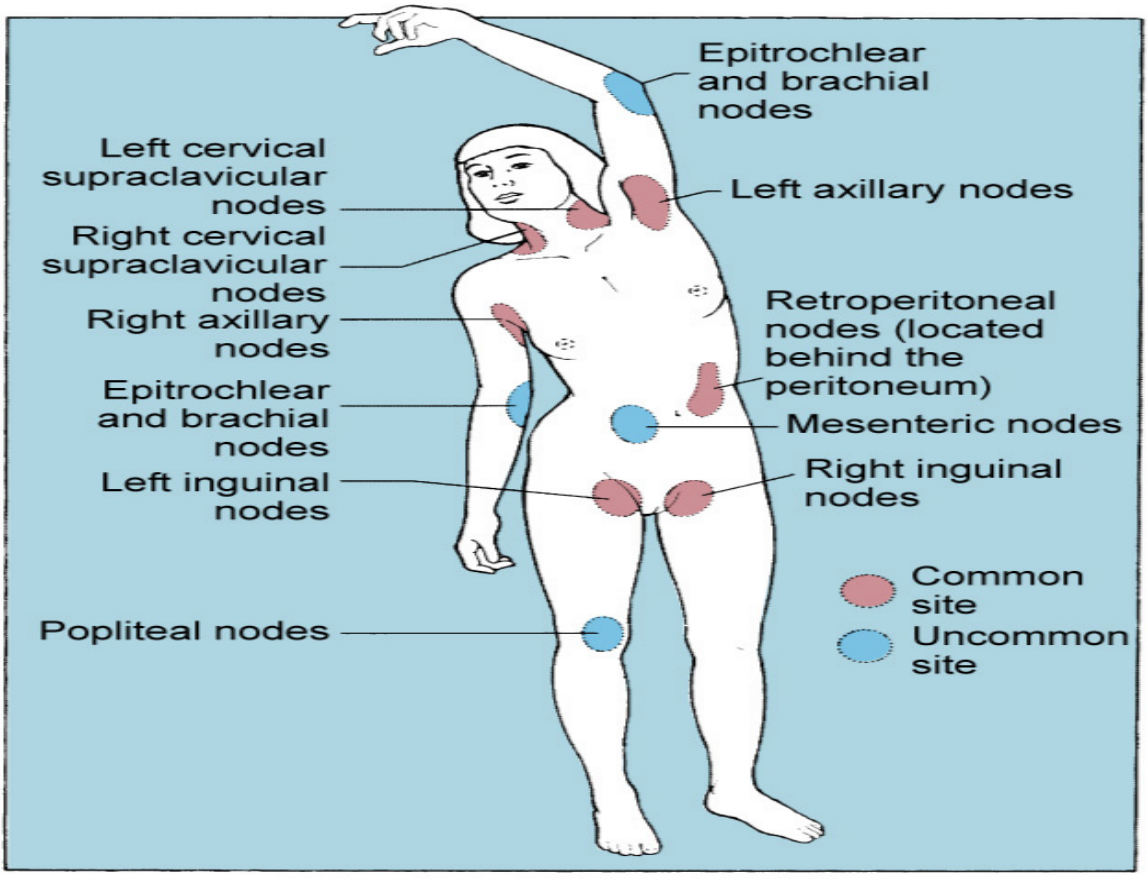
- Hodgkin lymphoma
- Non-Hodgkin lymphoma

Hodgkin Lymphoma

- Characterized by the presence of Reed-Sternberg cells in the lymph nodes
    - Reed-Sternberg cells are necessary for diagnosis, but they are not specific to Hodgkin lymphoma
    - Classical Hodgkin lymphoma
    - Nodular lymphocyte predominant Hodgkin lymphoma

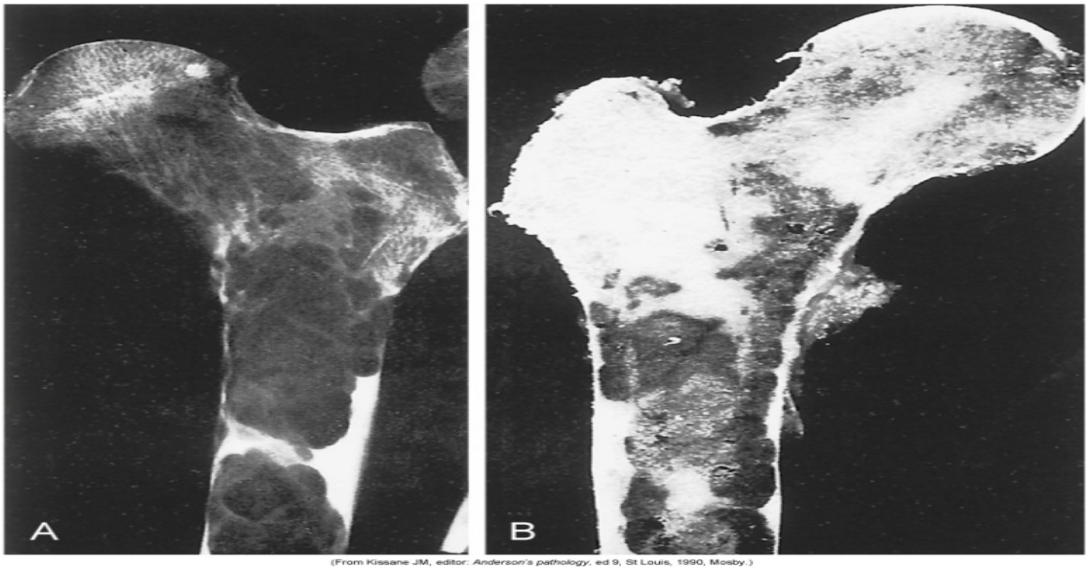
Hodgkin Lymphoma

- Physical findings
    - Adenopathy, mediastinal mass, splenomegaly, and abdominal mass
- Symptoms
    - Fever, weight loss, night sweats, pruritus
- Laboratory findings
    - Thrombocytosis, leukocytosis, eosinophilia, elevated ESR, and elevated alkaline phosphatase



Non-Hodgkin Lymphoma

- Generic term for a diverse group of lymphomas
- Differentiated based on etiology, unique features, and response to therapies
- Non-Hodgkin lymphomas are linked to chromosome translocations, viral and bacterial infections, environmental agents, immunodeficiencies, and autoimmune disorders



(From Kissane JM, editor: *Anderson's pathology*, ed 9, St Louis, 1990, Mosby.)

Multiple Myeloma

- Malignant proliferation of plasma cells
- Infiltrate bone marrow and aggregate into tumor masses in skeletal system
- Bence Jones protein
- Hypercalcemia, renal failure, bone lesions

Disorders of Platelets

- Thrombocytopenia
    - Platelet count <150,000/mm^3
        - <50,000/mm^3: hemorrhage from minor trauma
        - <15,000/mm^3: spontaneous bleeding
        - <10,000/mm^3: severe bleeding
    - Causes:
        - Hypersplenism
        - Autoimmune disease
        - Hypothermia

        - Viral or bacterial infections that cause disseminated intravascular coagulation (DIC)
- Immune (ideopathic) thrombocytopenic purpura (ITP)
    - IgG antibody that targets platelet glycoproteins
    - Antibody-coated platelets are sequestered and removed from the circulation
    - The acute form of ITP that often develops after a viral infection is one of the most common childhood bleeding disorders
- Immune (ideopathic) thrombocytopenic purpura (ITP) (cont'd)
    - Manifestations:
        - Petechiae and purpura
        - Progressing to major hemorrhage
- Thrombotic thrombocytopenic purpura (TTP)
    - A thrombotic microangiopathy
        - Platelets aggregate, form microthrombi, and cause occlusion of arterioles and capillaries
    - Chronic relapsing TTP
    - Acute idiopathic TTP
- Essential (primary) thrombocythemia (thrombocytosis)
    - Thrombocythemia is characterized by platelet counts >600,000/mm^3
    - Myeloproliferative disorder of platelet precursor cells
        - Megakaryocytes in the bone marrow are produced in excess
    - Microvasculature thrombosis occurs

Alterations of Platelet Function

- Qualitative alterations in platelet function demonstrate an increased bleeding time in the presence of a normal platelet count
- Platelet function disorders result from platelet membrane glycoprotein and von Willebrand factor deficiencies
- Manifestations:
    - Petechiae
    - Purpura
    - Mucosal bleeding
    - Gingival bleeding
    - Spontaneous bruising
- Disorders can be congenital or acquired

Alterations of Coagulation

- Vitamin K deficiency
    - Vitamin K is necessary for synthesis and regulation of prothrombin, the prothrombin factors
- Liver disease
    - Liver disease causes a broad range of hemostasis disorders:
        - Defects in coagulation
        - Fibrinolysis

- Platelet number and function