**Hematology Pathology  
Pathology 1 - Dr. Gary Mumaugh**

**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 B12 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 B12 absorption
* Results in vitamin B12 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 B12

**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

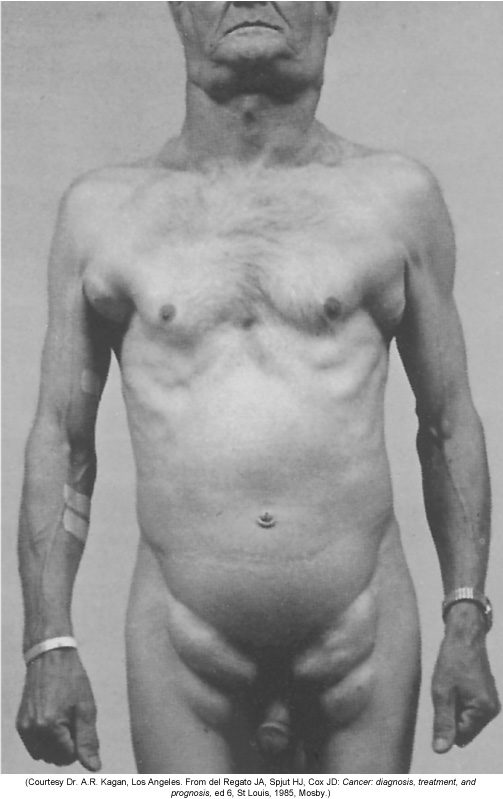
**Quantitative Alterations of Leukocytes**

* 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

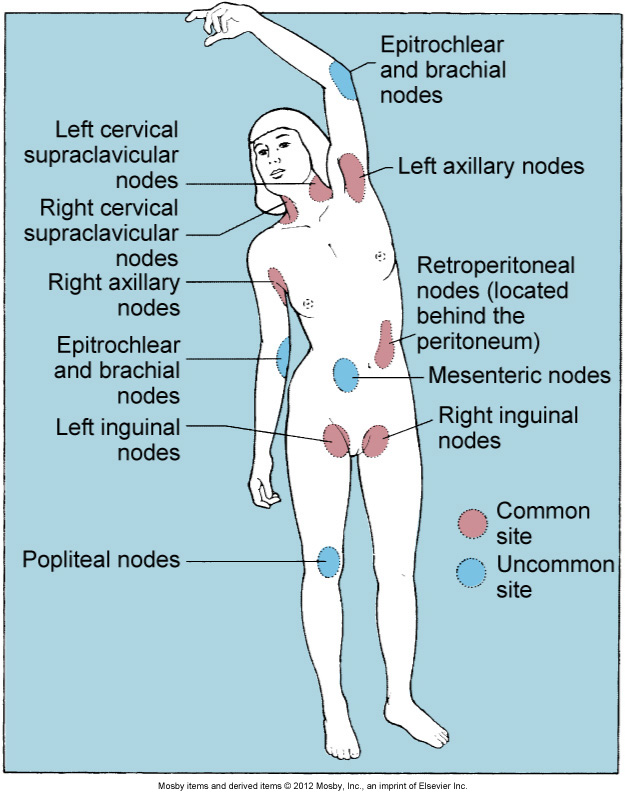


**Hodgkin Lymphoma**

* 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

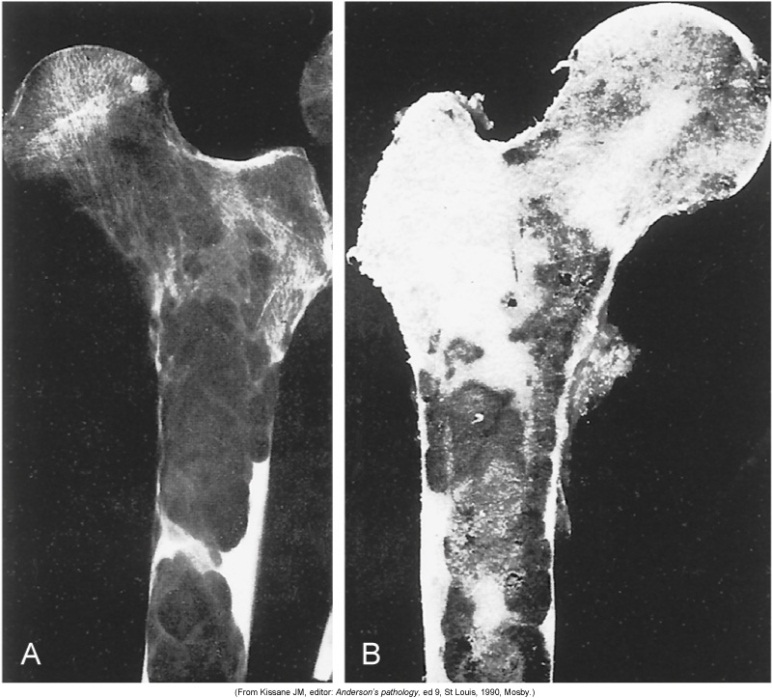


**Non-Hodgkin Lymphoma**

* 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

**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/mm3
    - <50,000/mm3: hemorrhage from minor trauma
    - <15,000/mm3: spontaneous bleeding
    - <10,000/mm3: 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/mm3
  + 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