**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)

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**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