Chapter 11

The Hematopoietic and Lymphatic Systems
Composition of Human Blood (1 of 6)

• Transports substances to tissues:
  – Oxygen, nutrients, hormones, leukocytes, red cells, platelets, antibodies
  – Carbon dioxide and other waste products of cell metabolism to the excretory organs of the body

• Volume of blood: about 5 quarts, but varies according to size of individual

• Almost half of blood consists of cellular elements suspended in plasma (viscous fluid)
Composition of Human Blood (2 of 6)

• Stem cells: precursor cells in bone marrow and differentiate to form red cells, white cells, and platelets

• Cellular elements are:
  – Red cells
  – Leukocytes
    • Neutrophils
    • Monocytes
    • Eosinophils
    • Lymphocytes
    • Basophils
  – Platelets
Composition of Human Blood (3 of 6)

- **Red cells**
  - Primarily concerned with transport of oxygen
  - Most numerous cells
  - Survive 4 months (120 days)
  - Erythroblast: precursor cell in bone marrow
  - Hemoglobin: oxygen-carrying protein formed by the developing red cell

- **Leukocytes**
  - Less numerous
  - Different types
Lymphocytes may last for several years
Lymphocytes also produced in the bone marrow but mainly produced in lymph nodes and spleen
Types of leukocytes
- Neutrophils
  - Most numerous in adults
  - Make up 70% of total circulating white cells
  - Actively phagocytic
  - Predominant in inflammatory reactions
- Monocytes
  - Actively phagocytic
  - Increased in certain types of chronic infection
Composition of Human Blood (5 of 6)

– Eosinophils
  • Increased in allergic reactions
  • Increased in presence of animal-parasite infections

– Lymphocytes
  • Next most common leukocytes in adults
  • Predominant leukocytes in children
  • Mostly located in lymph nodes, spleen, lymphoid tissues
  • Take part in cell-mediated and humoral defense reactions
Composition of Human Blood (6 of 6)

– Platelets
  • Essential for blood coagulation
  • Much smaller than leukocytes
  • Represent bits of the cytoplasm of megakaryocytes, largest precursor cells in the bone marrow
  • Short survival, about 10 days
Normal Hematopoiesis (1 of 4)

• Hematopoiesis: formation and development of blood cells
• Bone marrow replenishes the blood cells
• Substances necessary for hematopoiesis
  – Protein
  – Vitamin $B_{12}$
  – Folic acid (one of the vitamin B group)
  – Iron
• Red cell production: regulated by oxygen content of the arterial blood
• White cell production: not well understood
• Factors that may cause white cell production
  – Products of cell necrosis
  – Hormone secretion by adrenals and endocrine glands
Iron uptake, transport, storage, and utilization for hemoglobin synthesis
**Normal Hematopoiesis (2 of 4)**

- Red cells: develop from erythroblasts, large precursor cells in bone marrow
- Hemoglobin: tetramer composed of 4 subunits, each one consisting of heme and globin
- Heme: porphyrin ring that contains an iron atom
- Globin: largest part of hemoglobin; forms different chains designated by Greek letters such as alpha, beta, gamma, delta, and epsilon
- Porphyrin ring: produced by the mitochondria; iron inserted to form heme
- Globin chains: produced by the ribosomes; joined to heme to form a hemoglobin unit
Normal Hematopoiesis (3 of 4)

• Four subunits aggregate to form the complete hemoglobin tetramer
• Red cell accumulates increasing amounts of hemoglobin as it matures
• Nucleus extruded when 80% of total hemoglobin has been synthesized; cell discharged from the marrow into the circulation where it completes its maturation process in the next 24 hours
• Reticulocyte: young red cell without a nucleus but retains some of organelles; identified by special stains
• In 24 hours, reticulocyte matures and survives in the circulation for about 4 months
Normal Hematopoiesis (4 of 4)

- Worn out red cells removed in the spleen
  - Hemoglobin degraded and excreted as bile by liver
  - Porphyrin ring cannot be salvaged
  - Globin chains broken down and used to make other proteins
  - Iron extracted and saved to make new hemoglobin
- Red cell production regulated by O₂ content of arterial blood
  - Reduced O₂ supply stimulates erythropoiesis
  - Reduced O₂ tension does not act directly on bone marrow but mediated by the kidneys, which produce erythropoietin
Anemia: Etiologic Classification

(1 of 2)

• Reduction in red blood cells or subnormal level of hemoglobin
• Inadequate production of red cells
• Insufficient raw materials
  – Iron deficiency
  – Vitamin B₁₂ deficiency
  – Folic acid deficiency
• Inability to deliver adequate red cells into circulation due to marrow damage or destruction (aplastic anemia), replacement of marrow by foreign or abnormal cells
Anemia: Etiologic Classification (2 of 2)

• Excessive loss of red cells
  – External blood loss (hemorrhage)
  – Shortened survival of red cells in circulation
  – Defective red cells: hereditary hemolytic anemia
  – Accelerated destruction of cells from antibodies to red blood cell or by mechanical trauma to circulating red cells
Classification of anemia based on the “bone marrow factory” concept

- **Raw materials**
  - Protein
  - Vitamin B12
  - Folic acid
  - Iron

- **Factory**
  - Red cells
  - Leukocytes
  - Platelets

- **Finished product**
  - External loss
  - Hemolysis

- **Inadequate production**
  - Insufficient raw materials

- **Excessive loss**
  - Factory damaged

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Anemia: Morphologic Classification

(1 of 2)

- Classification based on red cell appearance suggests the etiology of the anemia:
  - Normocytic anemia: normal size and appearance
  - Macrocytic anemia: cells larger than normal
    - Folic acid deficiency
    - Vitamin B₁₂ deficiency
  - Microcytic anemia: cells smaller than normal
Anemia: Morphologic Classification (2 of 2)

- Hypochromic anemia: reduced hemoglobin content
- Hypochromic microcytic anemia: smaller than normal and reduced hemoglobin content
Iron-Deficiency Anemia (1 of 2)

- Most common type of anemia
- Hypochromic microcytic anemia
- Iron absorbed from duodenum, transferred via transferrin, stored as ferritin

- Pathogenesis
  - Inadequate iron intake in diet
  - Infants during periods of rapid growth
  - Adolescents subsisting on inadequate diet
  - Inadequate reutilization of iron present in red cells due to chronic blood loss

- Laboratory tests
  - Serum ferritin
  - Serum iron
  - Serum iron-binding capacity
Iron-Deficiency Anemia (2 of 2)

- Characteristic laboratory profile
  - Low serum ferritin and serum iron
  - Higher than normal serum iron-binding protein
  - Lower than normal percent iron saturation

- Treatment
  - Primary focus: learn cause of anemia
  - Direct treatment towards cause than symptoms
  - Administer supplementary iron

- Examples
  - Infant with a history of poor diet
  - Adults: common cause is chronic blood loss from GI tract (bleeding ulcer or ulcerated colon carcinoma)
  - Women: excessive menstrual blood loss
  - Too-frequent blood donations
Normal red cells
Cells of hypochromic microcytic anemia
Vitamin B$_{12}$ Deficiency Anemia (1 of 2)

- Vitamin B$_{12}$: meat, liver, and foods rich in animal protein
- Folic acid: green leafy vegetables and animal protein foods
  - Both required for normal hematopoiesis and normal maturation of many other types of cells
- Vitamin B$_{12}$: for structural and functional integrity of nervous system; deficiency may lead to neurologic disturbances
Vitamin $B_{12}$ Deficiency Anemia (2 of 2)

- Absence or deficiency of vitamin $B_{12}$ or folic acid
  - Abnormal red cell maturation or megaloblastic erythropoiesis with formation of large cells called megaloblasts
  - Mature red cells formed are larger than normal or macrocytes; corresponding anemia is called macrocytic anemia
  - Abnormal development of white cell precursors and megakaryocytes: leukopenia, thrombocytopenia
Pernicious Anemia

• Lack of intrinsic factor results in macrocytic anemia
  – Vitamin $\text{B}_{12}$ in food combines with intrinsic factor in gastric juice
  – Vitamin $\text{B}_{12}$ intrinsic factor complex absorbed in ileum

• Causes
  – Gastric mucosal atrophy; also causes lack of secretion of acid and digestive enzymes
  – Gastric resection and bypass: vitamin $\text{B}_{12}$ not absorbed
  – Distal bowel resection or disease: impaired absorption of vitamin $\text{B}_{12}$ intrinsic factor complex
  – May develop among middle-aged and elderly
  – Associated with autoantibodies against gastric mucosal cells and intrinsic factor
Folic Acid Deficiency Anemia

- Relatively common
- The body has very limited stores, which rapidly become depleted if not replenished continually
- Pathogenesis
  - Inadequate diet: encountered frequently in chronic alcoholics
  - Poor absorption caused by intestinal disease
  - Occasionally occurs in pregnancy with increased demand for folic acid
Diagnostic Evaluation of Anemia

- History and physical examination
- Complete blood count: to assess degree of anemia, leukopenia, and thrombocytopenia
- Blood smear: determine if normocytic, macrocytic, or hypochromic microcytic
- Reticulocyte count: assess rate of production of new red cells
- Lab tests: determine iron, B\textsubscript{12}, folic acid
- Bone marrow study: study characteristic abnormalities in marrow cells
- Evaluation of blood loss from gastrointestinal tract to localize site of bleeding
Bone Marrow Suppression, Damage, or Infiltration (1 of 2)

• Conditions that depress bone marrow function:
  – Anemia of chronic disease: mild suppression of bone marrow function
  – Aplastic anemia: marrow injured by radiation, anticancer drugs, chemicals, or autoantibodies
  – Marrow infiltrated by tumor or replaced by fibrous tissue
Bone Marrow Suppression, Damage, or Infiltration (2 of 2)

- Treatment depends on cause
  - Blood and platelet transfusions
  - Immunosuppressive drugs
  - Bone marrow transplant in highly selected cases of aplastic anemia
  - In many cases, there is no specific treatment
Hemolytic Anemia (1 of 2)

- Hereditary hemolytic anemia
  - Genetic abnormality prevents normal survival
- Abnormal shape: hereditary spherocytosis
- Abnormal hemoglobin: hemoglobin S (sickle hemoglobin); hemoglobin C; both found predominantly in persons of African descent
- Defective hemoglobin synthesis: thalassemia minor and major; globin chains are normal but synthesis is defective (Greek and Italian ancestry)
- Enzyme defects: glucose-6-phosphatase dehydrogenase deficiency predisposes to episodes of acute hemolysis
Hemolytic Anemia (2 of 2)

- Acquired hemolytic anemia
  - Normal red cells but unable to survive due to a “hostile environment”
  - Attacked and destroyed by antibodies
  - Destruction of red cells by mechanical trauma
  - Passing through enlarged spleen (splenomegaly)
  - In contact with some part of artificial heart valve
Distortion of red cells containing sickle hemoglobin when incubated under reduced oxygen tension.
Distortion of red calls containing sickle hemoglobin when incubated under reduced oxygen tension. Higher magnification view.
A stained blood film from subject with hereditary spherocytosis
Polycythemia (1 of 2)

• Secondary polycythemia
  – Reduced arterial $O_2$ saturation leads to compensatory increase in red blood cells (increased erythropoietin production)
  – Emphysema, pulmonary fibrosis, congenital heart disease; increased erythropoietin production by renal tumor

• Primary/Polycythemia vera
  – Manifestation of diffuse marrow hyperplasia of unknown etiology
  – Overproduction of red cells, white cells, and platelets
  – Some cases evolve into granulocytic leukemia
Polycythemia (2 of 2)

• **Complications**
  – Clot formation due to increased blood viscosity and platelet count

• **Treatment**
  – Primary polycythemia: treated by drugs that suppress marrow function
  – Secondary polycythemia: periodic removal of excess blood
Hemochromatosis

• Common genetic disease transmitted as autosomal recessive trait
• Iron overload but excreted with difficulty
• Iron accumulation leads to organ damage followed by scarring and permanent derangement of organ function
• Manifestations of disease take years to develop
  – Tan to brown skin
  – Diabetes
  – Cirrhosis
  – Heart failure
• Treatment: periodic removal of blood (phlebotomy) until iron stores are depleted
Thrombocytopenia

• Secondary thrombocytopenic purpura
  – Damage to bone marrow from drugs or chemicals
  – Bone marrow infiltrated by leukemic cells or metastatic carcinoma

• Primary thrombocytopenic purpura
  – Associated with platelet antibodies
  – Bone marrow produces platelets but are rapidly destroyed
  – Encountered in children and subsides spontaneously after a short time
  – Tends to be chronic in adults
Lymphatic System Diseases (1 of 2)

- Lymphadenitis: inflamed and enlarged lymph nodes
- Infectious mononucleosis: caused by Epstein-Barr virus, EBV
  - Infection of B lymphocytes causes diffuse lymphoid hyperplasia of spleen, lymph nodes, lymphoid tissues
  - Cytotoxic (CD8+) lymphocytes and antibodies produced by plasma cells destroy most of infected B cells
  - Characterized by enlarged and tender lymph nodes
  - Mostly encountered by young adults transmitted by close contact, usually kissing
  - Avoid body contact sports until spleen is no longer enlarged to avoid risk of splenic rupture
  - Persons with compromised immune system, unrestrained B cell proliferation may give rise to B cell lymphoma
Lymphatic System Diseases (2 of 2)

- **Neoplasms**
  - Metastatic tumors: breasts, lung, colon, other sites
  - Nodes first affected lie in immediate drainage area of tumor
  - Tumor spreads to more distant lymph nodes through lymphatic channels

- **Malignant lymphoma**
  - Hodgkin’s lymphoma
  - Non-Hodgkin’s lymphoma

- **Lymphocytic leukemia**: from lymphoid precursor cells; acute (primitive forms) or chronic (mature cells)
Spleen

• Phagocytosis
• Antibody formation: prompt elimination of pathogenic organisms
• Reasons for splenectomy
  – Traumatic injury: to prevent fatal hemorrhage
  – Blood diseases: excessive destruction of blood cells in the spleen (hereditary hemolytic anemia)
  – Patients with Hodgkin’s disease prior to treatment
• Effects
  – Less-efficient elimination of bacteria
  – Impaired production of antibodies
  – Predisposed to systemic infections
• Treatment: antibacterial vaccines; antibiotic prophylaxis