Chapter 12

Blood
Objectives

• Describe the primary functions of blood
• Describe the characteristics of blood plasma
• List the formed elements of blood and identify the most important function of each
• Discuss anemia in terms of red blood cell numbers and hemoglobin content
Objectives

• Explain the steps involved in blood clotting
• Describe ABO and Rh blood typing
• Understand the medical terms associated with blood: hematocrit, leukocytosis, leukopenia, polycythemia, sickle cell, phagocytosis, acidosis, thrombosis, erythroblastosis, fetalis, serum, fibrinogen, Rh factor, anemia, hemophilia, thrombocytopenia
• Name two common disorders associated with each type of blood cell
Blood Composition and Volume

• Blood components
  – Liquid fraction of whole blood (extracellular part) called *plasma*
  – Cellular components make up the formed elements

• Normal volumes of blood
  – Plasma—2.6 L
  – Formed elements—2.4 L
  – Whole blood—4 to 6 L average or 7% to 9% of total body weight
Buffy Coat

• White blood cells and platelets
Blood Composition and Volume

• Blood pH
  – Blood is alkaline—pH 7.35 to pH 7.45
  – Blood pH decreased toward neutral creates a condition called acidosis

• Blood donations
  – Approximately 14 million units donated annually
  – Plasma volume expanders (such as albumin) can only maintain blood volume after hemorrhage for short periods
  – Storage of donated blood limited to 6 weeks
Blood Composition and Volume

• Blood types
  – ABO system
    • Type A blood—type A antigens in RBCs; anti-B type antibodies in plasma
    • Type B blood—type B antigens in RBCs; anti-A type antibodies in plasma
    • Type AB blood—type A and type B antigens in RBCs; no anti-A or anti-B antibodies in plasma; called universal recipient blood
    • Type O blood—no type A or type B antigens in RBCs; both anti-A and anti-B antibodies in plasma; called universal donor blood
To understand blood is to understand clumping

<table>
<thead>
<tr>
<th>Recipient's blood</th>
<th>Reactions with donor's blood</th>
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<tbody>
<tr>
<td><strong>RBC antigens</strong></td>
<td><strong>Plasma antibodies</strong></td>
</tr>
<tr>
<td>None (Type O)</td>
<td>Anti-A Anti-B</td>
</tr>
<tr>
<td>A (Type A)</td>
<td>Anti-B</td>
</tr>
<tr>
<td>B (Type B)</td>
<td>Anti-A</td>
</tr>
<tr>
<td>AB (Type AB)</td>
<td>(None)</td>
</tr>
</tbody>
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Normal blood  Agglutinated blood
Blood Composition and Volume

• Blood types
  – Rh system
    • Rh-positive blood—Rh factor antigen present in RBCs
    • Rh-negative blood—no Rh factor present in RBCs; no anti-Rh antibodies present naturally in plasma; anti-Rh antibodies, however, appear in the plasma of Rh-negative persons if Rh-positive RBCs have been introduced into their bodies
    • Erythroblastosis fetalis—may occur when Rh-negative mother carries a second Rh-positive fetus; caused by mother’s Rh antibodies reacting with baby’s Rh-positive cells
Blood Composition and Volume

• Blood plasma
  – Liquid fraction of whole blood minus formed elements
  – Composition—water containing many dissolved substances including:
    • Foods, salts
    • About 3% of total $O_2$ transported in blood
    • About 5% of total $CO_2$
Blood Composition and Volume

• Blood plasma
  – Composition
    • Most abundant solutes dissolved in plasma are plasma proteins
      – Albumins
      – Globulins
      – Fibrinogen
      – Prothrombin
  – Plasma minus clotting factors called serum
    • Serum is liquid remaining after whole blood clots
    • Serum contains antibodies
Blood Composition and Volume

• Formed elements
  – Types
    • RBCs (erythrocytes)
    • WBCs (leukocytes)
      – Granular leukocytes—neutrophils, eosinophils, and basophils
      – Nongranular leukocytes—lymphocytes and monocytes
      – Platelets or thrombocytes
Blood Composition and Volume

• Formed elements
  – Numbers
    • RBCs—4.2 to 6.2 million/mm$^3$ of blood
    • WBCs—5000 to 10,000/mm$^3$ of blood
    • Platelets—140,000 to 340,000/mm$^3$ of blood
  – Formation
    • Red bone marrow (myeloid tissue) forms all blood cells except some lymphocytes and monocytes
    • Most other cells formed by lymphatic (lymphoid) tissue in the lymph nodes, thymus, and spleen
Mechanisms of Blood Disease

• Most blood diseases result from failure of myeloid and lymphatic tissues
  – Causes include toxic chemicals, radiation, inherited defects, nutritional deficiencies, and cancer, including leukemia
Mechanisms of Blood Disease

• Aspiration biopsy cytology (ABC) permits examination of blood-forming tissues to assist in diagnosis of blood diseases
• Bone marrow, cord blood, and hematopoietic stem cell transplants may be used to replace diseased or destroyed blood-forming tissues
Erythrocytes (RBCs)

• Excellent example of how structural adaptation affects biologic function
  – Tough and flexible plasma membrane deforms easily allowing RBCs to pass through small-diameter capillaries
  – Biconcave disk (thin center and thicker edges) results in large cellular surface area
  – Absence of nucleus and cytoplasmic organelles limits life span to about 120 days but provides more cellular space for red pigment called hemoglobin (Hb)
Erythrocytes (RBCs)

- Iron (Fe), folate (a B vitamin), and vitamin B_{12} are among the critical nutrients needed to manufacture red blood cells in the red bone marrow.
- Named according to size: normocytes (normal size about 7-9 μm in diameter); microcytic (small size); macrocytic (large size).
- Named according to hemoglobin content of cell: normochromic (normal Hb content); hypochromic (low Hb content); hyperchromic (high Hb content).
Erythrocytes (RBCs)

• General functions
  – Transport of respiratory gases (O₂ and CO₂)
    • Combined with hemoglobin
      – Oxyhemoglobin (Hb + O₂)
      – Carbaminohemoglobin (Hb + CO₂)
    • CO₂ inside the RBC as bicarbonate
  – Important role in homeostasis of acid base balance
Erythrocytes (RBCs)

• General functions
  – Complete blood cell count (CBC)—battery of laboratory tests used to measure the amounts or levels of many blood constituents
  – Hematocrit (packed cell volume or PCV) is the percentage of whole blood that is RBCs
Red Blood Cell Disorders

• Most often related to either overproduction of RBCs—called *polycythemia* or to low oxygen-carrying capacity of blood—called *anemia*

• Polycythemia
  – Cause is generally cancerous transformation of red bone marrow
  – Dramatic increase in RBC numbers—often in excess of 10 million/mm³ of blood—hematocrit may reach 60%
Red Blood Cell Disorders

• Polycythemia
  – Signs and symptoms
    • Increased blood viscosity or thickness
    • Slow blood flow and coagulation problems
    • Frequent hemorrhages
    • Distention of blood vessels and hypertension
Red Blood Cell Disorders

• Polycythemia
  – Treatment
    • Blood removal
    • Irradiation and chemotherapy to suppress RBC production
Red Blood Cell Disorders

• Anemia
  – Caused by low numbers or abnormal RBCs or by low levels or defective types of hemoglobin
    • Normal Hb levels 12-14 g/100 mL of blood
    • Low Hb level (below 9 g/100 mL of blood) classified as anemia
Red Blood Cell Disorders

• Anemia
  – Majority of clinical signs of anemia related to low tissue oxygen levels
    • Fatigue; skin pallor
    • Weakness; faintness; headache
    • Body compensates by increasing heart and respiratory rates
Red Blood Cell Disorders

• Anemia
  – Hemorrhagic anemia
    • Acute—blood loss is immediate (e.g., surgery or trauma)
    • Chronic—blood loss occurs over time (e.g., ulcers or cancer)
  – Aplastic anemia
    • Characterized by low RBC numbers and destruction of bone marrow
    • Often caused by toxic chemicals, irradiation or certain drugs
Red Blood Cell Disorders

– Deficiency anemias—caused by inadequate supply of some substance needed for RBC or hemoglobin production
  
  • Pernicious anemia
    – Caused by vitamin $B_{12}$ deficiency
    – Genetic-related autoimmune disease
    – Decreased RBC, WBC, and platelet numbers
    – RBCs are macrocytic
    – Classic symptoms of anemia coupled with CNS impairment
    – Treatment is repeated vitamin $B_{12}$ injections
Red Blood Cell Disorders

– Deficiency anemias
  • Folate deficiency anemia
    – Caused by folate (vitamin B<sub>9</sub>) deficiency
    – Decreased RBC count
    – Common in alcoholism and malnutrition
Red Blood Cell Disorders

• Iron deficiency anemia
  – Caused by deficiency or inability to absorb iron needed for Hb synthesis (dietary iron deficiency is common worldwide)
  – RBCs are microcytic and hypochromic
  – Hematocrit is decreased
  – Treatment is oral administration of iron compounds
Red Blood Cell Disorders

– Hemolytic anemias

• Caused by decreased RBC life span or increased RBC rate of destruction
• Symptoms, such as jaundice, swelling of spleen, gallstone formation, and tissue iron deposits, are related to retention of RBC breakdown products
Red Blood Cell Disorders

– Hemolytic anemias
  • Sickle cell anemia
    – Genetic disease resulting in formation of abnormal hemoglobin (HbS) primarily in black race
    – RBCs become fragile and assume sickled shape when blood oxygen levels decrease
    – Sickle cell trait is mild (one defective gene)
    – Sickle cell disease more serious (two defective genes); causes blood stasis, clotting and “crises” that may be fatal
    – Affects 1 in every 600 black newborns
Question 5

Ryan Byers—What is sickle cell anemia?
Red Blood Cell Disorders

- **Thalassemia**
  - Group of inherited hemolytic anemias occurring primarily in people of Mediterranean descent
  - RBCs microcytic and short lived
  - Present as mild thalassemia trait and severe thalassemia major
  - Hb levels often fall below 7 mcg/100 mL of blood in thalassemia major
Red Blood Cell Disorders

• Thalassemia
  – Classic symptoms of anemia coupled with skeletal deformities and swelling of spleen and liver
  – Marrow and stem cell transplantation needed for long-term treatment success
Red Blood Cell Disorders

• Hemolytic disease of newborn and erythroblastosis fetalis
  – Caused by blood ABO or Rh factor incompatibility during pregnancy between developing baby and mother
  – Maternal antibodies against “foreign” fetal RBCs or Rh factor can cross placenta, enter the fetal circulation, and destroy the unborn baby’s red cells
  – Symptoms in developing fetus related to decline in RBC numbers and Hb levels; jaundice, intravascular coagulation, and heart and lung damage are common
• Hemolytic disease of newborn and erythroblastosis fetalis
  – Treatment may include utero blood transfusions and early delivery of the baby
  – Prevention of Rh factor incompatibility now possible by administration of RhoGAM to Rh-negative mothers
Leukocytes (WBCs)

- Categorized by presence of granules (granulocytes) or absence of granules (agranulocytes)
- WBC count—normal range is 5000 to 10,000/mm$^3$ of blood
  - Leukopenia—abnormally low WBC count (below 5000/mm$^3$ of blood)
    - Occurs infrequently
    - May occur with malfunction of blood-forming tissues or diseases affecting immune system, such as AIDS
Leukocytes (WBCs)

- WBC count
  - Leukocytosis—abnormally high WBC count (over 10,000/mm³ of blood)
    - Frequent finding in bacterial infections
    - Classic sign in blood cancers (leukemia)
  - Differential WBC count—component test in CBC; measures proportions of each type of WBC in blood sample
Leucocytes in blood smears

A Neutrophil
B Eosinophil
C Basophil
D Lymphocyte
E Monocyte
Leukocytes (WBCs)

Leukocyte types and functions

Granulocytes—include neutrophils; eosinophils; basophils

- **Neutrophils**
  - Most numerous type of phagocyte
  - Numbers increase in bacterial infections

- **Eosinophils**
  - Weak phagocyte
  - Active against parasites and parasitic worms
  - Involved in allergic reactions
Leukocytes (WBCs)

– Granulocytes
  • Basophils
    – Related to mast cells in tissue spaces
    – Both mast cells and basophils secrete histamine (related to inflammation)
    – Basophils also secrete heparin (an anticoagulant)
Leukocytes (WBCs)

– Agranulocytes—monocytes in peripheral blood (macrophages in tissues); lymphocytes—B lymphocytes (plasma cells) and T lymphocytes

• Monocytes
  – Largest leukocyte
  – Aggressive phagocyte—capable of engulfing larger bacteria and cancer cells
  – Develop into much larger cells called macrophages after leaving blood to enter tissue spaces
Leukocytes (WBCs)

- Agranulocytes
  - Lymphocytes
    - B lymphocytes involved in immunity against disease by secretion of antibodies—kind of like a navy ship using land mines at sea that wait
    - Mature B lymphocytes called plasma cells
    - T lymphocytes involved in direct attack on bacteria or cancer cells (not antibody production)
      Like a direct attack by a dive bomber air plane
• Two major types of WBC cancers or neoplasms
  – Lymphoid neoplasms—result from B and T lymphocyte precursor cells or their descendendent cell types
  – Myeloid (marrow) neoplasms—result from transformation of precursor cells of granulocytic WBCs, monocytes, RBCs, and platelets
White Blood Cell Disorders

• Multiple myeloma
  – Cancer of B lymphocytes called *plasma cells*
  – Most deadly blood cancer in people over age 65
  – Causes bone marrow dysfunction and production of defective antibodies
White Blood Cell Disorders

• Multiple myeloma –think marrow!
  – Characterized by:
    • Recurrent infections and anemia
    • Destruction and fracture of bones
  – Treatment includes chemotherapy, drug, antibody therapy, and marrow and stem cell transplantation
White Blood Cell Disorders

• Leukemias—WBC-related blood cancers
  – Characterized by marked leukocytosis
  – Identified as:
    • Acute—rapid development of symptoms
    • Chronic—slow development of symptoms
    • Lymphoid
    • Myeloid—pertaining to bone marrow
White Blood Cell Disorders

• Common types of leukemia
  – Chronic lymphocytic leukemia (CLL)
    • Average age of onset is 65; rare under age 30
    • More frequent in men than women
    • Often diagnosed unexpectedly in routine physical exams with discovery of marked B lymphocytic leukocytosis
    • Generally mild symptoms include anemia, fatigue, and enlarged often painless lymph nodes
    • Most patients live many years following diagnosis
    • Treatment of severe cases involves chemotherapy and irradiation
Many B lymphocytes found in acute lymphocytic leukemia
– Acute lymphocytic leukemia (ALL)

- Primarily a disease of children between 3 and 7 years of age; 80% of children who develop leukemia have this form of the disease
- Highly curable in children but less so in adults
White Blood Cell Disorders

– Chronic myeloid leukemia (CML)
  • Accounts for about 20% of all cases of leukemia
  • Occurs most often in adults between 25 and 60 years of age
  • Caused by cancerous transformation of granulocytic precursor cells in the bone marrow
  • Onset and progression of disease is slow with symptoms of fatigue, weight loss, and weakness
– Chronic myeloid leukemia (CML)
  • Diagnosis often made by discovery of marked granulocytic leukocytosis and extreme spleen enlargement
  • Treatment by new “designer drug” Gleevec or bone marrow transplants is curative in over 70% of cases
The Case of Don Klock

- Diagnosed with chronic myeloid leukemia last year.
- Could not afford drug Gleevec costing $2000 per month.
- Bought prescription in Canada for $800.00 month
- Leukemia symptoms gone within five months after taking!!!
White Blood Cell Disorders

– Acute myeloid leukemia (AML)
  • Accounts for 80% of all cases of acute leukemia in adults and 20% of acute leukemia in children
  • Characterized by sudden onset and rapid progression
  • Symptoms: leukocytosis, fatigue, bone and joint pain, spongy bleeding gums, anemia, recurrent infections
  • Prognosis is poor with only about 50% of children and 30% of adults achieving long-term survival
  • Bone marrow and stem cell transplantation has increased cure rates in selected patients
White Blood Cell Disorders

- Infectious mononucleosis
  - Noncancerous WBC disorder
  - Highest incidence between 15 and 25 years of age
  - Caused by virus in saliva
  - Leukocytosis of atypical lymphocytes with abundant cytoplasm and large nuclei
White Blood Cell Disorders

• Infectious mononucleosis
  – Symptoms include fever, severe fatigue, sore throat, rash, and enlargement of lymph nodes and spleen
  – Generally self-limited and resolves without complications in about 4 to 6 weeks
Typical lymphocyte on left
Atypical on right
Platelets and Blood Clotting

• Platelets
  – Play essential role in blood clotting
    • Blood vessel damage causes platelets to become sticky and form a “platelet plug”
    • Accumulated platelets release additional clotting factors that enter into the clotting mechanism
Platelets and Blood Clotting

- Clotting mechanism
  - Damaged tissue cells release clotting factors leading to formation of prothrombin activator, which combines with platelet-produced prothrombin activator
  - Prothrombin activator and calcium convert prothrombin to thrombin
  - Thrombin reacts with fibrinogen to form fibrin
  - Fibrin threads form a tangle to trap RBCs (and other formed elements) to produce a blood clot
Note the fibrin mesh trapping the blood cells
Platelets and Blood Clotting

• Altering the blood clotting mechanism
  – Application of gauze (rough surface) to wound causes platelet aggregation and release of clotting factors
  – Administration of vitamin K increases synthesis of prothrombin
  – Coumadin (drug) delays clotting by inhibiting prothrombin synthesis
Platelets and Blood Clotting

• Altering the blood clotting mechanism
  – Heparin delays clotting by inhibiting conversion of prothrombin to thrombin
  – Drug called tissue plasminogen activator (TPA) used to dissolve clots that have already formed
Platelets and Blood Clotting

• Clotting disorders
  – Thrombus—stationary blood clot
  – Embolus—circulating blood clot (TPA used to dissolve clots that have already formed)
An embolism
Platelets and Blood Clotting

- Clotting disorders - The Disease of Young Nikolai of Russia
  - Hemophilia - X-linked inherited disorder that results from inability to produce factor VIII (a plasma protein) responsible for blood clotting
    - Most serious “bleeding disease” worldwide; hemophilia A most common form
    - Characterized by easy bruising, deep muscle hemorrhage, blood in urine, and repeated episodes of bleeding into joints causing pain and deformity
    - Treatment includes administration of factor VIII, injury prevention, and avoiding drugs such as aspirin that alter the clotting mechanism
Platelets and Blood Clotting

- Clotting disorders
  - Thrombocytopenia—caused by reduced platelet counts
    - Characterized by bleeding from small blood vessels, most visibly in the skin and mucous membranes
    - Platelet count below 20,000/mm$^3$ may cause catastrophic bleeding (normal platelet count 150,000-400,000/mm$^3$)
    - Most common cause is bone marrow destruction by drugs, chemicals, radiation, and diseases such as cancer, lupus, and HIV/AIDS
    - Treatment may involve transfusion of platelets, corticosteroid type drugs, or removal of the spleen