Blood
Section 1: Plasma and Formed Elements

Learning Outcomes

17.1 List the components of the cardiovascular system, and describe several important functions of blood.

17.2 Describe the important components and major properties of blood.

17.3 Explain the origins and differentiation of the formed elements.
Module 17.1: Blood is the fluid portion of the cardiovascular system

Cardiovascular system consists of heart, blood vessels, blood

1. **Heart**—pumps blood; maintains blood pressure

2. **Blood vessels**
   - **Arteries** carry blood away from heart
   - **Capillaries** permit exchange between blood and interstitial fluids
   - **Veins** return blood to heart
Functions of blood

- Transport dissolved gases, nutrients, hormones, and metabolic wastes
  - Oxygen—lungs to peripheral tissues
  - Carbon dioxide—tissues to lungs
  - Nutrients—from digestive tract or storage in adipose or liver
  - Hormones—gland to target
  - Wastes—to kidneys (excretion)
Functions of blood (continued)

- Regulate pH and ion composition of interstitial fluids (IF)
  - Absorbs/neutralizes acids
  - Diffusion between blood and IF balances ion concentrations
- Restrict fluid loss at injury sites
  - Enzymes/other substances initiate clotting when vessel wall is broken; clot = temporary patch
- Defend against toxins and pathogens
  - Transports white blood cells and antibodies to fight infection
Module 17.1: Blood functions

Functions of blood (continued)

- Stabilize body temperature
  - Absorbs heat generated in one area; distributes to other tissues
  - High body temperature—blood directed closer to skin
  - Low body temperature—blood directed to brain, internal organs
Functions of Blood

- Transport dissolved gases, nutrients, hormones, and metabolic wastes
- Regulate the pH and ion composition of interstitial fluids
- Restrict fluid losses at injury sites
- Defend against toxins and pathogens
- Stabilize body temperature
Module 17.1: Review

A. Identify the components of the cardiovascular system.

B. What are the functions of blood?

*Learning Outcome:* List the components of the cardiovascular system, and describe several important functions of blood.
Module 17.2: Blood is a fluid connective tissue containing plasma and formed elements

- Blood = fluid connective tissue
- Whole blood = blood with all components
  - **Plasma** = liquid matrix
  - **Formed elements** = cells and cell fragments
  - 5–6 liters (5.3–6.4 quarts) blood in males
  - 4–5 liters (4.2–5.3 quarts) blood in females
Properties of Whole Blood

- Blood temperature is about 38°C (100.4°F), slightly above normal body temperature.
- Blood is five times as viscous as water—that is, five times as resistant to flow. Blood’s high viscosity results from interactions among dissolved proteins, formed elements, and water molecules in the plasma.
- Blood is slightly alkaline, with a pH between 7.35 and 7.45 (average: 7.4).
Module 17.2: Blood composition

Plasma = 55 percent of the volume of whole blood

- Similar to interstitial fluid (IF)—constant exchange of water, ions, small solutes across capillary walls
  - Primary differences
    - Respiratory gases (oxygen, carbon dioxide)
    - Dissolved proteins (plasma proteins cannot cross capillary walls)
Module 17.2: Blood composition

Formed elements = blood cells/fragments; ~45 percent of whole blood

- 99 percent of formed elements are red blood cells
- **Hematocrit (packed cell volume, PCV)**
  - Percentage of whole blood from formed elements
  - Overall average 45 percent (range 37–54 percent)
  - Males average 47 percent; females average 42 percent (androgens stimulate RBC production)
Module 17.2: Blood composition

Plasma proteins

- In solution
- Each 100 mL has ~7.6 g of protein (~5× more than IF)
- Large, globular shapes prevent leaving bloodstream
- Liver synthesizes >90 percent of plasma proteins

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Module 17.2: Blood composition

**Albumins** ~60 percent of plasma proteins; for osmotic pressure

**Globulins** ~35 percent of plasma proteins

- **Antibodies (immunoglobulins)** attack foreign proteins, pathogens
- **Transport globulins** bind ions, hormones, lipids, other compounds

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**Plasma Proteins 7%**
- Albumins
- Globulins
- Fibrinogen
- Enzymes and hormones

**Other Solutes 1%**
- Electrolytes
- Organic nutrients
- Organic wastes

**Plasma**

- 55% (Range 46–63%)

**Other Solute**

**Water**

**Water 92%**
Module 17.2: Blood composition

Fibrinogen ~4 percent of plasma proteins

- Blood clotting—form large insoluble fibrin strands
- Plasma also contains active and inactive enzymes and hormones
Module 17.2: Blood composition

Plasma solutes (water = 92 percent of plasma)

- **Electrolytes**—essential for vital cellular activities
  - Major ions: Na\(^+\), K\(^+\), Ca\(^{2+}\), Mg\(^{2+}\), Cl\(^-\), HCO\(_3\)^-, HPO\(_4\)^-, SO\(_4\)^{2-}\n
- **Organic nutrients** include lipids, carbohydrates, and amino acids
  - Used for cell ATP production, growth, and maintenance
Module 17.2: Blood composition

Plasma solutes (continued)

- **Organic wastes** carried to sites of breakdown or excretion
  - *Examples*: urea, uric acid, creatinine, bilirubin, \( \text{NH}_4^+ \)
Module 17.2: Blood composition

Formed elements

- **Platelets** < 0.1 percent of formed elements
  - Small membrane-bound cell fragments involved in clotting
- **White blood cells** (WBCs, leukocytes) < 0.1 percent of formed elements
  - Body defense; five classes, each with different functions
Module 17.2: Blood composition

Formed elements (continued)

- **Red blood cells** (RBCs, erythrocytes) = 99.9 percent of formed elements
  - Oxygen transport
Summary of the composition of whole blood

- **Plasma Proteins 7%**
  - Albumins
  - Globulins
  - Fibrinogen
  - Enzymes and hormones

- **Other Solute 1%**
  - Electrolytes
  - Organic nutrients
  - Organic wastes

- **Water 92%**

- **Formed Elements 45% (Range 37–54%)**
  - Platelets
  - White Blood Cells
  - Red Blood Cells

- **Red Blood Cells 99.9%**
  - Neutrophils
  - Eosinophils
  - Basophils
  - Lymphocytes
  - Monocytes

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Module 17.2: Review

A. Identify the two components making up whole blood, and list the composition of each.

B. Define hematocrit.

C. Which specific plasma proteins would you expect to be elevated during an infection?

**Learning Outcome:** Describe the important components and major properties of blood.
Module 17.3: Formed elements are produced by stem cells in red bone marrow

Development of formed elements = hemopoiesis/hematopoiesis

- Occurs in red bone marrow

**Hemocytoblasts** from **hematopoietic stem cells (HSCs)**

- Produce two types of stem cells
  1. *Lymphoid stem cells* produce lymphocytes (type of WBC)
  2. *Myeloid stem cells* produce RBCs, other WBCs
Module 17.3: Hemopoiesis

Two types of stem cells produced by hemocytoblasts

1. **Lymphoid stem cells** produce lymphocytes (immune response)
   - Originate in red bone marrow; some stay
   - Others migrate to **lymphoid tissues** (thymus, spleen, lymph nodes)

2. **Myeloid stem cells** give rise to all other formed elements
Module 17.3: Hemopoiesis

Lymphoid stem cells to lymphocytes

Lymphoid stem cells → lymphoblasts → prolymphocytes → lymphocytes

Colony-stimulating factors = hormones released by activated lymphocytes and other cells during immune response to stimulate blood cell formation
Module 17.3: Hemopoiesis

Myeloid stem cells to immature blast cells

- Myeloid stem cells differentiate into three types of progenitor cells that, in turn, differentiate into:
  1. Monoblasts and myeloblasts
  2. Megakaryocytes
  3. Proerythroblasts

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Module 17.3: Hemopoiesis

Myeloid stem cells to monoblasts to monocytes

- Monoblasts differentiate into promonocytes
- Promonocytes differentiate into monocytes
Module 17.3: Hemopoiesis

Myeloid stem cells to myeloblasts to WBCs

- Myeloblasts differentiate into three types of myelocytes
- Myelocytes differentiate into band cells
- Band cells differentiate into neutrophils, eosinophils, basophils
Module 17.3: Hemopoiesis

Myeloid stem cells to megakaryocytes to platelets

- Myeloid stem cells differentiate into **megakaryocytes**
  - Megakaryocytes are enormous cells with large nuclei
  - Eventually shed cytoplasm in small, membrane-enclosed packets = *platelets*

<table>
<thead>
<tr>
<th>Structure and Function of Platelets</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Appearance in a Stained Blood Smear</strong></td>
</tr>
<tr>
<td>Platelets are flattened discs that appear round when viewed from above and appear spindle shaped in section or in a blood smear.</td>
</tr>
</tbody>
</table>
Module 17.3: Hemopoiesis

Myeloid stem cells to proerythroblasts to RBCs

- Myeloid stem cells differentiate into proerythroblasts
- Proerythroblasts differentiate to erythroblasts, which shed their nuclei, and then on to anucleate reticulocytes
- Reticulocytes differentiate to erythrocytes (red blood cells/RBCs)

Stimulated by erythropoietin (EPO)
Module 17.3: Hemopoiesis

Erythropoietin (EPO)
- Released into plasma in response to low tissue oxygen levels = hypoxia (hypo, below + oxy, presence of oxygen)
Erythropoietin (EPO) (continued)

- Stimulus for EPO release:
  - Anemia
  - Reduced blood flow to kidneys
  - $O_2$ content in lungs decreased from disease or high altitude
  - Lung damage

- Stimulates stem cells and developing RBCs in red bone marrow
The process of hemopoiesis
Module 17.3: Review

A. Define *hemocytoblasts*.
B. Describe platelets and their origin.
C. Compare the types of cells that lymphoid stem cells and myeloid stem cells produce.

*Learning Outcome:* Explain the origins and differentiation of the formed elements.
Section 2: Structure and Function of Formed Elements

Learning Outcomes

17.4 Define hematology, describe the elements of a complete blood count (CBC), and give examples of red blood cell lab tests.

17.5 List the characteristics and functions of red blood cells, and describe the structure and functions of hemoglobin.

17.6 Describe how the components of aged or damaged red blood cells are recycled.
Section 2: Structure and Function of Formed Elements

Learning Outcomes (continued)

17.7 Explain the importance of blood typing and the basis for ABO and Rh incompatibilities.

17.8 **Clinical Module:** Describe hemolytic disease of the newborn, explain the clinical significance of the cross-reaction between fetal and maternal blood types, and cite preventive measures.
Section 2: Structure and Function of Formed Elements

Learning Outcomes (continued)

17.9 Categorize the various types of white blood cells on the basis of their structures and functions.

17.10 Discuss the mechanisms that control blood loss after an injury, and describe the reaction sequences responsible for blood clotting.

17.11 **Clinical Module:** Explain how blood disorders are detected, and describe examples of the various categories of blood disorders.
Module 17.4: Hematology is the study of blood and blood-forming tissues

Hematology

- Important information about a person’s health
- Can detect disorders (anemia, infection, clotting disorders)
- Dyscrasias = blood disorders; can have systemic effects

Reasons for performing blood tests

- Determine blood type
- Evaluate types/numbers of RBCs, WBCs, and platelets
- Abnormal values may indicate underlying medical conditions

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Module 17.4: Hematology

Complete blood count (CBC)
- Determines following in 1 cubic millimeter (1 microliter or μL) of blood:
  - RBC count
  - WBC count
  - Erythrocyte indices (hemoglobin)
  - Hematocrit
  - Others

WBC differential count
- Identifies numbers of each type of white blood cell
Module 17.4: Hematology

Red blood cell tests

- Several common tests
- Assess number, size, shape, maturity of circulating RBCs
- Can detect problems that lack obvious signs (internal bleeding)

<table>
<thead>
<tr>
<th>RBC Tests and Related Terminology</th>
<th>Determines</th>
<th>Terms Associated with Abnormal Values</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Elevated</td>
</tr>
<tr>
<td>Hematocrit (Hct)</td>
<td>Percentage of formed elements in whole blood Normal = 37–54%</td>
<td>Polycythemia</td>
</tr>
<tr>
<td>Hemoglobin Concentration (Hb, Hgb)</td>
<td>Concentration of hemoglobin in blood Normal = 12–18 g/dL</td>
<td>Polycythemia</td>
</tr>
<tr>
<td>Mean Corpuscular Hemoglobin Concentration (MCH)</td>
<td>Average weight of Hb in one RBC Normal = 27–34 μg/RBC (normochromic)</td>
<td>Hyperchromic</td>
</tr>
<tr>
<td>Mean Corpuscular Volume (MCV)</td>
<td>Average volume of one RBC Normal = 82–101 μm³/cell (normocytic)</td>
<td>Macrocytic</td>
</tr>
<tr>
<td>RBC Count</td>
<td>Number of RBCs per μL of whole blood Normal = 4.2–6.3 million cells/μL</td>
<td>Erythrocytosis/polycythemia</td>
</tr>
<tr>
<td>Reticulocyte Count (Retic.)</td>
<td>Percentage of circulating reticulocytes Normal = 0.8%</td>
<td>Reticulocytosis</td>
</tr>
</tbody>
</table>
Module 17.4: Review

A. What is hematology?
B. Describe a complete blood count (CBC).
C. Which condition would a patient have if she had a depressed hematocrit level?

*Learning Outcome:* Define hematology, describe the elements of a complete blood count (CBC), and give examples of red blood cell lab tests.
Module 17.5: Red blood cells, the most common formed elements, contain hemoglobin that transports respiratory gases

Red blood cells (RBCs)

- Roughly one-third of all cells in the body
- Single drop of whole blood contains ~260 million RBCs
  - Average adult ~25 trillion RBCs = one-third of all cells in body
Module 17.5: Red blood cells

- **Red blood cell count**
  (standard test)
  - Number of RBCs per microliter (µL), or cubic millimeter (mm³), of whole blood
  - Adult males: 4.5–6.3 million RBCs/µL
  - Adult females: 4.2–5.5 million RBCs/µL
RBCs are biconcave discs—thinner centers, thicker edges
Module 17.5: Red blood cells

Functional aspects of red blood cells

- Large surface area–to–volume ratio
  - Packed with hemoglobin (= protein that carries oxygen)
  - Allows more oxygen exchange
  - Total RBC surface area (adult) equals ~2000 times total surface area of body
- Form stacks (rouleaux)—facilitate transport in small vessels
- Flexible—RBCs can move through narrowest capillaries with diameters smaller than RBC

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Functional Aspects of Red Blood Cells

- Large surface area-to-volume ratio.
- RBCs can form stacks
- Flexibility
Module 17.5: Red blood cells

Red blood cell characteristics

- Lose most organelles during development
- Mature RBCs lack nuclei (anucleate) and ribosomes
  - Cannot divide/repair
- Life span < 120 days
- Primary function—transport respiratory gases
  - 95 percent of RBC intracellular proteins are hemoglobin molecules
  - **Hemoglobin** (Hb) content, whole blood:
    - 14–18 g/dL males
    - 12–16 g/dL females
Module 17.5: Red blood cells

Hemoglobin

- Complex quaternary structure
- Each Hb molecule has:
  - Two alpha (α) chains
  - Two beta (β) chains
- Similar to myoglobin in muscle cells
- Each chain has a single heme molecule
Module 17.5: Red blood cells

Hemoglobin (continued)

- Each heme contains an iron ion that interacts with oxygen molecule to form oxyhemoglobin ($\text{HbO}_2$)
  - Makes oxygenated blood bright red
- Oxygen binding is reversible
  - Deoxyhemoglobin = hemoglobin not bound to oxygen; blood is dark red
Module 17.5: Red blood cells

Hemoglobin (continued)

- An RBC has ~280 million Hb molecules
- Each Hb molecule has four heme units
- So, each RBC can carry >1 billion oxygen molecules
- ~98.5 percent of oxygen in blood is bound to Hb; rest is dissolved in plasma
Module 17.5: Review

A. Describe the functional aspects of RBCs.
B. Describe hemoglobin.
C. Compare oxyhemoglobin with deoxyhemoglobin.

Learning Outcome: List the characteristics and functions of red blood cells, and describe the structure and functions of hemoglobin.
Module 17.6: Red blood cells are continually produced …

- ~1 percent of circulating RBCs are replaced each day (short lifespan)
- ~3 million new RBCs enter circulation each second

End of RBC life
- Plasma membrane ruptures (hemolysis) or
- RBC is engulfed by macrophages in spleen, liver, or bone marrow
Module 17.6: Red blood cells are continually produced ...

**Erythropoiesis** = red blood cell formation

- Occurs only in red bone marrow, or *myeloid tissue*, in vertebrae, ribs, sternum, skull, scapulae, pelvis, and ends of limb bones.
- Fatty yellow bone marrow can convert to red bone marrow in cases of severe, sustained blood loss and make RBCs.
Module 17.6: RBC production and breakdown

- **Erythroblasts** begin producing Hb
- **Normoblasts** lose their nuclei and become reticulocytes
- **Reticulocytes** contain ~80 percent of the Hb of mature RBCs; enter bloodstream after 2 days
Events occurring in macrophages

- Fe²⁺ transported in bloodstream by transferrin
- Amino acids
- Heme
- Biliverdin
- Bilirubin

Macrophages in spleen, liver, and bone marrow

After 24 hours in circulation, the reticulocytes complete their maturation and resemble other mature RBCs. Reticulocytes account for about 0.8% of the circulating RBCs.

Average life span of RBC is 120 days

90% Old and damaged RBCs
10% Bilirubin

In the bloodstream, the rupture of RBCs is called hemolysis.
Module 17.6: RBC production and breakdown

Events occurring in macrophages (continued)

- Macrophages monitor condition of circulating RBCs
  - Engulf old RBCs before rupture (hemolyze)
  - Remove Hb molecules/cell fragments

- Heme units stripped of iron
  - Iron is stored in phagocyte or enters blood and binds to transferrin (plasma protein)
  - Heme $\rightarrow$ biliverdin $\rightarrow$ bilirubin $\rightarrow$ bloodstream $\rightarrow$ liver

- Globular proteins disassembled and amino acids recycled
Events occurring in macrophages (continued)

- Hemoglobin that is not phagocytized breaks down into its protein chains and is excreted in urine
- Breakdown of an abnormally large number of RBCs results in red or brown urine; condition is hemoglobinuria
Module 17.6: RBC production and breakdown

Events occurring in the liver

- Bilirubin is excreted in bile
- Blocked bile ducts or inability to process bilirubin causes bilirubin levels to increase
  - Bilirubin diffuses into peripheral tissues
  - Causes yellow color in skin and eyes = jaundice
Module 17.6: RBC production and breakdown

Events occurring in large intestine

- Bacteria convert bilirubin to **urobilins** and **stercobilins**; they enter feces, giving it yellow-brown or brown color.
Module 17.6: RBC production and breakdown

Events occurring in kidneys

- Excrete hemoglobin and urobilins—gives urine yellow color
- **Hematuria** = presence of intact RBCs; occurs only after urinary tract damage
Summary of the production and clearance of RBCs

1. Events Occurring in the Red Bone Marrow
   - Developing RBCs absorb amino acids and Fe²⁺ from the bloodstream and synthesize new Hb molecules.
   - Proerythroblasts
     - Day 1
   - Erythroblasts
     - Basophilic erythroblast
     - Day 2
     - Polychromatophilic erythroblast
     - Day 3
     - Normoblast
     - Day 4
   - Ejection of nucleus
   - Reticulocyte

2. Events Occurring in Macrophages
   - Fe²⁺ transported in bloodstream by transferrin
   - Amino acids
   - Macrophages in spleen, liver, and bone marrow
   - Hemoglobin in macrophage
   - Biliverdin
   - Bilirubin
   - Liver
   - Bilirubin bound to albumin in bloodstream
   - Bilirubin excreted in bile
   - Urobilins, urobilinogen, and bilirubin in large intestine

3. Events Occurring in the Liver
   - Bilirubin
   - Liver
   - Bilirubin excreted in bile

4. Events Occurring in the Large Intestine
   - Urobilins, urobilinogen, and bilirubin
   - Eliminated in feces

5. Events Occurring in the Kidney
   - Kidney
   - Hb
   - Urobilins
   - Eliminated in urine

6. Average life span of RBC is 120 days
   - 90% Old and damaged RBCs
   - 10% Hemoglobin is not phagocytized
   - Hemoglobin breaks down, and the alpha and beta chains are excreted in urine

7. Events Occurring in the Bone Marrow
   - Reticulocytes account for about 0.9% of circulating RBCs

8. Events Occurring in the Bloodstream
   - Fe²⁺ transported in bloodstream by transferrin
   - Amino acids
A. In what way would a liver disease affect the level of bilirubin in the blood?

Learning Outcome: Describe how the components of aged or damaged red blood cells are recycled.
Module 17.7: Blood type is determined by the presence or absence of specific surface antigens on RBCs

Blood types

- **Antigens** = substances that can elicit immune response
- Our cells have **surface antigens** embedded in their plasma membranes; recognized as normal, or self, by immune system
Module 17.7: Blood type

Blood types (continued)

- Blood type determined genetically by which surface antigens are present in RBC plasma membranes
  - > 50 blood cell surface antigens
  - Three most important:
    - A
    - B
    - Rh (or D)
Module 17.7: Blood type

ABO blood group

- Based on the presence or absence of A and B surface antigens (or agglutinogens)
- Plasma has antibodies that will attack “foreign” surface antigen(s)
- Four ABO blood types

<table>
<thead>
<tr>
<th>Antigens and Antibodies by Blood Type</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Type A</strong></td>
</tr>
<tr>
<td>Surface antigen A</td>
</tr>
<tr>
<td>Anti-B antibodies in plasma</td>
</tr>
<tr>
<td><strong>Type B</strong></td>
</tr>
<tr>
<td>Surface antigen B</td>
</tr>
<tr>
<td>Anti-A antibodies in plasma</td>
</tr>
<tr>
<td><strong>Type AB</strong></td>
</tr>
<tr>
<td>Neither anti-A nor anti-B antibodies in plasma</td>
</tr>
<tr>
<td><strong>Type O</strong></td>
</tr>
<tr>
<td>Both anti-A and anti-B antibodies in plasma</td>
</tr>
</tbody>
</table>
Module 17.7: Blood type

Agglutination = clumping together of RBCs

- Occurs when surface antigens (agglutinogens) are exposed to corresponding antibodies (agglutinins) from another blood type
  - *Example*: Giving type A blood to someone who is type B
Agglutination (continued)

- Called a **cross-reaction**
  - Forms dangerous clumps/fragments of RBCs; can block small blood vessels—cuts blood supply, damages/destroys tissues
- Cells may undergo hemolysis
Module 17.7: Blood type

Rh blood group

- Based on presence or absence of Rh surface antigen on RBCs
- “Rh” comes from original discovery in *Rhesus* monkeys
- **Rh positive** (Rh\(^+\)) has Rh surface antigen
  - Indicates presence of Rh surface antigen
- **Rh negative** (Rh\(^-\)) lacks Rh surface antigen
- Included in full blood type as + or –
  
  *Examples*: O negative (O\(^-\)), AB positive (AB\(^+\))
<table>
<thead>
<tr>
<th>Population</th>
<th>Percentage with Each Blood Type</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>O</td>
</tr>
<tr>
<td>United States</td>
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<tr>
<td>Black American</td>
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</tr>
<tr>
<td>Caucasian</td>
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<tr>
<td>Chinese American</td>
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<td>Filipino American</td>
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<td>Korean American</td>
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<td>Native North American</td>
<td>79</td>
</tr>
<tr>
<td>Native South American</td>
<td>100</td>
</tr>
<tr>
<td>Australian Aborigine</td>
<td>44</td>
</tr>
</tbody>
</table>
Module 17.7: Blood type

Blood typing tests

- Drops of person’s blood are mixed with solutions containing antibodies to surface antigens A, B, and Rh
- Clumping (agglutination) occurs where sample contains the corresponding antigen
  - Example: Type A blood will clump with anti-A antibodies
- Typing is necessary to avoid transfusion reactions (cross-reactions occurring from transfusing mismatched blood)
  - Donor and recipient blood types must be compatible (will not cross-react)
### Results of blood typing tests

<table>
<thead>
<tr>
<th>Anti-A Antibodies</th>
<th>Anti-B Antibodies</th>
<th>Anti-Rh Antibodies</th>
<th>Blood type</th>
<th>Can receive blood from</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clumping</td>
<td>No clumping</td>
<td>Clumping</td>
<td>A⁺</td>
<td>A⁺, O⁺, O⁻</td>
</tr>
<tr>
<td>No clumping</td>
<td>Clumping</td>
<td>Clumping</td>
<td>B⁺</td>
<td>B⁺, O⁺, O⁻</td>
</tr>
<tr>
<td>Clumping</td>
<td>Clumping</td>
<td>Clumping</td>
<td>AB⁺</td>
<td>A⁺, B⁺, AB⁺, O⁺, O⁻ (universal recipient)</td>
</tr>
<tr>
<td>No clumping</td>
<td>No clumping</td>
<td>No clumping</td>
<td>O⁻</td>
<td>O⁻ (universal donor)</td>
</tr>
</tbody>
</table>
Module 17.7: Blood type

Genetics of blood type

- Presence of anti-A and/or anti-B antibodies is genetically determined
  - Exposure to foreign RBCs not needed to develop the antibodies

- Anti-Rh antibodies are not automatically present
  - Rh-negative person will not have any anti-Rh antibodies until exposed to Rh-positive RBCs (sensitized); then develops anti-Rh antibodies
Module 17.7: Review

A. What is determined by the surface antigens on RBCs?

B. What is the most common blood type in the United States?

C. Which blood type(s) can be safely transfused into a person with type O\(^-\) blood?

D. Why can’t a person with type A blood safely receive blood from a person with type B blood?

Learning Outcome: Explain the importance of blood typing and the basis for ABO and Rh incompatibilities.
Module 17.8: Clinical Module: Hemolytic disease of the newborn is an RBC-related disorder caused by a cross-reaction between fetal and maternal blood types

Background

- Blood type is determined by combining genes from both parents
  - Child can have blood type different from either parent
- During pregnancy, mother’s antibodies may cross the placenta and attack/destroy fetal RBCs.
- Condition is **hemolytic diseases of the newborn (HDN)**
- Many forms—some very dangerous, others undetectable.
Module 17.8: Hemolytic disease of the newborn

- Most common involves Rh− mother who has carried Rh+ fetus

- First pregnancy—rarely poses a problem because fetal cells are mostly isolated from maternal blood—mom’s immune system is not stimulated to produce anti-Rh antibodies
Module 17.8: Hemolytic disease of the newborn

- **Birth**: bleeding at placenta/uterus mixes fetal and maternal blood
  - Mother exposed to Rh antigens; stimulates her immune system to produce anti-Rh antibodies (= sensitization)
  - ~20 percent of Rh− mothers who carried Rh+ children are sensitized within 6 months of delivery, but first child usually not affected (antibodies develop after delivery)
Module 17.8: Hemolytic disease of the newborn

Subsequent pregnancy with Rh\(^+\) fetus:

- Maternal anti-Rh antibodies can cross placenta; destroy fetal RBCs, causing severe anemia
- Fetal demand for RBCs increases; erythroblasts enter bloodstream before maturity—leads to alternative name, **erythroblastosis fetalis**
- High fatality rate without treatment
- Newborn with severe HDN is anemic/jaundiced (from high bilirubin concentrations)
Module 17.8: Hemolytic disease of the newborn

- Maternal antibodies remain active 1–2 months after delivery
  - May require replacement of infant’s entire blood volume
- HDN can be prevented by giving mother anti-Rh antibodies (RhoGAM) at weeks 26–28 of pregnancy and during/after delivery
- The antibodies destroy fetal RBCs that crossed placenta before RBCs stimulate maternal immune response (= no sensitization)
Overview of hemolytic disease of the newborn

First Pregnancy of an Rh- Mother with an Rh+ Infant

- Very few fetal cells enter the maternal bloodstream during the first pregnancy.

Second Pregnancy of an Rh- Mother with an Rh+ Infant

- In future pregnancy with Rh+ fetus, maternal anti-Rh antibodies can cross the placenta and destroy fetal RBCs, causing erythroblastosis fetalis (hemolytic disease of the newborn).

During First Pregnancy
- Maternal blood supply and tissue
- Fetal blood supply and tissue

Hemorrhaging at Delivery
- Maternal RBC
- Rh antigen on fetal red blood cells

During Second Pregnancy
- Maternal blood supply and tissue
- Fetal blood supply and tissue

Maternal Antibody Production
- Maternal blood supply and tissue
- Maternal antibodies to Rh antigen

During First Pregnancy
- Placenta

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Module 17.8: Review

A. Define *hemolytic disease of the newborn (HDN)*.

B. Why is RhoGAM administered to pregnant Rh− women?

C. Does an Rh+ mother carrying an Rh− fetus require a RhoGAM injection? Explain your answer.

*Learning Outcome*: Describe hemolytic disease of the newborn, explain the clinical significance of the cross-reaction between fetal and maternal blood types, and cite preventive measures.
Module 17.9: The various types of white blood cells contribute to the body’s defenses

White blood cells (WBCs), or leukocytes

- Have nuclei and other organelles, unlike RBCs, but no hemoglobin
- Five types—“Never Let Monkeys Eat Bananas”
  1. Neutrophils
  2. Lymphocytes
  3. Monocytes
  4. Eosinophils
  5. Basophils
Characteristics of WBCs

Shared Properties of WBCs

- WBCs circulate for only a short portion of their life span, using the bloodstream primarily to travel between organs and to rapidly reach areas of infection or injury. WBCs spend most of their time migrating through loose and dense connective tissues throughout the body.

- All WBCs can migrate out of the bloodstream. When circulating WBCs in the bloodstream become activated, they contact and adhere to the vessel walls and squeeze between adjacent endothelial cells to enter the surrounding tissue. This process is called emigration, or diapedesis (di-ah-peh-DĒ-sis; dia, through + pedesis, a leaping).

- All WBCs are attracted to specific chemical stimuli. This characteristic, called positive chemotaxis (kē-mō-TAK-sis), guides WBCs to invading pathogens, damaged tissues, and other active WBCs.

- Neutrophils, eosinophils, and monocytes are capable of phagocytosis. They can engulf pathogens, cell debris, or other materials. Macrophages are monocytes that move from the bloodstream into peripheral tissues (see Module 4.11).
Module 17.9: White blood cells

White blood cell counts

- Number can be increased in response to infection, inflammation, or allergic responses
- **WBC differential count** identifies types and numbers of WBCs in a blood sample; reported as percentage (per 100 WBCs)
Module 17.9: White blood cells

Two classes of white blood cells

1. **Granular leukocytes**, or *granulocytes*
   - Abundant cytoplasmic granules (secretory vesicles and lysosomes) that absorb histological stains

2. **Agranular leukocytes**, or *agranulocytes*—smaller secretory vesicles/lysosomes that don’t absorb stains
The agranular leukocytes are monocytes and lymphocytes

<table>
<thead>
<tr>
<th>White Blood Cells</th>
<th>Quantity (Average Number per μL)</th>
<th>Appearance in a Stained Blood Smear</th>
<th>Functions</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Monocytes</strong></td>
<td>456 (range: 200–950) Differential count: 2–8%</td>
<td>Very large cell; nucleus kidney bean–shaped; abundant cytoplasm</td>
<td>Enter tissues and become macrophages; engulf pathogens or debris</td>
<td>Move into tissues after 1–2 days; survive for months or longer; produced primarily in red bone marrow</td>
</tr>
<tr>
<td><strong>Lymphocytes</strong></td>
<td>2185 (range: 1500–4000) Differential count: 20–40%</td>
<td>Generally round cell, slightly larger than RBC; round nucleus; very little cytoplasm</td>
<td>Cells of lymphatic system; provide defense against specific pathogens or toxins</td>
<td>Survive for months to decades; circulate from blood to tissues and back; produced in red bone marrow and lymphoid tissues</td>
</tr>
</tbody>
</table>
Module 17.9: Review

A. Identify the five types of white blood cells.
B. How do basophils respond to tissue damage?
C. Which type of white blood cell would you find in the greatest numbers in an infected cut?

Learning Outcome: Categorize the various types of white blood cells on the basis of their structures and functions.
Module 17.10: The clotting response is a complex cascade of events that reduces blood loss

**Hemostasis** (*haima*, blood + *stasis*, halt)

- Process responsible for stopping blood loss through walls of damaged blood vessels
- Establishes framework for tissue repairs
- Three Phases
  1. Vascular phase
  2. Platelet phase
  3. Coagulation phase
Module 17.10: Hemostasis

Vascular phase of hemostasis

- Lasts ~ 30 minutes after injury
- Dominated by endothelial response and **vascular spasm** (smooth muscle contracts)
- Exposed endothelium in contact with blood; releases chemicals/local hormones
Vascular phase of hemostasis (continued)

- Endothelial cells release chemicals and local hormones, including endothelins:
  1. Cause smooth muscle contraction; promote vascular spasms
  2. Stimulate division of endothelial cells, smooth muscle cells, fibroblasts for repair
     - Endothelial plasma membranes become “sticky”
Module 17.10: Hemostasis

Platelet phase of hemostasis

- Begins with attachment of platelets to sticky endothelial surfaces, basement membrane, exposed collagen fibers, and other platelets.
Module 17.10: Hemostasis

Chemicals released by platelets:

- Adenosine diphosphate (ADP) stimulates platelet aggregation and secretion
- Chemicals that stimulate vascular spasms (smooth muscle contraction)
- **Platelet factors**—proteins that play role in clotting
- **Platelet-derived growth factor (PDGF)**—promotes vessel repair
- Calcium ions—required for platelet aggregation and clotting process
Module 17.10: Hemostasis

Coagulation phase of hemostasis

- Starts 30 seconds or more after damage
- Coagulation (blood clotting) involves complex sequence of steps leading to conversion of circulating fibrinogen to insoluble fibrin
- Blood cells and platelets are trapped in fibrin network (blood clot)
Coagulation phase of hemostasis (continued)

- **Procoagulants** (clotting factors) play a key role
  - Calcium and 11 different proteins (I–XI)
  - Many are **proenzymes** (inactive)
  - Activated enzymes lead to chain reaction (**cascade**)
Module 17.10: Hemostasis

Coagulation phase of hemostasis (continued)

- Two pathways lead to common pathway—extrinsic and intrinsic

  1. **Extrinsic pathway**
     - Begins with release of *tissue factor* (factor III) from damaged endothelial cells or peripheral tissues
     - Tissue factor combines with Ca$^{2+}$ and another clotting factor to activate factor X (first step in common pathway)
Coagulation phase of hemostasis (continued)

- Two pathways (continued)

2. **Intrinsic pathway**
   - Begins with activation of proenzymes exposed to collagen fibers at injury site
   - Pathway proceeds with assistance of PF-3 (factor released by aggregating platelets)
   - Sequence of enzyme activations leads to factor X
Module 17.10: Hemostasis

Coagulation phase of hemostasis (continued)

- **Common pathway**
  - Activated factor X activates prothrombin activator, a complex that converts the prothrombin (a proenzyme) to the enzyme thrombin
  - Thrombin converts fibrinogen to fibrin
    - Completes clotting process

- **Clot retraction**
  - RBCs and platelets stick to the fibrin threads
  - Platelets contract to form tighter clot and pull edges together
  - Continues for 30–60 minutes
Fibrinolysis

- Process of clot dissolving
- Begins with activation of:
  - Plasminogen by thrombin (from common pathway)
  - Tissue plasminogen activator, or t-PA, from damaged tissues
- Produces plasmin—erodes the clot
Module 17.10: Review

A. Define hemostasis.

B. Briefly describe the vascular, platelet, and coagulation phases of hemostasis.

C. Describe the events that follow the coagulation phase.

**Learning Outcome:** Discuss the mechanisms that control blood loss after an injury, and describe the reaction sequences responsible for blood clotting.
Module 17.11: Blood disorders can be classified by their origins and the changes in blood characteristics

Obtaining blood for diagnosis

- **Venipuncture** (*vena*, vein + *punctura*, a piercing)
  - Withdrawal of whole blood from superficial vein, such as median cubital vein
Obtaining blood for diagnosis (continued)

- Commonly used because:
  1. Easy to locate superficial veins
  2. Vein walls are thinner than walls of comparable arteries
  3. Venous blood pressure is relatively low, so vein seals quickly
Nutritional blood disorders

- **Iron deficiency anemia**
  - Insufficient iron intake (needed to form functional hemoglobin)
  - Resulting RBCs are small (*microcytic*); transport less oxygen
  - More common in women—iron reserves half the reserves of a typical man
Nutritional blood disorders (continued)

- **Pernicious anemia**
  - Vitamin $B_{12}$ deficiency prevents normal stem cell divisions
  - Fewer RBCs produced; often misshaped, large (macrocytic)
  - Can be from lack of intrinsic factor—secreted in stomach; needed for vitamin $B_{12}$ absorption

- **$Ca^{2+}$ and vitamin K deficiencies**
  - Calcium is required for all clotting pathways
  - Vitamin K is required by liver to synthesize clotting factors
Module 17.11: Blood disorders

Congenital blood disorders

- **Sickle cell disease (SDC)**—group of inherited RBC disorders
  
  - Genetic mutation affects amino acid sequence of the beta globin subunit in hemoglobin
  
  - RBCs take on sickle shape when they release oxygen
    - RBCs more fragile, easily damaged
    - Can get stuck in smaller vessels, block flow
Module 17.11: Blood disorders

Congenital blood disorders (continued)

- **Sickle cell anemia**—most severe type of sickle cell disease
  - Requires two copies of the sickling gene
    - People with one copy have the *sickling trait*, but not disorder
    - Having the trait increases person’s resistance to malaria
      - Infected RBCs sickle
      - Sickled cells are destroyed by macrophages—malarial pathogen destroyed with infected cells
Congenital blood disorders (continued)

- **Hemophilia**—Inherited bleeding disorder
  - Affects 1 person in 10,000; ~80–90 percent are males
  - Caused by missing or reduced production of a clotting factor
  - Severity of disorder varies
  - In severe cases, extensive bleeding occurs with minor contact
    - Bleeding also occurs at joints and around muscles
Module 17.11: Blood disorders

Congenital blood disorders (continued)

- **Thalassemias**—diverse group of inherited disorders
  - Unable to adequately produce normal Hb protein subunits
  - Severity depends on which/how many subunits are abnormal
Blood infections

- Caused by pathogens entering the blood through wound or infection
  - **Bacteremia**—bacteria circulate in blood, do not multiply there
  - **Viremia**—viruses circulating in blood, but not multiplying there
Blood infections (continued)

• **Sepsis**
  – Widespread infection of body tissue

• **Septicemia**
  – Sepsis of the blood (“blood poisoning”)
  – Pathogens present, multiplying in blood, and spreading

Infant with septicemia from meningococcal bacteria
Module 17.11: Blood disorders

Blood infections (continued)

- **Malaria**—parasitic disease caused by several species of *Plasmodium*
  - Kills 1.5–3 million people per year (up to half are under age 5)
  - Transmitted by mosquito
  - Initially infects liver; later infects RBCs
    - Every 2–3 days, all infected RBCs rupture, release more parasites
    - Causes cycles of fever/chills; dead RBCs block vessels to vital organs
Module 17.11: Blood disorders

Blood cell cancers

- **Leukemias**—cancers of blood-forming tissues
  - Cancerous cells spread from origin in red bone marrow
  - First symptoms appear with presence of immature and abnormal WBCs in circulation
  - Fatal if untreated
  - Two types
    - Myeloid leukemia
    - Lymphoid leukemia
    - Both have elevated WBCs

Abnormal WBCs (*) seen in a blood smear of a patient with myeloid leukemia
Module 17.11: Blood disorders

Degenerative blood disorders

- **Disseminated intravascular coagulation (DIC)**
  - Bacterial toxins activate steps in coagulation process
    - Converts too much fibrinogen to fibrin; small clots may block small vessels and damage nearby tissue
    - Phagocytes and plasmin work to remove fibrin
  - Liver tries to maintain adequate fibrinogen levels; if cannot keep up, uncontrolled bleeding may occur
Module 17.11: Review

A. Compare pernicious anemia with iron deficiency anemia.

B. Identify the two types of leukemia.

C. Explain why venipuncture is a common clinical procedure for obtaining blood for examination.

**Learning Outcome:** Explain how blood disorders are detected, and describe examples of the various categories of blood disorders.