Blood

- **Functions include**
  - **Transport**
    - Delivering O\(_2\) and nutrients
    - Transporting metabolic wastes and water
    - Transporting hormones
  - **Regulation**
    - Maintaining body temperature
      - fluid warmed in one area of body distributes heat to cooler areas
    - Maintaining normal pH (both blood and tissues) using buffer substances
      - Buffered solution = a solution that resists changes in pH when acid or alkali is added to it
    - Maintaining adequate fluid volume
      - Osmotic pressure exerted by blood colloids and solutes
  - **Protection**
    - Preventing blood loss – plugging, clotting
    - Preventing infection – using cells and proteins

Physical Characteristics and Volume

- Blood is a sticky, opaque fluid with metallic taste
- Color varies with O\(_2\) content
  - High O\(_2\) levels show a scarlet red
  - Low O\(_2\) levels show a dark red
- pH = 7.35–7.45
- Approximately 8% of body weight
  - Average volume:
    - Males: 5–6 L
    - Females: 4–5 L (likely the result of body size difference)

Components of Blood

Blood, a connective tissue, is the only fluid tissue in body
Plasma Composition

Plasma proteins are heavier than lighter (but more numerous) solutes

![Image of plasma composition]

Table 17.1 Composition of Plasma

<table>
<thead>
<tr>
<th>CONSTITUENT</th>
<th>DESCRIPTION AND IMPORTANCE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Water</td>
<td>90% of plasma volume; dissolving and suspending medium for solutes of blood, absorbs heat</td>
</tr>
<tr>
<td>Solutes</td>
<td></td>
</tr>
<tr>
<td>Electrolytes</td>
<td>Most abundant solutes by number; cations include sodium, potassium, calcium, magnesium; anions include chloride, phosphate, sulfate, and bicarbonate. Help to maintain plasma osmotic pressure and normal blood pH.</td>
</tr>
<tr>
<td>Plasma proteins</td>
<td>8% by weight of plasma; aid in osmotic pressure and maintain water balance in body and tissue, all have other functions (transport, enzymes, etc.) as well.</td>
</tr>
<tr>
<td>Albumin</td>
<td>68% of plasma proteins; produced by liver; main contributor to osmotic pressure.</td>
</tr>
<tr>
<td>Globulins</td>
<td>30% of plasma proteins; produced by liver; aid in osmotic pressure.</td>
</tr>
<tr>
<td>Alpha, beta</td>
<td>Produced by liver; mediate transport proteins that bind to fats, metal ions, and fat-soluble vitamins;</td>
</tr>
<tr>
<td>Gamma</td>
<td>Antibodies released by plasma cells during immune response.</td>
</tr>
<tr>
<td>Fibrogen</td>
<td>4% of plasma proteins; produced by liver; form fibrin threads of blood clot</td>
</tr>
</tbody>
</table>

Table 17.1 Composition of Plasma (continued)

<table>
<thead>
<tr>
<th>CONSTITUENT</th>
<th>DESCRIPTION AND IMPORTANCE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nonprotein nitrogenous substances</td>
<td>By-products of cellular metabolism, such as urea, uric acid, creatinine, and ammonium salts</td>
</tr>
<tr>
<td>Nutrients (organic)</td>
<td>Materials absorbed from digestive tract and transported for use throughout body; include glucose and other simple carbohydrates, amino acids (protein digestion products), fatty acids, glycerol and triglycerides (fat digestion products), cholesterol, and vitamins</td>
</tr>
<tr>
<td>Respiratory gases</td>
<td>Oxygen and carbon dioxide; oxygen mostly bound to hemoglobin inside RBCs; carbon dioxide transported dissolved as bicarbonate or CO₂ or bound to hemoglobin in RBCs</td>
</tr>
<tr>
<td>Hormones</td>
<td>Steroid and thyroid hormones carried by plasma proteins</td>
</tr>
</tbody>
</table>
**Formed Elements**

**Hematocrit**: percent of blood volume that is RBCs

Normal values:
- Males: 47% ± 5%
- Females: 42% ± 5%

How does altitude affect hematocrit?

**WBCs and platelets in Buffy coat (< 1%)**

**Leukocytes**
- Neutrophils
- Lymphocytes
- Monocytes
- Eosinophils

**Erythrocytes**
- Erythrocytes
- Platelets

**Photomicrograph of a human blood smear, Wright's stain (610x)**

**SEM of blood (1800x, artificially colored)**

**Structural Characteristics**
- biconcave disc
- Anucleate
- Essentially has no organelles
- RBC diameters are larger than some capillaries
  - Possess a skeleton of spectrin protein that allow cell to fold and return to shape

**Side view (cut)**

**Top view**
RBC Characteristics

• Three features make for efficient gas transport:
  – Biconcave shape offers huge surface area relative to volume for gas exchange
  – Hemoglobin makes up 97% of cell volume (not counting water)
  – RBCs have no mitochondria
    • ATP production is anaerobic, so they do not consume O$_2$ they transport

• Hemoglobin consists of globin (two alpha and two beta polypeptide chains) and four heme groups.

  – Hemoglobin (Hb) binds reversibly with oxygen
  – Hemoglobin consists of red heme pigment bound to the protein globin
    – A heme pigment is bonded to each globin chain
      • Gives blood red color
      • Each heme’s central iron atom binds one O$_2$

Function of Erythrocytes (cont.)

• Each Hb molecule can transport four O$_2$
• Each RBC contains 250 million Hb molecules
• O$_2$ loading in lungs
  – Produces oxyhemoglobin (ruby red)
• O$_2$ unloading in tissues
  – Produces deoxyhemoglobin, or reduced hemoglobin (dark red)
• CO$_2$ loading in tissues
  – 20% of CO$_2$ in blood binds to Hb, producing carbaminohemoglobin
**Hematopoiesis**: formation of all blood cells

- **Occurs in** red bone marrow
  - In adult, found in axial skeleton, girdles, and proximal epiphyses of humerus and femur
- **Hematopoietic stem cells** (hemocytoblasts)
  - Stem cell that gives rise to all formed elements
  - Hormones and growth factors push cell toward specific pathway of blood cell development
  - Committed cells cannot change

**Erythropoiesis**: formation of red blood cells.

- **Hematopoietic stem cell** (hemocytoblast)
  - Proerythroblast
  - Basophilic erythroblast
  - Polychromatic erythroblast
  - Orthochromatic erythroblasts
  - Reticulocyte
  - Erythrocyte

- **Phase 1**: Ribosome synthesis
- **Phase 2**: Hemoglobin accumulation
- **Phase 3**: Ejection of nucleus

These can sometimes be seen in blood smears

**Regulation and Requirements of Erythropoiesis**

- Too few RBCs lead to tissue hypoxia
- Too many RBCs increase blood viscosity
- > 2 million RBCs are made per second
- Balance between RBC production and destruction depends on:
  - **Hormonal controls**
    - Erythropoietin (EPO) released by kidney, liver
  - **Dietary requirements**
    - Availability of Fe, amino acids, vitamins B₁₂ and folate
Fate and Destruction of Erythrocytes

- Life span: 100–120 days
  - anucleate, so cannot synthesize new proteins, or repair or divide
  - Old RBCs become fragile, and Hb begins to degenerate
- Can get trapped in smaller circulatory channels, especially in spleen where macrophages engulf
- RBC breakdown: heme, iron, and globin are separated
  - Iron binds to ferritin or hemosiderin and is stored for reuse
  - Heme is degraded to yellow pigment bilirubin
    - Liver secretes bilirubin (in bile) into intestines, where it is degraded to pigment urobilinogen
      - Urobilinogen is transformed into brown pigment stercobilin that leaves body in feces
    - Globin is metabolized into amino acids which are reused

Leukocytes

General Structure and Functional Characteristics

- **Leukocytes**, or WBCs, are only formed element that is complete cell with nuclei and organelles
- Make up <1% of total blood volume
  - 4800 to 10,800 WBCs per µl blood
- Function in defense against disease
  - Can leave capillaries via diapedesis
  - Move through tissue spaces by amoeboid motion and positive chemotaxis
  - Leukocytosis – infection-stimulated increase in WBC numbers

<table>
<thead>
<tr>
<th>Formed elements (not drawn to scale)</th>
<th>Differential WBC count (All total 4800–10,800/µl)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Platelets</td>
<td>Increase is a normal response to infection</td>
</tr>
<tr>
<td>Leukocytes</td>
<td></td>
</tr>
<tr>
<td>Granulocytes</td>
<td></td>
</tr>
<tr>
<td>Neutrophils (50–70%)</td>
<td></td>
</tr>
<tr>
<td>Eosinophils (2–4%)</td>
<td></td>
</tr>
<tr>
<td>Basophils (0.5–1%)</td>
<td></td>
</tr>
<tr>
<td>Agranulocytes</td>
<td></td>
</tr>
<tr>
<td>Lymphocytes (25–45%)</td>
<td></td>
</tr>
<tr>
<td>Monocytes (3–8%)</td>
<td></td>
</tr>
</tbody>
</table>
**Neutrophils**
- Most numerous WBCs
  - Account for 50–70% of WBCs
- About twice the size of RBCs
- Also called polymorphonuclear leukocytes (PMNs or polys)
  - Cell has anywhere from three to six lobes
- Granules stain with both acid and basic dyes
- Granules contain either hydrolytic enzymes or antimicrobial proteins, **defensins**
- Active phagocytes
  - Referred to as "bacteria slayers" – numbers increase with bacterial infections
  - Kill by process called **respiratory burst**
    - Cell synthesizes potent oxidizing substances (bleach or hydrogen peroxide)
    - Defensin granules merge with phagosome
      - Form "spears" that pierce holes in membrane of ingested microbe

**Eosinophils**
- Account for 2–4% of all leukocytes
- Nucleus has two lobes connected by a broad band; resembles ear muffs
- Red-staining granules contain digestive enzymes
  - Release enzymes on large parasitic worms, digesting their surface
- Also play role as immune response modulators
Basophils

• Rarest WBCs, accounting for only 0.5–1% of leukocytes
• Nucleus deep purple with one to two constrictions
• Large, purplish black (basophilic) granules contain histamine
  – Histamine: inflammatory chemical that acts as vasodilator and attracts WBCs to inflamed sites
• Are functionally similar to mast cells

Lymphocytes

• Second most numerous WBC, accounts for 25%
• Large, dark purple, circular nuclei with thin rim of blue cytoplasm
• Mostly found in lymphoid tissue (example: lymph nodes, spleen), but a few circulate in blood
• Crucial to immunity
• Two types of lymphocytes
  – T lymphocytes (T cells) act against virus-infected cells and tumor cells
  – B lymphocytes (B cells) give rise to plasma cells, which produce antibodies

Monocytes

• Largest of all leukocytes; 3–8% of all WBCs
• Abundant pale blue cytoplasm
• Dark purple-staining, U- or kidney-shaped nuclei
• Leave circulation, enter tissues, and differentiate into macrophages
  – Actively phagocytic cells; crucial against viruses, intracellular bacterial parasites, and chronic infections
• Activate lymphocytes to mount an immune response
Platelets

- fragments of larger megakaryocyte
- Function: form temporary platelet plug that helps seal breaks in blood vessels
  - Contain several chemicals involved in plug formation and clotting process
- Circulating platelets are kept inactive and mobile by nitric oxide (NO) and prostacyclin from endothelial cells lining blood vessels
- Platelets age quickly and degenerate in about 10 days

**Summary of Formed Elements of the Blood**

<table>
<thead>
<tr>
<th>Cell Type</th>
<th>Illustration</th>
<th>Description</th>
<th>Cell/μL in Circulating Blood</th>
<th>Duration of Development/Use and Life Span</th>
<th>Function</th>
</tr>
</thead>
<tbody>
<tr>
<td>Erythrocyte (Red Blood cells, RBC)</td>
<td></td>
<td>Spherical, biconcave disc, non-nucleated</td>
<td>4.4 million</td>
<td>120 days</td>
<td>Transport oxygen and carbon dioxide</td>
</tr>
<tr>
<td>Leukocytes (White Blood cells, WBC)</td>
<td></td>
<td>Spherical, nucleated</td>
<td>4,000–10,000</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Eosinophils (Eosinophils)</td>
<td></td>
<td>Multinucleated; large eosinophilic granules; diameter 12–15 μm</td>
<td>0.3–0.8</td>
<td>4 days</td>
<td>Phagocytosis, Basophilia</td>
</tr>
<tr>
<td>Neutrophils (Neutrophils)</td>
<td></td>
<td>Multinucleated; toxic granules; diameter 10–15 μm</td>
<td>0.3–0.8</td>
<td>7 days</td>
<td>Phagocytosis, Basophilia</td>
</tr>
<tr>
<td>Basophils (Basophils)</td>
<td></td>
<td>Large, polychromatophilic; diameter 20–30 μm</td>
<td>0.01–0.02</td>
<td>24–48 hrs</td>
<td>Phagocytosis, Basophilia</td>
</tr>
<tr>
<td>Monocytes</td>
<td></td>
<td>Mononuclear, with few granules; diameter 15–20 μm</td>
<td>0.005–0.02</td>
<td>7–10 days</td>
<td>Phagocytosis, Basophilia</td>
</tr>
<tr>
<td>B lymphocytes</td>
<td></td>
<td>Spherical, small, with few granules; diameter 7–8 μm</td>
<td>0.001–0.002</td>
<td>7–10 days</td>
<td>Phagocytosis, Basophilia</td>
</tr>
<tr>
<td>T lymphocytes</td>
<td></td>
<td>Small, lymphoblast-like; diameter 10–15 μm</td>
<td>0.001–0.002</td>
<td>7–10 days</td>
<td>Phagocytosis, Basophilia</td>
</tr>
<tr>
<td>Platelets</td>
<td></td>
<td>Fragment of larger megakaryocyte; diameter 2–3 μm</td>
<td>400,000–600,000</td>
<td>10 days</td>
<td>Function: form temporary platelet plug that helps seal breaks in blood vessels; Contain several chemicals involved in plug formation and clotting process; Circulating platelets are kept inactive and mobile by nitric oxide (NO) and prostacyclin from endothelial cells lining blood vessels; Platelets age quickly and degenerate in about 10 days</td>
</tr>
</tbody>
</table>

*Appearance when stained with Wright's stain.*
Hemostasis

- **Hemostasis**: fast series of reactions for stoppage of bleeding
- Requires **clotting factors** and substances released by platelets and injured tissues
- Three steps involved
  
  **Step 1: Vascular spasm**
  
  **Step 2: Platelet plug formation**
  
  **Step 3: Coagulation (blood clotting)**

**Step 1: Vascular Spasm**

- Vessel responds to injury with vasoconstriction of smooth muscle in vessel wall
- Triggered by:
  - Direct injury to vascular smooth muscle
  - Chemicals released by endothelial cells and platelets
  - Pain reflexes
- Most effective in smaller blood vessels not large arteries or veins
- Can significantly reduce blood flow until other mechanisms can kick in
Step 2: Platelet Plug Formation

- Platelets stick to collagen fibers that are exposed when a vessel’s layered wall is damaged
  - Intact vessel walls have no exposed collagen and release paracrine inhibitors of aggregation
- Platelets adhering to free collagen are further bound by plasma protein von Willebrand factor
- Platelets activate, change shape which stimulates more aggregation, release granules which act as messengers in plug formation and clotting
- Platelet plugs are fine for small vessel tears, but larger breaks in vessels need additional step

Step 3: Coagulation

- Blood clotting reinforces platelet plug with fibrin threads
  - Effective in sealing larger vessel breaks
  - Can be complete in 3-6 minutes
- CAUTION: clotting must be carefully controlled
  - Uncontrolled clotting can occlude vessels or create emboli (emboli) – both may have serious consequences
  - Clotting “cascade” requires initiating substances, aggregated platelet surface, presence of intermediate messengers, presence of Ca²⁺, presence of plasma proteins
  - Initiating substances and platelet surfaces are most concentrated at site of damage, clotting should be limited to these areas
  - Circulating substances with anticoagulant properties also suppress clotting in areas that are not damaged
- Coagulation occurs in three phases
Step 3: Coagulation (cont.)

- **Intrinsic pathway**
  - Called “intrinsic” because clotting factors are present *within* the blood
  - Triggered by negatively charged surfaces such as activated platelets, collagen, or even glass of a test tube

- **Extrinsic pathway**
  - Called “extrinsic” because factors needed for clotting are located *outside* blood
  - Triggered by exposure to *tissue factor (TF)*; also called *factor III*
  - Bypasses several steps of intrinsic pathway, so faster pathway
Clot Retraction and Fibrinolysis

- Clot must be stabilized and removed when damage has been repaired
- **Clot retraction**
  - Platelet contraction pulls on attached fibrin strands
  - Draws ruptured blood vessel edges together
  - Initiation of repair:
    - Platelet-derived growth factor (PDGF) – repair underlying CT
    - Vascular endothelial growth factor – repair endothelium
- **Fibrinolysis**
  - Process whereby clots are removed after repair is completed
  - Begins within 2 days and continues for several days until clot is dissolved
  - Plasminogen, plasma protein that is trapped in clot, is converted to plasmin, a fibrin-digesting enzyme