Introduction to the Cardiovascular System

- A circulating transport system
  - A pump (the heart)
  - A conducting system (blood vessels)
- A fluid medium (blood)
  - Is specialized fluid of connective tissue
  - Contains cells suspended in a fluid matrix
Introduction to the Cardiovascular System

- To transport materials to and from cells
  - Oxygen and carbon dioxide
  - Nutrients
  - Hormones
  - Immune system components
  - Waste products
Functions of Blood

- Transport of dissolved substances
- Regulation of pH and ions
- Restriction of fluid losses at injury sites
- Defense against toxins and pathogens
- Stabilization of body temperature
Physical Characteristics of Blood

- **Whole Blood**
  - **Plasma**
    - Fluid consisting of:
      - water
      - dissolved plasma proteins
      - other solutes
  - **Formed elements**
    - All cells and solids
Physical Characteristics of Blood

Figure 19–1 The Composition of Whole Blood
## Physical Characteristics of Blood

### Figure 19–1b The Composition of a Typical Sample of Plasma

#### Plasma Proteins
- **Albumins (60%)**: Major contributors to osmotic pressure of plasma; transport lipids, steroid hormones.
- **Globulins (35%)**: Transport ions, hormones, lipids; immune function.
- **Fibrinogen (4%)**: Essential component of clotting system; can be converted to insoluble fibrin.
- **Regulatory proteins (<1%)**: Enzymes, proenzymes, hormones.

#### Plasma Composition
- **Plasma proteins**: 7%
- **Other solutes**: 1%
- **Water**: 92%
  - Transports organic and inorganic molecules, formed elements, and heat.

#### Other Solute Compartments
- **Electrolytes**: Normal extracellular fluid ion composition essential for vital cellular activities. Ions contribute to osmotic pressure of body fluids.
  - Major plasma electrolytes are Na⁺, K⁺, Ca²⁺, Mg²⁺, Cl⁻, HCO₃⁻, HPO₄⁻, SO₄²⁻.
- **Organic nutrients**: Used for ATP production, growth, and maintenance of cells; include lipids (fatty acids, cholesterol, glycerides), carbohydrates (primarily glucose), and amino acids.
- **Organic wastes**: Carried to sites of breakdown or excretion; include urea, uric acid, creatinine, bilirubin, ammonium ions.
Physical Characteristics of Blood

Figure 19–1c The Composition of Formed Elements of Blood
Physical Characteristics of Blood

- Three Types of Formed Elements
  - Red blood cells (RBCs) or erythrocytes
    - Transport oxygen
  - White blood cells (WBCs) or leukocytes
    - Part of the immune system
  - Platelets
    - Cell fragments involved in clotting
Physical Characteristics of Blood

- Hemopoiesis
  - Process of producing formed elements
  - By myeloid and lymphoid stem cells

- Fractionation
  - Process of separating whole blood for clinical analysis
    - Into plasma and formed elements
Physical Characteristics of Blood

Three General Characteristics of Blood

- 38°C (100.4°F) is normal temperature
- High viscosity
- Slightly alkaline pH (7.35–7.45)
Physical Characteristics of Blood

- Blood volume (liters) = 7% of body weight (kilograms)
  - Adult male: 5 to 6 liters
  - Adult female: 4 to 5 liters
Plasma

- Makes up 50–60% of blood volume
- More than 90% of plasma is water
- Extracellular fluids
  - Interstitial fluid (IF) and plasma
  - Materials plasma and IF exchange across capillary walls
    - Water
    - Ions
    - Small solutes
Plasma

- Differences between Plasma and IF
  - Levels of $O_2$ and $CO_2$
  - Concentrations and types of dissolved proteins
    - Plasma proteins do not pass through capillary walls
Plasma Proteins

- **Albumins (60%)**
  - Transport substances such as fatty acids, thyroid hormones, and steroid hormones

- **Globulins (35%)**
  - Antibodies, also called immunoglobulins
  - Transport globulins (small molecules): hormone-binding proteins, metalloproteins, apolipoproteins (*lipoproteins*), and steroid-binding proteins

- **Fibrinogen (4%)**
  - Molecules that form clots and produce long, insoluble strands of fibrin
Plasma

- Serum
  - Liquid part of a blood sample
    - In which dissolved fibrinogen has converted to solid fibrin

- Other Plasma Proteins
  - 1% of plasma
    - Changing quantities of specialized plasma proteins
    - Enzymes, hormones, and prohormones
Plasma

- Origins of Plasma Proteins
  - 90% + made in liver
  - Antibodies made by plasma cells
  - Peptide hormones made by endocrine organs
Red Blood Cells

- Red blood cells (RBCs) make up 99.9% of blood’s formed elements

- Hemoglobin
  - The red pigment that gives whole blood its color
  - Binds and transports oxygen and carbon dioxide
Red Blood Cells

- **Abundance of RBCs**
  - **Red blood cell count**: the number of RBCs in 1 microliter of whole blood
    - Male: 4.5–6.3 million
    - Female: 4.2–5.5 million
  - **Hematocrit** (packed cell volume, PCV): percentage of RBCs in centrifuged whole blood
    - Male: 40–54
    - Female: 37–47
Red Blood Cells

- Structure of RBCs
  - Small and highly specialized discs
  - Thin in middle and thicker at edge

- Importance of RBC Shape and Size
  - High surface-to-volume ratio
    - Quickly absorbs and releases oxygen
  - Discs form stacks called *rouleaux*
    - Smooth the flow through narrow blood vessels
  - Discs bend and flex entering small capillaries:
    - 7.8 µm RBC passes through 4 µm capillary
Red Blood Cells

Figure 19–2a–c The Anatomy of Red Blood Cells
Figure 19–2d The Anatomy of Red Blood Cells

(d) Sectional view of capillaries
Red Blood Cells

- Lifespan of RBCs
  - Lack nuclei, mitochondria, and ribosomes
    - Means no repair and *anaerobic* metabolism
    - Live about 120 days
Red Blood Cells

- Hemoglobin (Hb)
  - Protein molecule, that transports respiratory gases
  - Normal hemoglobin (adult male)
    - 14–18 g/dL whole blood
  - Normal hemoglobin (adult female)
    - 12–16 g/dL, whole blood
Hemoglobin Structure

- Complex quaternary structure
- Four globular protein subunits:
  - Each with one molecule of heme
  - Each heme contains one iron ion
- Iron ions
  - Associate easily with oxygen (oxyhemoglobin)
    - OR
  - Dissociate easily from oxygen (deoxyhemoglobin)
Figure 19–3 The Structure of Hemoglobin
Red Blood Cells

- Fetal Hemoglobin
  - Strong form of hemoglobin found in embryos
  - Takes oxygen from mother’s hemoglobin
Red Blood Cells

- Hemoglobin Function
  - Carries oxygen
  - With low oxygen (peripheral capillaries)
    - Hemoglobin releases oxygen
    - Binds carbon dioxide and carries it to lungs
      - Forms carbaminohemoglobin
Red Blood Cells

Figure 19–4 "Sickling" in Red Blood Cells
Red Blood Cells

- **RBC Formation and Turnover**
  - 1% of circulating RBCs wear out per day
    - About 3 million RBCs per second
  - Macrophages of liver, spleen, and bone marrow
    - Monitor RBCs
    - Engulf RBCs before membranes rupture (*hemolyze*)
Red Blood Cells

- Hemoglobin Conversion and Recycling
  - Phagocytes break hemoglobin into components
    - Globular proteins to amino acids
    - Heme to **biliverdin**
    - Iron
  - Hemoglobinuria
    - Hemoglobin breakdown products in urine due to excess hemolysis in bloodstream
  - Hematuria
    - Whole red blood cells in urine due to kidney or tissue damage
Red Blood Cells

- Iron Recycling
  - Iron removed from heme leaving biliverdin
  - To transport proteins (*transferrin*)
  - To storage proteins (*ferritin* and *hemosiderin*)
Red Blood Cells

- Breakdown of Biliverdin
  - Biliverdin (green) is converted to **bilirubin** (yellow)
    - Bilirubin is:
      - excreted by liver (bile)
      - **jaundice** is caused by bilirubin buildup
      - converted by intestinal bacteria to **urobilins** and **stercobilins**
Red Blood Cells

Figure 19–5 Recycling of Red Blood Cell Components
Red Blood Cells

- RBC Production
  - Erythropoiesis
    - Occurs only in myeloid tissue (red bone marrow) in adults
    - Stem cells mature to become RBCs
  - Hemocytoblasts
    - Stem cells in myeloid tissue divide to produce
      - Myeloid stem cells: become RBCs, some WBCs
      - Lymphoid stem cells: become lymphocytes
Red Blood Cells

- Stages of RBC Maturation
  - Myeloid stem cell
  - Proerythroblast
  - Erythroblasts
  - Reticulocyte
  - Mature RBC
Figure 19–6 Stages of RBC Maturation
Red Blood Cells

- Regulation of Erythropoiesis
  - Building red blood cells requires
    - Amino acids
    - Iron
    - Vitamins B\textsubscript{12}, B\textsubscript{6}, and folic acid:
      - pernicious anemia
        - low RBC production
        - due to unavailability of vitamin B\textsubscript{12}
# Red Blood Cells

## TABLE 19–1  RBC Tests and Related Terminology

<table>
<thead>
<tr>
<th>Test</th>
<th>Determines</th>
<th>Terms Associated with Abnormal Values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hematocrit (Hct)</td>
<td>Percentage of formed elements in whole blood</td>
<td>Polycythemia (may reflect erythrocytosis or leukocytosis)</td>
</tr>
<tr>
<td></td>
<td>Normal = 37–54%</td>
<td>Anemia</td>
</tr>
<tr>
<td>Reticulocyte count (Retic.)</td>
<td>Percentage of circulating reticulocytes</td>
<td>Reticulocytosis</td>
</tr>
<tr>
<td></td>
<td>Normal = 0.8%</td>
<td></td>
</tr>
<tr>
<td>Hemoglobin concentration (Hb)</td>
<td>Concentration of hemoglobin in blood</td>
<td>Anemia</td>
</tr>
<tr>
<td></td>
<td>Normal = 12–18 g/dL</td>
<td></td>
</tr>
<tr>
<td>RBC count</td>
<td>Number of RBCs per μL of whole blood</td>
<td>Erythrocytosis/polycythemia</td>
</tr>
<tr>
<td></td>
<td>Normal = 4.2–6.3 million/μL</td>
<td>Anemia</td>
</tr>
<tr>
<td>Mean corpuscular volume (MCV)</td>
<td>Average volume of single RBC</td>
<td>Macrocytic</td>
</tr>
<tr>
<td></td>
<td>Normal = 82–101 μm³ (normocytic)</td>
<td></td>
</tr>
<tr>
<td>Mean corpuscular hemoglobin concentration (MCHC)</td>
<td>Average amount of Hb in one RBC</td>
<td>Hyperchromic</td>
</tr>
<tr>
<td></td>
<td>Normal = 27–34 pg/μL (normochromic)</td>
<td></td>
</tr>
</tbody>
</table>

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Red Blood Cells

- Stimulating Hormones
  - Erythropoietin (EPO)
    - Also called *erythropoiesis*-stimulating hormone
    - Secreted when oxygen in peripheral tissues is low (hypoxia)
    - Due to disease or high altitude
Blood Typing

- Are cell surface proteins that identify cells to immune system
- Normal cells are ignored and foreign cells attacked

- Blood types
  - Are genetically determined
  - By presence or absence of RBC surface antigens A, B, Rh (or D)
Blood Typing

- Four Basic Blood Types
  - A (surface antigen A)
  - B (surface antigen B)
  - AB (antigens A and B)
  - O (neither A nor B)
Blood Typing

Figure 19–7a Blood Types and Cross-Reactions
Blood Typing

- Agglutinogens
  - Antigens on surface of RBCs
  - Screened by immune system
  - Plasma antibodies attack and agglutinate (clump) foreign antigens
Blood Typing

- Blood Plasma Antibodies
  - Type A
    - Type B antibodies
  - Type B
    - Type A antibodies
  - Type O
    - Both A and B antibodies
  - Type AB
    - Neither A nor B antibodies
Blood Typing

- The Rh Factor
  - Also called D antigen
  - Either Rh positive (Rh\(^+\)) or Rh negative (Rh\(^-\))
    - Only *sensitized* Rh\(^-\) blood has anti-Rh antibodies
Figure 19–9 Rh Factors and Pregnancy
Figure 19–9 Rh Factors and Pregnancy
Blood Typing

- Cross-Reactions in Transfusions
  - Also called transfusion reaction
  - Plasma antibody meets its specific surface antigen
  - Blood will agglutinate and hemolyze
  - Occur if donor and recipient blood types not compatible
Blood Typing

Figure 19–7b Blood Types and Cross-Reactions
Blood Typing

- Cross-Match Testing for Transfusion Compatibility
  - Performed on donor and recipient blood for compatibility
  - Without cross-match, type O⁻ is universal donor
Blood Typing

Figure 19–8 Blood Type Testing
# Blood Typing

## TABLE 19–2 Differences in Blood Group Distribution

<table>
<thead>
<tr>
<th>Population</th>
<th>O</th>
<th>A</th>
<th>B</th>
<th>AB</th>
<th>Rh⁺</th>
</tr>
</thead>
<tbody>
<tr>
<td>U.S. (AVERAGE)</td>
<td>46</td>
<td>40</td>
<td>10</td>
<td>4</td>
<td>85</td>
</tr>
<tr>
<td>African American</td>
<td>49</td>
<td>27</td>
<td>20</td>
<td>4</td>
<td>95</td>
</tr>
<tr>
<td>Caucasian</td>
<td>45</td>
<td>40</td>
<td>11</td>
<td>4</td>
<td>85</td>
</tr>
<tr>
<td>Chinese American</td>
<td>42</td>
<td>27</td>
<td>25</td>
<td>6</td>
<td>100</td>
</tr>
<tr>
<td>Filipino American</td>
<td>44</td>
<td>22</td>
<td>29</td>
<td>6</td>
<td>100</td>
</tr>
<tr>
<td>Hawaiian</td>
<td>46</td>
<td>46</td>
<td>5</td>
<td>3</td>
<td>100</td>
</tr>
<tr>
<td>Japanese American</td>
<td>31</td>
<td>39</td>
<td>21</td>
<td>10</td>
<td>100</td>
</tr>
<tr>
<td>Korean American</td>
<td>32</td>
<td>28</td>
<td>30</td>
<td>10</td>
<td>100</td>
</tr>
<tr>
<td>NATIVE NORTH AMERICAN</td>
<td>79</td>
<td>16</td>
<td>4</td>
<td>1</td>
<td>100</td>
</tr>
<tr>
<td>NATIVE SOUTH AMERICAN</td>
<td>100</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>100</td>
</tr>
<tr>
<td>AUSTRALIAN ABORIGINE</td>
<td>44</td>
<td>56</td>
<td>0</td>
<td>0</td>
<td>100</td>
</tr>
</tbody>
</table>
White Blood Cells

- Also called leukocytes
- Do not have hemoglobin
- Have nuclei and other organelles
- WBC functions
  - Defend against pathogens
  - Remove toxins and wastes
  - Attack abnormal cells
White Blood Cells

- WBC Circulation and Movement
  - Most WBCs in
    - Connective tissue proper
    - Lymphoid system organs
  - Small numbers in blood
    - 5000 to 10,000 per microliter
White Blood Cells

WBC Circulation and Movement

Characteristics of circulating WBCs

- Can migrate out of bloodstream
- Have amoeboid movement
- Attracted to chemical stimuli (positive chemotaxis)
- Some are phagocytic:
  - neutrophils, eosinophils, and monocytes
White Blood Cells

- Types of WBCs
  - Neutrophils
  - Eosinophils
  - Basophils
  - Monocytes
  - Lymphocytes
White Blood Cells

(a) Neutrophil
(b) Eosinophil
(c) Basophil

Figure 19–10a-c White Blood Cells
Figure 19–10d-e White Blood Cells
White Blood Cells

- Neutrophils
  - Also called polymorphonuclear leukocytes
  - 50–70% of circulating WBCs
  - Pale cytoplasm granules with
    - Lysosomal enzymes
    - Bactericides (hydrogen peroxide and superoxide)
White Blood Cells

- Neutrophil Action
  - Very active, first to attack bacteria
  - Engulf pathogens
  - Digest pathogens
    - Degranulation:
      - removing granules from cytoplasm
      - *defensins* (peptides from lysosomes) attack pathogen membranes
  - Release prostaglandins and leukotrienes
  - Form pus
White Blood Cells

- **Eosinophils**
  - Also called *acidophils*
  - 2–4% of circulating WBCs
  - Attack large parasites
  - Excrete toxic compounds
    - Nitric oxide
    - Cytotoxic enzymes
  - Are sensitive to allergens
  - Control inflammation with enzymes that counteract inflammatory effects of neutrophils and mast cells
White Blood Cells

- Basophils
  - Are less than 1% of circulating WBCs
  - Are small
  - Accumulate in damaged tissue
  - Release histamine
    - Dilates blood vessels
  - Release heparin
    - Prevents blood clotting
White Blood Cells

- **Monocytes**
  - 2–8% of circulating WBCs
  - Are large and spherical
  - Enter peripheral tissues and become macrophages
  - Engulf large particles and pathogens
  - Secrete substances that attract immune system cells and fibrocytes to injured area
White Blood Cells

- Lymphocytes
  - 20–30% of circulating WBCs
  - Are larger than RBCs
  - Migrate in and out of blood
  - Mostly in connective tissues and lymphoid organs
  - Are part of the body’s specific defense system
White Blood Cells

- Three Classes of Lymphocytes
  - T cells
    - Cell-mediated immunity
    - Attack foreign cells directly
  - B cells
    - Humoral immunity
    - Differentiate into plasma cells
    - Synthesize antibodies
  - Natural killer (NK) cells
    - Detect and destroy abnormal tissue cells (cancers)
White Blood Cells

- The Differential Count and Changes in WBC Profiles
  - Detects changes in WBC populations
  - Infections, inflammation, and allergic reactions
White Blood Cells

- WBC Disorders
  - Leukopenia
    - Abnormally low WBC count
  - Leukocytosis
    - Abnormally high WBC count
  - Leukemia
    - Extremely high WBC count
White Blood Cells

- **WBC Production**
  - All blood cells originate from hemocytoblasts
    - Which produce myeloid stem cells and lymphoid stem cells
  - **Myeloid Stem Cells**
    - Differentiate into *progenitor cells*, which produce all WBCs except lymphocytes
  - **Lymphoid Stem Cells**
    - *Lymphopoiesis*: the production of lymphocytes
White Blood Cells

- **WBC Development**
  - WBCs, except monocytes
    - Develop fully in bone marrow
  - Monocytes
    - Develop into macrophages in peripheral tissues
White Blood Cells

- Regulation of WBC Production
- Colony-stimulating factors = CSFs
  - Hormones that regulate blood cell populations:
    1. **M-CSF** stimulates monocyte production
    2. **G-CSF** stimulates granulocyte (neutrophils, eosinophils, and basophils) production
    3. **GM-CSF** stimulates granulocyte and monocyte production
    4. **Multi-CSF** accelerates production of granulocytes, monocytes, platelets, and RBCs
# White Blood Cells

<table>
<thead>
<tr>
<th>Cell</th>
<th>Abundance (average number per µL)</th>
<th>Appearance in a Stained Blood Smear</th>
<th>Functions</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>RED BLOOD CELLS</td>
<td>5.2 million (range: 4.4–6.0 million)</td>
<td>Flattened, circular cell; no nucleus, mitochondria, or ribosomes; red</td>
<td>Transport oxygen from lungs to tissues and carbon dioxide from tissues to lungs</td>
<td>Remain in bloodstream; 120-day life expectancy; amino acids and iron recycled; produced in bone marrow</td>
</tr>
</tbody>
</table>
# White Blood Cells

## SUMMARY TABLE 19–3  Formed Elements of the Blood

<table>
<thead>
<tr>
<th>Cell</th>
<th>Abundance (average number per µL)</th>
<th>Appearance in a Stained Blood Smear</th>
<th>Functions</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>WHITE BLOOD CELLS</td>
<td>7000 (range: 5000–10,000)</td>
<td>Round cell; nucleus lobed and may resemble a string of beads; cytoplasm contains large, pale inclusions</td>
<td>Phagocytic: Engulf pathogens or debris in tissues, release cytotoxic enzymes and chemicals</td>
<td>Move into tissues after several hours; may survive minutes to days, depending on tissue activity; produced in bone marrow</td>
</tr>
<tr>
<td>Neutrophils</td>
<td>4150 (range: 1800–7300) Differential count: 50–70%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Eosinophils</td>
<td>165 (range: 0–700) Differential count: 2–4%</td>
<td>Round cell; nucleus generally in two lobes; cytoplasm contains large granules that generally stain bright red</td>
<td>Phagocytic: Engulf antibody-labeled materials, release cytotoxic enzymes, reduce inflammation; increase in allergic and parasitic situations</td>
<td>Move into tissues after several hours; survive minutes to days, depending on tissue activity; produced in bone marrow</td>
</tr>
<tr>
<td>Basophils</td>
<td>44 (range: 0–150) Differential count: &lt;1%</td>
<td>Round cell; nucleus generally cannot be seen through dense, blue-stained granules in cytoplasm</td>
<td>Enter damaged tissues and release histamine and other chemicals that promote inflammation</td>
<td>Survival time unknown; assist mast cells of tissues in producing inflammation; produced in bone marrow</td>
</tr>
</tbody>
</table>
**White Blood Cells**

<table>
<thead>
<tr>
<th>SUMMARY TABLE 19–3</th>
<th>Formed Elements of the Blood</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cell</strong></td>
<td><strong>Abundance</strong> (average number per µL)</td>
</tr>
<tr>
<td>Monocytes</td>
<td>456 (range: 200–950) Differential count: 2–8%</td>
</tr>
<tr>
<td>Lymphocytes</td>
<td>2185 (range: 1500–4000) Differential count: 20–30%</td>
</tr>
</tbody>
</table>
# White Blood Cells

<table>
<thead>
<tr>
<th>Cell</th>
<th>Abundance (average number per µL)</th>
<th>Appearance in a Stained Blood Smear</th>
<th>Functions</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>PLATELETS</td>
<td>350,000 (range: 150,000–500,000)</td>
<td>Round to spindle-shaped cytoplasmic fragment; contain enzymes, proenzymes, actin, and myosin; no nucleus</td>
<td>Hemostasis: Clump together and stick to vessel wall (platelet phase); activate intrinsic pathway of coagulation phase</td>
<td>Remain in bloodstream or in vascular organs; remain intact for 7–12 days; produced by megakaryocytes in bone marrow</td>
</tr>
</tbody>
</table>
White Blood Cells

Figure 19–11 The Origins and Differentiation of Formed Elements
Platelets

- Cell fragments involved in human clotting system
  - Nonmammalian vertebrates have thrombocytes (nucleated cells)
- Circulate for 9–12 days
- Are removed by spleen
- 2/3 are reserved for emergencies
Platelets

- **Platelet Counts**
  - 150,000 to 500,000 per microliter
- **Thrombocytopenia**
  - Abnormally low platelet count
- **Thrombocytosis**
  - Abnormally high platelet count
Three Functions of Platelets:

1. Release important clotting chemicals
2. Temporarily patch damaged vessel walls
3. Actively contract tissue after clot formation
Platelets

- **Platelet Production**
  - Also called *thrombocytopoiesis*
    - Occurs in bone marrow
  - **Megakaryocytes**
    - Giant cells in bone marrow
    - Manufacture platelets from cytoplasm
Platelets

- Platelet Production
  - Hormonal controls
    - Thrombopoietin (TPO)
    - Interleukin-6 (IL-6)
    - Multi-CSF
Hemostasis

- Hemostasis is the cessation of bleeding
- Consists of three phases
  - Vascular phase
  - Platelet phase
  - Coagulation phase
Hemostasis

- The Vascular Phase
  - A cut triggers vascular spasm that lasts 30 minutes
  - Three steps of the vascular phase
    - Endothelial cells contract:
      - expose basal lamina to bloodstream
    - Endothelial cells release:
      - chemical factors: ADP, tissue factor, and prostacyclin
      - local hormones: endothelins
      - stimulate smooth muscle contraction and cell division
    - Endothelial plasma membranes become “sticky”:
      - seal off blood flow
Hemostasis

The Platelet Phase

- Begins within 15 seconds after injury

  - **Platelet adhesion** (attachment)
    - To sticky endothelial surfaces
    - To basal laminae
    - To exposed collagen fibers

- Platelet aggregation (stick together)
  - Forms **platelet plug**
  - Closes small breaks
Hemostasis

- **Platelet Phase**
  - Activated platelets release clotting compounds
    - Adenosine diphosphate (ADP)
    - Thromboxane A$_2$ and serotonin
    - Clotting factors
    - Platelet-derived growth factor (PDGF)
    - Calcium ions
Hemostasis

- Factors that limit the growth of the platelet plug
  - **Prostacyclin**, released by endothelial cells, inhibits platelet aggregation
  - Inhibitory compounds released by other white blood cells
  - Circulating enzymes break down ADP
  - Negative (inhibitory) feedback: from serotonin
  - Development of blood clot isolates area
Hemostasis

Figure 19–12 The Vascular and Platelet Phases of Hemostasis.
Hemostasis

- The Coagulation Phase
  - Begins 30 seconds or more after the injury
  - Blood clotting (coagulation)
    - Cascade reactions:
      - chain reactions of enzymes and proenzymes
      - form three pathways
      - convert circulating fibrinogen into insoluble fibrin
Hemostasis

- Clotting Factors
  - Also called procoagulants
  - Proteins or ions in plasma
  - Required for normal clotting
# Hemostasis

## TABLE 19–4 Clotting Factors

<table>
<thead>
<tr>
<th>Factor</th>
<th>Structure</th>
<th>Name</th>
<th>Source</th>
<th>Concentration in Plasma (μg/mL)</th>
<th>Pathway</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Protein</td>
<td>Fibrinogen</td>
<td>Liver</td>
<td>2500–3500</td>
<td>Common</td>
</tr>
<tr>
<td>II</td>
<td>Protein</td>
<td>Prothrombin</td>
<td>Liver, requires vitamin K</td>
<td>100</td>
<td>Common</td>
</tr>
<tr>
<td>III</td>
<td>Lipoprotein</td>
<td>Tissue factor (TF)</td>
<td>Damaged tissue, activated platelets</td>
<td>0</td>
<td>Extrinsic</td>
</tr>
<tr>
<td>IV</td>
<td>Ion</td>
<td>Calcium ions</td>
<td>Bone, diet, platelets</td>
<td>100</td>
<td>Entire process</td>
</tr>
<tr>
<td>V</td>
<td>Protein</td>
<td>Proaccelerin</td>
<td>Liver, platelets</td>
<td>10</td>
<td>Extrinsic and intrinsic</td>
</tr>
<tr>
<td>VI</td>
<td>(No longer used)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>VII</td>
<td>Protein</td>
<td>Proconvertin</td>
<td>Liver, requires vitamin K</td>
<td>0.5</td>
<td>Extrinsic</td>
</tr>
<tr>
<td>VIII</td>
<td>Protein factor (AHF)</td>
<td>Antihemophilic</td>
<td>Platelets, endothelial cells</td>
<td>15</td>
<td>Intrinsic</td>
</tr>
<tr>
<td>IX</td>
<td>Protein factor</td>
<td>Plasma thromboplastin</td>
<td>Liver, requires vitamin K</td>
<td>3</td>
<td>Intrinsic</td>
</tr>
<tr>
<td>X</td>
<td>Protein</td>
<td>Stuart–Prower factor</td>
<td>Liver, requires vitamin K</td>
<td>10</td>
<td>Extrinsic and intrinsic</td>
</tr>
<tr>
<td>XI</td>
<td>Protein antecedent (PTA)</td>
<td>Plasma thromboplastin</td>
<td>Liver</td>
<td>&lt;5</td>
<td>Intrinsic</td>
</tr>
<tr>
<td>XII</td>
<td>Protein</td>
<td>Hageman factor</td>
<td>Liver</td>
<td>&lt;5</td>
<td>Intrinsic; also activates plasmin</td>
</tr>
<tr>
<td>XIII</td>
<td>Protein factor (FSF)</td>
<td>Fibrin-stabilizing</td>
<td>Liver, platelets</td>
<td>20</td>
<td>Stabilizes fibrin, slows fibrinolysis</td>
</tr>
</tbody>
</table>
Hemostasis

- Three Coagulation Pathways
  - **Extrinsic pathway**
    - Begins in the vessel wall
    - Outside bloodstream
  - **Intrinsic pathway**
    - Begins with circulating proenzymes
    - Within bloodstream
  - **Common pathway**
    - Where intrinsic and extrinsic pathways converge
Hemostasis

- The Extrinsic Pathway
  - Damaged cells release tissue factor (TF)
  - TF + other compounds = enzyme complex
  - Activates Factor X
Hemostasis

- The Intrinsic Pathway
  - Activation of enzymes by collagen
  - Platelets release factors (e.g., PF–3)
  - Series of reactions activates Factor X
Hemostasis

- The Common Pathway
  - Forms enzyme prothrombinase
  - Converts prothrombin to thrombin
  - Thrombin converts fibrinogen to fibrin
Hemostasis

- Stimulates formation of tissue factor
  - Stimulates release of PF-3
  - Forms positive feedback loop (intrinsic and extrinsic)
    - Accelerates clotting
Figure 19–13a The Coagulation Phase of Hemostasis
Hemostasis

Figure 19–13b The Coagulation Phase of Hemostasis
Hemostasis

- Clotting: Area Restriction
  - Anticoagulants (plasma proteins)
    - Antithrombin-III
    - Alpha-2-macroglobulin
  - Heparin
  - Protein C (activated by thrombomodulin)
  - Prostacyclin
Hemostasis

- Calcium Ions, Vitamin K, and Blood Clotting
  - Calcium ions (Ca$^{2+}$) and vitamin K are both essential to the clotting process
Hemostasis

- **Clot Retraction**
  - After clot has formed
    - Platelets contract and pull torn area together
  - Takes 30–60 minutes
Fibrinolysis

- Slow process of dissolving clot
  - Thrombin and tissue plasminogen activator (t-PA):
    - activate plasminogen

- Plasminogen produces plasmin
  - Digests fibrin strands