Cardiovascular System

Blood

Introduction

• Circulatory system – 2 divisions
  — Blood vascular system
    • Blood
    • Heart
    • Blood vessels
  — Lymphatic system
    • Lymph
    • Lymph vessels
    • Lymph nodes

Blood

• Components
  — Cellular portion = formed elements
  — Fluid portion = plasma

• Arterial = blood leaving the heart
  — Highly oxygenated
    • Exception: pulmonary artery

• Venous = blood returning to the heart
  — Depleted of oxygen
    • Exception: pulmonary vein

Blood

• ~8% of body weight
• Average volume
  — Males: 5–6 L
  — Females: 4–5 L
  — ~10% taken in a blood donation
• ~92% water

Blood

• More viscous than water
• Color depends on oxygenation
  — More oxygen = bright red
  — Less oxygen = dark red
• pH
  — 7.35–7.45
  — Maintained through several buffer systems
• Temperature
  — 38°C (99° F)
Functions of Blood

1. Transport
   - Oxygen and carbon dioxide
   - Nutrients
   - Metabolic wastes
   - Hormones and enzymes

2. Regulation
   - Body temperature
   - pH
   - Water content of cells through distribution of dissolved ions

3. Protection against
   - Fluid loss
     - Plasma proteins and platelets initiate clot formation
   - Infection (immune response)
     - Antibodies
     - WBCs

Structure of Blood

- Formed elements 45%
- Plasma 55%

Plasma

- Water 90%
  - Solvent
- Proteins 7-9%
  - Albumin
    - Made in the liver
    - Viscosity
    - Osmolarity – keeps fluid from leaking out of your blood vessels
  - Globulins
    - Transport of fat-soluble compounds
    - Immunity (immunoglobulins)
    - Fibrinogen
    - Clotting
Plasma

- Electrolytes
  - Na⁺, K⁺, Ca²⁺, Cl⁻, HCO₃⁻
- Nutrients
  - Glucose, carbohydrates, amino acids, lipids
- Gases
  - O₂ and CO₂
- Wastes
  - Lactic acid from muscles
  - Urea, ketones, uric acid from liver

Formed Elements

- Erythrocytes
  - No nuclei or organelles
- Leukocytes
  - 5 types
    - Granular
    - Agranular
- Thrombocytes (platelets)
  - Cell fragments

Formed Elements

- General
  - Most survive in the bloodstream for only a few days
  - RBC’s = 120 days
  - Most blood cells originate in bone marrow, are amitotic

Erythrocytes

- Appearance
  - Biconcave discs
  - Non-nucleated
  - 8 nm in diameter
Erythrocytes

- Properties
  - Filled with hemoglobin (Hb) for gas transport
  - Major factor contributing to blood viscosity
  - Survive 120 days
- Hematocrit (ratio rbc volume:total blood volume)
  - Males 47%
  - Females 42%

Erythrocytes

- **Gas transport**
  - Biconcave shape
  - Larger surface area
  - Essentially bags of hemoglobin
  - 33% of weight
  - No mitochondria
    - ATP production is anaerobic (no O$_2$ is used in generation of ATP)

Erythrocytes

- **Hemoglobin structure**
  - Globin: protein
  - Heme: iron
- Each Hb molecule can transport 4 O$_2$
- Each RBC has about 250 million Hb molecules!

Erythrocytes

- **Hemoglobin roles**
  - O$_2$ loading in the lungs
  - O$_2$ unloading in the tissues
  - CO$_2$ loading in the tissues
**CO Poisoning**

- Hemoglobin binds to CO 200X more strongly than O₂
- Reduces oxygen carrying capacity of blood
- Leads to slow suffocation
- Sources of CO = wherever carbon-containing fuels burn
  - Exhaust fumes
  - Cigarette smoke
  - Furnaces, fireplaces
  - Water heaters
  - Clothes dryers
  - Power tools
  - Lawn equipment

**Hematopoiesis**

- Blood cell formation = hematopoiesis
- Red blood cell formation = erythropoiesis
- Embryo = yolk sac
- Fetus = liver
- After birth = red bone marrow

**Erythropoiesis**

- Spongy bone
  - Sternum, ribs, cranium
- Epiphyses
  - Femur and humerus
- Vertebral bodies

**Hematopoiesis**

**Erythropoiesis**

**Hematopoiesis**

**Erythropoiesis**

**Erythropoiesis**

Figure 17.5

Stem cell

Committed cell

Developmental pathway

Phase 1: Ribosome synthesis

Phase 2: Hemoglobin accumulation

Phase 3: Ejection of nucleus

Nucleus being expelled from a forming red blood cell
Erythropoiesis

- Regulation
  - Too few RBCs leads to tissue hypoxia
  - Too many RBCs increases blood viscosity
  - Balance between RBC production and destruction depends on
    - Hormonal controls (renal erythropoietic factor)
    - Adequate supplies of iron, amino acids and B vitamins

- Hormonal control
  - Hypoxemia
    - Kidneys release REF
  - Plasma protein converted to erythropoietin (EPO)
  - RBC production stimulated in bone marrow

Erythropoiesis

- EPO is used to treat anemia due to kidney failure or cancer treatment
  - More rapid maturation of committed bone marrow cells
  - Increased circulating reticulocyte count in 1–2 days

Erythrocytes

- Fate
  - Life span
  - Old RBCs become fragile and Hb begins to degenerate
  - Macrophages engulf dying RBCs in the spleen
Leukocytes

- Make up <1% of total blood volume
- Defense

Diapedesis

- Leukocytes can move against the direction of bloodflow
- Exit the circulatory system and migrate to sites of injury or infection

Leukocytes

- Granulocytes
  - Neutrophils, eosinophils and basophils
    - Cytoplasmic granules
    - Larger and shorter-lived than RBCs
    - Lobed nuclei
    - All are capable of diapedesis
    - All phagocytic to some degree
Neutrophils
- AKA: Polymorphonuclear leukocytes (PMNs)
- Most numerous WBC
- Granules contain hydrolytic enzymes
  - Bacteria slayers
    - Numbers increase during acute infection

Eosinophils
- Granules
  - Antihistamines
  - Lysozyme like substances
  - Cytokines
- Defend against parasites, certain viruses
- Allergic response
  - Accumulate in nasal mucosa in allergic rhinitis

Basophils
- Rare WBC
- Large, purplish-black granules
  - Histamine
    - Inflammatory chemical vasodilation
    - Increases capillary permeability
    - Attracts other WBC’s to inflamed sites
  - Heparin
    - Prevents clotting

Mast Cells
- Another rare WBC
- May have lobed or large round nucleus
- Abundant large, purplish-black granules
  - Histamine
- Largely known for role in anaphylaxis
- Also important in wound healing, angiogenesis, blood-brain barrier function
Mast Cells
- Anaphylaxis involves massive degranulation of mast cells
- Chemicals from basophils then amplify the inflammation

Mast Cells vs Basophils

Leukocytes
- Agranulocytes
  - Lymphocytes and monocytes
    - Lack visible cytoplasmic granules
    - Lymphocytes = spherical nucleus
    - Monocytes = U-shaped or kidney-shaped nucleus

Figure 17.10d, e
(d) Small lymphocyte; large spherical nucleus
(e) Monocyte; kidney-shaped nucleus

Lymphocytes
- Nuclei
  - Large, dark purple
- Lymphoid tissue
  - Few circulate in the blood
- Crucial to immunity
  - Antibodies
- 2nd most common WBC

Lymphocytes
- Three types
  - T cells
    - Act against virus-infected cells and tumor cells
  - B cells
    - Give rise to plasma cells
  - Natural killer (NK) cells
    - Innate immune response, viral infection
Monocytes

- Largest leukocyte
- Phagocytic
- Nuclei
  - Dark purple-staining, U- or kidney shaped

Monocytes

Leave circulation → enter tissues → macrophages

- Actively phagocytic cells
  - Viruses
  - Intracellular bacterial parasites
  - Chronic infections

Arrive later than neutrophils but arrive in larger numbers and destroy more microbes

Platelets (Thrombocytes)

- Small fragments of cells
- Platelet plug (clot)
  - Helps seal breaks in blood vessels

Stem cell Developmental pathway

- Megakaryocytes are huge!
Complete Blood Count (CBC)

- Screens for anemia and various infections
- Includes
  - RBC count
  - WBC count with differential
  - Platelets
  - Hematocrit (% of RBC)
  - Hemoglobin

CBC

- Normal WBC – 4,000 – 11,000 cells/mm³
  - Leukocytosis = increase in WBC
    - Indicates infection
  - Leukopenia = decrease in WBC
    - Viral infections, chemotherapy, some cancers, some mineral deficiencies
    - Leaves a person vulnerable to infection

Differential – indicates relative numbers of WBC

- Useful for diagnosing disease
- Normal:
  - Neutrophils: 40-70%
  - Eosinophils: 1-4%
  - Basophils: 0.5-1%
  - Lymphocytes: 20-45%
  - Monocytes: 4-8%

Erythrocyte Tests

- Men 5.1-5.8 million cells/mm³
- Women 4.3-5.2 million cells/mm³
- Variations
  - Anemia
  - Polycythemia

Erythrocyte Disorders

- Anemia
  - Blood has abnormally low O₂ carrying capacity
  - Leads to fatigue, paleness, shortness of breath, chills

Causes of Anemia

1) Insufficient erythrocytes
2) Low hemoglobin content
3) Abnormal hemoglobin
Causes of Anemia

1. Insufficient erythrocytes
   - Hemorrhagic anemia: acute or chronic loss of blood
   - Hemolytic anemia: RBCs rupture prematurely
   - Aplastic anemia: destruction or inhibition of red bone marrow (usually due to radiation or chemotherapy exposure)

Causes of Anemia

2. Low hemoglobin content
   - Iron-deficiency anemia
     • Secondary result of hemorrhagic anemia or
     • Inadequate intake of iron-containing foods or
     • Impaired iron absorption
     • Can lead to microcytes (small RBC)

Causes of Anemia

3. Abnormal hemoglobin
   - Pernicious anemia
     • Deficiency of vitamin B₁₂
       - Necessary for formation of normal RBC's
     • Macrocytes
     • Lack of intrinsic factor in stomach?
       - Made by parietal cells in stomach, necessary for B₁₂ absorption

Causes of Anemia

3. Abnormal hemoglobin
   - Thalassemias
     • Absent or faulty globin chain
     • RBCs are thin, delicate, and deficient in hemoglobin

Causes of Anemia

3. Abnormal hemoglobin
   - Sickle-cell anemia
     • Defective gene codes for abnormal hemoglobin (HbS)
     • Causes RBCs to become sickle shaped in low-oxygen situations

Figure 17.8

(a) Normal erythrocyte has normal hemoglobin amino acid sequence in the beta chain.

(b) Sickled erythrocyte results from a single amino acid change in the beta chain of hemoglobin.
Erythrocyte Disorders

• **Polycythemia**
  - Increased RBCs  → increased blood viscosity
  - Causes
    • Polycythemia vera
    • Secondary polycythemia
      – Less O₂ is available (high altitude)
      – EPO production increases
      – Blood doping

Leukocyte Disorders

• **Leukopenia**
  - Chemotherapy

• **Leukocytosis**
  - Infection
  - Leukemia

Leukemia

• Bone marrow occupied with cancerous leukocytes
  - Immature non-functional WBC's in the bloodstream

• Death from internal hemorrhage and infections

• Treatments
  - Irradiation
  - Antileukemic drugs
  - Stem cell transplants
Leukemia

- Leukemia
  - Acute leukemia
    - Blast-type cells and primarily affects children
  - Chronic leukemia
    - Older people

Infectious Mononucleosis

- Epstein-Barr Virus
  - Increased agranulocytes
- Typically infects young adults
  - Healthy individuals recover in 2-3 weeks

Blood Types

- Cell surface antigens
  - Proteins
- Antigen-antibody interactions

Human Blood Groups

- At least 30 types of RBC glycoprotein antigens exist
  - Perceived as foreign if transfused blood is mismatched
  - Unique to each individual
  - Promoters of agglutination
- Presence or absence of each antigen is used to classify blood cells into different groups

Blood Groups

- ABO and Rh blood groups
  - Vigorous transfusion reactions
- Other blood groups
  - MNS, Duffy, Kell and Lewis
    - Usually weak antibody-antigen interactions

ABO Blood Groups

- Types A, B, AB, and O
  - Based on the presence or absence of A and B antigens on the surface of the RBC's
  - Blood may contain anti-A or anti-B antibodies (naturally, without prior exposure)

*Antibodies to all other antigens are only produced after exposure to the antigen*
Transfusion Reactions

- Occur if mismatched blood is transfused
- Donor’s cells
  - Attacked by the recipient’s plasma antibodies
  - Rupture and release free hemoglobin into the bloodstream
- Result
  - Diminished oxygen-carrying capacity
  - Hemoglobin in kidney tubules — renal failure

Terminology

- Used to distinguish from adaptive immune antibodies
- Agglutinogen = antigen
- Agglutinins = antibody

ABO Blood Typing

<table>
<thead>
<tr>
<th>Blood Type Being Tested</th>
<th>RBC Agglutinogens</th>
<th>Serum Reaction</th>
</tr>
</thead>
<tbody>
<tr>
<td>AB</td>
<td>A and B</td>
<td>+ +</td>
</tr>
<tr>
<td>B</td>
<td>B</td>
<td>– +</td>
</tr>
<tr>
<td>A</td>
<td>A</td>
<td>+ –</td>
</tr>
<tr>
<td>O</td>
<td>None</td>
<td>– –</td>
</tr>
</tbody>
</table>

Blood being tested

- Type AB (contains agglutinogens A and B; agglutinates with both sera)
- Type A (contains agglutinogen A; agglutinates with anti-A)
- Type B (contains agglutinogen B; agglutinates with anti-B)
- Type O (contains no agglutinogens; does not agglutinate with either serum)

Red Blood Cell Compatibility Table

<table>
<thead>
<tr>
<th>Recipient</th>
<th>Donor</th>
</tr>
</thead>
</table>
| O−        | O+    | Y
| O−        | A−    | Y
| O−        | A+    | Y
| O−        | B−    | Y
| O−        | B+    | Y
| O−        | AB−   | Y
| O−        | AB+   | Y
| O+        | A−    | Y
| O+        | A+    | Y
| O+        | B−    | Y
| O+        | B+    | Y
| O+        | AB−   | Y
| O+        | AB+   | Y
| A−        | A−    | Y
| A−        | A+    | Y
| A−        | B−    | Y
| A−        | B+    | Y
| A−        | AB−   | Y
| A−        | AB+   | Y
| A+        | A−    | Y
| A+        | A+    | Y
| A+        | B−    | Y
| A+        | B+    | Y
| A+        | AB−   | Y
| A+        | AB+   | Y
| B−        | A−    | Y
| B−        | A+    | Y
| B−        | B−    | Y
| B−        | B+    | Y
| B−        | AB−   | Y
| B−        | AB+   | Y
| B+        | A−    | Y
| B+        | A+    | Y
| B+        | B−    | Y
| B+        | B+    | Y
| B+        | AB−   | Y
| B+        | AB+   | Y
| AB−       | A−    | Y
| AB−       | A+    | Y
| AB−       | B−    | Y
| AB−       | B+    | Y
| AB−       | AB−   | Y
| AB−       | AB+   | Y
| AB+       | A−    | Y
| AB+       | A+    | Y
| AB+       | B−    | Y
| AB+       | B+    | Y
| AB+       | AB−   | Y
| AB+       | AB+   | Y

Y = no adverse reaction
Rh Factor

- 45 different Rh agglutinogens (Rh factors)
  - C, D and E are most common
  - Rh\(^+\) indicates presence of D

- Anti-Rh antibodies are not spontaneously formed in Rh\(^-\) individuals
  - Antibodies form if an Rh\(^-\) individual receives Rh\(^+\) blood
  - Second exposure to Rh\(^+\) blood  \(\rightarrow\) transfusion reaction

Erythroblastosis fetalis

- Rh\(^-\) mother carries Rh\(^+\) fetus
  - Synthesize anti-Rh antibodies
  - Second pregnancy anti-Rh antibodies cross the placenta and destroy the RBCs of an Rh\(^+\) fetus

- RhoGAM serum
  - anti-Rh can prevent the Rh\(^-\) mother from making antibodies
  - Complexes with fetal RBCs in maternal blood supply before maternal antibody production can be activated
  - The baby can be treated with prebirth transfusions and exchange transfusions after birth

Hemolytic Disease

- Rh blood group
  - People whose RBCs have the Rh antigen are Rh\(^+\)
  - People who lack the Rh antigen are Rh\(^-\)
  - Normally blood plasma does not contain anti-RH antibodies
  - Hemolytic disease of the newborn (HDN) - blood from Rh\(^+\) fetus passes to Rh\(^-\) mother through placenta or during birth = anti-Rh antibodies made
    - Affect is on second Rh\(^+\) baby

Blood Clotting

- Largely dependent on platelets

Figure 17.12

Stem cell Developmental pathway

- Hemocytoblast
  - Megakaryoblast
  - Promegakaryocyte
  - Megakaryocyte
  - Platelets
Hemostasis

Fast series of reactions for stoppage of bleeding
1. Vascular spasm
   - Vasoconstriction triggered by prostaglandins
2. Platelet plug formation
3. Coagulation (blood clotting)

Vascular Spasm

- Vasoconstriction of damaged blood vessel
  - Triggered by
    - Direct injury
    - Chemicals released by endothelial cells and platelets

Platelet Plug

- Platelets attracted to injured vessel wall
  - Collagen and glycoprotein
  - Actin and myosin

Coagulation

- Blood is transformed from a liquid to a gel
- Reinforces platelet plug

Coagulation

<table>
<thead>
<tr>
<th>Damaged cells, platelets</th>
<th>release</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thromboplastin (enzyme)</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Prothrombin (inactive proenzyme)</th>
<th>Thrombin (active enzyme)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fibrinogen (soluble, globular)</td>
<td>Fibrin (insoluble, stringy)</td>
</tr>
</tbody>
</table>
Clinical Considerations

- **Bleeding disorders**
  - Prevent normal clot formation

- **Thromboembolic disorders**
  - Undesirable clot formation

**Bleeding Disorders**

- **Hemophilia**
  - Several similar hereditary bleeding disorders
  - Symptoms
    - Prolonged bleeding
  - Treated
    - Plasma transfusions
    - Injection of missing factors

**Bleeding Disorders**

- **Thrombocytopenia**
  - Deficiency of circulating platelets
  - Causes
    - Dehydration, vitamin B12 deficiency, bone marrow disease, leukemia, liver failure, sepsis, Dengue fever, immune diseases, some medications, Lyme disease, snake bites
  - Symptoms
    - Spontaneous bleeding, petechiae
  - Treatment
    - Transfusion of concentrated platelets

**Thromboembolic Conditions**

- **Thrombus**: clot that develops and persists in an unbroken blood vessel
  - May block circulation, leading to tissue death

- **Embolus**: a thrombus freely floating in the blood stream
  - Pulmonary emboli
  - Cerebral emboli

**Thromboembolic Conditions**

- **Atherosclerosis**, inflammation, sedentary states

- **Prevention**
  - Aspirin
  - Heparin
  - Warfarin (Coumadin)
    - Important medication
    - Also the active ingredient in some rat poisons