Biol. 2402
Chapter 17
Cardiovascular & Blood

CVS and Public Health

The 10 Leading Causes of Death as a Percentage of All Deaths
United States, 1990 and 1996

1900
Pneumonia
Tuberculosis
Diabetes
Heart Disease
Stoke
Struma
Liver Disease
Varies
Cancer
Cerebral
Septicemia
Chronic Liver Disease

1996
Heart Disease
Cancer
Stroke
Chronic Liver Disease
Accidents
Pneumonitis/hemorrhage
Diabetes
HIV
Suicide

The average life expectancy in 1900 was 47.3 years of age. In 1990, it was 73.7 years of age.

SOURCE: CDC, National Center for Health Statistics

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CVS and Public Health

Total Cardiovascular Disease Deaths, 1996
Age-adjusted death rates per 100,000 population

- 127-149
- 150-164
- 165-191
- 192-231
- United States - 172

Source: National Vital Statistics System, National Center for Health Statistics, CDC

Cardio Vascular System
Functions of Blood

- Transportation of dissolved gases, nutrients, hormones, and metabolic wastes
- Regulation of the pH and electrolyte composition of interstitial fluids throughout the body
- Restriction of fluid losses
- Defense against toxins and pathogens
- Stabilization of body temperature

Blood and Transportation

- Red blood cells are packed with the protein hemoglobin (Hb) which carries $O_2$
- $CO_2$ is carried by Hb, and dissolved in plasma in multiple ways
- Nutrients absorbed at the GI tract, or released by the liver or adipocytes, are distributed by blood
- Hormones (blood-borne chemical messengers) are transported from the endocrine glands where they’re produced to their target organs via the bloodstream
- Metabolic wastes produced by tissue cells are absorbed by the blood and carried to the kidneys for excretion
**Blood and Regulation**

- Blood absorbs heat from active skeletal muscles and distributes it to other tissues.
- If body $T^\circ$ is already high, that heat will be lost across the skin surface. If body $T^\circ$ is too low, that heat will be directed to the brain and to other $T^\circ$ sensitive organs.
- The blood absorbs and neutralizes the acids generated by active tissues (e.g., lactic acid from skeletal muscles).
- The blood acts as both a conduit and reservoir for important electrolytes ($\text{Na}^+$, $\text{Ca}^{2+}$, etc.).
- Blood volume is regulated in response to the body's water levels.

The above represents a relative distribution of blood in response to warm and cold ambient temperatures.

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**Blood Characteristics**

- Adult male contains 5 - 6 L
- Adult female contains 4 - 5 L
- $T^\circ$ is about 100.4° F
  - *Is this higher or lower than normal body $T^\circ$?*
- 5 times as viscous as water
  - *Is it more or less resistant to flow than water?*
  - *What accounts for its viscosity?*
- pH ranges from 7.35 – 7.45 (slightly alkaline)
- Color ranges from scarlet (oxygenated blood) to a deep red (deoxygenated blood).
Blood Composition

Whole Blood

Plasma (46-63%)
- 1. Water (92%)
- 2. Plasma Proteins (7%)
- 3. Other Solute (1%)

Formed Elements (37-54%)
- 1. Red Blood Cells (99.9%)
- 2. Platelets (0.1%)
- 3. White Blood Cells

Blood Composition

Blood

- Plasma
- Buffy coat
- Red blood cells

Plasma (20-40%)
- Fluid portion of blood
- Contains: 91-98% water, albumin, globulin, used to transport nutrients, hormones, clotting factors, and pH balance

Red Cells (40-45%)
- Transports oxygen from the lungs to all tissues of the body and returns carbon dioxide back to the lungs

White Cells
- Protect against diseases & infections

Platelets
- Small platelet-shaped cells that clump together to help form blood clots upon bleeding occurs
Plasma Water (92%) 

Plasma Proteins (7%) 

Other Solutes (1%) 

Transports, organic and inorganic molecules, formed elements, and heat 

Albumins (60%): Contribute to plasma osmotic pressure; Transport lipids, steroid hormones 

Globulins (35%): Transport ions, hormones, lipids; Immune function 

Fibrinogen (4%): Essential component of clotting system 

Regulatory Proteins (<1%): Enzymes, Hormones 

Electrolytes: Ions necessary for vital cellular activity. Contribute to osmotic pressure of body fluids. Major electrolytes are Na+, K+, Ca2+, Mg2+, Cl-, HCO3-, HPO42-, SO42-. 

Organic Nutrients: Used for ATP production, cell growth and maintenance; Includes lipids, carbohydrates, and amino acids 

Organic Wastes: Carried to sites of breakdown or excretion; Includes urea, uric acid, creatinine, bilirubin, and ammonium ions 

The Formed Elements 

- 95% Red blood cells (erythrocytes) 
- 4.9% White blood cells (leukocytes) 
  - Granulocytes 
    - Neutrophils 
    - Eosinophils 
    - Basophils 
  - Agranulocytes 
    - Lymphocytes 
    - Monocytes 
- Platelets (thrombocytes)
Hematopoiesis

• is the process blood cell development
• occurs in red bone marrow of long and flat bones
• all blood cell originate from a **pluripotent hematopoietic stem cell or hemocytoblast**
• differentiation of these stem cells is regulated by hormones, cytokines and paracrine agents
• all of these factors are called **hematopoietic growth factors**

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Hematopoiesis

- All blood cells develop from stem cells called hemocytoblasts
- Interleukin-7 stimulates formation of Lymphoid stem cells
  - they will form Lymphoid cells
- **Thrombopoetin (TPO)** stimulates the formation of Myeloid stem cells
  - they will form all the other blood cells

![Hematopoiesis Diagram](image-url)
Hematopoiesis

Hemocytoblast → Lymphoid Stem Cell → Lymphocyte

- IL-7

Myeloid Stem Cell → Megakaryocyte → Platelet
- IL-11
- TPO

Erythrocyte
- EPO

Where does all of this take place?

IL = InterLeukin
TPO = Thrombopoietin
EPO = Erythropoietin
Red Blood Cells (Erythrocytes)

- Most abundant blood cells (99.9% of formed elements)
  - In males, 1µL of blood contains 4.5-6.3 million RBCs
  - In females, 1µL of blood contains 4.2-5.5 million RBCs
- Contains the red pigment hemoglobin which binds and transports O₂ and CO₂
- Each RBC is a biconcave disc
  
  Diameter → 7.5µm  
  Thickness → 2.0µm

Contains the red pigment hemoglobin which binds and transports O₂ and CO₂

- Why a biconcave disc?
  - Provides a large surface area for O₂ entry/exit
  - Enables them to bend and flex when entering small capillaries
- RBCs lack a nucleus and most organelles.
  - Instead they are simply membranous bags of hemoglobin
  - What is a functional advantage of the fact that the RBC lacks mitochondria?

Here, we have an RBC bending to fit thru a small capillary
Hemoglobin

- Large protein consisting of 4 polypeptides
  - 2 $\alpha$ chains and 2 $\beta$ chains
- Each chain contains a single molecule of heme, an iron-containing pigment
  - The iron ion in heme is able to reversibly bind an oxygen molecule.
  - Meaning, $O_2$ can bind to Hb at the lungs and then be released at the tissues
- Based on the above, how many molecules of $O_2$ can each Hb protein bind?

Each RBC has roughly 250 million Hb molecules
Hemocytoblast | *Pluripotential stem cell*
---|---
Myeloid Stem Cell | *Could become RBC, several types of WBC or platelets*
Proerythroblast | *Destined to become an RBC*
Erythroblast | *Various stages. Actively synthesize Hb*
Reticulocyte | *Just lost its nucleus. Enters the circulation after 2d in bone marrow.*
Erythrocyte | *Mature RBC. (After a reticulocyte has been in the blood stream for 24hrs)*

**ERYTHROPOEISIS : Hematopoiesis of RBC**
Control of RBC production

- We have roughly 5.4 million RBC per microliter
- Breakdown of RBC is 1% of total RBC per day
- This corresponds to ~250 billion RBC

To maintain the balance we need to make the same #’s per day

What is required?

- the basic elements for synthesis
- a feedback system

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Control of RBC production

**Required elements for synthesis**

- Dietary Iron (needed for the heme group)
- Amino acids (needed for the globins)
- Folic Acid (needed for DNA synthesis in dividing cells)
- Vitamin B₁₂ (needed for action of Folic Acid)

**Feedback system**

- Erythropoietin (EPO) = hormone produced by kidney cells
- Stimulates Erythropoiesis
- Is produced whenever the kidney experiences a chronic oxygen deficiency
Control of RBC production

Erythropoietin Mechanism

- Increases $\text{O}_2$-carrying ability of blood
- Reduces $\text{O}_2$ levels in blood
- Enhanced erythropoiesis increases RBC count
- Erythropoietin stimulates red bone marrow
- Kidney (and liver to a smaller extent) releases erythropoietin

Start

Stimulus: Hypoxia due to decreased RBC count, decreased amount of hemoglobin, or decreased availability of $\text{O}_2$

Endressation: Normal blood oxygen levels

Lifecycle of an RBC

- RBCs are subjected to incredible mechanical stress.
  - Why are they unable to synthesize replacements for damaged parts?

- After $\approx 120$ d, the RBC cell membrane ruptures, or the damage is detected by phagocytic cells and the RBC is engulfed.

- If the RBC hemolyzes, its contained Hb will be excreted by the kidneys
Fate of Hb after RBC breakdown

1. Globular proteins
   - Disassembled into component amino acids and metabolized by the cell or released into the circulation for use by other cells

2. Heme
   - Stripped of its iron and converted to bilirubin, which has an orange-yellow color.
   - Bilirubin is released into the circulation where it binds to albumin and is transported to the liver.
   - Here it is stored in the galbladder as a component of bile
   - When secreted into the intestine, bilirubin becomes converted to urobilinogens and stercobilinogens by intestinal bacteria

Abnormalities in RBC production

Occurs whenever RBC depletion is greater than RBC production

Results in a condition where the blood has an abnormally low oxygen-carrying capacity = ANEMIA

Anemia can be due to
   - lower than normal RBC (thus low hematocrit)
   - or, a lower Hb content per RBC

Since Anemia can have several causes, it not a disease in itself but a symptomatic display of an abnormal process.
3. Iron
   • Binds to Transferrin protein for transport in the blood (shuttles it to the liver and bone marrow)
   • In the liver, it becomes stored by binding to Ferritin.
   • 50% of iron is stored in the liver as Fe-Ferritin. Stripped of its iron and converted to bilirubin, which has an orange-yellow color.

Note: If the bile ducts are blocked, or if the liver is unable to absorb/excrete bilirubin, plasma [bilirubin] rises and diffuses into peripheral tissues where it can impart a yellow color to the skin and sclera of the eye (jaundice).
Fate of Hb after RBC breakdown

- Iron is bound to transferrin and released to blood from liver as needed for erythropoesis.
- Bilirubin is picked up from blood by liver, secreted into intestine in bile, metabolized to stercobilin by bacteria and excreted in feces.
- Food nutrients, including amino acids, Fe, B12, and folic acid are absorbed from intestine and enter blood.
- Raw materials are made available in blood for erythrocyte synthesis.

1. Mixture of Fe$^{2+}$ and Fe$^{3+}$ is ingested
2. Stomach acid converts Fe$^{3+}$ to Fe$^{2+}$
3. Fe$^{2+}$ binds to gastroferritin
4. Gastroferritin transports Fe$^{2+}$ to small intestine and releases it for absorption
5. In blood plasma, Fe$^{2+}$ binds to transferrin
6. In liver, some transferrin releases Fe$^{2+}$ for storage
7. Fe$^{2+}$ binds to apoferritin to be stored as ferritin
8. Remaining transferrin is distributed to other organs where Fe$^{2+}$ is used to make hemoglobin, myoglobin, etc.
## Types of Anemia

- **Hemorrhagic**
  - Results from blood loss (i.e., RBC loss)
  - Can be acute (stab wound perhaps) or chronic (due to hemorrhoids or an undiagnosed bleeding ulcer)

- **Hemolytic**
  - RBCs rupture (lyse) prematurely
  - Can be due to hemoglobin abnormalities, mismatched blood transfusions, parasitic or bacterial infection, or autoimmune.

- **Nutritional**
  - Inadequate diet
  - Low iron intake, low protein intake
  - Low Vit. B12 intake

## Types of Anemia

- **Pernicious**
  - Due to a lack of Vitamin B\textsubscript{12} intake or absorption.
  - Stomach mucosa produces a substance called intrinsic factor which is necessary for Vitamin B\textsubscript{12} absorption.
  - Lack of intrinsic factor is often a cause of pernicious anemia

- **Renal Anemia**
  - Due to a lack of EPO production

- **Aplastic**
  - Results from destruction of red bone marrow from bacterial toxins, drugs, or radiation
  - Impacts all blood cells

Compare the 2 slides of red bone marrow. Blue dots indicates developing blood cells. Left-hand slide is during aplastic anemia; right-hand slide is almost back to normal.
**Abnormal Hb Production Diseases**

**Thalassemias (= ‘Anemia by the sea’)**

- Genetic disease
- Faulty production of alpha or beta chain of Hb
- Causes ineffective Erythropoiesis and Hemolysis
- Originally seen in people of Mediterranean origin. But now also noticed in Africa, Malyasia, China, SE Asia

**Types of Anemia**

**Sickle Cell Disease**

- A single mutation in the gene for the β chain of the globin molecule results in abnormal hemoglobin (HbS)
- Due to the structural change, the β chains link together and become stiff rods under low-O$_2$ conditions.
- This causes the RBCs to become sickle-shaped and these malformed RBCs can then block and clog small blood vessels.
- Strikes 1 in every 400 African Americans
Polycythemia

- An elevated hematocrit with a normal blood volume
- I.e., an increase in the number of erythrocytes in the blood.
- May be primary (polycythemia vera) and due to cancer of the bone marrow
- May be secondary when O₂ is not available or EPO production increases.
- How does polycythemia affect blood viscosity and thus affect blood flow?
- Polycythemia can be treated by blood dilution – removing blood and replacing it with isotonic saline.
- Endurance athletes often attempt to induce polycythemia as a means of increasing their athletic performance. Why?