Blood

- Functions: Transport, Stability of interstitial fluid, distribute heat, hemostasis, prevent infection

- Normal blood volume = 5L
  - 45% of blood (% hematocrit)
  - 55% of blood

Blood Cell Counts

- Number of RBCs reflects blood's oxygen carrying capacity
- Anemia – deficiency of RBCs or Hb in RBCs; reduces O₂ carrying capacity of blood

- The average life span of an RBC is about 120 days
- Iron is carried in the blood by transferrin to red bone marrow, liver
- Porphyrin from worn out RBCs is converted into biliverdin and bilirubin
White Blood Cells and Platelets

# WBCs - 5,000 – 10,000 per mm³ (or μl) of blood

- **leukopenia** (-penia = deficiency of cell number)
  - low WBC count
  - typhoid fever, flu, measles, mumps, chicken pox, AIDS
- **leukocytosis** (-cytosis = increase in cell number)
  - high WBC count
  - acute infections, vigorous exercise, great loss of body fluids

# Platelets - 150,000 – 500,000 per mm³ of blood (average ≈ 350,000 per μl)

- **cytosis** = abnormal increase in cell number
- **penia** = abnormal decrease in cell number

Hemoglobin

**General structure:**
- Four polypeptides chains
- A porphyrin
- An iron atom

Heme

Blood Viscosity and Osmolarity

- **Viscosity (thickness)**
  - Resistance to flow of blood
  - Whole blood is about 5x as viscous as water
  - Changes in viscosity can put strain on the heart
  - Erythrocytosis (polycythemia) ↑ viscosity

- **Osmolarity**
  - Due to NUMBER of particles dissolved, not the type
  - Na⁺, proteins, erythrocytes
  - Osmolarity determines fluid flow between blood and tissues
Blood Clots

• After forming, blood clot retracts (~60%) and pulls the edges of a broken vessel together

• Platelet-derived growth factor stimulates smooth muscle cells and fibroblasts to repair damaged blood vessels

• Thrombus – blood clot
• Embolus – blood clot moving through blood

Serum is the fluid expressed from a clot, i.e., the plasma minus clotting factors

White Blood Cells

Two major classes of leukocytes (WBC)

<table>
<thead>
<tr>
<th>Neutrophils</th>
<th>First to arrive at infections, phagocytic, 55% - 65% of leukocytes, elevated in bacterial infections</th>
</tr>
</thead>
<tbody>
<tr>
<td>Basophils</td>
<td>Release histamine and heparin in allergic reactions &lt; 1%</td>
</tr>
<tr>
<td>Eosinophils</td>
<td>Participate in allergic reactions, defend against parasitic worm infestations 1-3%</td>
</tr>
<tr>
<td>Monocytes</td>
<td>Precursors of macrophages, elevated in viral infections, inflammation, 3-9% of leukocytes</td>
</tr>
<tr>
<td>Lymphocytes</td>
<td>Important in immunity, produce antibodies, 25% - 33% of leukocytes</td>
</tr>
</tbody>
</table>

WBCs leave the bloodstream and enter tissues by the process of diapedesis

Plasma Proteins

Albumins
• Most numerous plasma proteins (~55%)
• ‘Transport’ proteins
• Origin in liver
• Help maintain osmotic pressure of blood

Alpha and Beta Globulins
• Originate in liver
• Transport lipids and fat-soluble vitamins

Fibrinogen
• Originates in liver
• Plays key role in blood coagulation

Gamma Globulins
• Origin in lymphatic tissues (plasma cells)
• Constitute the antibodies of immunity
Hemostasis

- **cessation of bleeding**

**Blood Vessel Spasm**
- smooth muscle in vessel contracts (vascular spasm)

**Platelet Plug Formation**
- platelets adhere to rough surface to form a plug

**Blood Coagulation**
- blood clot forms
- clotting cascade

1. Vascular phase
2. Platelet phase
3. Coagulation phase

Substances released by platelets:
- ADP (platelet activator)
- thromboxane A$_2$ and serotonin (vessel constriction)
- clotting factors
- Ca$^{2+}$ (aids in coagulation)
- PDGF

Blood Coagulation

Three cascades:
1. **Intrinsic**
2. **Extrinsic**
3. **Common**

Coagulation is an example of positive feedback

Figure from: Martini, Anatomy & Physiology, Prentice Hall, 2001

Prevention of Coagulation

- The smooth lining (endothelium) of blood vessels discourages the accumulation of platelets
- **Prostacyclin** released by endothelial cells (aspirin)
- Some cells secrete **heparin** (an anticoagulant)
- As a clot forms, **fibrin** absorbs thrombin and prevents the reaction from spreading
- **Antithrombin** (in plasma) interferes with the action of excess thrombin
- **Plasmin** digests blood clots (generated from plasminogen via the action of a plasma enzyme, kallikrein)
**Pathway of Blood Through Heart**

1. Blood enters a right atrium from superior and inferior vena cava.
2. Blood exits right atrium through right A-V valve into right ventricle.
3. Contraction of right ventricle forces pulmonary valve open.
4. Blood flows through pulmonary valve into pulmonary trunk.
5. Blood leaves the heart via pulmonary trunk.
7. Blood flows into left ventricle.
8. Contraction of left ventricle simultaneously with relaxation of aortic valve.
10. Blood flows to every organ in the body, where it exchanges CO₂ and picks up O₂.
11. Blood returns to heart via vena cava.

**Heart Valves**

- **Atrioventricular (A V) valves**
  - **Tricuspid Valve**
    - right A-V valve
    - between right atrium and right ventricle
    - Attached to chordae tendineae
  - **Bicuspid (Mitra) Valve**
    - left A-V valve
    - between left atrium and left ventricle
    - Attached to chordae tendineae

- **Pulmonary Valve**
  - semilunar valve
  - between right ventricle and pulmonary trunk

- **Aortic Valve**
  - semilunar valve
  - between left ventricle and aorta

**Wall/Coverings of Heart**

- **endocardium**
  - forms protective inner lining
  - membrane of epithelial and connective tissues
- **myocardium**
  - cardiac muscle
  - contracts to pump blood
- **epicardium**
  - serous membrane (visceral pericardium)
  - protective covering
  - contains capillaries and nerve fibers

Know all the layers depicted in the diagram, and know their correct order.
Cardiac Conduction System

Specialized myocardial cells.

Instead of contracting, they initiate and distribute impulses throughout the heart.

Pacemaker firing rates:
- SA Node = 80-100 / min
- AV Node = 40-60 / min
- Purkinje = 30-40 / min

Electrocardiogram

- recording of electrical changes that occur in the myocardium during the cardiac cycle
- used to assess heart's ability to conduct impulses, heart enlargement, and myocardial damage

Important points to remember:
- Depolarization precedes contraction
- Repolarization precedes relaxation

P wave – atrial depolarization
QRS wave – ventricular depolarization
T wave – ventricular repolarization

Three waves per heartbeat

Regulation of Cardiac Rate

Tachycardia > 100 bpm
Bradycardia < 60 bpm

Parasympathetic impulses reduce CO (↓rate). Why not strength?

Sympathetic impulses increase CO (↑rate/strength)
### Summary of Factors Affecting CO - Table Form

<table>
<thead>
<tr>
<th>Effect on CO</th>
<th>Affect HR, SV, or both?</th>
<th>How?</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>DECREASE</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Atrial reflex</td>
<td>HR</td>
<td>1 HR</td>
</tr>
<tr>
<td>Hypothalamic stimulation</td>
<td>HR and SV</td>
<td>1 HR, 1 SV</td>
</tr>
<tr>
<td>Sympathetic discharge</td>
<td>HR and SV</td>
<td>1 HR, 1 SV</td>
</tr>
<tr>
<td>1-Packed, Heart failure Mechanism</td>
<td>SV</td>
<td>1 RV, 2 GSV</td>
</tr>
<tr>
<td>1-Compresses</td>
<td>SV</td>
<td>1 LSV</td>
</tr>
<tr>
<td>1: Viscosity, 1: CVP</td>
<td>HR and SV</td>
<td>1 Packed, 1 atrial reflex</td>
</tr>
<tr>
<td>1: Ca²⁺ (Hypercalcemia)</td>
<td>SV</td>
<td>1 Contractility, 1 LSV</td>
</tr>
<tr>
<td>1: Temperature</td>
<td>HR</td>
<td>1 HR</td>
</tr>
<tr>
<td><strong>INCREASE</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Parasympathetic stimulation (vagus nerve)</td>
<td>HR</td>
<td>1 HR</td>
</tr>
<tr>
<td>1: Dehydrated</td>
<td>SV</td>
<td>1 GSV</td>
</tr>
<tr>
<td>1: Co²⁺ (Hypercalcemia)</td>
<td>SV</td>
<td>1 Contractility, 1 LSV</td>
</tr>
<tr>
<td>1: K⁺ (Hyperkalemia)</td>
<td>HR, SV</td>
<td>Arrhythmia, cardiac arrest</td>
</tr>
<tr>
<td>1: K⁺ (Hypokalemia)</td>
<td>HR, SV</td>
<td>Arrhythmia, cardiac arrest</td>
</tr>
<tr>
<td>1: Temperature</td>
<td>HR</td>
<td>1 HR</td>
</tr>
</tbody>
</table>

### Coronary Circulation

Coronary vessels fill mainly during diastole.

### Systole and Diastole

Systole = contraction; Diastole = relaxation

**Atrial Systole/Ventricular Diastole**

**Atrial Diastole/Ventricular Systole**

![Diagram of heart systole and diastole](attachment:diagram.png)
Review of Events of the Cardiac Cycle

1. Atrial contraction begins
2. Atria eject blood into ventricles
3. Atrial systole ends; AV valves close (S1)
4. Isovolumetric ventricular contraction
5. Ventricular ejection occurs
6. Semilunar valves close (S2)
7. Isovolumetric relaxation occurs
8. AV valves open; passive atrial filling

Figure from: Martini, Anatomy & Physiology, Prentice Hall, 2004

Regulation of Cardiac Output

Recall: SV = EDV - ESV

CO = heart rate (HR) x stroke volume (SV)

Factors Affecting Cardiac Output

CO – Cardiac Output (~5L/min); CO = Stroke Volume (SV: 70 ml) x Heart Rate (HR)
CVP – Central Venous Pressure; Pressure in vena cava near the right atrium (affects preload; Starling mechanism)
Contractility – Increase in force of muscle contraction without a change in starting length of sarcomeres
Afterload – Load against which the heart must pump, i.e., pressure in pulmonary artery or aorta
ESV – End Systolic Volume; Volume of blood left in heart after it has ejected blood (~50 ml)
EDV – End Diastolic Volume; Volume of blood in the ventricle before contraction (~120-140 ml)

Figure adapted from: Aaronson & Ward, The Cardiovascular System at a Glance, Blackwell Publishing, 2007
The Frank-Starling Mechanism

- Amount of blood pumped by the heart each minute (CO) is almost entirely determined by the venous return

- Frank-Starling mechanism
  - Intrinsic ability of the heart to adapt to increasing volumes of inflowing blood
  - Cardiac muscle reacts to increased stretching (venous filling, preload) by contracting more forcefully
  - Increased stretch of cardiac muscle causes optimum overlap of cardiac muscle (length-tension relationship)

Comparison of Skeletal and Cardiac Muscle

Ca^{2+} ions enter from:
1. Extracellular fluid (20%)
2. Sarcoplasmic reticulum (80%)

So, Cardiac muscle is very sensitive to Ca^{2+} changes in extracellular fluid via slow Ca^{2+} channels

Recall that tetanic contractions usually cannot occur in a normal cardiac muscle cell

Overview of the Cardiovascular System (CVS)

CVS = Heart + Blood Vessels
Overview of Blood Vessels

Large/med sized arteries regulate blood flow to organ systems; high press.
Arterioles regulate blood flow to capillary beds
Capillaries are site of fluid exchange
Arteries and veins are constructed of three layers:
1) tunica intima
2) tunica media
3) tunica externa
Veins return blood to heart, hold most of body’s blood and have valves; low press.

Capillaries
• smallest diameter blood vessels (fit 1 RBC at a time)
• extensions of inner lining of arterioles
• walls consist of endothelium and basement membrane
  only – NO smooth muscle
• semipermeable (plasma fluid can escape, but not proteins)

  3 types:
  • continuous (muscle)
  • fenestrated (endocrine glands, kidney, small intestine)
  • sinusoids (liver, spleen, bone marrow)

Exchange in the Capillaries
• major mechanism involved in exchange of solutes is diffusion
• substances move in and out along the length of the capillaries according to their respective concentration gradients
• Fluid movement in systemic capillaries is determined by two major factors
1. hydrostatic pressure; varies along portions of capillary
2. osmotic pressure; remains about the same along the length of the capillary

Excess tissue fluid is drained via lymphatics
Arterial Blood Pressure

Blood Pressure – force the blood exerts against the inner walls of the blood vessels

Arterial Blood Pressure
• rises when ventricles contract
• falls when ventricles relax
• systolic pressure – maximum pressure
• diastolic pressure – minimum pressure

Pulse pressure – difference between systolic and diastolic pressures (systolic : diastolic : pulse pressure ~ 3:2:1)

- Pulse pressures usually rise with age because of an increase in blood vessel resistance (arteriosclerosis)

Recall: Blood Flow (CO) \( \propto \) Pressure / Resistance

Mean Arterial Pressure

Mean Arterial Pressure (MAP) – Average effective pressure driving blood flow through the systemic organs

\[ \text{MAP} = \text{CO} \times \text{Total Peripheral Resistance (TPR)} \]

Thus ALL changes in MAP result from changes in either cardiac output or peripheral resistance

If CO increases, MAP \\
If TPR decreases, MAP \\
If TPR decreases, what must be done to keep MAP the same? \\
If blood volume decreases, what must be done to keep MAP the same?

MAP can be estimated by the equation:

\[ \text{diastolic bp} + \frac{\text{pulse pressure}}{3} \]

(Roughly 1/3 of the way between systolic and diastolic pressures

Factors Affecting Blood Pressure (MAP)

Factors affecting MAP include:
- CO
- Contractility
- HR
- ESV
- EDV
- CVP
- Parasympathetic
- Sympathetic

The MAP is dependent upon CO and TPR, i.e., MAP = CO \( \times \) TPR. TPR – Total Peripheral Resistance depends upon *blood vessel radius, vessel length, blood viscosity, and turbulence*
Factors Affecting Blood Pressure (MAP)

MAP = \frac{X \cdot TPR}{1 \cdot \text{radius}^4} \cdot \text{Viscosity} \cdot \text{Turbulence}

Autoregulation of Blood Flow/Pressure

- Local vasodilators increase blood flow
  - Decreased O_2 (except pulmonary circulation) or increased CO_2
  - Increase in lactic acid production
  - Release of nitric oxide (NO)
  - Increased K^+ or H^+
  - Mediators of inflammation (histamine, NO)
  - Elevated local temperature, prostaglandins (some)
- Local vasoconstrictors decrease blood flow
  - Thromboxanes (released by activated platelets and WBCs), serotonin, prostaglandins (some)
  - Endothelins released by damaged endothelial cells

Central Venous Pressure

- Central Venous Pressure = pressure in the vena cava near the right atrium (~ 2-4 mm Hg)
- determines the filling pressure of the right ventricle
  - determines the EDV of the right ventricle which
  - determines ventricular stroke volume (Frank-Starling)
- affects pressure within the peripheral veins
- weakly beating heart causes an increase in central venous pressure (backup of blood)
- increase in central venous pressure causes blood to back up into peripheral veins
Hepatic Portal Vein

Portal circulation: one set of capillaries and leads to another set of capillaries before it becomes a vein

Note that veins in the abdominal cavity drain into the hepatic portal vein

Aorta and Its Principal Branches

**Need to know this table: if I give you an artery, you need to know which branch of the aorta it arises from

<table>
<thead>
<tr>
<th>Major Branches</th>
<th>Arteries</th>
<th>Branches</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ascending aorta</td>
<td>Right subclavian</td>
<td>Brachiocephalic</td>
</tr>
<tr>
<td>Descending aorta</td>
<td>Left subclavian</td>
<td>Femoral</td>
</tr>
<tr>
<td>Thoracic aorta</td>
<td>Brachial</td>
<td>Radial</td>
</tr>
<tr>
<td>Abdominal aorta</td>
<td>Celiac</td>
<td>Duodenum</td>
</tr>
<tr>
<td>Abdominal aorta</td>
<td>Superior mesenteric</td>
<td>Ileocecal</td>
</tr>
<tr>
<td>Abdominal aorta</td>
<td>Inferior mesenteric</td>
<td>Left colic</td>
</tr>
<tr>
<td>Abdominal aorta</td>
<td>Left gastric</td>
<td>Left gastroepiploic</td>
</tr>
</tbody>
</table>

Major Veins - Upper Limb and Shoulder

Median cubital vein is often used to draw blood (venipuncture)

- Right internal jugular v.
- Right subclavian v.
- Right brachiocephalic v.
- Axillary v.
- Brachial v.
- Cephalic v.
- Basilic v.
- Median cubital v.
- Radial v.
- Ulnar v.
- Dorsal arch v.
- Left brachio-cephalic v.
- Superior vena cava
Arteries to Neck, Head, and Brain

Superficial temporal a.
Posterior auricular a.
Basilar a.
Occipital a.
Internal carotid a.
External carotid a.
Carotid sinus
Vertebral a.
 Thyrocervical axis
Subclavian a.
Anterior choroid a.
Maxillary a.
Facial a.
Lingual a.
Superior thyroid a.
Common carotid a.
Brachiocephalic a.

Major Veins of the Brain, Head, and Neck

External jugular v. 
Drains blood from face, scalp, and superficial neck regions

Venous sinuses
Leads to internal jugular veins

Superior ophthalmic v.
Anterior facial v.
Right internal jugular v.
Drains internal structures of brain

Arteries to Shoulder and Upper Limb

Right common carotid a.
Right subclavian a.
Axillary a.
Anterior circumflex a.
Posterior circumflex a.
Deep brachial a.
Brachial a.
Radial recurrent a.
Radial a.
Principal artery of thumb
Ulnar recurrent a.
Ulnar a.
Deep volar arch a.
Superficial volar arch a.
Digital a.
Cerebral Arterial Circle

• Also called the Circle of Willis
• Formed by anterior and posterior cerebral arteries, which join the internal carotid and basilar arteries.

Know the names of the vessels that make up the cerebral arterial circle.

Lymphatic System and Immunity

Functions of the Lymphatic System

• network of vessels that assist in circulating fluids
• transports excess fluid away from interstitial spaces
• transports fluid to the bloodstream
• aids in absorption of dietary fats
• help defend the body against disease

Lymphatic Pathways

Know the pathway.
Lymphatic Ducts

- Thoracic duct – drains left side of body above diaphragm and all lower body
- Right lymphatic duct
  - Drains right side of body above diaphragm and right arm

- Lymph
  - Is eventually returned to the subclavian veins
  - Is tissue fluid that has entered a lymphatic capillary
  - Contains lymphocytes, interstitial fluid, and plasma proteins

Lymph Movement

- Action of skeletal muscles
- Respiratory movements
- Smooth muscle in larger lymphatic vessels
- Valves in lymphatic vessels

Anatomical and physiological mechanisms similar to veins!!

Lymphatic Tissues

- Aggregations of lymphocytes in the connective tissues of mucous membranes and various organs
  - Diffuse lymphatic tissue (scattered, rather than densely clustered), e.g., in respiratory, digestive, urinary, and reproductive tracts. Known as MALT (mucosa-associated lymphatic tissue)
  - Lymphatic nodules (follicles) – densely clustered cell masses in lymph nodes, tonsils, appendix, small intestine (Peyer’s patches)
Lymphatic Tissues

- Lymph nodes filter the lymph, carry out immune surveillance, and serve as an early warning system for pathogens
  - The structural unit of the LN is the nodule
  - Some tissues contain isolated nodules
- Lymph nodes are usually located in clusters/ chains
  - Cervical, axillary, inguinal, pelvic, abdominal, thoracic, and supratrochlear
- The thymus is the site of ‘education’ of T lymphocytes
- The spleen is the filter of the blood; destroys worn out RBCs

Innate (Nonspecific) Defenses

- Species Resistance
  - resistance to certain diseases to which other species are susceptible
- Mechanical Barriers
  - skin
  - mucous membranes
- Chemical Barriers
  - enzymes in various body fluids
  - pH extremes in stomach
  - high salt concentrations
  - interferons
  - defensins
  - collectins

These are not specific to a particular pathogen (disease causing agent)

Innate Defenses (continued)

- Natural Killer Cells
  - type of lymphocyte
  - lysis of viral-infects cells and cancer cells
- Phagocytosis
  - neutrophils
  - monocytes
  - macrophages
  - ingestion and destruction of foreign particles
- Complement System
  - ‘complements’ the action of antibodies
  - helps clear pathogens

These are not specific to a particular pathogen

- Inflammation
  - tissue response to injury
  - helps prevent spread of pathogen
  - promotes healing
  - blood vessels dilate
  - capillaries become leaky
  - white blood cells attracted to area
  - clot forms
  - fibroblasts arrive
  - phagocytes are active

- Fever
  - inhibits microbial growth
  - increases phagocytic activity

These are not specific to a particular pathogen
Adaptive (Specific) Immunity
• resistance to particular pathogens or to their toxins or metabolic by-products
• ** based on the ability of lymphocytes to distinguish “self” from “non-self”
• antigens = cell surface proteins that can provoke immune responses
• Adaptive (Specific) Immunity demonstrates: 1) specificity and 2) memory
• T cells – cell-mediated immunity; B cells – humoral immunity

The Immune Response – A Summary
Antigen Presenting Cell (APC) + MHC + antigen $\rightarrow$ T_{H} + Cytokines
$\rightarrow$ T_{CMI} + antigen
$\rightarrow$ B Cell + antigen $\rightarrow$ Plasma Cell
$\rightarrow$ Direct Killing (T_{CMI} Cells - Cell Mediated Immunity)
$\rightarrow$ Antibodies (B Cells - Humoral Immunity)

Types of Immunoglobulins (Ig)
Immunoglobulins are the ‘gamma globulins’ in plasma

IgM
• located in plasma; too large to escape
• reacts with naturally occurring antigens on RBCs following certain blood transfusions
• activates complement

IgG
• located in tissue fluid and plasma
• activates complement
• defends against bacteria, viruses, and toxins
• can cross the placenta

IgA
• located in exocrine gland secretions
• defends against bacteria and viruses in membranes
• can cross the placenta
**Types of Immunoglobulins**

**IgD**
- located on surface of most B lymphocytes
- plays a role in B cell activation

**IgE**
- located in exocrine gland secretions
- promotes inflammation and allergic reactions

**Actions of Antibodies**
- agglutination
- precipitation
- neutralization
- activation of complement

---

**The Complement Cascade**

Activation of the complement cascade stimulates inflammation, attracts phagocytes, and enhances phagocytosis

---

**Immune Responses**

A primary immune response is slower and produces a lesser concentration of antibodies than a secondary immune response

Know this:
- Secondary response (anamnestic) (IgG)
- Primary response (mainly IgM; also IgG)
Practical Classification of Immunity

- Natural
  - Active (live pathogens)
  - Passive (maternal Ig)
- Artificial
  - Active (vaccination)
  - Passive (Ig or antitoxin)

Know this

Autoimmunity/Types of grafts

- Autoimmunity
  - Inability to distinguish “self” from “non-self”
  - Immune response generated against self

Types of grafts (transplantation)

- Isograft – identical twin
- Autograft – self graft
- Allograft – same species
- Xenograft – different species

Allergic Response

IgE mediates allergic reactions by binding to mast cells
Mast cells release histamine and heparin

Anaphylaxis is a severe allergic reaction involving the whole body caused by histamine release.