

CARDIOVASCULAR SYSTEM:

The Blood

- The blood is a connective tissue composed of a liquid extracellular matrix called blood plasma that dissolves and suspends various cells and cell fragments.

***Interstitial Fluid** – the fluid that bathes body cells and is constantly renewed by the blood.

Functions of Blood:

- a. Transportation of:
 - Gases (oxygen and carbon dioxide), nutrients from gastrointestinal tract, waste products
 - Processed molecules
 - Regulatory molecules – hormones
- b. Regulation of pH (by the use of buffers) and osmosis
 - Buffer systems include **Protein, Phosphate and Bicarbonate buffers**
- c. Maintenance of body temperature
 - Normal body temperature is 36.5 – 37 degrees Celsius
- d. Protection against foreign substances
 - White blood cells protect via phagocytosis
- e. Clot formation
 - *12 clotting factors but actually 13 – no number 6 (Prothrombinase is a combination of factors V and X)
- f. Blood performs a number of functions dealing with:
 - Substance distribution
 - Regulation of blood levels of particular substances
 - Body protection

Blood Functions: Distribution

Blood transports:

- Oxygen from the lungs and nutrients from the digestive tract
 - *Nutrients include Vitamins:
 - Vitamin B12 - Cyanocobalamin
 - Vitamin B6 - Pyridoxine
 - Vitamin B1 - Thiamine
 - Vitamin B2 - Riboflavin
 - Vitamin B3 - Niacinamide
- Metabolic waste from cells to the lungs and kidneys for elimination
- Hormones from endocrine glands to target organs

Blood Functions: Regulation

Blood maintains:

- Appropriate body temperature by absorbing and distributing heat to other parts of the body
- The plasma also has a cooling effect because of its water properties
- Blood osmotic pressure can influence the water content of cells.
- Normal pH in the body tissues using buffer systems
 - * Normal pH in the body is 7.35 – 7.45
- Adequate fluid volume in the circulatory system

Blood Functions: Protection

- a. **Blood prevents blood loss by:**
 - Activating plasma proteins and platelets
 - *Plasma proteins include albumin, immunoglobulins, fibrinogens, alpha 1-antitrypsin, regulatory proteins etc.
 - *Immunoglobulins include alpha, beta and gamma (IgA, IgD, IgE, IgG, IgM)
 - Initiating clot formation when a vessel is broken
- b. **Blood prevents infection by:**
 - Synthesizing and utilizing antibodies
 - Activating complement proteins
 - Activating WBCs to defend the body against foreign invaders
 - Several types of blood proteins, including antibodies, interferons and complement, help the body fight against infection

Methods of collecting blood

- a. Venipuncture – most common method
- b. Finger stick – measure capillary blood glucose level
- c. Heel Stick – usually done in infants
- d. Arterial Stick – getting blood sample from arteries, to determine levels of oxygen in blood
- e. Venesection – cutting a section in a vein for samples
 - ***Phlebotomy** - is the name of the procedure for drawing blood (it is different from venipuncture)

Physical Characteristics of Blood

- a. **Average volume of blood:**
 - 5-6 L for males and 4-5 L for females (Normovolemia)
 - Hypovolemia – low blood volume
 - Hypervolemia – high blood volume
- b. **Viscosity (thickness)**
 - 4-5 (where water is 1)
 - Blood is denser and more viscous than water and it feels slightly sticky
- c. **The pH of blood**
 - 7.35 – 7.45 (average is 7.4) – slightly alkaline
- d. **Osmolarity**
 - 300 mOsm or 0.3 Osm
 - This reflects the concentration of solutes in the plasma
- e. **Salinity**
 - 0.85 % (isotonic)
 - Reflects the concentration of NaCl in the blood
- f. **Temperature**
 - 38 °C (*normal is 36.5 – 37*)
 - *Slightly higher than the normal body temperature and is the same with rectal temperature (1°C higher than normal)*
- g. **Blood accounts for approximately 8% of total body weight**
- h. **Color**
 - Color of the blood varies with its oxygen content
 - When it has high oxygen content, it is bright red

Components of Blood

a. 2 Major Components

- Liquid = plasma (55%)
 - Formed Elements (45%)
 - Erythrocytes, or red blood cells (RBCs)
 - Leukocytes, or white blood cells (WBCs)
 - Platelets – cell fragments of megakaryocytes in Marrow
- ***Buffy Coat** – WBCs and platelets
 - middle part after centrifugation

Percentage by Weight

Other fluids and Tissues (92%)

Blood (8%)

- **Plasma** (55% by volume)
 - Proteins (7% by weight)
 - Albumins (58%)
 - Globulins (38%)
 - Fibrinogen (4%)
 - Water (91% by weight)
 - Other solutes (2% by weight)
 - Ions (Na, Cl, Ca, Mg, K, HPO₄, SO₄, etc.)
 - Nutrients
 - Waste products
 - Gases
 - Regulatory substances (hormones)
- **Formed Elements** (45% by volume)
 - Platelets (250-400 thousand per mm³)
 - White blood Cells (5-9 thousand per mm³)
 - Neutrophils (60% - 70%)
 - Lymphocytes (20% - 25%)
 - Monocytes (3% - 8%)
 - Eosinophils (2% - 4%)

- Basophils (0.5% - 1%)
- Red Blood Cells (4.2-6.2 million per mm³)

***Dengue fever** – platelet and hematocrit might go down as low as 20, no intervention since it is a vigorous intravenous infection

Components of Whole Blood

Steps in Separating Blood:

- a. Withdraw blood and place in tube
 - Median Cubital Vein – common site for venipuncture, next choice is the cephalic vein
 - Cephalic, Median Cubital, and Basilic Veins
Origin is the Axillary vein
Lateral → Vein → Artery → Nerve → Medial
 - Hematocrit- Males: 47% ± 5%
Females: 42% ± 5%

Cellular Components of Blood

Component	Normal Range	Function
a. RBC	Male: 4.2-5.4 M/ μ l Female: 3.6-5M/ μ l	Oxygen transport; Carbon Dioxide transport
b. Platelets	150,000-400,000/ μ l	Essential for clotting
c. WBC	5000-10,000/ μ l	Immunity
d. Neutrophils	About 60% of WBC	Phagocytosis
e. Eosinophils	1-3% of WBC	Same role in allergic response
f. Basophils	1% of WBC	May play a role in prevention of clotting in the body
g. Lymphocytes	25-35% of WBC	Produce antibodies; Destroy foreign cells
h. Monocytes	6% of WBC	Differentiate in tissues to macrophages

*Athletes - limiting factor is delivery of oxygen
- induced polycythemia to increase

RBC

hematocrit in 3 ways:

- Blood Doping** – 1 month before game, extract 500 cc of blood from the athlete, store it in a cold temperature, then return it to the body a day before the game
- Higher Altitude** – lower oxygen content thereby increasing erythropoiesis because of decrease in oxygen; decreased oxygen therefore increases RBC

- Synthetic Hormones** – Epoetin alpha is injected 7 days before the game. It is a hormone that increases erythropoiesis.

Hematocrit – it is the percentage of total blood volume occupied by RBCs. A hematocrit of 40 indicates that 40% of the volume of blood is occupied by RBCs. Significant drop in hematocrit is called anemia.

Blood Plasma

- **Blood plasma components:**
 - Water** - 90-92%, liquid portion
 - Proteins** - 6-8%, exert colloid osmotic pressure, which helps maintain water balance between blood and tissues and regulates blood volume
 - Albumins** – maintain osmotic pressure of the blood
 - Transport for several steroid hormones for fatty acids
 - It is produced in the liver
 - Globulins** – Alpha and beta globulins are used for transport purposes; Gamma globulins are the immunoglobulins (IgG, IgA, etc.). They help in attacking viruses and bacteria
 - produced by liver and plasma cells
 - Fibrinogen** – a clotting protein
 - Produced by the liver
 - Organic Nutrients** – glucose, carbohydrates, amino acids, fatty acids, vitamins and minerals
 - Electrolytes** – sodium, potassium, calcium, chloride, bicarbonate, phosphate etc.

- e. **Non-protein Nitrogenous substances**
 - Lactic acid, urea, creatinine, creatine, ammonia, bilirubin, uric acid
- f. **Respiratory Gases** – oxygen, carbon dioxide, and nitrogen

***Leukocytes** – complete cells because they have nucleus

Lymphocytes - with or without nucleus

RBC with nucleus might indicate leukemia

*Chemotherapy for breast cancer has 6 cycles but cancer might relapse and become more invasive

*RBC lifespan – 110-120 days

WBC lifespan – 6-8 days

Platelets lifespan – 5-9 days

Formed Elements

- a. **Red Blood Cells** - erythrocytes
- b. **White Blood cells** – leukocytes
 - WBCs are whole cells
- 1. **Granulocytes** (contains conspicuous granules)
 - Neutrophils
 - Eosinophils
 - Basophils
- 2. **Agranulocytes** (no granules are visible)
 - Lymphocytes (T and B are natural killer cells)
 - Monocytes
- c. **Platelets** – thrombocytes
 - Platelets are cell fragments
 - Formed elements comprise 45% of blood
 - Erthrocytes, leukocytes, and platelets make up the formed elements
 - Only WBCs are complete cells
 - RBCs have no nuclei or organelles, and platelets are just cell fragments

Most formed elements survive in the bloodstream for only a few days

Hematopoiesis/Hemopoiesis

- the process by which the formed elements of blood develop

a. Site of hematopoiesis (Fetus)

- Liver
- Thymus gland – rudimentary gland
- Spleen
- Lymph tissues or nodes
- Bone marrow (primary site in at least 3 months before birth)

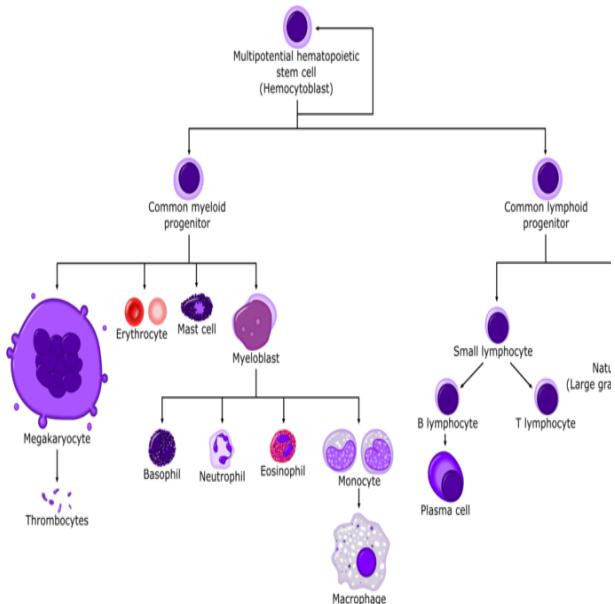
*Thymus is a **rudimentary gland** like the appendix, it is surgically removed if does not disappear in 1 year because it will release hormones that could disturb the homeostasis of the body

b. Sites of hematopoiesis (after birth)

- Lymph tissue
- Bone marrow

*All formed elements are derived from one population of cells called **Stem Cells or Pluripotent Cells or Hemocytoblast**. These cells are capable of developing into different types of cells.

*Spleen is retroperitoneal and is usually damaged during blunt trauma; surgical intervention could cause massive bleeding; function is production and storage of blood.



Production of Formed Elements

- Hematopoiesis or hemopoiesis is the process of blood cell production
- Pluripotent Stem Cells: All formed elements derived from single population
 - a. **Proerythroblast** – develop into red blood cells
 - b. **Myeloblast** – develop into basophils, neutrophils, eosinophils
 - c. **Lymphoblast** – develop into lymphocytes
 - d. **Monoblast** – develop into monocytes
 - e. **Megakaryoblasts** – develop into platelets

Red Blood Cells: Erythrocytes

- They contain the oxygen-carrying protein hemoglobin, which is a pigment that gives whole blood its red color.

Characteristics:

a. Biconcave Disc

- Folding increases surface area by 30%
- Plasma membrane contains **Spectrin** which gives erythrocytes their flexibility

b. Anucleate, no centrioles, no organelles

- All their internal space is available for oxygen transport
- End result: no cell division
- No mitochondria means they generate ATP anaerobically – it prevents consumption of oxygen being transported

c. Filled with **Hemoglobin (Hb)** – 97% of cell contents

- Hb functions in gas transport
- $\text{Hb} + \text{oxygen} \rightleftharpoons \text{HbO}_2$ (oxyhemoglobin)

d. Most numerous of the formed elements

- Females: 4.3 – 5.2 million cells/cubic millimeter
- Males: 5.2 – 5.8 million cells/cubic millimeter
 - *side view- $2.0\mu\text{m}$
 - Top view- $7.5\mu\text{m}$

Erythrocyte/RBC function

- a. Erythrocytes are dedicated to respiratory gas transport
- b. Hemoglobin reversibly binds with oxygen and most oxygen in the blood is bound to hemoglobin
- c. **Composition of hemoglobin:**
 - A protein called **Globin** – made up of 2 alpha and 2 beta chains.
 - Contains four polypeptide chains

- A **Heme** molecule – each heme group bears an atom of iron, which can **bind to one oxygen** molecule; each hemoglobin molecule thus can transport **four molecules** of oxygen

Hemoglobin

- **Consists of:**
 - 4 globin molecules:** transport carbon dioxide (carbonic anhydrase involved), nitric oxide produced by the endothelial cells of the blood vessels also binds to hemoglobin
 - 4 heme molecules:** transport oxygen
 - Iron is required for oxygen transport

A. Oxyhemoglobin - hemoglobin bound to oxygen

- oxygen leading takes place in the lungs

B. Deoxyhemoglobin – hemoglobin after diffuses into

Tissues (reduced Hb)

C. Carbaminohemoglobin – hemoglobin bound to carbon

Dioxide

- Carbon dioxide

loading takes

place in the tissues

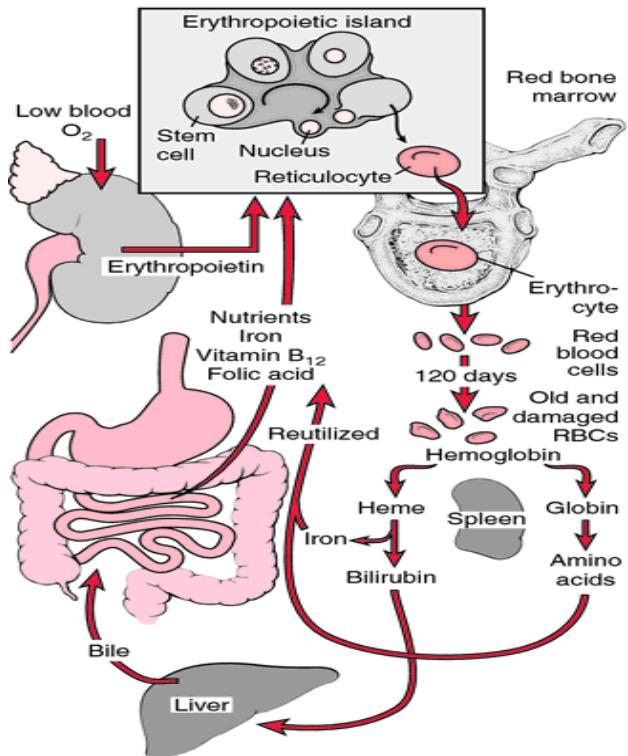
and has 6

times affinity

*Carbon monoxide is caused by incomplete combustion of vehicles

Life Cycle of Red Blood Cells

*Erythropoiesis is for hypoxia or low oxygen levels



1. Macrophages in the spleen, liver, or red bone marrow phagocytize ruptured and worn-out red blood cells.
2. The globin and heme portions of hemoglobin are split apart.
3. Globin is broken down into amino acids, which can be reused to synthesize other proteins.
4. Iron is removed from the heme portion in the form of Ferric, which associates with the plasma protein **transferrin**, a transporter for Ferric ion in the bloodstream.
5. In muscle fibers, liver cells, and macrophages of the spleen and liver, Ferric ion detaches from transferrin and attaches to an iron-storage protein called **ferritin**.
6. Upon release from a storage site or absorption from the gastrointestinal tract, Ferric ion reattaches to transferrin.

7. The Ferric ion transferrin complex is then carried to red bone marrow, where RBC precursor cells take it up through receptor-mediated endocytosis for use in hemoglobin synthesis. Iron is needed for the heme portion of the hemoglobin molecule, and amino acids are needed for the globin portion. Vitamin B12 is also needed for the synthesis of hemoglobin.
 8. Erythropoiesis in red bone marrow results in the production of red blood cells, which enter the circulation.
 9. When iron is removed from heme, the non-iron portion of heme is converted to, a green pigment, and then into **bilirubin** a yellow orange pigment.
 10. Bilirubin enters the blood and is transported to the liver.
 11. Within the liver, bilirubin is released by liver cells into bile, which passes into the small intestine and then into the large intestine.
 12. In the large intestine, bacteria convert bilirubin into **urobilinogen**
 13. Some urobilinogen is absorbed back into the blood, converted to a yellow pigment called **urobilin**, and excreted in urine.
 14. Most urobilinogen is eliminated in feces in the form of a brown pigment called **stercobilin**, which gives feces its characteristic color.
- Stored as **Hemosiderin** or **Ferritin** in tissues
- Transported in plasma by beta-globulins as **Transferrin**
- *Increase in **Bilirubin** in blood stream could cause **Jaundice**
- It is the yellowing of the person and the sclera of his/her eyes
- *amino acid and iron is needed for erythropoiesis
- *Black Feces – **melena** – upper gastrointestinal tract gastroenteritis or gastritis

Hemoglobin Breakdown

Old RBCs → Macrophage of liver or spleen → Hgb
 → Globin → Recycled
 → Heme → Iron → Bone marrow → Erythropoiesis
 → Bilirubin → Blood → Liver → Intestines → Kidney
 - feces - urine

Erythropoiesis

- RBC production starts in the red bone marrow with a precursor cell called proerythroblast.
- Proerythroblast divides several times and becomes a reticulocyte.
- Compounds needed for Erythropoiesis:
 1. Iron
 2. Folic Acid/ Folate
 3. Vitamin B12/ Cyanocobalamin
- It is a negative feedback system
- Stimulus for erythropoiesis: decreased Blood Oxygen or **Hypoxia**
 - a. Decreased RBC/Hgb Count
 - b. Increased oxygen demand (exercise)

Fate and destruction of Erythrocytes

- The life span of an erythrocytes is 100-120 days
- Old erythrocytes become rigid and fragile, and their hemoglobin begins to degenerate
- Dying erythrocytes are engulfed by macrophages
- Heme and globin are separated
 - Iron is removed from the heme and salvaged for reuse

- c. Lung disease
- d. Cardiovascular disease
- e. High altitude

Erythropoiesis

- Stem cells → proerythroblast → early erythroblast → intermediate erythroblast → late erythroblast → reticulocytes
- **Erythropoietin** – hormone to stimulate RBC production

Regulation and Requirements for Erythropoiesis

- **Circulating Erythrocytes** – the number remains constant and reflects a balance between Red blood cell production and destruction
 - Too few red blood cells leads to tissue hypoxia
 - Too many red blood cells causes undesirable viscosity
- **Erythropoiesis** is hormonally controlled and depends on adequate supplies of iron, amino acids, and B vitamins

***Cell Apoptosis** – programmed cell death

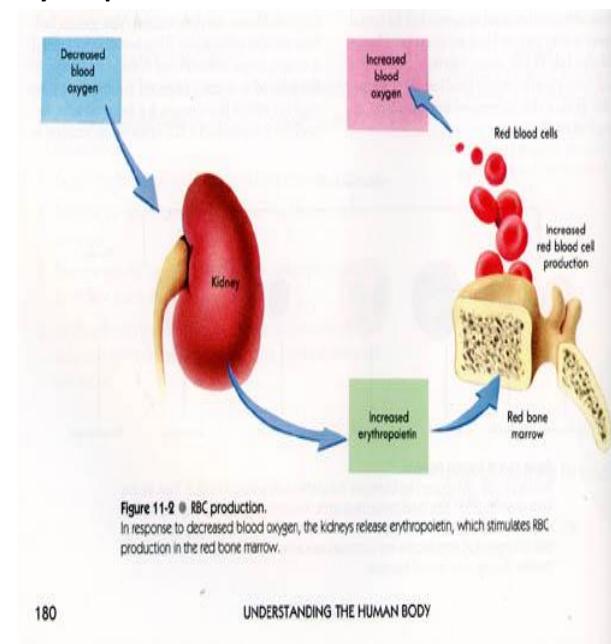
Hormonal Control of Erythropoiesis

- **Erythropoietin (EPO)** released by the kidneys is triggered by:
 - Hypoxia due to decreased RBCs
 - Decreased oxygen availability
 - Increased tissue demand for oxygen

- **Enhanced erythropoiesis** increases the:
 - RBC count circulating in the blood
 - Oxygen carrying ability of the blood

*The rate of erythropoiesis is measured by a reticulocyte count

Erythropoietin Mechanism



Dietary Requirements of Erythropoiesis

- a. **Erythropoiesis requires:**
 - Proteins, lipids and carbohydrates
 - Iron, Vitamin B12 and Folic acid
- b. The body stores iron in Hemoglobin(65%), the liver, spleen, and bone marrow
- c. Intracellular iron is stored in protein-iron complexes such as ferritin and hemosiderin
- d. Circulating iron is loosely bound to the transport protein transferring

Erythrocyte Disorders

a. Polycythemia

- Abnormal excess of erythrocytes
- Increases viscosity, decreases flow rate of blood
- Decrease pumping action of the heart

b. Anemia

- Blood has abnormally low oxygen-carrying capacity
- It is a symptom rather than a disease itself
- Blood oxygen levels cannot support normal metabolism
- Signs/symptoms include fatigue, paleness, shortness of breath and chills
 - **Paleness- vertigo**
- Compare hands to know, look in the **palpebra** of eyes

Anemia: Insufficient Erythrocytes

a. Hemorrhagic Anemia – result of acute or chronic loss of blood

- Occur from surgical procedure and may be acute or chronic

b. Hemolytic Anemia – prematurely ruptured erythrocytes

- Common on newborns

c. Aplastic Anemia – destruction or inhibition of red bone marrow

- Occurs when exposed to benzene, toluene and other chemicals
- Eat iron rich foods like liver, malunggay, and fibers

Anemia: Decreased Hemoglobin Content

a. Iron-deficiency anemia results from:

- A secondary result of hemorrhagic anemia
- Inadequate intake of iron-containing foods

- Impaired iron absorption
- Do complete blood count to know

b. Pernicious Anemia results from:

- Deficiency of vitamin B12
- Lack of intrinsic factor needed for absorption of vitamin B12
- Treatment is intramuscular injection of vitamin B12
- Could cause tumor in colon, cut in colon

*Intestinal Anastomosis

Anemia: Abnormal Hemoglobin

a. Thalassemias – absent or faulty globin chain in hemoglobin and may be alpha or beta

- Erythrocytes are thin, delicate and deficient in hemoglobin
- **Normocytic Anemia** - an anemia with a Mean Corpuscle Volume of 80-100 which is the normal range. However, the hematocrit and hemoglobin is decreased.

- **Normochromic Anemia** - is a form of anemia in which the concentration of hemoglobin in the red blood cells is within the standard range. However, there are insufficient numbers of red blood cells.

***Mean Corpuscle Volume** - is a measure of the average red blood cell size that is reported as part of a standard complete blood count.

b. Sickle-cell Anemia – results from a defective gene

- Codes for an abnormal hemoglobin called **Hemoglobin S (Hbs)**
- This defect causes RBCs to become sickle-shaped in low oxygen situations
- Caused by radiation

- **Polycythemia** – may be induced
- **Polycythemia Vera** - hereditary

Leukocytes (WBCs)

- These are the cells that have no nuclei and hemoglobin.
- a. **Leukocytes, the only blood components that are complete cells:**
 - 4,800 – 10,000/ cubic millimeter
 - Protect the body from infectious microorganisms
 - Can leave capillaries via chemotaxis/diapedesis or the passage of blood cells through capillary walls
 - Move through tissue spaces (amoeboid motion)
 - Many are phagocytic (possess numerous lysosomes)
- b. **Two major types of Leukocytes**
 - **Granulocytes:** Neutrophils, Eosinophils, Basophils
 - **Agranulocytes:** Monocytes, Lymphocytes
- c. **Leukocytosis** – WBC count over 11,000/mm³
 - Normal response to bacterial or viral invasion
 - Bacterial or viral in origin, example is Urinary Tract Infection
- d. **Leukopenia** – a decrease in WBC count below 4,800/mm³
 - Could be caused by chronic use of drugs or steroids
- e. **Leukemia** – a cancer of White Blood Cells

Leukocytes

- a. Protect the body against microorganisms and remove dead cells and debris

b. Movement

- Ameboid
- Diapedesis
- Chemotaxis
- Passive immunity
- Active immunity
- Antigen-Antibody

c. Types

A. Granular Leukocytes

- **Neutrophils** – most common phagocytic cells that destroy bacteria (60%)
- **Eosinophils** – detoxify chemicals and reduce inflammation (4%)
- **Basophils** – Allergic reactions, releases **histamine** (from mast cells) and **heparin** (anti-coagulant and anti-thrombin), increases inflammation response (1%)
***Serotonin** – 5-hydroxy-tryptophan
- Catecholamines

B. Agranular Leukocytes

- **Lymphocytes** – Immunity, 2 types (B and T cell types, IgG-infection, IgM-microbes, IgA-respiratory and GI, IgE-allergy, IgD-immune response)
- **Monocytes** – become macrophages

Granulocytes

a. Granulocytes – neutrophils, eosinophils, basophils

- Contain cytoplasmic granules that stain specifically (acidic, basic, or both) with **Wright's stain**
- Are larger and usually shorter-lived than RBCs
- Have lobed nuclei
- Are all phagocytic cells

Granulocytes: Neutrophils (Polymorphonuclear Leukocytes)

- a. **Account for 65-75% of total WBCs**
- b. **Neutrophils have two types of granules that:**
 - Take up both acidic and basic dyes
 - Give the cytoplasm a lilac color
 - Contain peroxidases, hydrolytic enzymes, and defensins (antibiotic-like proteins)
 - Low count may indicate radiation exposure, drug toxicity, or Systematic Lupus Erythematosus
 - High count may indicate infections, burns, stress and inflammation
 - **Functions:**
 - Neutrophils are our body's bacteria slayers
 - Functions for phagocytosis

Granulocytes: Eosinophils

- a. Eosinophils account for 1-4% of WBCs
 - Have red-staining bilobed nuclei
 - Have red to crimson granules
 - High count may indicate allergic reactions, parasitic infections, autoimmune diseases
 - Low count may indicate drug toxicity and stress
 - **Functions:**
 - Lead the body's counterattack against parasitic infections
 - Lessen the severity of allergies by phagocytizing immune complexes (ending allergic reactions)

Granulocytes: Basophils

- a. Account for 0.5-1% of all WBCs
 - Have U or S-shaped nuclei with two or three conspicuous constrictions
 - Are functionally similar to mast cells
 - Have large, purplish-black (Basophilic) granules that contain histamine
 - High count may indicate allergic reactions, leukemias, cancers, hypothyroidism
 - Low count may indicate pregnancy, ovulation, stress or hyperthyroidism
 - **Function:**
 - Liberate heparin, histamine, and serotonin in allergic reactions

Agranulocytes: lymphocytes

- a. **Account for 20-25% or more of WBCs and:**
 - Have large, dark-purple, circular nuclei with a thin rim of blue cytoplasm
 - Are found mostly enmeshed in lymphoid tissue and some circulate in the blood
 - High count may indicate viral infections, some leukemias
 - Low count may indicate prolonged illness, immunosuppression, or treatment with cortisol
 -
- b. **Most important cells of the immune system**
- c. **There are two types of lymphocytes: T cells and B cells**
 - T cells attack foreign cells directly
 - B cells give rise to plasma cells, which produce antibodies

Monocytes

- a. Monocytes account for 3-7% of leukocytes
 - They are the largest leukocytes
 - They have purple-staining, U or kidney-shaped nuclei
 - They leave the circulation, enter tissue, and differentiate into macrophages
 - High count may indicate viral or fungal infections, tuberculosis, leukemias, chronic diseases
 - Low count may indicate bone marrow suppression, treatment with cortisol
 - **Function:**
 - For phagocytosis

Production of Leukocytes

- **Leukopoiesis** – is hormonally stimulated by two families of cytokines (hematopoietic factors) – interleukins and colony-stimulating factors (CSFs)
 - Interleukins are numbered (e.g. IL-1, IL-2), whereas CSFs are named for the WBCs they stimulate (e.g. granulocyte-CSF stimulates granulocytes)
- All leukocytes originate from hemocytoblasts o the mother of all blood stem cells
- Macrophages abd T cells are the most important source of cytokines
- Many hematopoietic hormones are used clinically to stimulate bone marrow

***Emigration** – process where white blood cells leave the blood stream.

***Adhesion Molecules** – molecules that help white blood cells stick to the endothelium.

Blood Disorders

- **Erythrocytosis:** RBC overabundance
- **Anemia:** Deficiency of hemoglobin
 - Iron-deficiency
 - Pernicious
 - Hemorrhagic
 - Hemolytic
 - Sickle-cell
- **Hemophilia** – A or B(9) clotting factors
- **Thrombocytopenia** – decrease in platelets
- **Leukemia**
- **Septicemia** – generalized infection of blood
- **Infectious Mononucleosis**
- **Hepatitis**
 - Hepatitis A – oral-fecal route
 - Hepatitis B – blood transfusion, hepatocellular carcinoma
 - Hepatitis C – use of drugs
 - Hepatitis D – superimposition of hepatitis B
 - Hepatitis E – oral-fecal route

Leukocytes Disorders: Leukemias

- Leukemia refers to cancerous conditions involving white blood cells
- Leukemias are named according to the abnormal white blood cells involved
 - **Myelocytic Leukemia** – involves myeloblast
 - **Lymphocytic Leukemia** – involves lymphocytes

- **Acute Leukemia** involves blast-type cells and primarily affects children, they have usually 2 years to live
- **Chronic Leukemia** is more prevalent in older people
- Immature white blood cells are found in the blood stream in all leukemias
- Bone marrow becomes totally occupied with cancerous leukocytes
- Severe anemia ensues due to excess production of white blood cells
- The white blood cells produced, though numerous, are not functional
- Death is caused by internal hemorrhage and overwhelming infections
- Treatment includes radiation, antileukemic drugs (chemotherapy, can cause baldness) and bone marrow transplants

***Bone Marrow Transplant** – is the replacement of cancerous or abnormal red bone marrow with healthy red bone marrow in order to establish normal blood cell counts.

Thrombocytes (Platelets)

- Cell fragments that splinter from megakaryocytes in red bone marrow and then enter the blood circulation
- Are disc-shaped, 2-3 μm in diameter
- Has many vesicles but no nucleus
- Life span: 5-9 days
- Between 150,000 and 400,000 platelets are present in each μl of blood
- **Function:**

- Help stop blood loss from damaged blood vessels by forming a platelet plug
- Their granules contain chemicals that, once released, promote blood clotting and vascular spasm
*Endothelin and thromboxane are powerful vasoconstrictors

- Under the influence of **Thrombopoietin**, myeloid stem cells develop into megakaryocyte-colony-forming cells that develop into megakaryoblasts.
Megakaryocytes then would form megakaryocyte

Hemostasis

- Sequence of responses that stops bleeding
- Prevents **hemorrhage** or the loss of a large amount of blood from the blood vessels

1. **Vascular Spasm** – the smooth muscle of a blood vessel wall contracts which slows blood loss
 - It is caused by the damage to the smooth muscle, by substances released from activated platelets, and by reflexes initiated by pain receptor
 - Temporary vasoconstriction
2. **Platelet Plug Formation** – very effective in preventing blood loss in a small vessel
 - Combine with collagen fibers of injured tissue

- Platelet-derived Growth factor (PGDF)
- A hormone that can cause proliferation of vascular endothelial cells, vascular smooth, muscle fibers, and fibroblasts
- **Platelet Plug Formation occurs as follows:**
 - a. **Platelet Adhesion**
 - platelets contact and stick to parts of a damaged blood vessels, such as collagen fibers of the connective tissue underlying the damaged endothelial cells
 - b. **Platelet Release Reaction**
 - due to adhesion, the platelets become activated, and their characteristics change dramatically
 - They extend many projections that enable them to contact and interact with one another
 - They begin to liberate the contents of their vesicles
 - b. **Platelet Aggregation**
 - the release of ADP makes the other platelets in the area sticky
 - Fibrinogen is the clotting factor, fibrin clots
 - The stickiness of the newly recruited and activated platelets causes them to adhere to the originally activated platelets
 - The gathering of the platelets is called platelet aggregation
 - **Platelet Plug** – the accumulation and attachment of large number of platelets forming a mass

3. Blood Clotting

- If blood is drawn from the body, it thickens and forms a gel. Eventually, the gel separates from the liquid. The straw-colored liquid, called **serum** is simply blood plasma minus the clotting proteins. The gel is called a **clot**.
- **Terms:**
 - **Clot** – a network of insoluble protein fibers(fibrin) in which formed elements of blood are trapped
 - **Clotting/Coagulation** – is a series of chemical reactions that culminates in formation of fibrin threads
 - **Thrombosis** – clotting in an undamaged blood vessels
 - **Clotting Factors** – substances involved clotting
- **Extrinsic Pathway** – this pathway has fewer steps than intrinsic pathway and occurs rapidly within a matter of seconds if trauma is severe. It is named so because of a protein called **Tissue Factor** leaks into blood from outside blood vessels and initiates formation of prothrombinase
- **Intrinsic Pathway** – this pathway is more complex and slower, usually requiring several minutes. It is named so because its activators are either in direct contact with blood or contained within the blood.

- **The Clot Retraction** – it is the consolidation or tightening of the fibrin clot, The fibrin threads attached to the damaged surfaces of the blood vessel gradually contract as platelets pull them in.

Blood Clotting

- Platelets adhere to collagen fibers of damaged blood vessels and release ADP
- Platelets release chemicals that convert **Prothrombin** to **Thrombin**
- Thrombin causes fibrinogen molecules to join together to form strands called **Fibrin**
- Many strands of fibrin form a mesh or clot that
- stops the bleeding

Steps in Clotting:

Thromboplastin(trigger blood clot formation)
 → reacts with **Calcium ions** and **Protein Factors**
 → with **Prothrombin Activator** → converted to **Prothrombin** → to **Thrombin** → **Fibrinogen** → **Fibrin** → **RBC platelets** that are insoluble → **Clot**

Clotting factors – refer to other handout

Factor	Name
I	Fibrinogen
II	Prothrombin
III	Tissue factor or thromboplastin
IV	Calcium ions
V	Proaccelerin (Labile factor)
VII	Proconvertin (Stable factor)
VIII	Antihemophilic factor A, Antihemophilic globulin
IX	Antihemophilic factor B, Plasma thromboplastin component, Christmas factor

X	Stuart-Prower factor
XI	Plasma thromboplastin antecedent, Haemophilia C, Rosenthal syndrome
XII	Hageman factor
XIII	Fibrin stabilising factor, Laki-Lorand factor

Blood clotting tissue factor (**Thromboplastin**)

Hemostatic Control Mechanism

- **Blood clotting Stages:**
 1. Thromboplastin, which is the substance that triggers clotting mechanism will react with protein factors and calcium ion
 2. Protein factors and calcium ion will activate prothrombin activator
 3. Prothrombin activator will convert prothrombin to thrombin
 4. Thrombin will react with fibrinogen (soluble) converting it to fibrin (insoluble)/network of threads

- **Terms:**

- **Fibrinolytic System** – dissolves small, inappropriate clots. It also dissolves clots at a site of the damage once the damage is repaired
- **Fibrinolysis** – dissolution of clot
- **Plasminogen** – an inactive plasma enzyme incorporated into the clot
- **Plasmin** – an active plasma enzyme

Human Blood Groups

- RBC membranes have glycoprotein antigens on their external surfaces
- These antigens are:
 - Unique to the individual
 - Recognized as foreign if transfused into another individual
 - Promoter of agglutination and are referred to as agglutinogens
- Presence or absence of these antigens is used to classify blood groups
- Humans have 30 varieties of naturally occurring RBC antigens
- The antigens of the ABO and Rh(Rhesus factor) blood groups cause vigorous transfusion reactions when they are improperly transfused
- Other blood groups (M, N, Duffy, Kell, and Lewis) are mainly used for legalities, common in America

Blood Grouping

- Determined by antigens(agglutinogens) on surface of RBCs
- Antibodies (agglutinins) can bind to RBC antigens, resulting in agglutination (clumping) or hemolysis (rupture) of RBCs
- **Groups:**
 - ABO and Rh

ABO Blood Groups

- The ABO blood groups consists of:
 - Two antigens (A and B) on the surface of the RBCs
 - Two antibodies in the plasma (anti-A and anti-B)

- An individual with ABO blood may have various types of antigens and spontaneously preformed antibodies
- Agglutinogens and their corresponding antibodies cannot be mixed without serious hemolytic reactions

Type	Antigen	Antibody
A	A	Anti-B
B	B	Anti-A
AB	A and B	(-)
O	(-)	A and B

Rh Blood Groups

- Presence of the Rh agglutinogens on RBCs is indicated as Rh+, 85% of the population is positive
- Lack of antigen indicated as Rh-, 15% of population
- Anti-Rh antibodies are not spontaneously formed only in Rh- individuals
- However, if an Rh- individual receives Rh+ blood, anti-rh antibodies form
- First studied in rhesus monkeys
- **Types:**
 - Rh positive: Have these antigens present on surface of RBCs
 - Rh negative: Do not have these antigens present

Hemolytic Disease of the Newborn (HDN)

- **Erythroblastosis Fetalis**
- Mother produces anti-Rh antibodies that cross placenta and cause agglutination and hemolysis of fetal RBCs

- May occur in an Rh- mom pregnant with an rh+ fetus
 - Hemolytic disease of the newborn – Rh+ antibodies of a sensitized Rh- mother cross the placenta and attack and destroy the RBCs of an Rh+ baby
 - Rh- mother becomes sensitized when rh+ blood (from a previous pregnancy of an Rh+ baby or a Rh+ transfusion) causes her body to synthesize Rh+ antibodies
 - The drug RhoGAM can prevent the Rh- mother from becoming sensitized
 - Treatment of hemolytic disease of the newborn involves pre-birth transfusions and exchange transfusions after birth
- Complete blood count
 - Red blood count
 - Hemoglobin measurement
 - Hematocrit measurement
 - White blood count
 - Differential white blood count – age of leukocytes
 - Clotting time and bleeding time

Transfusion Reactions

- Transfusion reactions occur when mismatched blood is infused
- Donor's cells are attacked by the recipient's plasma agglutinins causing:
 - Diminished oxygen-carrying capacity
 - Clumped cells that impede blood flow
 - Ruptured RBCs that release free hemoglobin into the bloodstream
- Circulating hemoglobin precipitates in the kidneys and causes renal failure
- Agglutination and hemolysis of recipients blood causing fever

Diagnostic Blood Tests

- Type and crossmatch (3 steps)

Routine Blood Tests

- **Complete blood Count:**
 - **HgB: Hemoglobin**
 - M: 14-17 g/dl
 - F: 12-15 g/dl
 - **Hct: Hematocrit** – M: 42-52%
-F: 36-46%
 - **WBC count:** white blood cells/unit
 - **RBC count:** red blood cells/unit
 - **Differential cell count:** % WBC types
 - **Plt:** platelets/unit
 - **PT:** Prothrombin time – 12 seconds

Medical Terminologies

- **Cyanosis** – slightly bluish/dark-purple skin discoloration, most easily seen in the nail beds and mucous membranes, due to increased quantity of reduced hemoglobin in systemic blood.
- **Gamma Globulin** – solution of immunoglobulins from blood consisting of antibodies that react with specific pathogens.
- **Hemachromatosis** – disorder of iron metabolism characterized by excessive absorption of ingested and excess deposit of iron in tissues.

- **Acute Normovolemic Hemodilution**
 - removal of blood immediately before surgery and its replacement with a cell-free solution to maintain sufficient blood volume for adequate circulation
 - **Autologous preoperative Transfusion** – donating one's blood; this procedure eliminates the risk of incompatibility and blood-borne disease. Also called **predonation**
 - **Blood Bank** – a facility that collects and stored a supply of blood for future use by the donors or others
 - **Hemorrhage** – loss of large amount of blood. Can be external or internal
 - **Jaundice** – an abnormal yellowish discoloration of the sclera of the eyes, skin, and mucous membranes due to excess bilirubin in the blood.
 - **Phlebotomist** – a technician who specializes in withdrawing blood.
 - **Septicemia** – toxins or disease-causing bacteria in the blood. Also called "blood poisoning"
 - **Thrombocytopenia** – very low platelet count that results in a tendency to bleed from capillaries
 - **Venesection** – opening of a vein for withdrawal of blood
- *Central Venous Access** – slit to the right atrium, it is invasive because it goes inside the person
- *Non-invasive** – includes ECG, 2-D echo, X-ray
- **Whole blood** – blood containing all formed elements, plasma and plasma solutes in natural concentrations

- **Hemophilia** – is an inherited deficiency of clotting in which bleeding may occur spontaneously or after only a minor trauma. It is the oldest known hereditary bleeding disorder.

Blood Trivia

- a. **How long does it take a drop of blood to travel away from the heart and back again?**
 - 20 to 60 seconds.
- b. **Why do mosquitos feed on blood?**
 - Adult mosquitos actually eat the nectar of flowers. But mosquito babies need protein, not sugar, to grow. So their mothers feed on blood. Bloodsucking mosquito moms find you by sensing your body heat and breath. Then, with their proboscis, they drill a hole through your skin, into a capillary. Their saliva keeps the blood from clotting while they drink.
- c. Your blood takes a very long trip through your body. If you could stretch out all of a human's blood vessels, they would be about 60,000 miles long. That's enough to go around the world twice.

The HEART

General Info:

- Major pumping organ of the cardiovascular system
- Consists of cardiac muscle fibers
- Involuntary action
- Has a beat average of 100, 000 per day and 33 million beats per year
- Located in the mediastinum
- Pumps 14,000 liters of blood in a day, and 5 million liters of blood per year

Anatomy of the Heart:

Location of the Heart:

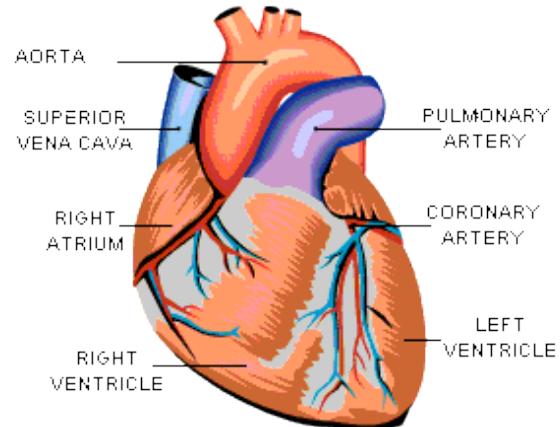
- Located in the mediastinum
- About 2/3 of the heart mass lies to the left of the body's midline
- The apex is formed by the tip of the left ventricle and rests on the diaphragm
- The base of the heart is its posterior surface which is formed by the atria of the heart

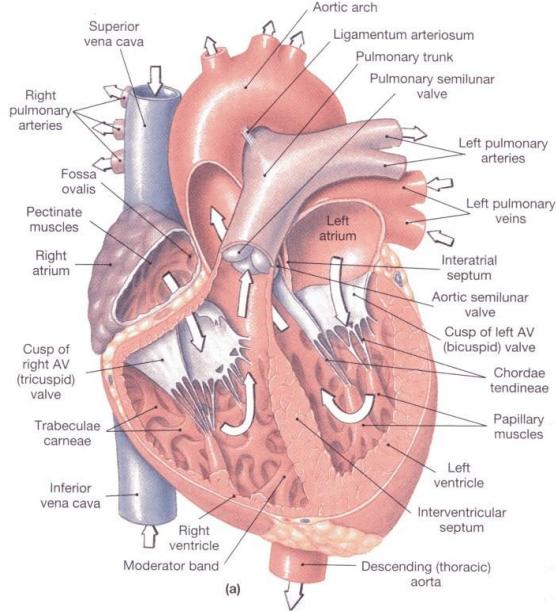
3 Layers of the wall of the heart:

1. Epicardium
 - Outermost layer
 - Composed of 2 layers:
 - Visceral Layer of the Serous Pericardium (Mesothelium)
 - Fibroelastic and adipose tissue layer
2. Myocardium
 - Middle layer
 - Responsible for the pumping action of the heart
 - Composed of cardiac muscle tissue
3. Endocardium
 - Innermost layer
 - Thin layer of endothelium overlying a thin layer of connective tissue
 - Provides a smooth lining for the chambers of the heart and covers the valves of the heart
 - Minimizes surface friction as blood passes through the heart

Chambers of the Heart:

- The heart has 4 chambers:
- 2 Superior chambers called atria and 2 inferior chambers called ventricles.
- Atria receive blood from blood vessels returning blood to the heart, called veins.
- Ventricles eject blood from the heart into blood vessels called arteries.





- Sulcus
- Grooves on the surface of the heart
 - Deep coronary sulcus
- Encircles most of the heart and marks the external boundary between the superior atria and inferior ventricles
 - Anterior interventricular sulcus
- Shallow groove on the anterior surface of the heart that marks the external boundary between the right and left ventricles.
 - Posterior interventricular sulcus
- Marks the external boundary between the ventricles on posterior aspect of the heart

1. RIGHT ATRIUM

- Forms the right border of the heart
- Receives blood from three veins: the superior vena cava, inferior vena cava, and coronary sinus.
- About 2-3 mm in thickness.

- Inside of posterior wall is smooth while the inside of the anterior wall is rough, which is due to muscular ridges called pectinate muscles.
- Between the right and left atria is a thin partition called the interatrial septum.

Valves present:

- Tricuspid valves
- Prevent backflow of blood towards the right atrium.
- Also known as the right atrioventricular valve

2. RIGHT VENTRICLE

- Forms the anterior surface of the heart
- About 4-5 mm in thickness
- The inside contains a series of ridges formed by raised cardiac muscle fibers called **trabeculae carneae** which help in the heart's conduction system
- Separated from the left ventricle via the **interventricular septum**.

- Chordae Tendinae
- Tendon-like chords that connect to the tricuspid valve and cone-shaped trabeculae carneae called **papillary muscles**.

- Blood passes from the right ventricle through the **pulmonary valve** into a large artery called the **pulmonary trunk**, which divides into right and left pulmonary arteries and carries blood to the lungs.
- Arteries always take blood from the heart

3. Left Atrium

- Receives blood from the lungs through four **pulmonary veins**.
- Roughly the same thickness as the right atrium at 2-3 mm thickness
- Has both a smooth posterior wall and a smooth anterior wall
- Blood passes from the left atrium into the left ventricle through the **bicuspid valve**, also called the left atrioventricular valve.

4. Left Ventricle

- Thickest chamber of the heart at 10-15 mm in thickness
- Forms the apex of the heart
- Also contains trabeculae carneae and chordate tendinae that anchor the bicuspid valve to papillary muscles.
- Blood passes from the left ventricle through the **aortic valve** into the ascending aorta.

Fibrous Skeleton of the Heart:

- Consists of four dense connective tissue rings that surround the valves of the heart, fuse together, and merge with the interventricular septum.
- Forms structural foundation for heart valves
- Prevents overstretching of the heart valves as blood passes through them.
- Serves as an electrical insulator between the atria and ventricles

Veins and Arteries of the Heart

1. Coronary Arteries

- There are two coronary arteries:
 - Right coronary artery
- Supplies small branches to the right atrium
- Continues inferior to the right auricle and divides into the posterior interventricular and marginal branches
- The **posterior interventricular branch** follows the posterior interventricular sulcus and supplies the walls of the two ventricles with oxygenated blood.
- Left coronary artery
- Passes inferior to the left auricle and divides into the **anterior interventricular sulcus** and supplies oxygenated blood to the walls of both ventricles.

2. Coronary Veins

- 4 major coronary veins:
 - Great Cardiac Vein
- Anterior interventricular sulcus
- Drains blood from areas of the heart supplied by left coronary artery
 - Middle Cardiac Vein
- Posterior interventricular sulcus
- Drains blood from areas of the heart supplied by the posterior interventricular branch of the right coronary artery
 - Small Cardiac Vein
- Coronary sulcus
- Drains blood from the right atrium and right ventricle

- Anterior Cardiac veins
- Drains blood from the right ventricle and open directly into the right atrium

Histology of Cardiac Muscle Tissue

- Compared to skeletal muscle fibers, cardiac muscle fibers are shorter in length and less circular in transverse section.
- Exhibit branching
- Typical cardiac muscle fiber is 50-100 μm long and has a diameter of about 14 μm .
- Usually has one centrally located nucleus present in one fiber
- Occasional cells may have two nuclei
- Ends of cardiac muscle fibers connect to neighboring fibers by irregular transverse thickenings of the sarcolemma called **intercalated discs**.
 - Intercalated discs
- Contains **desmosomes** that hold fibers together and;
- **Gap junctions** which allow muscle action potentials to conduct from one muscle fiber to its neighbors

Blood Vessel

Structure of Blood Vessel

Outer Layer

The walls of the larger blood vessels, the arteries and veins have three layers. The outermost layer of blood vessel is the *TUNICA ADVENTITIA* in Latin it means “coat that comes first” referring to how it is found during the dissection of a vessel. This layer is made up of strong, flexible fibrous connective tissue. It helps hold vessels open; prevents tearing of vessels during body movements.

Middle Layer

The middle layer of blood vessel is called the *TUNICA MEDIA*, which means “middle coat” for Latin. It is a layer of smooth muscle tissue sandwiched together with a layer of elastic connective tissue. Tunica media permits changes in blood vessel diameter.

⑩The middle layer smooth muscle is innervated by autonomic nerves and supplied with blood by tiny *vasa vasorum*.

Inner Layer

The innermost layer of a blood vessel is called the *TUNICA INTIMA*, which is a Latin for “innermost coat”. It is made up of endothelium; in arteries, completely smooth lining; in veins in forms of semilunar valves.

Types of Blood Vessel

There are three kinds of blood vessels which are ARTERIES, VEINS, and CAPILLARIES.

An ARTERY is a vessel that carries blood away from the heart, while small arteries are called **arterioles**.

A VEIN, on the other hand, is a vessel that carries blood toward the heart. All veins carry deoxygenated blood except the

pulmonary vein. Small veins are called *venules*, but often, very large venous spaces are called the *sinuses*.

⑩Both veins and arteries are macroscopic structures.

A CAPILLARY carries blood from small arteries to small veins, that is, from arterioles to venules. They are very tiny but very numerous in number.

Functions of Blood Vessel

The functions of different types of Blood vessels are determined upon their structures.

CAPILLARIES

These are the most important type of blood vessel in the body. Functionally, because they allow the delivery and collection of substances called the exchange of vessels.

Capillaries are often called the primary exchange vessels. They only contain one layer, the endothelium so the capillary wall is thin enough to allow effective exchanges of material between the plasma and interstitial fluid.

⑩ *microcirculation* – is the flow of blood through the capillary bed

ARTERIES

Arteries serve mainly as “distributors”, carrying the blood to the arterioles. They maintain normal blood pressure and circulation and they also serve as the *resistance vessels* of the cardiovascular. They are the blood vessels that carry blood from the heart to the other parts of the body.

Smooth muscle cell walls in the walls of arterioles acts as *precapillary sphincters* near the point at which a capillary originates.

VEINS

Veins function both as collectors and as reservoir vessels. They not only return blood to the heart, but they can also accommodate varying amounts of blood. Veins have the greatest ability to be stretched. This ease of stretch is called *capacitance*, for which they are referred to as "capacitance vessel".

CIRCULATORY ROUTES OF BLOOD

The term circulation of blood suggests its meaning, the blood flow through vessels arranged to form a circuit or circular pattern. There are two types of circulation occurring in the body; namely, the **Systematic Circulation** and **Pulmonary Circulation**.

ANATOMY OF ARTERIES

Systematic Circulation

Blood flows from the heart through the blood vessels then to all parts of the body and back to the heart. It receives oxygen-rich blood from the lungs.

Systemic Arteries

The **AORTA** is the major artery that serves as the main trunk of the entire systemic arterial system. The Aorta is consist of 3 main parts.

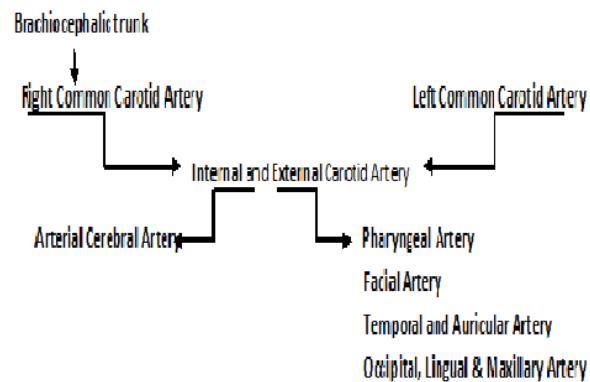
- a. **Ascending Aorta** – the region where the aorta conducts blood upward out of the left ventricle of the heart.
- b. **Arch of Aorta / Aortic Arch** – region where the aorta turns 180° downward.
- c. **Descending Aorta** – the region where the arterial blood is conducted downwards the arc of aorta.

General Principles about Arteries

Arteries are the major pipeline distributing blood from the heart to the various organs and that, in each organ of the body. Arteries continue to branch and rebranch, forming **arterioles** then to much smaller vessel called **capillaries**.

ARTERIES OF THE HEAD AND NECK

The left side of the head is supplied of blood by the **left common carotid artery** while the **brachiocephalic artery** supplies the right side of the head and neck.



Basilar Artery – located undersurface of the brainstem where vertebral arteries unite, which shortly branches into right and left posterior cerebral arteries.

Communicating Arteries – joins the anterior and posterior cerebral arteries in such a way as to form an **ARTERIAL CIRCLE** (circle of Willis) at the base of the brain. E.g Arterial Anastomosis.

ARTERIES OF THE EXTREMITIES AND TRUNK

The arteries of the upper extremities gradually branches from Subclavian Artery. The subclavian Artery branches out to Acromial, Axillary, Subscapular, Brachial, Radial and Ulnar Artery. The Radial Artery and Ulnar Artery forms the Palmar Arch and Digital Arteries.

® The distal part of the RADIAL ARTERY is often used to assess a person's pulse.

In the lower extremities, the ABDOMINAL AORTA supplies arterial vessels. Abdominal aorta branches out as other arteries in Hips, Thighs and Legs.

Hip	Thighs	Legs
Iliac Artery	Femoral Artery	Fibular Artery
Sacral Artery	Genicular Artery	Tibial Artery
Pudendal Artery	Popliteal Artery (in knees)	Pedis Artery
Gluteal Artery		Plantar Artery
Obturator		Digital Artery

THE ANATOMY OF THE VEINS

- Veins are most likely blue-colored in majority of diagrams in blood vessels. The veins are the large blood vessels responsible for returning deoxygenated blood back to the heart for oxygenation.

The structure of the Veins

- Venous structure resembles the arteries although with difference in layer thickness. It may have a thickness range of 0.1 millimeters to more than 1 millimeter. Many of the veins feature valves, which are fold of the inner layer (tunica interna) which forms cusps that extend to the lumen and pointing toward the heart. These valves prevent backflow of blood when blood travels back to the heart.

Layers:

a. Tunica Externa- This is the thickest layer in the veins that consist primarily of collagen and elastic fibers.

b. Tunica Media- Compared to arteries, this layer of the veins is thinner composed of thin smooth muscles and elastic fibers. Veins also lack the external elastic lamina which decreases the ability of veins to adapt to varying pressure in the blood flow.

c. Tunica Interna (or Intima)- This layer of the veins are thinner compared to arteries. It is composed of an endothelium (a lining of simple squamous epithelium) and a basement membrane. The internal elastic lamina present in arteries is absent in the veins contributing to the veins lack of resistance to high blood pressure.

The lumen of the vein is relatively wider than a counterpart artery, and may often appear collapsed.

Venules

- Before blood from capillaries reach the veins, they enter venules. Venules are small veins formed through the unification of several capillaries having a diameter ranging from 10 – 100 micrometers. They function to collect and deliver blood from the capillaries to the veins. The venules have a tunica media and tunica interna and few smooth muscle fibers. The walls of these venules are porous like the capillaries that may function as gateways for white blood cells to enter.

Medical complications of veins:

a. Superficial Thrombophlebitis

-Formation of a clot on a superficial vein most commonly in the lower limb or calf which appears as a red streak that is accompanied by swelling. This condition usually occurs in the varicose veins. If cancer is the known cause for the superficial blood clots, this is referred to as Trousseau's syndrome.

b. Deep Vein Thrombosis

- This occurs when a clot forms in one of the deeper veins most commonly in the legs. Symptoms may include pain during walking and leg swelling.

c. Chronic Venous Insufficiency

- Results from the insufficient drainage of blood for a significant period of time in a deep vein. This may be a result of faulty venous valves. This complication can be characterized by pain and swelling, a change in skin color and the coarsening of skin in the affected area. Changes in skin color and texture result from the deposit of dead red blood cells over a long period of time.

- This can also occur superficially in the case of varicose veins.

d. Aneurysm

- this is the bulging out of a weakened section of an artery or vein that may burst if left untreated resulting to internal hemorrhage. Causes may be due to congenital disorders, trauma, fat deposits or syphilis.

VEINS IN THE CIRCULATORY SYSTEM

Veins of the Head and Neck

1. The internal Jugular veins

- Drains the brain (through the dural venous sinuses), face, and neck

2. External Jugular veins

- Drains parts of the head, the scalp, superficial and deep regions of the face
- Become very prominent during heavy straining or coughing

3. Vertebral veins

- Drain the deep structures in the neck, like the cervical spinal cord and several neck muscles

Veins of the Upper limbs

A. Superficial

1. Cephalic veins

- A major draining vein in the upper limbs
- Drains the lateral aspect of the upper limbs

2. Basilic Veins

- Drain the anterior aspect of the upper limbs
- Connect to the cephalic vein anteriorly to the elbow to form the median cubital vein
- Merge with the brachial veins to form the axillary vein

3. Median antebrachial veins

- Drain the palms and the forearms

B. Deep

1. Radial veins

- Drain the lateral aspects of the forearms
- Merges with the ulnar vein to form the brachial vein

2. Ulnar veins

- Paired and larger than the radial veins
- Drain the medial aspects of the forearm

3. Brachial veins

- Accompany the brachial arteries, drains the forearm, elbow joints, and humerus

4. Axillary veins

- Become the subclavian veins as they reach the outer borders of the first ribs
- Drains the arms, axillas and superolateral chest wall

5. Subclavian veins

- Unite with the internal jugular veins to form the brachiocephalic veins
- Drains the arms, neck and thoracic wall

Veins of the Thorax

1. Brachiocephalic vein

- Collects blood from the head, neck, upper limbs, mammary glands, and superior thorax

2. Azygos vein

- Drains the right side of the thoracic wall, thoracic viscera, and abdominal wall
- Receives blood from most of the right posterior intercostal, hemiazygos, accessory hemiazygos esophageal, mediastinal, pericardial, and bronchial veins.

3. Hemiazygos vein

- Drains the left side of the thoracic wall, thoracic viscera, and abdominal wall.
- Specifically receives blood from the 9th to 11th left posterior intercostal, esophageal, mediastinal and sometimes the accessory hemiazygos veins.

4. Accessory Hemiazygos vein

- Drains the left side of the thoracic wall
- Receives blood from the 4th to 8th left posterior intercostal veins, left bronchial, and ,mediastinal veins

Veins of the Abdomen and Pelvis

1. Inferior Vena cava

- Drains blood to the heart from the lower body
- Formed by the two common iliac veins that unite

2. Common iliac veins

- Drain the pelvis, external genitals, and lower limbs

3. Internal iliac veins

- Drain the thigh, buttocks, external genitals and pelvis

4. External iliac veins

- Drain the lower limbs, cremaster muscle in males, and the abdominal wall

5. Lumbar veins

- Drain blood from both sides of the posterior abdominal wall, vertebral canal, spinal cord and the meninges

6. Gonadal veins

- Called testicular veins in males, draining the testes, and called ovarian veins in females draining the ovaries

7. Renal veins

- Drain the kidneys

8. Suprarenal veins

- Drain the adrenal glands

9. Inferior Phrenic veins

- Drain the diaphragm

10. Hepatic veins

- Drain the liver

Veins of the Lower limbs

A. Superficial veins

1. Great Saphenous veins

- Longest veins in the body
- Drain mainly the medial side of the leg and thigh, the groin, external genitals, and abdominal wall
- May have 10 – 20 valves

2. Small Saphenous veins

- Drain the foot and the posterior aspect of the leg
- May have 9 – 12 valves

B. Deep veins

1. Posterior tibial veins

- Unite with the anterior tibial veins to form the popliteal veins
- Drain the foot and posterior leg muscles

2. Anterior tibial veins

- Drain the ankle joint, knee joint, tibiofibular joint, and anterior portion of the leg

3. Popliteal veins

- Drain the knee joint, the skin, muscles and bone of portions of the calf and thigh around the knee joint

4. Femoral veins

- Drain the thigh muscles, femurs, external genitalia, and superficial lymph nodes

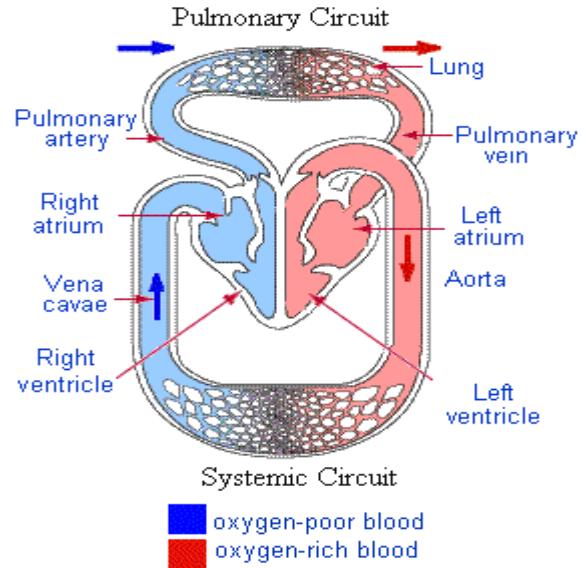
PHYSIOLOGY OF THE CARDIOVASCULAR SYSTEM

HEMODYNAMICS- a term used to describe a collection of mechanisms that influence the active and changing circulation of blood

Blood Circulation:

- Pulmonary Circulation
- Un oxygenated blood flows through the superior and inferior vena cava, and the coronary sinus into the right atrium. The tricuspid valve opens as the blood flows into the right ventricle. The pulmonary valve is opened while the tricuspid valve closes as the blood is pushed into the pulmonary trunk and pulmonary arteries.

- Systemic Circulation
- In the pulmonary capillaries, blood loses CO₂ and gains Oxygen. Oxygenated blood flows through the pulmonary veins into the left atrium. The bicuspid valve opens as blood enters the left ventricle. The aortic valve opens while the bicuspid valve closes as the blood is pushed into the aorta and systemic arteries.



Conduction System of the Heart

- Consists of the Sinoatrial (SA) node, Atrioventricular (AV) node, AV bundle, and Purkinje system
 - Structures are made up of highly specialized cardiac muscle tissue
 - Structures are not contractile; permit only generation or rapid conduction of an action potential
- 1) Sinoatrial (SA) node
 - a) Pacemaker cells in the node possess an intrinsic rhythm
 - b) *Intrinsic rhythm*- initiate impulses at regular intervals even without stimulation by nerve impulses from the brain and spinal cord
 - c) Interatrial bundle facilitates rapid conduction to the left atrium
 - 2) Atrioventricular (AV) node
 - a) Action potential enters AV nodes via intermodal bundles
 - b) Slow conduction
 - 3) AV bundle (bundle of His)
 - a) Conduction velocity increases

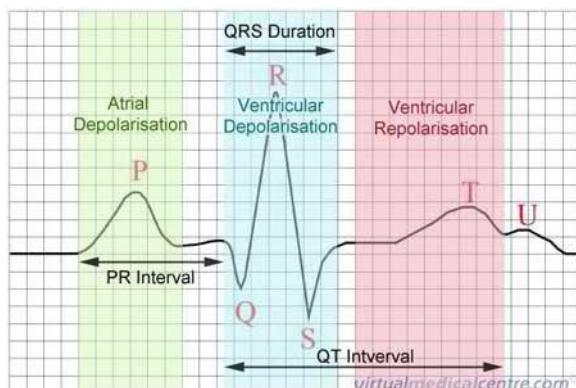
- b) Impulse is conducted to the ventricles via AV bundles
 - 4) Purkinje system
- Ectopic pacemakers-* pacemakers other than the SA node; rate of discharge are slower than SA node

Electrocardiogram (ECG)

Electrocardiogram- a graphic record of heart's activity, and its conduction of impulses

Electrocardiograph- visible records of the heart's electrical activity

ECG waves



- 1) P Wave
 - Depolarization of the atria
- 2) QRS Complex
 - Depolarization of the ventricles
 - Q, R, and S represent the entire process of ventricular depolarization
- 3) T Wave
 - Repolarization of the ventricles
- 4) U Wave
 - A tiny hump at the end of the T wave
 - Repolarization of Purkinje fibers

Cardiac Cycle

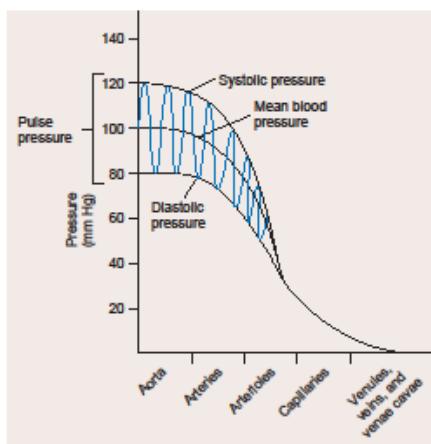
- Systole- Contraction
- Diastole- Relaxation

- 1) Atrial Systole
 - a) The contracting force of the atria empty the blood out of the atria into the ventricles
- 2) Isovolumetric Ventricular Contraction
 - a) Start of ventricular systole and the opening of semilunar valves
 - b) The onset of ventricular systole coincides with the R wave of the ECG
- 3) Ejection
 - a) Semilunar Valves open and blood is ejected from the heart when the pressure gradient in the ventricles exceeds pressure in the pulmonary artery and aorta
 - b) *Residual volume-* a considerable quantity of blood that normally remains in the ventricles at the end of ejection
- 4) Isovolumetric ventricular Relaxation
 - a) Closure of the semilunar valves and opening of the atrioventricular valves
 - b) The atrioventricular valves do not open until the pressure in the atrial chambers increases above that in relaxing ventricles
- 5) Passive Ventricular Filling
 - a) *Diastasis-* a later longer period of slow ventricular filling at the end of ventricular diastole
 - b) The abrupt inflow of blood that occurred after opening the atrioventricular valves is followed by a slow continuous flow of venous blood into atria, and then through the open atrioventricular valve into the ventricles

Heart Sounds

First, or systolic, sound is caused primarily by the contraction of the ventricles and also by vibrations of the closing atrioventricular, or cuspid, valves. It is longer and lower than the second, or diastolic, sound which is caused by vibrations of the semilunar valves.

Primary Principle of Circulation

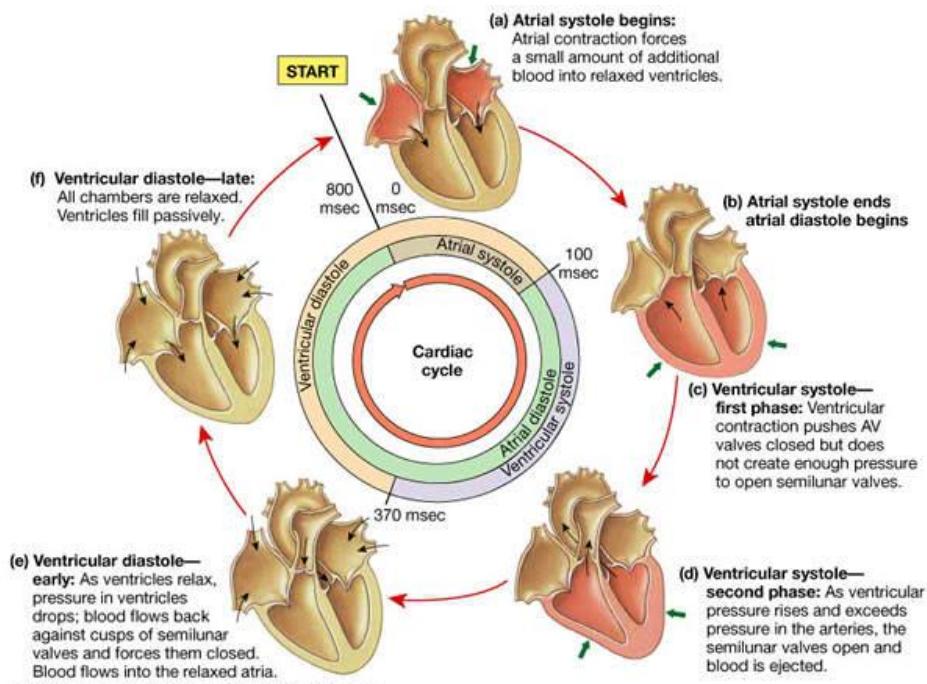


Fluid always travels from an area of high pressure to an area of low pressure. Blood flows

from an area of high average pressure at the beginning of the aorta (100 mm Hg) toward the area of lowest pressure at the end of the venae cavae (0 mm Hg). As seen on the illustration, the progressive fall in pressure as blood passes through the circulatory system is directly related to resistance. The lower the resistance, the lower the pressure; the higher the resistance, the lower the pressure.

Arterial Blood pressure

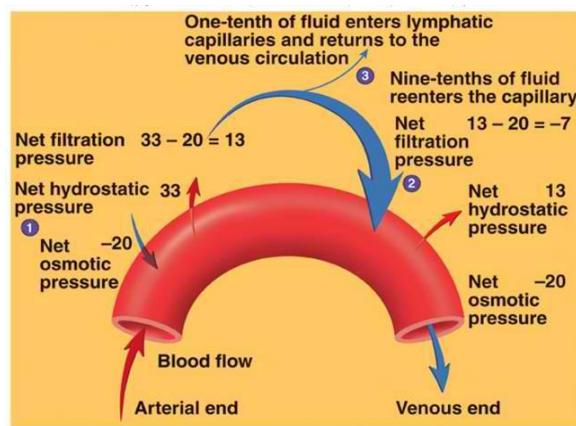
- High pressure in the arteries must be maintained to keep blood flowing
 - An increase in arterial blood volume tends to increase in arterial pressure and vice versa
 - Two of the most important factors determining arterial volume is *cardiac output* and *peripheral output*
- 1) Cardiac output
 - a) Determined by volume of blood pumped out of the ventricles by each beat and by heart rate



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- b) Stroke volume- the amount of blood pumped by one stroke of the ventricle
- c) The greater the stroke volume, the greater the cardiac output ;
 $SV \text{ (volume /beat)} \times HR \text{ (beat/ min)}$
 $= CO \text{ (volume/ min)}$
- d) Because heart's rate and stroke volume determine its output, anything that changes the rate of the heartbeat or its stroke volume tends to change Cardiac output, arterial volume and blood pressure in the same direction
- 2) Peripheral output
- Helps determine arterial blood pressure—arterial blood pressure vary directly with peripheral resistance
 - Peripheral resistance- the resistance to blood flow imposed by the force of friction between blood and the walls of its vessels
 - Peripheral resistance helps determine arterial pressure by controlling the rate of “arterial runoff,” the amount of blood that runs out of the arteries and arterioles
- 1) Venous pumps
- a) Respiratory pump
 - alternately decreasing thoracic pressure during inspiration (pulls blood into central veins) and increasing pressure in the thorax during expiration (pushes central venous blood into the heart)
 - b) Skeletal Muscle pump
 - Promotes venous return by contracting and squeezing soft veins—“milking” the blood inside the veins and move them towards the heart
 - Moves blood through veins

Capillary Exchange and Total Blood Volume



Venous Returns to the Heart

- the amount of blood that is returned to the heart by way of the veins

- 1) Starling’s Law of the Capillaries
- Several factors govern the movement of fluid (and solutes contained in the fluid) back and forth across the capillary wall
- 2) Osmotic pressure
- Promotes diffusion of fluid into plasma

- Blood colloids in the plasma that cannot cross vessel wall draws water osmotically into plasma
 - At the arterial end of capillary, the potential osmotic pressure is small and thus generates only a small inwardly directed force
 - At the venous end, loss of water (due to hydrostatic pressure) increases blood colloid osmotic pressure—promoting osmosis of water back into plasma
- 3) Hydrostatic pressure gradient
- Promote filtration across capillary wall
 - At the arterial end, blood pressure in the vessel is greater than the hydrostatic pressure of the interstitial fluid thus producing a net loss of blood volume
 - 10% of the fluid lost is recovered by the lymphatic system and returned to the venous blood before it reaches the heart

Changes in Total Blood Volume

- 1) ADH mechanism
- ADH increases the amount of water that kidneys reabsorb from urine; thus, more water is reabsorbed into the blood, and the greater the blood plasma volume would become

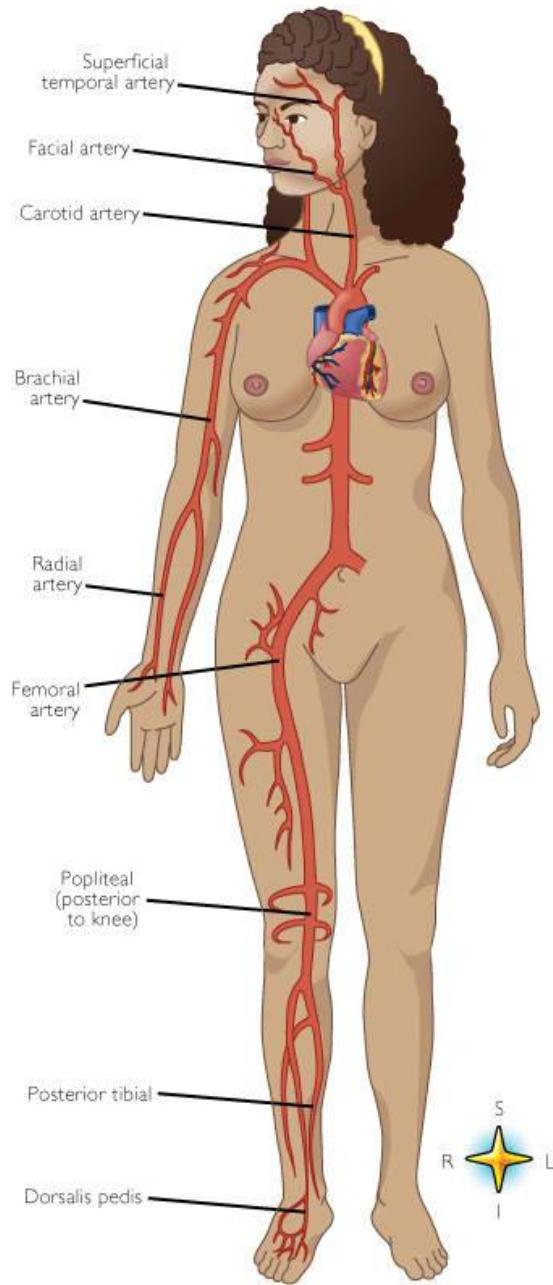
- 2) Renin- angiotensin mechanism
- Renin triggers secretion of aldosterone, which in turn promotes sodium retention by the kidney; the latter results to the stimulation of the osmotic flow of water from kidney tubules back to the blood plasma
- 3) ANH mechanism
- ANH adjusts venous return back down to its set point value by promoting the loss of water from the plasma and the resulting decrease in blood volume.

PULSE

- Alternate expansion and recoil of an artery
- 1) Clinical Significance: reveals important information regarding cardiovascular system, blood vessels and circulation
 - 2) Physiological Significance: expansion stores energy generated by the heart and maintaining relatively constant blood flow
 - 3) Reasons for the existence of pulse
 - a) Alternating increase and decrease of pressure in the vessel
 - b) Elasticity of arterial walls allows walls to expand with increased pressure and recoil with decreased pressure

Pulse points

- Radial artery- at wrist
- Temporal artery- in front of ear or above and to outer side of eye
- Common carotid artery- along anterior edge of sternocleidomastoid muscle at level of lower margin of thyroid cartilage
- Facial artery- at lower margin of jawbone on a line with corners of mouth and in groove in mandible about one third of way forward from angle
- Brachial artery- at bend of elbow along inner margin of biceps muscle
- Popliteal artery- behind knee
- Posterior tibial artery- behind the medial malleolus (inner "ankle bone")
- Dorsalis pedis artery- on the dorsum (upper surface) of the foot



Diseases and Disorders Related to the Cardiovascular System

a. Congestive heart failure

- This disorder is a general term referring to the failure of the heart to meet demand of the body for circulating blood for the processes of metabolism. Heart failure may be the chronic or acute types, high or low level input failure, left or right sided biventricular failure. Various diseases and disorders may be the cause of heart failure.

b. Coronary Artery disease

- This disease is caused by the accumulation of plaque, due to high cholesterol levels in the blood, in the coronary arteries which results to partial obstruction of blood into the myocardium. Its risk of occurrence could be increased by smoking, hypertension and other blood related diseases.

c. Acute Myocardial Infarction

- Results from the obstruction of blood through the coronary arteries by accumulated atherosclerotic plaque. This can lead to cardiac arrest and probable death.

d. Hypertension

- Hypertension is when the blood pressure of an individual rises above normal. Blood pressure is the product between the blood volume pumped by the heart and the resistance to the flow by the blood vessels. A systolic pressure of 165 mmHg and a diastolic pressure of 95 mmHg can be considered as high blood pressure.

e. Cardiomegaly

- Refers to the condition in which the heart is enlarged beyond the normal range. It is due to the thickening of the myocardial wall resulting from genetic inconsistencies (hypertrophic cardiomyopathy). The overwork of the heart can also cause the heart cells to hypertrophy due to an increase in the oxygen demand.

f. Cardiac Arrhythmia

- Also called as dysrhythmia, cardiac arrhythmia refers to a defect in the conduction system of the heart that results to an irregular heartbeat.

Types of Arrhythmia

1. *Bradycardia*- refers to a slow heart rate lower than 50 beats per minute.

2. *Tachycardia*- quick, rapid heart rate of over 100 beats per beat.

② *Supraventricular tachycardia (SVT)*- a regular but rapid heart rate of 160 – 200 beats per minute that comes from the atria. It may last for a few minutes to many hours.

③ *Ventricular tachycardia (VT)*- The ventricles of the heart beat at a rate of more than 120 beats per minute. Ventricular tachycardia is associated with heart disease of infarction and may develop ventricular fibrillation.

3. *Fibrillation*- these are rapid and uncoordinated heart beats.

④ *Ventricular fibrillation*- The most dangerous type of arrhythmia. Fibers of the ventricles do not contract in coordination and therefore no net contraction of the ventricles is seen. Blood ejection ceases and may cause death if medical help does not intervene.

⑤ *Atrial fibrillation*- a common arrhythmia in where the atria contract up to 600 beats per minute and in an uncoordinated manner that atrial pumping stops.

Other types of arrhythmia:

⑥ *Heart block*- a type of arrhythmia from the inhibition of the electrical pathways between the atria and the ventricles that slows the transmission of nerve impulses. The most common site of inhibition is the atrioventricular node (Atrioventricular block).

② **Atrial flutter**- the occurrence rapid, regular atrial contraction of 240- 360 beats per minute with an atriventricular block when the nerve impulse from the SA node to the AV node is weakened.

③ **Ventricular premature contraction**- A region of the heart other than the conduction system (ectopic focus) becomes abnormally excitable that causes an occurrence of an action potential. This causes premature contraction of the ventricles.

g. Congenital Heart defects

These defects that are present at birth can affect the individual depending on its severity.

1. **Coarctation**- This is the condition in which a segment of the aorta is too narrow. This decreases blood flow thus making the left ventricle pump harder which increases the blood pressure.

2. **Patent ductus arteriosus (PDA)**- after birth, a blood vessel between the aorta and the pulmonary trunk, which is supposed to be closed, remains open. This allows aortic blood to flow into the pulmonary trunk increasing the pulmonary trunk pressure and overworking both ventricles.

3. **Septal defect**- May occur in the midst of the atria (atrial septal defect) or the ventricles (ventricular septal defect) in which the septum dividing the chambers from left to right is not completely closed resulting to the contamination of oxygenated blood.

4. **Tetralogy of Fallot**- A defect in which four complications are combined – an interventricular septal defect, an aorta emerges from both ventricles, a stenosed pulmonary valve and an enlarged right ventricle. This causes cyanosis (“blue baby” in infants) but could be successfully treated by surgery.

Other Blood Diseases:

1. **Blackfan Diamond Anemia** - is present at birth but can be difficult to identify. In about one-third of children born with the disorder, there are physical defects such as hand deformities or heart defects, but a clear set of signs hasn't been identified. The symptoms may also vary greatly, from very mild to severe and life-threatening.
2. **Myelodysplastic Syndromes** - There are several subtypes of myelodysplastic syndromes (MDS), but they are all disorders in which the cells in the bone marrow don't function normally and not enough normal blood cells are produced. MDS usually occurs in older people, typically starting after age 50. Myelodysplastic syndrome is rarely inherited. For many people, it develops without any known cause. In other people, MDS may develop after being exposed to chemotherapy or radiation therapy. Exposures to industrial chemicals such as benzene are also linked to the development of MDS.
3. **Paroxysmal nocturnal hemoglobinuria** - (PNH) is an acquired blood stem cell disorder. It was originally named for its symptom of dark-colored urine (hemoglobinuria) produced in the morning. It was thought that the abnormal breakdown of red blood cells (hemolysis) that caused the dark urine occurred in bursts (paroxysms) that occurred at night. Research has shown, however, that the hemolysis in PNH, caused by a biochemical defect, occurs throughout the day and does not occur in bursts. The change in urine color may occur at any time, but is most dramatic in concentrated nighttime urine.

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