

The Cardiovascular System: The Blood

Fluids of the Body

- Cells of the body are serviced by 2 fluids
 - blood
 - composed of plasma and a variety of cells
 - transports nutrients and wastes
 - interstitial fluid
 - bathes the cells of the body
- Nutrients and oxygen diffuse from the blood into the interstitial fluid & then into the cells
- Wastes move in the reverse direction

Functions of Blood

- Transportation
 - O₂, CO₂, metabolic wastes, nutrients, heat & hormones
- Regulation
 - helps regulate pH through buffers
 - helps regulate body temperature
 - coolant properties of water
 - vasodilatation of surface vessels dump heat
 - helps regulate water content of cells by interactions with dissolved ions and proteins
- Protection from disease & loss of blood

Physical Characteristics of Blood

- Thicker (more viscous) than water and flows more slowly than water
- Temperature of 100.4 degrees F
- pH 7.4 (7.35-7.45)
- 8 % of total body weight
- Blood volume
 - 5 to 6 liters in average male
 - 4 to 5 liters in average female
 - hormonal negative feedback systems maintain constant blood volume and osmotic pressure

Techniques of Blood Sampling

Components of Blood

- Hematocrit
 - 55% plasma
 - 45% cells
 - 99% RBCs
 - < 1% WBCs and platelets

Blood Plasma

- Over 90% water
- 7% plasma proteins
 - created in liver
 - confined to bloodstream
 - albumin
 - maintain blood osmotic pressure
 - globulins (immunoglobulins)
 - antibodies bind to foreign substances called antigens
 - form antigen-antibody complexes
 - fibrinogen
 - for clotting
- 2% other substances
 - electrolytes, nutrients, hormones, gases, waste products

Formed Elements of Blood

- Red blood cells (erythrocytes)
- White blood cells (leukocytes)
 - granular leukocytes
 - neutrophils
 - eosinophils
 - basophils
 - agranular leukocytes
 - lymphocytes = T cells, B cells, and natural killer cells
 - monocytes
- Platelets (special cell fragments)

Hematocrit

- Percentage of blood occupied by cells
 - female normal range
 - 38 - 46% (average of 42%)
 - male normal range
 - 40 - 54% (average of 46%)
 - testosterone
- Anemia
 - not enough RBCs or not enough hemoglobin
- Polycythemia
 - too many RBCs (over 65%)
 - dehydration, tissue hypoxia, blood doping in athletes

Formation of Blood Cells

- Most blood cells types need to be continually replaced
 - die within hours, days or weeks
 - process of blood cells formation is hematopoiesis or hemopoiesis
- In the embryo
 - occurs in yolk sac, liver, spleen, thymus, lymph nodes & red bone marrow

- In adult
 - occurs only in red marrow of flat bones like sternum, ribs, skull & pelvis and ends of long bones

Hematopoiesis Stages of Blood Cell Formation

- Pluripotent stem cells
 - .1% of red marrow cells
 - replenish themselves as they differentiate into either myeloid or lymphoid stem cells
- Myeloid stem cell line of development continues:
 - progenitor cells(colony-forming units) no longer can divide and are specialized to form specific cell types
 - example: CFU-E develops eventually into only red blood cells
 - next generation is blast cells
 - have recognizable histological characteristics
 - develop within several divisions into mature cell types
- Lymphoid stem cell line of development
 - pre-B cells & prothymocytes finish their develop into B & T lymphocytes in the lymphatic tissue after leaving the red marrow

Hemopoietic Growth Factors

- Regulate differentiation & proliferation
- Erythropoietin (EPO)
 - produced by the kidneys increase RBC precursors
- Thrombopoietin (TPO)
 - hormone from liver stimulates platelet formation
- Cytokines are local hormones of bone marrow
 - produced by some marrow cells to stimulate proliferation in other marrow cells
 - colony-stimulating factor (CSF) & interleukin stimulate WBC production

Red Blood Cells or Erythrocytes

- Contain oxygen-carrying protein hemoglobin that gives blood its red color
 - 1/3 of cell's weight is hemoglobin
- Biconcave disk 8 microns in diameter
 - increased surface area/volume ratio
 - flexible shape for narrow passages
 - no nucleus or other organelles
 - no cell division or mitochondrial ATP formation
- Normal RBC count
 - male 5.4 million/drop ---- female 4.8 million/drop
 - new RBCs enter circulation at 2 million/second

Hemoglobin

- Globin protein consisting of 4 polypeptide chains

- One heme pigment attached to each polypeptide chain
 - each heme contains an iron ion (Fe^{+2}) that can combine reversibly with one oxygen molecule

Transport of O_2 , CO_2

- Each hemoglobin molecule can carry 4 oxygen molecules from lungs to tissue cells
- Hemoglobin transports 23% of total CO_2 waste from tissue cells to lungs for release
 - combines with amino acids in globin portion of Hb

RBC Life Cycle

- RBCs live only 120 days
 - wear out from bending to fit through capillaries
 - no repair possible due to lack of organelles
- Worn out cells removed by fixed macrophages in spleen & liver
- Breakdown products are recycled

Recycling of Hemoglobin Components

- In macrophages of liver or spleen
 - globin portion broken down into amino acids & recycled
 - heme portion split into iron (Fe^{+3}) and biliverdin (green pigment)

Fate of Components of Heme

- Iron(Fe^{+3})
 - stored in liver, muscle or spleen
 - in bone marrow being used for hemoglobin synthesis
- Biliverdin (green) converted to bilirubin (yellow)
 - bilirubin secreted by liver into bile
 - converted to urobilinogen then stercobilin (brown pigment in feces) by bacteria of large intestine
 - if reabsorbed from intestines into blood is converted to a yellow pigment, urobilin and excreted in urine

Normal Reticulocyte Count

- Should be .5 to 1.5% of the circulating RBC's
- Low count in an anemic person might indicate bone marrow problem
 - leukemia, nutritional deficiency or failure of red bone marrow to respond to erythropoietin stimulation
- High count might indicate recent blood loss or successful iron therapy

WBC Anatomy and Types

- All WBCs (leukocytes) have a nucleus and no hemoglobin
- Granular or agranular classification based on presence of cytoplasmic granules made visible by staining
 - granulocytes are neutrophils, eosinophils or basophils
 - agranulocytes are monocytes or lymphocytes

Classification of Leukocytes: Granulocytes

- Granulocytes – neutrophils, eosinophils, and 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

Agranulocytes

- Agranulocytes – lymphocytes and monocytes:
 - Lack visible cytoplasmic granules
 - Are similar structurally, but are functionally distinct and unrelated cell types
 - Have spherical (lymphocytes) or kidney-shaped (monocytes) nuclei

Neutrophils (Granulocyte)

- Polymorphonuclear Leukocytes or Polys
- Nuclei = 2 to 5 lobes connected by thin strands
 - older cells have more lobes
 - young cells called band cells because of horseshoe shaped nucleus (band)
- Fine, pale lilac practically invisible granules
- Diameter is 10-12 microns
- 60 to 70% of circulating WBCs

Eosinophils (Granulocyte)

- Nucleus with 2 or 3 lobes connected by a thin strand
- Large, uniform-sized granules stain orange-red with acidic dyes
 - do not obscure the nucleus
- Diameter is 10 to 12 microns
- 2 to 4% of circulating WBCs

Basophils (Granulocyte)

- Large, dark purple, variable-sized granules stain with basic dyes
 - obscure the nucleus
- Irregular, s-shaped, bilobed nuclei
- Diameter is 8 to 10 microns
- Less than 1% of circulating WBCs

Lymphocyte (Agranulocyte)

- Dark, oval to round nucleus
- Cytoplasm sky blue in color
 - amount varies from rim of blue to normal amount
- Small cells 6 - 9 microns in diameter
- Large cells 10 - 14 microns in diameter
 - increase in number during viral infections
- 20 to 25% of circulating WBCs

Monocyte (Agranulocyte)

- Nucleus is kidney or horse-shoe shaped
- Largest WBC in circulating blood
 - does not remain in blood long before migrating to the tissues
 - differentiate into macrophages
 - fixed group found in specific tissues
 - alveolar macrophages in lungs
 - kupffer cells in liver
 - wandering group gathers at sites of infection
- Diameter is 12 - 20 microns
- Cytoplasm is a foamy blue-gray
- 3 to 8% of circulating WBCs

WBC Physiology

- Less numerous than RBCs
 - 5000 to 10,000 cells per drop of blood
 - 1 WBC for every 700 RBC
- Leukocytosis is a high white blood cell count
 - microbes, strenuous exercise, anesthesia or surgery
- Leukopenia is low white blood cell count
 - radiation, shock or chemotherapy
- Only 2% of total WBC population is in circulating blood at any given time
 - rest is in lymphatic fluid, skin, lungs, lymph nodes & spleen

Neutrophil Function

- Fastest response of all WBC to bacteria
- Direct actions against bacteria
 - release lysozymes which destroy/digest bacteria
 - release defensin proteins that act like antibiotics & poke holes in bacterial cell walls destroying them
 - release strong oxidants (bleach-like, strong chemicals) that destroy bacteria

Monocyte Function

- Take longer to get to site of infection, but arrive in larger numbers
- Become wandering macrophages, once they leave the capillaries
- Destroy microbes and clean up dead tissue following an infection

Basophil Function

- Involved in inflammatory and allergy reactions
- Leave capillaries & enter connective tissue as mast cells
- Release heparin, histamine & serotonin
 - heighten the inflammatory response and account for hypersensitivity (allergic) reaction

Eosinophil Function

- Leave capillaries to enter tissue fluid

- Release histaminase
 - slows down inflammation caused by basophils
- Attack parasitic worms
- Phagocytize antibody-antigen complexes

Lymphocyte Functions

- B cells
 - destroy bacteria and their toxins
 - turn into plasma cells that produces antibodies
- T cells
 - attack viruses, fungi, transplanted organs, cancer cells & some bacteria
- Natural killer cells
 - attack many different microbes & some tumor cells
 - destroy foreign invaders by direct attack

Differential WBC Count

- Detection of changes in numbers of circulating WBCs (percentages of each type)
 - indicates infection, poisoning, leukemia, chemotherapy, parasites or allergy reaction
- Normal WBC counts
 - neutrophils 60-70% (up if bacterial infection)
 - lymphocyte 20-25% (up if viral infection)
 - monocytes 3 -- 8 % (up if fungal/viral infection)
 - eosinophil 2 -- 4 % (up if parasite or allergy reaction)
 - basophil <1% (up if allergy reaction or hypothyroid)

Platelet (Thrombocyte) Anatomy

- Disc-shaped, 2 - 4 micron cell fragment with no nucleus
- Normal platelet count is 150,000-400,000/drop of blood
- Other blood cell counts
 - 5 million red & 5-10,000 white blood cells

Platelets--Life History

- Platelets form in bone marrow by following steps:
 - myeloid stem cells to megakaryocyte-colony forming cells to megakaryoblast to megakaryocytes whose cell fragments form platelets
- Short life span (5 to 9 days in bloodstream)
 - formed in bone marrow
 - few days in circulating blood
 - aged ones removed by fixed macrophages in liver and spleen

Hemostasis

- Stoppage of bleeding in a quick & localized fashion when blood vessels are damaged
- Prevents hemorrhage (loss of a large amount of blood)
- Methods utilized

- vascular spasm
- platelet plug formation
- blood clotting (coagulation = formation of fibrin threads)

Vascular Spasm

- Damage to blood vessel produces stimulates pain receptors
- Reflex contraction of smooth muscle of small blood vessels
- Can reduce blood loss for several hours until other mechanisms can take over
- Only for small blood vessel or arteriole

Platelet Plug Formation

- Platelets store a lot of chemicals in granules needed for platelet plug formation
 - alpha granules
 - clotting factors
 - platelet-derived growth factor
 - cause proliferation of vascular endothelial cells, smooth muscle & fibroblasts to repair damaged vessels
- Steps in the process
 - (1) platelet adhesion (2) platelet release reaction (3) platelet aggregation

Platelet Adhesion

- Platelets stick to exposed collagen underlying damaged endothelial cells in vessel wall

Platelet Release Reaction

- Platelets activated by adhesion
- Extend projections to make contact with each other
- Release thromboxane A₂ & ADP activating other platelets
- Serotonin & thromboxane A₂ are vasoconstrictors decreasing blood flow through the injured vessel

Platelet Aggregation

- Activated platelets stick together and activate new platelets to form a mass called a platelet plug
- Plug reinforced by fibrin threads formed during clotting process

Blood Clotting

- Blood drawn from the body thickens into a gel
 - gel separates into liquid (serum) and a clot of insoluble fibers (fibrin) in which the cells are trapped
- If clotting occurs in an unbroken vessel is called a thrombosis
- Substances required for clotting are Ca⁺², enzymes synthesized by liver cells and substances released by platelets or damaged tissues
- Clotting is a cascade of reactions in which each clotting factor activates the next in a fixed sequence resulting in the formation of fibrin threads
 - prothrombinase & Ca⁺² convert prothrombin into thrombin
 - thrombin converts fibrinogen into fibrin threads

Overview of the Clotting Cascade

- Prothrombinase is formed by either the intrinsic or extrinsic pathway
- Final common pathway produces fibrin threads
 - Extrinsic Pathway
- Damaged tissues leak tissue factor (thromboplastin) into bloodstream
- Prothrombinase forms in seconds
- In the presence of Ca^{+2} , clotting factor X combines with V to form prothrombinase
 - Intrinsic Pathway
- Activation occurs
 - endothelium is damaged & platelets come in contact with collagen of blood vessel wall
 - platelets damaged & release phospholipids
- Requires several minutes for reaction to occur
- Substances involved: Ca^{+2} and clotting factors XII, X and V
 - Final Common Pathway
- Prothrombinase and Ca^{+2}
 - catalyze the conversion of prothrombin to thrombin
- Thrombin
 - in the presence of Ca^{+2} converts soluble fibrinogen to insoluble fibrin threads
 - activates fibrin stabilizing factor XIII
 - positive feedback effects of thrombin
 - accelerates formation of prothrombinase
 - activates platelets to release phospholipids
- Clot Retraction & Blood Vessel Repair
- Clot plugs ruptured area of blood vessel
- Platelets pull on fibrin threads causing clot retraction
 - trapped platelets release factor XIII stabilizing the fibrin threads
- Edges of damaged vessel are pulled together
- Fibroblasts & endothelial cells repair the blood vessel

Role of Vitamin K in Clotting

- Normal clotting requires adequate vitamin K
 - fat soluble vitamin absorbed if lipids are present
 - absorption slowed if bile release is insufficient
- Required for synthesis of 4 clotting factors by hepatocytes
 - factors II (prothrombin), VII, IX and X
- Produced by bacteria in large intestine

Blood Groups and Blood Types

- RBC surfaces are marked by genetically determined glycoproteins & glycolipids
 - agglutinogens or isoantigens
 - distinguishes at least 24 different blood groups
 - ABO, Rh, Lewis, Kell, Kidd and Duffy systems

ABO Blood Groups

- Based on 2 glycolipid isoantigens called A and B found on the surface of RBCs
 - display only antigen A -- blood type A
 - display only antigen B -- blood type B
 - display both antigens A & B -- blood type AB
 - display neither antigen -- blood type O
- Plasma contains isoantibodies or agglutinins to the A or B antigens not found in your blood
 - anti-A antibody reacts with antigen A
 - anti-B antibody reacts with antigen B

RH blood groups

- Antigen was discovered in blood of *Rhesus* monkey
- People with Rh agglutinogens on RBC surface are Rh+. Normal plasma contains no anti-Rh antibodies
- Antibodies develop only in Rh- blood type & only with exposure to the antigen
 - transfusion of positive blood
 - during a pregnancy with a positive blood type fetus
- Transfusion reaction upon 2nd exposure to the antigen results in hemolysis of the RBCs in the donated blood