Bio 12 Student Reference Guide

Prepared for

Kingsborough Learning Center

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Preface

This study guide is intended to be used as a supplement for lecture sessions, self study, and tutoring sessions. This guide is designed to provide background and basic explanations for complex topics. Do not attempt to use this guide as your sole source of information. Please remember that your professors will be creating assignments and tests based on the material they present, which may have some differences from the materials in this guide.

Endocrine System

Controls and regulates body functions through the use of hormones through negative feedback cycles. Compared to exocrine glands found in epithelial tissues, instead of releasing their secretions through a duct for transport, the endocrine organs release hormones into the blood for transport.

The Endocrine system complements the Nervous system (has similar function but different methods)

- Nervous system specializes in fast, short lasting signals sent to one specific target in the form of action potentials sent down neurons to a target tissue.
- Endocrine system specializes in slow, long lasting signals that affect large numbers of tissues, by releasing a hormone into the blood, which will bond to any cell with a receptor for that hormone

Major Organs of Endocrine System

Hypothalamus
The Hypothalamus is found in the Diencephalon of the brain. While the hypothalamus is an organ of the nervous system, it also plays a major role as an organ of the endocrine system. In the endocrine system, it regulates many of the other endocrine organs through the pituitary gland, as well as produces hormones that are released through the pituitary gland.

Pituitary Gland
Directly connected to the hypothalamus by the infundibulum. Separated into the anterior and posterior pituitary

- Anterior Pituitary - Produces its own hormones. will release those hormones when it receives the corresponding hormone from the hypothalamus
- Posterior Pituitary - Stores hormones produced by the hypothalamus. Releases these hormones when it receives a nerve signal from the hypothalamus

Pineal Gland
Located just above the posterior midbrain. Regulates sleep cycle (Circadian Rhythm)

Thyroid Gland
Located in the lower throat, with lobes on either side of the trachea. Regulates metabolism in body and calcium homeostasis

Parathyroid Glands
Located on the posterior surface of the Thyroid gland. Helps regulate calcium homeostasis

Thymus Gland
Located in the chest, just above the heart. Involved in the production and development of T-cells (type of immune cell)

Pancreas
Located in the abdomen, just below and behind the stomach. Regulates blood sugar levels

Adrenal Glands
Located just above the kidneys. Has an outer portion called the Adrenal Cortex, and an inner portion called the Adrenal Medulla
Adrenal Cortex has three layers-

- Zona Glomerulosa - produces mineralocorticoids such as aldosterone
- Zona Fasciculata - produces glucocorticoids such as cortisol
- Zona Reticularis - produces androgens and small amounts of estrogen

Adrenal Medulla produces hormones used by the Sympathetic Nervous System
Gonads: Testes and Ovaries
produce sex hormones, stimulates creation of gametes, secondary sexual characteristics, libido

Major Hormones of the Endocrine System

Hormones of the Hypothalamus	
Hormone	**Effects**
Thyrotropin-releasing Hormone (TRH)	Causes secretion of thyroid-stimulating hormone (TSH) and prolactin (PRL)
Corticotropin-releasing Hormone (CRH)	Causes secretion of adrenocorticotropic hormone (ACTH)
Gonadotropin-releasing Hormone (GnRH)	Causes secretion of follicle-stimulating hormone (FSH) and luteinizing hormone (LH)
Growth Hormone-releasing Hormone (GHRH)	Causes secretion of growth hormone (GH)
Prolactin-inhibiting Hormone (PIH)	Inhibits secretion of prolactin (PRL)
Somatostatin	Inhibits secretion of growth hormone (GH) and thyroid-stimulating hormone (TSH)

Hormones of the Pituitary Gland		
Hormone	**Target organ**	**Effects**
Anterior Pituitary		
Follicle-stimulating Hormone (FSH)	Ovaries, testes	Female: growth of ovarian follicles and secretion of estrogen Male: sperm production
Luteinizing Hormone (LH)	Ovaries, testes	Female: ovulation, maintenance of corpus luteum Male: testosterone secretion
Thyroid-stimulating Hormone (TSH)	Thyroid gland	Growth of thyroid, secretion of thyroid hormone
Adrenocorticotropic Hormone (ACTH)	Adrenal cortex	Growth of adrenal cortex, secretion of glucocorticoids
Prolactin (PRL)	Mammary glands, testes	Female: milk synthesis Male: increased LH sensitivity and testosterone secretion
Growth Hormone (GH)	Liver, bone, cartilage, muscle, fat	Widespread tissue growth

Posterior Pituitary		
Antidiuretic Hormone (ADH)	Kidneys	Water retention
Oxytocin (OT)	Uterus, mammary glands	Labor contractions, milk release, possibly involved in ejaculation, sperm transport, sexual affection, mother-infant bonding

Hormones of other organs		
Hormone	**Target organ**	**Effects**
Pineal gland		
Melatonin	Brain	May regulate timing of puberty, may influence mood
Thyroid Gland		
Thyroxine (T4) + Triiodothyronine (T3)	Most tissues	Elevate metabolic rate and heat production; increase respiratory rate, heart rate, and strength of heartbeat; stimulate appetite and accelerate breakdown of nutrients
Calcitonin	Bone	Stimulates bone deposition
Parathyroid Glands		
Parathyroid Hormone (PTH)	Bone, kidneys, small intestine	Raises blood calcium by stimulating bone resorption and inhibiting deposition, reducing urinary calcium excretion, and enhancing calcitriol synthesis
Thymus Gland		
Thymopoietin, thymosin, thymulin	Immune cells	Stimulates T-lymphocyte development and activity
Pancreas		
Glucagon	Liver	Stimulates gluconeogenesis, glycogen and fat breakdown, raises blood glucose and fatty acid levels
Insulin	Most tissues	Stimulates glucose and amino acid uptake in body tissues, lowers blood glucose levels, causes glycogen, fat, and protein synthesis
Adrenal Cortex		
Aldosterone	Kidney	Causes sodium and water retention and potassium excretion, maintains blood pressure and blood volume
Cortisol	Most tissues	Causes breakdown of fats and proteins for energy, gluconeogenesis, increases stress resistance and tissue repair
Adrenal Medulla		
Epinephrine, norepinephrine, dopamine	Most tissues	Promotes alertness, raises metabolic rate, stimulates circulation and respiratory rate, increases blood glucose levels, inhibits secretion of insulin, reduces glucose absorption of most tissues (other than brain)

Ovaries		
Estradiol	Many tissues	Stimulates female reproductive development and adolescent growth, regulates menstrual cycle and pregnancy
Progesterone	Uterus, mammary glands	Regulates menstrual cycle and pregnancy, prepares mammary glands for lactation
Inhibin	Anterior pituitary	Inhibits release of FSH
Testes		
Testosterone	Many tissues	Stimulates fetal and adolescent reproductive development, musculoskeletal growth, sperm production and libido
Inhibin	Anterior pituitary	Inhibits release of FSH

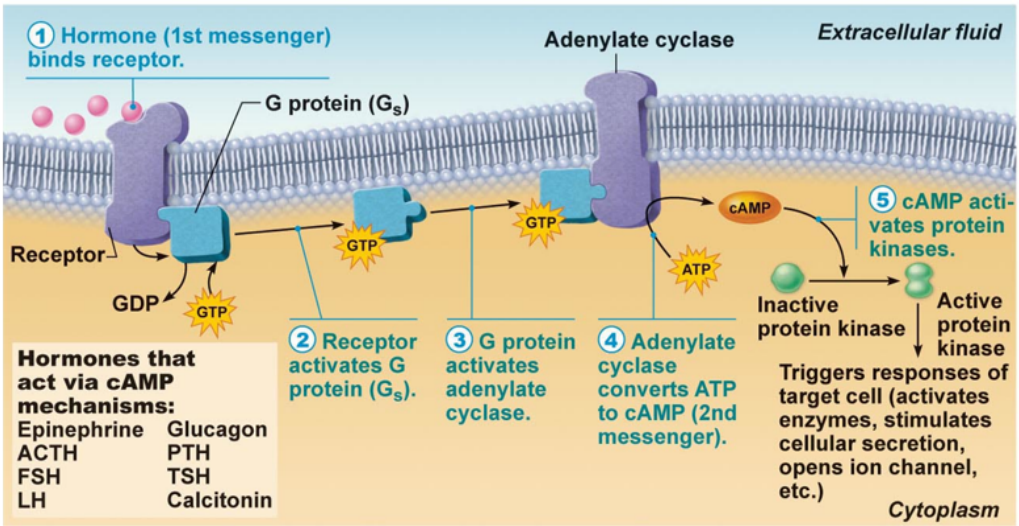
Receptors vs. Second Messenger system

There are two broad categories of hormones-hydrophobic (cannot mix with water) and hydrophilic (will mix with water)

Hydrophobic hormones are able to pass through the cell membrane because they can bond to the lipids of the membrane. These hormones will go directly to the nucleus and bond to the DNA, and will either trigger or cease the production of specific proteins in these cells.
These hormones can enter any cell in the body

Hydrophilic hormones cannot pass through the cell membrane.
These hormones rely on receptor proteins in the membrane to affect the cell. When hydrophobic hormones bond to a receptor, it will cause one of two things to happen- either activate gates on cell membrane to allow chemicals to enter or exit the cell, or they will activate the "second messenger system"
Hydrophobic hormones can only affect cells with the receptor for this particular hormone

Second Messenger system
When a hormone activates the second messenger system, it activates a series of reactions inside of the cell, ending with the creation of multiple molecules capable of opening gates, causing release of secretions by exocytosis of vesicles, or activating proteins such as enzymes in the cytoplasm.



Digestive System

The digestive system is designed to allow for the ingestion, digestion, absorption, and excretion of nutrients. The digestive system operates under control of hormones released from the digestive organs, and neural control by the autonomic nervous system.

Structure of the Digestive System

Alimentary Canal

The basis of the digestive system is a structure that forms during embryonic development called the alimentary canal. This embryonic tissue forms a tube which runs from what will develop into the mouth, to what will develop into the anus. Most of the organs of the digestive system develop from this tissue.

Layers of Alimentary Canal

The organs of the alimentary canal can be described as having four layers. The **Mucosa** is an epithelial tissue that forms the inner border between the organ and the lumen that ingested food passes through. The **Submucosa** is supportive connective tissue that provides mechanical support and blood supply to the mucosa. The **Muscularis** is a layer of smooth muscle that is used to move ingested food through the digestive system. The **Serosa** is an outer layer of fibrous connective tissue that isolates and protects the organs of the digestive system.

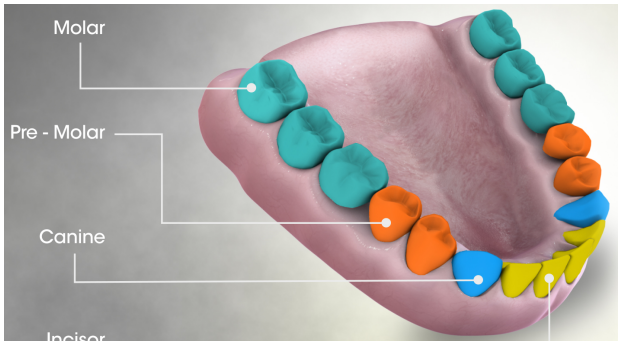
Primary vs Secondary Organs

Organs that come into contact with ingested food are described as primary organs. These primary organs were developed from the tissues of the alimentary canal. Organs that contribute materials to assist in digestion such as enzymes or other secretions are referred to as secondary organs.

Primary Digestive Organs

Mouth

The mouth is the entryway to the digestive system. It is designed to ingest food and mechanically process it before passing it along to later organs. To do this processing, we rely on the teeth, tongue, and salivary glands.



Adults possess 32 teeth, divided into two sets of 16 teeth in the upper and lower jaws.

There are four types of teeth, designed for different purposes, and having different shapes.

Incisors are narrow with a sharp edge, designed to chop through materials.
Canines are pointed, and used to hold food in place, to rip or tear food.
Premolars have a flat surface with a sharp edge that can be used for both cutting and grinding.
Molars have flat surfaces that are optimized for grinding food.

The tongue is used to manipulate food in the mouth. During **mastication** (chewing), the tongue pushes food in between the teeth in order to maximize their work. When swallowing, the tongue pushes food back in the mouth toward the esophagus.

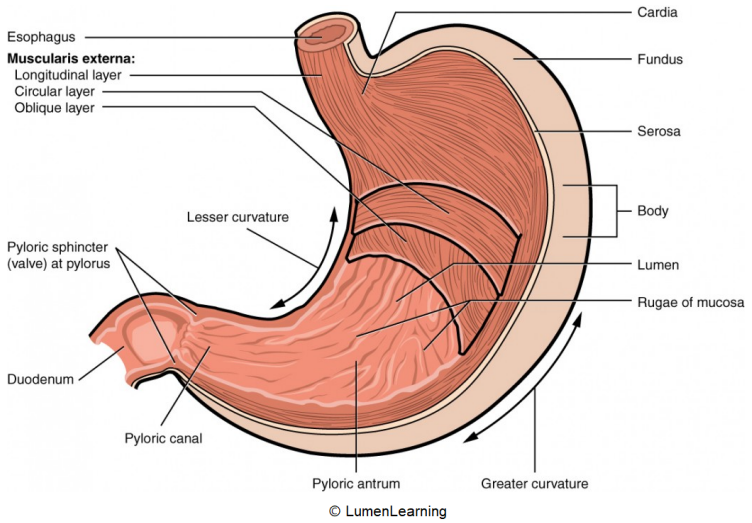
The salivary glands produce fluids that moisten food, making swallowing easier and containing enzymes that are used to break down chemicals within the food.

Esophagus

The esophagus is a tubular organ ringed with smooth muscle designed to transport food from the mouth to the stomach. During swallowing, food is pushed to the rear of the mouth by the tongue and cheek muscles, before an involuntary, wave-like muscle contraction called peristalsis forces food down the esophagus.
The esophagus passes through an opening in the diaphragm called the **esophageal hiatus**, to connect to the stomach. The border of the esophagus and stomach is sealed by a sphincter muscle, creating the cardiac sphincter.

Stomach

The stomach is located in the upper left quadrant of the abdomen. The stomach is notable for having a thick mucous lining on top of its mucosa, that protects the tissue of the stomach from the acids and digestive enzymes that are secreted into the stomach. The muscularis of the stomach has three layers of muscle, longitudinal, circular, and oblique compared to other portions of the digestive system which lack oblique muscles. This additional muscle layer is used to help churn the mixture of food and digestive secretions within the stomach.



The smooth muscle in the stomach and intestines is controlled by the **Myenteric Plexus**, a network of nerve tissue that regulates gastrointestinal motility (movement), through input of the sympathetic and parasympathetic nervous system.

The gastric epithelium has glands embedded in it to produce the digestive secretions. These glands form the gastric crypts, which seem to be holes or lines on the surface of the epithelium. In the gastric pits, there are **Chief cells** which produce digestive enzymes, and **Parietal cells** which produce the stomach acid.

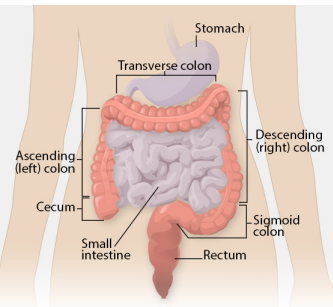
Gastric Cycle

The gastric cycle describes the series of events that cause the stomach secretions to be stimulated and then inhibited in the stomach.
The **Cephalic Phase** is triggered by the sight, scent, or thought of food. In this phase, the hypothalamus triggers signals that pass from the vagus nerve to the stomach, triggering the secretion of pepsinogen and hydrochloric acid.
The **Gastric Phase** occurs as food enters the stomach, triggering stretch receptors. As the stomach stretches, this triggers a reflex in the myenteric nerve plexus, and the vasovagal reflex. This results in the secretion of acetylcholine, histamine, and gastrin, increasing secretion of pepsinogen and hydrochloric acid.
The **Intestinal Phase** is triggered by the enterogastric reflex, which reduces secretion in the stomach. The enteroendocrine cells located just beyond the pyloric sphincter will trigger the release of secretin and cholecystokinin (CCK) as chyme enters the duodenum. These will inhibit gastric secretion and stimulate secretion of the pancreas.

Small Intestine

The small intestine is a long (approximately 20 feet), narrow, tubular organ that runs from the stomach to the large intestine. The small intestine is divided into three segments. The **Duodenum** is a short segment which receives food from the stomach, as well as secretions from the pancreas and gallbladder. The **Jejunum** makes up about 35% of the length of the small intestine, and is the main site of digestion and absorption of nutrients. The **Ileum** is the longest section of the small intestine, and is involved in absorption of nutrients and immune system activity. The small intestines are lined by simple columnar cells, whose surfaces are covered in microvilli, increasing their surface area for absorption.
In addition to moving food through the small intestines through peristalsis, the contractions of the smooth muscle of the muscularis will also isolate and churn food in a process called **segmentation**.
The epithelial cells that line the small intestine have enzymes bonded to their cell membranes that are responsible for the final breakdown of macromolecule nutrients, these enzymes are usually called the **brush-border enzymes**. The breakdown of the more complex forms of these nutrients relies on the secretion of enzymes and other substances from accessory digestive organs.

Large Intestine (Colon)



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The large intestine is a wider tubular organ that connects to the small intestine at the **ileocecal junction**, with the movement of digested food being regulated by the **ileocecal valve**.

The large intestine is divided into five segments. The **ascending colon** rises along the right lateral edge of the abdomen. The **transverse colon** passes from the right to the left side of the superior edge of the abdomen. The **descending colon** passes down the left lateral edge of the abdomen. The **sigmoid colon** passes medially along the lower abdomen. The **rectum** descends from the end of the sigmoid colon to the anus.

The large intestine is the site of water and electrolyte absorption. Additionally, the large intestine is host to many bacteria that have evolved to work with the human digestive system. These bacteria, called the **intestinal microflora** or the **gut microbiota**, produce Vitamin K and other substances needed by the body, and help prevent infection from harmful bacteria.

Both the small and large intestines have patches of immune cells, usually referred to as **Mucosa Associated Lymphatic Tissue** (**MALT**), or **Gut-Associated Lymphatic Tissue** (**GALT**). These immune tissues prevent bacteria or other harmful foreign organisms from entering the body through the digestive system.

Secondary (Accessory) Digestive Organs

Salivary Glands

In the mouth, there are three sets of salivary glands. These glands produce **saliva**, a hypotonic solution composed of water, several enzymes, mucous, antibodies, and electrolytes. The main enzymes found in the saliva are salivary amylase which helps break down carbohydrates, and lingual lipase which helps break down lipids.

The **parotid glands** are located anterior to the ear, at the back of the cheek. These glands will release their secretions through a duct located in the cheek, near the second molar. The **submandibular glands** are located medially to the body of the mandible. These glands will release their secretions through ducts near the **inguinal frenulum**, the strand of tissue that connects the midline of the tongue to the anterior floor of the mouth. The **sublingual gland** is located under the tongue, on the floor of the mouth. It releases its secretions through ducts that are located just posterior of the duct for the submandibular glands.

Pancreas

The pancreas produces multiple substances which mix to form what is called the **pancreatic juice**. The enzymes contained in the pancreatic juice are responsible for the vast majority of the chemical digestion that occurs in the small intestine. The pancreas produces enzymes for the breakdown of carbohydrates, proteins, lipids, and nucleic acids.
The pancreatic juice also contains bicarbonate, a base. The bicarbonate plays an important role in neutralizing the acid that is produced by the stomach. This protects the tissues of the small intestine from the acidity, as they lack the thick mucous and multiply layered tissue that protect the stomach.

The pancreatic juices are secreted through the **pancreatic duct**, combining with secretion from the gallbladder in the **hepatopancreatic ampulla**, before entering the duodenum.

Liver

The liver contains a huge number of hepatic lobules. These structures contain the **hepatic sinusoids**, blood vessels with large openings that allow the hepatic cells to come into contact with the plasma and proteins of the blood. The hepatocytes lining the sinusoids will filter out harmful chemicals from the blood, and secrete proteins such as albumin and clotting factors into the blood.

The liver is the site of **bile** production. Bile is an **emulsifier**, a chemical that can make bonds to hydrophobic lipids, and hydrophilic substances at the same time. The process of **emulsification** allows for lipids and water to mix and form a solution.
A major component of bile, **bilirubin** is created in the liver after removing the iron from hemoglobin recovered from destroyed RBCs. Bile that is not reabsorbed by the small intestine will be metabolized into **urobilinogen** by the bacteria of the large intestine, creating the brown pigment that colors feces.

Gallbladder

The gallbladder is a small, pear shaped organ attached to the posterior of the liver. It will receive bile from the liver through the **hepatic ducts**. In the gallbladder, the bile is concentrated as the gallbladder removes water from it. When triggered by cholecystokinin (CCK) and secretin, the gallbladder will secrete bile through the **bile duct**, to the hepatopancreatic ampulla, and into the duodenum

Digestion

Digestion is the process of transforming food into absorbable nutrients. In order to access the nutrients in your food, the body must transform the food both physically and chemically.

Mechanical Digestion

Mechanical digestion is a process that physically alters the food you ingest. This includes crushing, grinding, and moistening food in the mouth, as well as churning in the stomach. By transforming solid food into a liquid form, it makes it easier to transport through the digestive system and makes it easier for enzymes to access and chemically alter the food.

Chemical Digestion

Chemical digestion involves using enzymes to break down complex molecules (polymers) in food into simpler compounds (monomers) that can be absorbed.
Compounds that are chemically digested are carbohydrates, proteins, lipids, and nucleic acids.

Carbohydrate Digestion

In general, enzymes designed to break down the bonds between carbohydrates are referred to as amylase enzymes.
To break down carbohydrates in foods, we rely on several enzymes. **Salivary Amylase** is secreted from the salivary glands of the mouth and breaks down starches. **Pancreatic Amylase** is secreted from the pancreas and breaks polysaccharides into di and trisaccharides. The **Brush Border Enzymes** are a set of enzymes attached to the cell membranes of the epithelium of the small intestine that break down di and trisaccharides into monosaccharides.

Protein Digestion

Protein digestion relies on a set of enzymes called proteases. These enzymes are different when compared to other enzymes, as they are produced in an inactive form, called a **Zymogen**. These enzymes require a specific trigger that is capable of activating them before they become capable of breaking down proteins. This is done as a safety measure, to prevent these enzymes from damaging the proteins produced by our own cells.
Protein digestion occurs in two main locations, the stomach and small intestine. In the stomach, the enzyme **Pepsinogen** is secreted by the chief cells, before being activated into **Pepsin** by hydrochloric acid (HCl) secreted by parietal cells. Pepsin will then break proteins down into smaller polypeptide chains. In the small intestine, several enzymes are secreted by the pancreas, including **Trypsinogen**, **Chymotrypsinogen**, and **Procarboxypeptidase**. These enzymes are activated by the brush border enzymes of the small intestine, and will then break down polypeptides into di and tripeptides. The brush border enzymes will then break down the di and tripeptides into amino acids.

Lipid Digestion

Lipid digestion is complicated by the fact that lipids are hydrophobic, which makes it difficult for hydrophilic enzymes carried in the digestive juices to affect them. In order to digest these chemicals, the body uses bile which functions as an emulsifier that serves as a bridge to allow hydrophilic enzymes to interact with the lipids. Bile will be secreted from the gallbladder at the same time as pancreatic enzymes are released by the pancreas.
In the small intestine, bile will break down fat droplets into smaller, water soluble pieces called **micelles**. **Pancreatic amylase** secreted from the pancreas will then enter the micelle and break down triglycerides, forming new monoglycerides and fatty acid chains. The micelles are then absorbed by the intestinal epithelium, before being processed and repackaged into bundles called **chylomicrons**.

Absorption

Absorption in the Small Intestine

In the small intestine, the epithelium forms folds and finger-like projections called **villi** to increase the surface area and allow for more absorption. Most of the nutrients will be absorbed by active transport proteins in the intestinal epithelium. Once absorbed by the epithelium, most nutrients will be transported away by capillaries that provide blood supply in the villi. The exception to this is lipids, which are transported from the epithelium by lymphatic vessels called **lacteals**, since they are too large to fit into the smaller capillaries.

Absorption in the Large Intestine

In the large intestine, water, vitamins and electrolytes are removed from the lumen through active transport. This causes the material in the colon to solidify, forming feces over the course of 12-24 hours.

Defecation

As material moves through the colon and becomes the feces, it will accumulate in the rectum. As the rectum stretches, it will trigger the defecation reflexes. The **intrinsic defecation reflex** is activated by stretch receptors in the rectum, and triggers a peristaltic wave that pushes the feces downward. The **parasympathetic defecation reflex** is a spinal reflex with the same trigger that intensifies the response of the intrinsic defecation reflex.

The anus is held closed by two sets of sphincter muscles. The **internal anal sphincter** is controlled by the reflex arcs mentioned above. When the reflexes are activated, the internal sphincter relaxes. The **external anal sphincter** is a consciously controlled sphincter that allows people to delay the urge to defecate. In children and adults with nerve damage or deterioration, this sphincter may not be consciously controlled, and will result in **incontinence**.

Circulatory System: Blood

Responsible for transport of oxygen, nutrients, wastes, and heat in the body.
Carries cells and proteins that protect the body from infection.
Helps regulate acid/base balance, temperature, and fluid levels in body

Components of blood

Plasma
Liquid portion of the blood
~48-55% of the blood volume in men, 52-63% of the blood volume in women
Carries electrolytes and other chemicals in solution
Formed Elements
Cells and cell fragments carried in suspension
45-52% of the blood volume in men, 37-48% of the blood volume in women (Also referred to as Hematocrit)

- **Red Blood Cells (RBC)**, or Erythrocytes - carry oxygen to the tissues in the body. These cells do not have a nucleus, and as a result have an inward curving shape called a biconcave disc.
- **White Blood Cells (WBC)**, or Leukocytes - protect the body from harmful foreign cells and substances.
    - Granulocytes have visible granules (dots) in cytoplasm
        - **Neutrophils** - phagocytes, specialized for destroying bacteria
        - **Basophils** - produce histamine and heparin, cause inflammation
        - **Eosinophils** - phagocytes, specialized for destroying parasites
    - Agranulocytes no visible granules in cytoplasm
        - **Lymphocytes** - used to attack viruses and cancer cells
        - **Monocytes** - phagocytes, develop into macrophages

  WBC's from most common to least common:
  Neutrophils, Lymphocytes, Monocytes, Eosinophils, Basophils
  Mnemonic to remember this: **N**ever **L**et **M**onkeys **E**at **B**ananas

Platelets
Cell fragments responsible for creating blood clots and stopping blood loss

RBC life cycle

Red blood cells are vital for the body for their ability to carry oxygen. This is due to the hemoglobin protein found inside of RBCs. Hemoglobin is a quaternary protein, made from four heme groups. Each heme contains a single iron atom that is able to bond to and carry oxygen. Mature RBCs will circulate in the blood for about 120 days before being destroyed in the spleen.

Erythropoiesis (production of RBCs)

Occurs in the red bone marrow, triggered by the hormone **Erythropoietin (EPO)**
EPO is secreted by the kidney when blood oxygen levels drop. Reduced blood oxygen may be caused by low RBC levels, high altitude, or other factors

Hemocytoblasts will divide, creating an Erythroblast
Erythroblasts will begin producing Hemoglobin, the protein needed to carry oxygen.
After completing the production of Hemoglobin, the cell is now called a Reticulocyte, and will eject their nucleus
Reticulocytes will leave the bone marrow and enter the blood, becoming Erythrocytes within 1-2 days
Mature Erythrocytes can circulate for ~120 days before being removed from circulation in the Spleen or Liver
Iron, Folic acid, and vitamin B12 are vital for RBC production. Lack of these chemicals can slow or stop RBC production, leading to a low RBC count (**Anemia**)

Destruction of RBC occurs primarily in the red pulp of the Spleen
The red pulp has very narrow vessels which will cause older, less flexible RBC's to rupture (**hemolysis**). Macrophages will phagocytize the destroyed RBC, and break down many of the components of the cell. The heme portion (the section of the hemoglobin protein that carries oxygen) is transported to the liver. After having its iron removed, the heme is converted into bilirubin

Blood Types

Blood typing is a way of identifying compatibility between people and blood in the case of transfusion.
Antigens are structures on the surface of the cell that allow the body to identify a cell
Antibodies are immune proteins that can recognize and attack specific antigens

The **ABO system** identifies blood cells through the presence or absence of the A and B antigens.

- If only the A antigen is present, the blood is described as type A
- If only the B antigen is present, the blood is described as type B
- If both the A and B antigens are present, the blood is described as type AB
- If neither the A or B antigens are present, the blood is described as type O

The **Rh system** identifies blood cells through the presence or absence of the D (Rh) antigen

- If the Rh antigen is present, the blood is described as Rh+
- If the Rh antigen is absent, the blood is described as Rh-

In healthcare, we use a combination of these systems, with the letter type from the ABO system, followed by a +/- from the Rh system

Ex: A person whose blood has the B antigen and the Rh antigen would be type B+

If your body does not normally produce an antigen, you will instead produce an antibody designed to attack that antigen, as your body will see it as a foreign cell.

- People with type A blood will produce Anti-B antibodies
- People with type B blood will produce Anti-A antibodies
- People with type O will produce both Anti-A and Anti-B antibodies

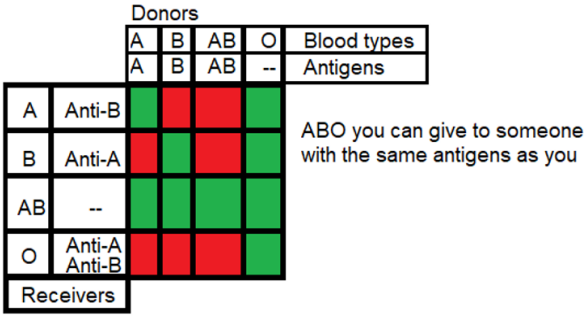
People who are Rh- will not immediately produce an Anti-Rh antibody, but will produce one if they are ever exposed to Rh+ blood. This is especially important for women who are Rh-, as antibodies can cross the placenta and attack the blood of an Rh+ fetus.

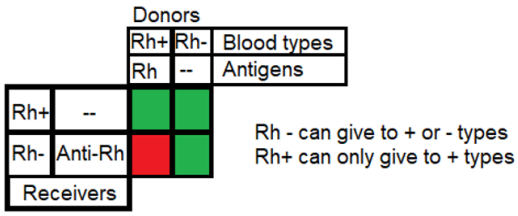
Transfusion reactions

Occur when the antigens of the blood cells received from a transfusion are not compatible with a person's antibodies. This results in the person's immune system destroying the transfused blood cells, which causes life threatening reactions.

To prevent transfusion reactions, always compare the **antigens of a donor's blood** to the **antibodies of the recipient's blood**.

In this chart, green squares indicate matches between donors and receivers that will not cause a transfusion reaction, while red squares indicate matches that will cause a reaction





Hemostasis

Process of stopping bleeding when a blood vessel has been damaged.

1. **Vascular Spasm**
   Smooth muscle in the wall of the blood vessel will constrict, narrowing the blood vessel and reducing blood flow to the damaged section, slowing blood loss
2. **Platelet plug formation**
   As blood escapes through the hole in the blood vessel, platelets in the blood will come into contact with collagen fibers in the connective tissue that supports the blood vessels. Platelets will stick to these fibers, and then begin sticking to each other, forming a clot to block the hole in the vessel
3. **Coagulation**
   Series of chemical reactions occur in the blood that cause a protein dissolved in the blood, Fibrinogen, to change into Fibrin. Fibrin will prevent the platelet plug from breaking up

Coagulation can be triggered by two methods, called the intrinsic and extrinsic pathways. The intrinsic pathway uses cells and chemicals found within the blood, while the extrinsic pathway requires the presence of a chemical found in the tissues surrounding the blood vessels.

The intrinsic pathway will sometimes cause clots to be formed without a broken blood vessel (**Thrombosis**), which can lead to reduced blood flow and reduced oxygen delivery to the tissues fed by that blood vessel (**Ischemia**).

The intrinsic pathway starts with a chemical released by platelets when they adhere to Collagen (Factor 12). This leads to a series of reactions-

- Factor 12 → Factor 11 → Factor 9 → Factor 8 → Factor 10

The extrinsic pathway requires the presence of what is sometimes called tissue factor (Factor 3) to enter the blood from the surrounding tissues. Due to the higher pressure in the blood vessels, this chemical usually cannot enter the blood until enough blood has been lost to cause a reduction in blood pressure.

- The extrinsic pathway combines factors 3 and Factor 7 to activate factor 10

Both intrinsic and extrinsic pathways will have the same end result, with the following series of reactions sometimes referred to as the combined coagulation pathway

- Factor 10 → Prothrombin activator (PTA) → Thrombin → Fibrin

Some medications will interfere with the coagulation reactions.

- Heparin will inhibit factor 10 and thrombin
- Warfarin (Coumadin) will inhibit factors 7,9,10

Hemophilia is a genetic disorder which prevents the body from producing certain coagulation factors

- Hemophilia A prevents the production of factor 8
- Hemophilia B prevents the production of factor 9
- Hemophilia C prevents the production of factor 11

Hemophilia is commonly treated by periodic injection of the missing coagulation factors

Circulatory System: Heart and Blood Vessels

The Cardiovascular System

The cardiovascular system consists of the heart and the blood vessels of the body that are used to transport blood to the tissues. At the tissues, oxygen and nutrients are dropped off and carbon dioxide and wastes are picked up. In order to sustain vital function, the blood needs to be pumped so that carbon dioxide can be removed and oxygen is picked up, and for wastes to be removed and nutrients picked up.

Circuits of Circulation
In the body, the various tissues consume oxygen and produce carbon dioxide, requiring delivery of additional oxygen and removal of carbon dioxide. To remove the carbon dioxide and collect additional oxygen, the blood must travel to the lungs, where gas exchange can occur with the surrounding air.

Pulmonary Circuit
The pulmonary circuit of circulation involves pumping of blood from the heart toward the lungs, before returning to the heart. Blood exiting the heart is high in carbon dioxide and low in oxygen, while blood returning to the heart is high in oxygen and low in carbon dioxide.

Systemic Circuit
The systemic circuit of circulation involves pumping blood from the heart out to the body, before returning to the heart. Blood exiting the heart is high in oxygen and low in carbon dioxide, while blood returning to the heart is high in carbon dioxide.and low in oxygen.

The Heart

The heart is a muscular four chambered pump, comprising three layers of tissue, and surrounded by a double walled sac.

The Pericardium

Double layer of dense irregular connective tissue that surrounds the heart, protecting it from contamination and damage. The space in between the pericardium and the heart tissue is known as the pericardial cavity. The pericardial cavity contains pericardial fluid, which reduces friction between the heart and pericardium.

Epicardium

Serous membrane on the surface of the heart. Composed of simple squamous epithelium and areolar connective tissue. Some areas of the heart have adipose tissue embedded in the epicardium, while others do not.

Myocardium

Muscular layer of the heart, composed of Cardiac Muscle tissue. Thickest layer of the heart, with the left side of the heart having much more muscle tissue than the right side. This muscle surrounds the chambers of the heart in a spiral arrangement, causing a twisting motion when the muscle contacts.

Endocardium

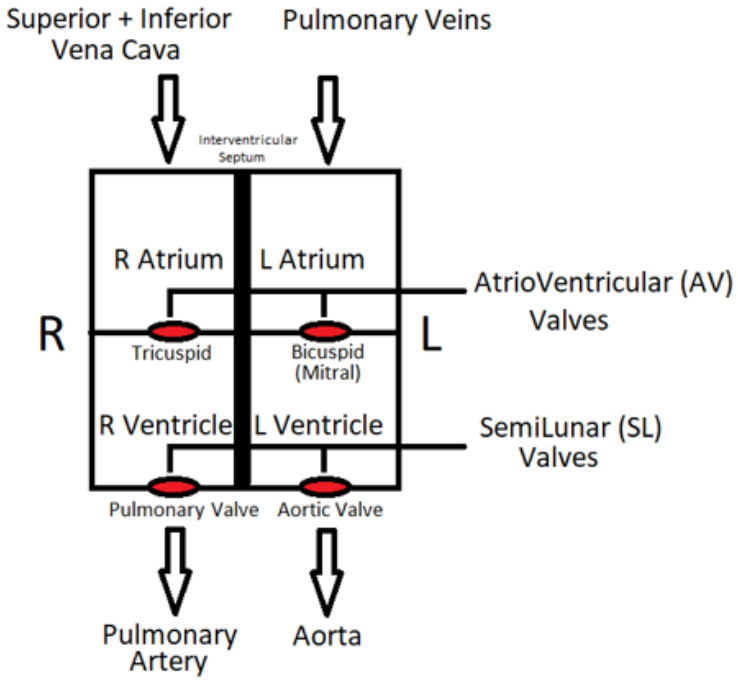
Serous membrane that lines the inside of the chambers of the heart.Composed of simple squamous epithelium and areolar connective tissue.

Chambers of the Heart

The heart contains a total of 4 chambers, with the right and left sides of the heart separated by the cardiac muscle, and the top (**atria**) and bottom (**ventricles**) separated by a set of valves. The **Interatrial Septum** separates the right and left sides of the atria, while the **Interventricular septum** separates the right and left ventricles. The myocardium of the left ventricle of the heart is visibly more muscular than that of the right ventricle.

Blood Flow Through the Heart

Blood enters the heart at the right and left atria. Blood is delivered to the right atrium through the Superior and Inferior Vena Cava, which collect blood from the major veins of the upper and lower body. Blood entering the left atrium enters from the pulmonary veins, which return blood from the lungs to the heart.
Blood will flow from the right atrium, through the tricuspid valve and into the right ventricle. Blood from the left atrium will flow through the bicuspid valve to enter the left ventricle.
From the right ventricle, blood will pass through the pulmonary valve before entering the **Pulmonary trunk**. From the left ventricle, blood will pass through the aortic valve before entering the **Aorta**.



Valves of the heart

The heart contains a total of 2 sets of valves that are designed to direct blood flow. In between the Atria and the Ventricles are the **Atrioventricular (AV) Valves**. These valves are designed to prevent the backflow of blood, preventing blood from going from the ventricle back into the atria. The AV valves will open or close based on the pressure difference between the atria and the ventricles. When there is higher pressure in the atria than the ventricles, the AV valves will open, and when pressure in the ventricles is higher than in the atria, the AV valves will close.
The right AV valve is also called the **Tricuspid valve**, while the left AV valve is called either the **Bicuspid or Mitral valve**.

In between the ventricle and the arteries there is a second set of valves, the **Semilunar (SL) Valves**. These valves prevent blood from flowing back from the arteries into the heart. The SL valves operate based on the relative pressure between the ventricles and the arteries. When there is higher pressure in the ventricles than the arteries, the SL valves will open. When the pressure in the arteries is higher than in the ventricles, the SL valves will close.
The right SL valve is also called the **Pulmonary valve**, while the left SL valve is called the **Aortic valve**.

Major Blood Vessels of the Chest

Superior and Inferior Vena Cava

The superior and Inferior Vena Cava are the largest veins of the body. The Superior Vena cava is formed from the brachiocephalic veins, which collect blood from the head and upper limbs. The Inferior Vena Cava is formed from the iliac veins, as well as the veins of the abdominal organs.

Pulmonary Veins

Composed of 2 sets of 2 veins from the right and left lungs, carries oxygenated blood from the lungs to the right atrium.

Pulmonary Trunk and Arteries

The pulmonary trunk is a short section leading from the right ventricle before branching into the right and left pulmonary arteries which carry deoxygenated blood from the heart toward the lungs.

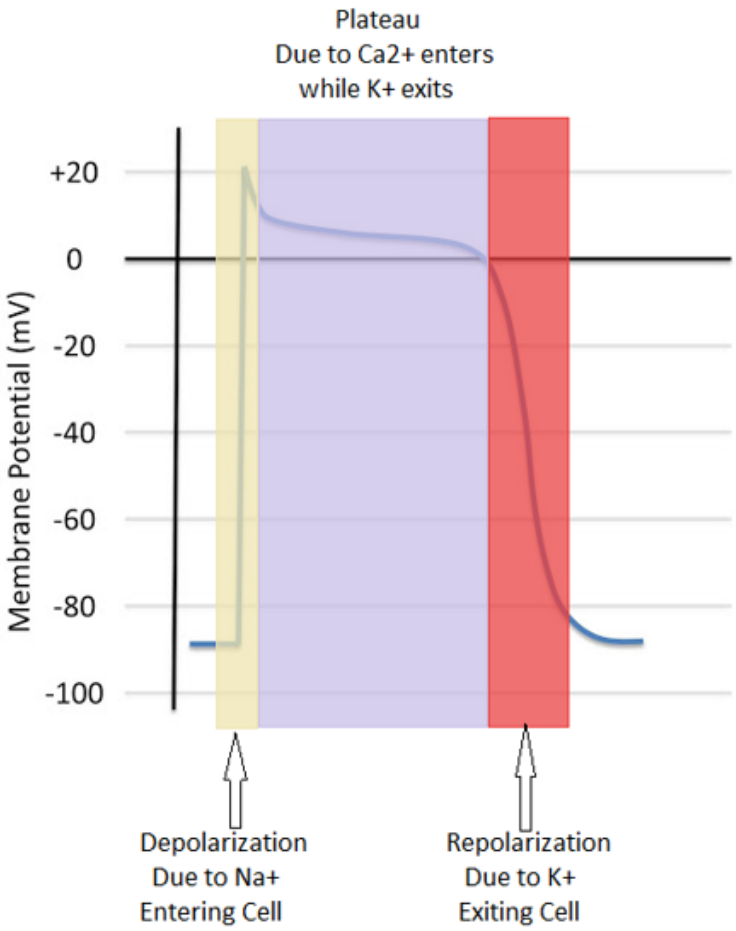
Aorta

The largest artery in the body, which carries oxygenated blood from the left ventricle out toward the organs of the body. Separated into the aortic arch, descending aorta, and the abdominal aorta. Branches out to form the arteries of the head, torso, abdomen, and appendages.

Circulatory System: Cardiovascular Physiology

Cardiac Action Potential

Similar to skeletal muscle tissue, cardiac muscle tissue is electrically excitable.Cardiac muscle tissue has an additional step designed to prolong the action potential, leading to an extended period of contraction compared to skeletal muscle tissue.



Depolarization

Cardiac muscle tissue will initially depolarize (have its voltage increase) due to sodium channels opening, allowing sodium to enter the cells.

Plateau

Once voltage in the cell peaks, the sodium channels will close, while potassium and calcium channels open. Calcium ions will enter the cell, while potassium ions will exit. Due to this, the incoming charges from the calcium will offset the loss of the charges from the exiting potassium, causing the voltage to remain steady rather than decrease. This prolongs the action potential, extending the contraction of the heart and enabling it to force more blood out into the arteries.

Repolarization

Once the calcium channels close, potassium continues to exit the cell, causing the voltage to rapidly decrease, bringing the voltage down below the level of the resting membrane potential.

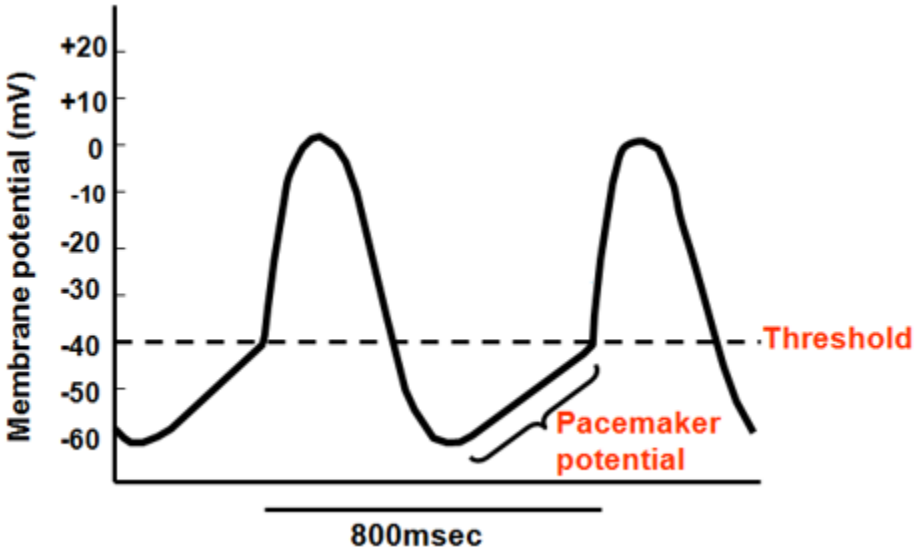
Cardiac Conduction System

The cardiac conduction system refers to the pathways that the action potentials follow as they move through the cardiac muscle tissue to cause the chambers of the heart to contract and relax.

Cardiac Pacemakers

Unlike skeletal muscle, cardiac action potentials are not triggered by nerve signals received from the central nervous system. Instead action potentials are created by special pacemaker cells. The autonomic nervous system is able to alter the rate that these pacemaker cells produce their action potentials, with the sympathetic nervous system increasing the rate, and the parasympathetic nervous system decreasing the rate.

Unlike normal cardiac muscle tissue, pacemaker cells have sodium channels that remain open, allowing for a constant stream of sodium ions entering the cell that will cause the voltage in the cell to continuously increase. When the voltage reaches the threshold, these cells will create an action potential which is spread to surrounding cells through gap junctions.

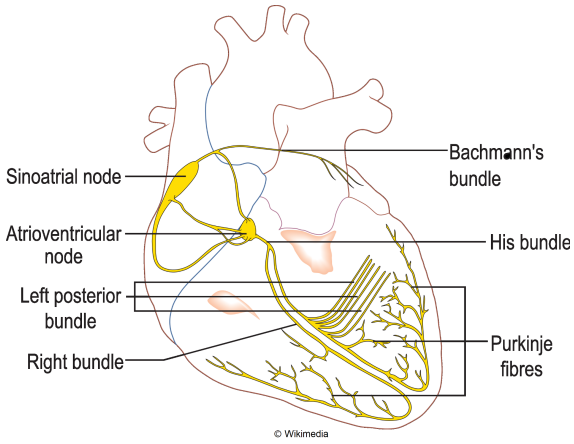


Cardiac Conduction Pathways

Action potentials originate at the **Sinoatrial node** (primary pacemaker), before radiating through the cardiac muscle of the atria.

In the medial inferior wall of the right atrium, these action potentials are received by the **Atrioventricular node** (secondary pacemaker).

The AV node will delay the action potential momentarily before passing it down the **Bundle of His** which carries the action potential to the **Left and Right Bundle Branches** that run through the interventricular septum.



At the apex (inferior margin) of the heart, the bundle branches will enter the myocardium of the right and left ventricles, before branching into **Purkinje Fibers** which deliver the action potential to the cardiac muscle of the ventricles.

Phases of the Cardiac Cycle

Due to the way that the electrical signals are transmitted through the cardiac conduction system, the Atria receive their action potential and contract before the Ventricles receive their action potentials and begin their own contraction.

The cardiac cycle refers to the actions occurring in the heart at different points in time due to the contraction and relaxation of the Atria and Ventricles.

Ventricular Filling

In this phase, the cardiac muscle of the Atria and Ventricles are completely relaxed. Due to blood entering the atria from the veins, there is more pressure in the atria during this phase. The Atrioventricular valves will open, allowing blood to flow down from the Atria into the Ventricles due to the force of gravity.
As the Atria contract, additional blood will be forced into the Ventricles, slightly expanding their capacity. Approximately 80% of ventricular filling occurs due to gravity, with the remaining 20% being due to atrial contraction.
When the ventricles begin to contact, pressure in the ventricles will increase forcing the AV valves to close. When the AV valves close, the first heart sound, S1 or “lub” can be heard. Once the AV valves close, ventricular filling ends and isovolumetric contraction begins.

Isovolumetric Contraction

In this phase the muscle of the ventricle is contracting, exerting more pressure on the blood within the ventricles. Until the pressure within the Ventricle is greater than the pressure in the

arteries, which will open the Semilunar Valves, blood is unable to leave the Ventricle. Due to this, the muscle of the Ventricle is in a state of isometric contraction, unable to change the volume of the Ventricle.
When the pressure in the Ventricle is greater than that of the Arteries, the SL valves will open, allowing blood to be pushed into the arteries. Once the SL valves open, isovolumetric contraction ends and ventricular ejection begins.

Ventricular Ejection

In this phase, blood is being pushed out of the Ventricles due to the contraction of the cardiac muscle. As blood exits the ventricle, pressure in the ventricle will begin to decrease, which causes the speed the blood exits the Ventricle to decrease over time. Once Ventricular contraction ends, pressure in the ventricle will sharply decrease
When the pressure in the Ventricle drops below the pressure in the Arteries, the SL valves will close. When the SL valves close, the second heart sound, S2 or “dub” can be heard. Once the SL valves close, ventricular ejection ends and isovolumetric relaxation begins.

Isovolumetric Relaxation

In this phase the cardiac muscle of the Ventricle is decreasing as the muscle tissue completes its contraction. At this point pressure in the Ventricle is lower than the arteries, while still higher than the Atria. As the relaxation continues, pressure in the Ventricle will continue to decrease until it reaches a point where there is more pressure in the Atria than the Ventricles.
When the pressure in the Ventricle drops below the pressure in the Atria, the AV valves open, ending isovolumetric contraction and beginning ventricular filling

Cardiac Volumes

To measure how much blood is being pumped by the heart, we estimate the volume of blood in the Ventricle at different points in time.

End Diastolic Volume
End Diastolic Volume (EDV) represents the amount of blood in the ventricle after the ventricle has finished filling with blood. EDV is measured at the end of the ventricular filling phase, when the AV valves close.

End Systolic Volume
End Systolic Volume represents the amount of blood in the ventricle after ventricular ejection has occurred. ESV is measured at the end of the ventricular ejection phase, when the SL valves close

Stroke Volume
By subtracting EDV-ESV, we can calculate the amount of blood that was pushed out of the ventricle by a contraction. This is referred to as the Stroke Volume.

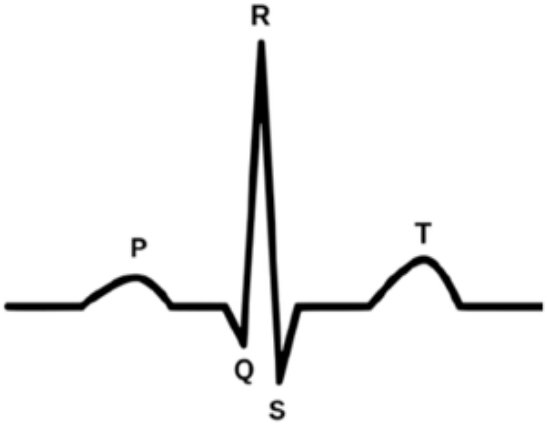
Cardiac Output
Cardiac output is an estimation of how much blood the heart pumps over a period of one minute. It is calculated by multiplying Stroke Volume and Heart Rate. This is often referenced in healthcare as a way of evaluating a patient's cardiac function. When cardiac output decreases, organs are unable to be adequately oxygenated, leading to decreased function or organ death.

Stroke volume and cardiac output are mainly affected by two factors we refer to as **preload** and **afterload**. Preload is referring to the amount of blood returning to the heart by venous return. As venous return increases, more blood is available to be pumped out to the body, increasing stroke volume and cardiac output. Afterload refers to the blood pressure in the arteries. Since the semilunar valves will not open before the pressure in the ventricle is higher than the pressure in the arteries, higher arterial blood pressure will make it harder to pump blood from the heart to the arteries, decreasing stroke volume and cardiac output.

Electrocardiogram (EKG)

Electrocardiograms are a diagnostic tool used to evaluate the function of the heart. An EKG uses a series of electrodes attached to the patient's body to detect changes in voltage in the heart. These voltage changes are displayed as a graph, usually called the EKG rhythm.

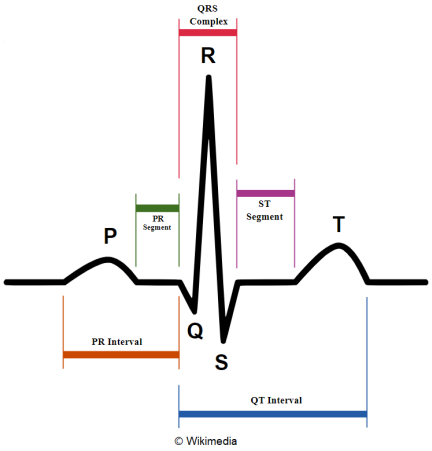
The various peaks and curves of the EKG correspond to physical and electrical activity within the heart



The P-wave represents the depolarization of the Atria, caused by the firing of the SA node and the conduction of the action potential through the atrial cardiac muscle.

The QRS complex represents the repolarization of the Atria, as well as the depolarization of the Ventricles.
The T-wave represents the repolarization of the Ventricles.

In addition to these main activities, additional information can be identified by measuring the timing between different waves.



The PR interval represents the time from the beginning of atrial depolarization to the beginning of ventricular depolarization. If this segment is abnormal, it indicates dysfunction in the SA node.

The PR segment represents the time in between the end of atrial depolarization and the beginning of ventricular depolarization. If this period is longer than normal, it indicates there is a conduction problem in the atria

The QRS duration represents the time when the action potential is passing through the muscles of the Ventricle. Abnormalities in this segment may indicate conduction problems in the bundle branches or the Purkinje fibers.

The ST segment represents the point where the Ventricle is contracting. Abnormalities may occur during a Myocardial Infarction (Heart Attack).

Circulatory System: Blood Vessels

Types of Blood Vessels

There are three major types of blood vessels: Arteries, Veins, Capillaries. Arteries carry blood away from the heart and toward the body. Veins carry blood from the body toward the heart. Capillaries are found in between the arteries and veins, and allow for exchange of oxygen and nutrients with the body tissues.

Structure of Blood vessels

Arteries and veins have three layers of tissue: Tunica Interna, Tunica Media, Tunica Externa. Capillaries only have Tunica Interna.

Tunica Interna
This layer surrounds the lumen (hollow inner portion) of the blood vessels. This layer is composed of a layer of simple squamous epithelium with a connective tissue backing.

Tunica Media
In arteries and veins, this is the thickest of the three layers. This layer is made of smooth muscle tissue and elastic connective tissue. Arteries will have a thicker Tunica Media than veins, with more smooth muscle, which provides additional ability to resist expansion when the heart pumps blood into the arteries.

Tunica Externa
This layer is made of fibrous connective tissue, and serves to protect the blood vessels from damage.

Types of capillaries

There are several types of capillaries that are designed to control what is allowed to be exchanged with different types of tissues in the body.

Continuous Capillaries

These are the most common type of capillary in the body. Like other capillaries, they are composed of simple squamous epithelium. The epithelium in continuous capillaries are connected by tight junctions to prevent fluid from leaking out into the tissues

Fenestrated Capillaries

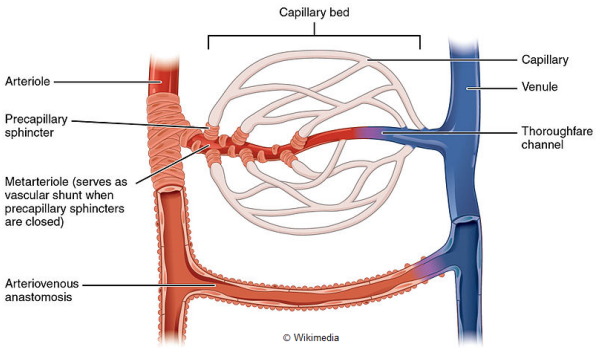
These capillaries have small pores along the wall of the capillary, and are designed to allow fluid and small particles to leak out and enter the tissues. Commonly found in the kidneys to allow wastes to be filtered from the blood

Sinusoidal Capillaries

These capillaries have large gaps in the walls of the capillary, and are designed to allow fluid and large particles to escape the blood and enter the tissues. These can be found in the liver, and allow the liver cells to remove and break down harmful chemicals carried in the blood.

Control of Capillary Blood Flow

Blood flow into capillary beds is regulated in order to maintain a sufficient level of oxygen and nutrients in the blood, while ensuring that tissues are adequately supplied.

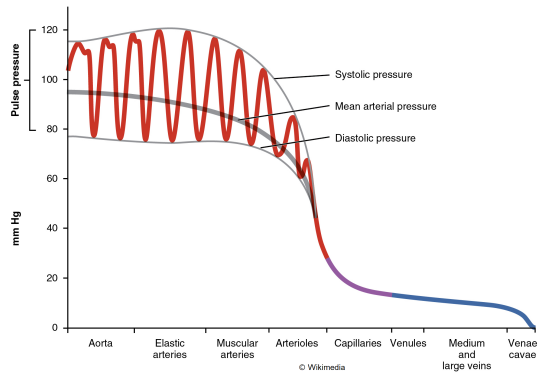


Capillaries have bands of smooth muscle surrounding the ends where they connect to arterioles (small arteries). When these muscles contract the entrance to the capillary is forced closed, which causes blood to bypass that capillary bed. Since these muscles use oxygen and nutrients at a faster rate than the tissues supplied by the capillary, the muscle will exhaust its supplies and reopen the capillary before the tissues run out of oxygen and nutrients

Arteriovenous anastomosis
These are direct connections between Arterioles and Venules, which allow blood to bypass tissue beds without depleting their oxygen and nutrients.

Blood Pressure

Blood pressure is the force that causes blood to move through the body. The larger the difference in blood pressure between two points is, the more blood will flow.



Blood pressure is highest in the large arteries near the heart. As the arteries branch out, the pressure in the blood vessels is divided, decreasing as distance to the heart increases.

Near the heart there is a change in pressure when the heart is pumping, compared to when it is at rest

Venous Adaptations

Due to the very low pressures in the veins, they require special adaptations to assist the return of blood to the heart. Most veins in the body contain small one way **valves**, which prevent blood from flowing back away from the heart. Veins are often located in between bones and skeletal muscle, which will put pressure on the veins when they contract, forcing blood forward toward the heart. This process is called the **skeletal muscle pump**. In the Thoracic cavity, pressure changes caused by respiration will exert pressure on the veins, forcing blood toward the heart in a process called the **thoracic pump**.

Measuring Blood Pressure

Blood pressure is measured using the units millimeters of mercury (mmHg).

Systolic Blood Pressure

As the heart pushes blood into the arteries, the pressure in the arteries increases. This causes the arteries to expand, which triggers the smooth muscle in the artery to contract in order to maintain its structural strength. Systolic blood pressure represents the peak pressure within the arteries

Diastolic Blood Pressure

Once the heart relaxes, the pressure exerted on the arteries decreases, while the contraction of the smooth muscle of the arteries continues to exert pressure on the blood in the artery. Diastolic blood pressure represents the lowest pressure measured in an artery.

Pulse Pressure

This is the difference between the systolic and diastolic blood pressure (SBP-DBP). This can be used as a way to measure the effort the heart is exerting in pumping blood. The higher the pulse pressure, the more force being exerted on the blood by the heart, causing more blood to be pushed into the arteries. When pulse pressure decreases, less force is exerted on the blood by the heart, causing less blood to be pushed into the arteries.

Peripheral Resistance

Peripheral resistance is a force which reduces the flow of blood through blood vessels. The amount of blood flow that is possible is a factor of both blood pressure and peripheral resistance. When peripheral resistance is higher, more pressure is required in order to make blood flow. When peripheral resistance is lower, less pressure is required to make blood flow. Peripheral resistance is caused by physical factors in the blood vessels,

Vessel Length

The longer a blood vessel is, the more blood is contained in that vessel. Since it is harder to move a larger quantity of blood than a smaller quantity, we can describe longer vessels as having higher peripheral resistance. A shorter vessel has less blood, and has less resistance toward moving that blood. Due to this, we can say there is a direct relationship between blood vessel length and peripheral resistance.

Vessel Radius

The wider a vessel is, the more space there is for blood to flow through. This makes it easier for blood to flow, and represents a decrease in peripheral resistance. As a vessel narrows, there is less room for blood to flow through, which causes an increase in peripheral resistance. There is an inverse relationship (opposite) between vessel radius and peripheral resistance

Blood Viscosity

Viscosity is a physical property of a fluid that describes how easily it can flow. Fluids with higher viscosity are harder to move, which would represent a higher peripheral resistance. Fluids with less viscosity are easier to move, and cause a lower peripheral resistance. There is a direct relationship between blood viscosity and peripheral resistance.

Control of Blood Flow

By controlling the peripheral resistance of blood vessels, it is possible to control the areas that blood will flow. By increasing resistance of one set of vessels, while lowering resistance in a second, blood that would have originally been carried by the first will be redirected to the second.

Vasodilation

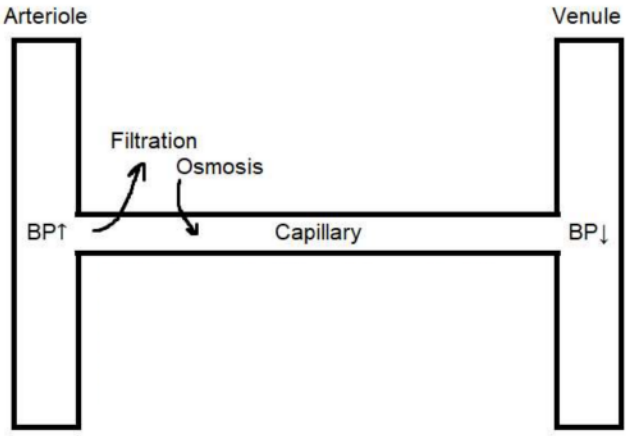
By relaxing the smooth muscles in arteries, the radius of the artery can be increased, decreasing resistance and increasing blood flow. Vasodilation is also used by the body when the heart is unable to pump blood with its normal force, to allow for normal blood flow using less blood pressure.

Vasoconstriction

By contracting the smooth muscle in arteries, the radius of the artery is decreased, increasing resistance and decreasing blood flow. This is usually used to redirect blood flow away from an area of the body. An example of this is the restriction of blood flow to the appendages in cold temperatures, causing the hands and feet to turn pale. In this case, the blood is redirected to prevent loss of body temperature to the environment

Capillary Exchange

When blood flows through a capillary, fluid is exchanged between the blood in the capillary and the **interstitial fluid** of the tissues. This helps transport electrolytes and other materials that are in solution with the plasma of the blood. Movement of fluid is regulated by filtration and osmosis.



Filtration
When fluid in the capillary is forced against the wall of the capillary by the blood pressure (**hydrostatic pressure**), some fluid is forced through the spaces in between the cells that make up the capillary wall

Osmosis
When fluids leave the capillary, the concentration of the remaining fluid in the blood increases. This causes fluid to be drawn from the tissues into the blood.

Since filtration is caused by blood pressure, filtration will be higher in regions of higher pressure, and lower when there is less pressure. Since there is more blood pressure in the arteriole end of the capillary, more fluid is forced out of the capillary on the arteriole end, while the venule end will have more fluid entering due to osmosis than leaving due to filtration.

Fluid homeostasis relies on the balancing of filtration and osmosis, and thus on the blood pressure and concentration of the blood plasma. Blood pressure changes will directly affect the amount of filtration that occurs. The quantity of blood electrolytes such as sodium will directly affect the concentration of the blood, increasing or decreasing the amount of fluid moved by osmosis.

Net Filtration Pressure
This term is used to describe the overall direction fluid is moving in between the blood and interstitial fluid. NFP = Forces pushing fluid out (filtration) - Forces pushing fluid in (osmosis).

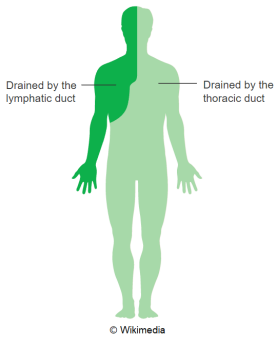
Lymphatic and Immune System

Lymphatic System

The lymphatic system performs three major functions in the body. It aids in the transport of lipids from the digestive system to the circulatory system, It recovers excess fluid from body tissues and returns them to the circulatory system, and finally it protects the body from infection.

Lymph and Lymphatic Vessels

The lymphatic system incorporates a wide network of vessels to collect and transport fluid. **Lymphatic capillaries** are the smallest of these vessels, and are present in most tissues of the body. These vessels collect fluid from the tissues, and transport it toward larger lymphatic vessels and organs. The fluid in these vessels is referred to as **lymph**. Lymphatic vessels operate under very low pressure, and incorporate similar measures to the veins to assist in movement of lymph, such as valves and the skeletal and thoracic pump.
The lymphatic capillaries converge and form larger vessels called **collecting vessels**. These collecting vessels are often colocated with arteries and veins. The collecting vessels will empty out into **lymph nodes**, which contain immune cells that will examine the lymph for signs of infection. From the lymph nodes, different collecting vessels will carry the fluid to converge in one of six **lymphatic trunks**, which are responsible for collecting fluid from major portions of the body.
These lymphatic trunks will then converge to form the **thoracic duct** and **right lymphatic duct**. The thoracic duct collects fluid from the left side of the head and neck, left chest, left arm, abdomen, and legs. The right lymphatic duct collects fluid from the right side of the head and neck, right chest, and right arm. The right lymphatic duct connects to and returns its fluid to the **right subclavian vein**, while the thoracic duct connects to and returns its fluid to the **left subclavian vein**.



Lymphatic Tissues and Organs

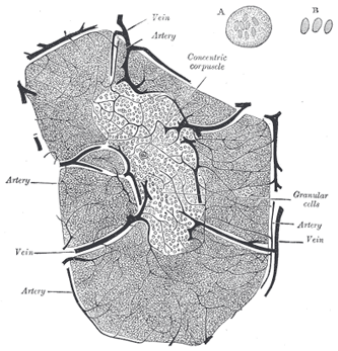
Lymphatic tissues are collections of lymphocytes in the connective tissues of mucous membranes and some organs. These tissues are often located near openings in the body to prevent invasion from foreign organisms. The respiratory, digestive, urinary, and reproductive tracts often have regions of this **mucosa associated lymphatic tissue (MALT)**. The ileum contains areas where lymphocytes and macrophages collect, called **peyer's patches** which serve a similar function.

Red Bone Marrow

Red bone marrow is the site of blood cell production, including production of white blood cells and other immune cells. Red bone marrow is found in most bones of the head, thorax, abdomen, and pelvis.

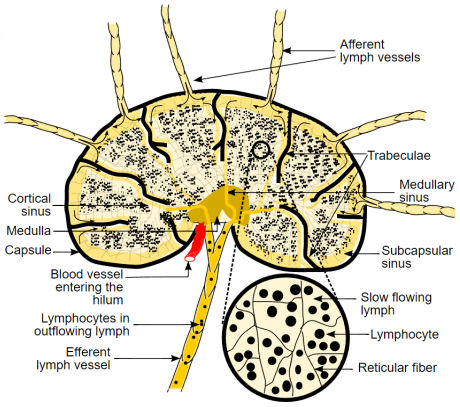
Thymus

The thymus is the site where lymphocytes develop, as well as having endocrine functions that regulate the production and function of lymphocytes. The Thymus is located between the sternum and the aortic arch.



Lymph nodes

Lymph nodes are the most common type of lymphatic organ. Their purpose is to cleanse the lymph as it passes through the nodes, and to be the site where B-Lymphocytes and T-Lymphocytes are activated by the immune system. Lymph enters through the afferent lymph vessels, and exits through the efferent lymph vessel.



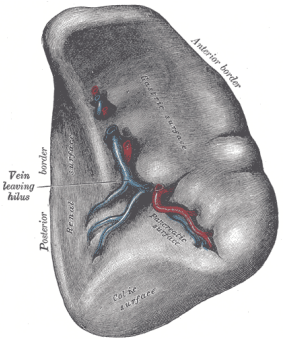
Lymph nodes are found throughout the body, but are found in clusters in the neck (**cervical lymph nodes**), armpits (**axillary lymph nodes**), thoracic cavity (**thoracic lymph nodes**), posterior abdominal wall (**abdominal lymph nodes**), intestines and mesentery (**intestinal and mesenteric lymph nodes**), groin (**inguinal lymph nodes**), and at the back of the knees (**popliteal lymph nodes**).

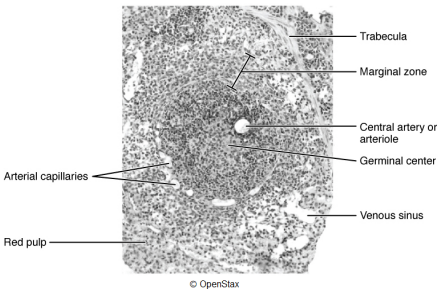
Tonsils

The tonsils are nodules located in the pharynx that protect the body from inhaled or ingested foreign organisms

Spleen

The spleen is the largest lymphatic organ. It is located on the left lateral thorax in between the diaphragm, stomach, and left kidney.





The spleen is separated into regions called the **red pulp**, and the **white pulp**. The red pulp makes up the majority of the spleen and filters out aged red blood cells. The white pulp surrounds the arterioles in the spleen, and monitors the blood for signs of infection

Immune system

When discussing the immune system, we are referring to all of the functions that work together to prevent organisms from entering the body, or to destroy foreign organisms after they have entered the body. Immunity is achieved when the body has the ability to destroy foreign organisms before they can impair the function of the body. Foreign organisms that can cause disease or damage are known as **pathogens**

Types of Immune function

To protect the body from pathogens, our body requires the ability to target and destroy foreign organisms. Targeting of foreign cells relies on antigens present on all cells.

Innate (Non-specific) Immunity

Innate immunity relies on the presence of “self-antigens”, a set of markers on the surface of your body's cells that identify it as belonging to you. Portions of the Innate immune system will target and attack any cell that does not have the correct self-antigen. In some cases, your immune system may mistake a self-antigen as a foreign antigen, causing the immune system to attack your own body in an **autoimmune reaction**

Adaptive (Specific) Immunity

Adaptive immunity relies on identifying and targeting a single specific antigen. Any cell that then displays that antigen can be attacked by the corresponding adaptive immune cell or protein. Since adaptive immunity is more specifically targeted, there is less of a concern regarding autoimmune reactions. This allows the body to mass produce these cells and proteins safely.

Layers of Defense

The immune system works as a series of responses, designed to prevent entry to foreign organisms, then to destroy them at the point of entry, followed by a body wide response.

First Layer - External Barriers

The skin and mucous membranes are designed to be impermeable to foreign organisms, denying them access to the body. By preventing entry, the body prevents these organisms from causing disease or damage

Second Layer - Innate Defenses

The second layer of defense is a series of responses that occur when the skin or mucous membranes are damaged, allowing pathogens to enter the body. These responses are designed to limit the spread and growth of pathogens to prevent systemic infection.

- **Fever** is caused by chemicals called **pyrogens** that cause the hypothalamus to increase body temperature. The goal of fever is to use the increased body heat to degrade the function of a pathogen's enzymes, reducing their ability to attack the body and reproduce. Some pathogens are capable of producing pyrogens that cause body temperatures to increase to unsafe levels.

- **Inflammation** creates swelling in tissues surrounding tissue damage and summons immune cells to the site of the damage. Inflammation is initiated by the release of inflammatory chemicals called **cytokines**. These chemicals will cause nearby capillaries to dilate, which will cause gaps to form in the wall of the capillary in a process called **margination**. Neutrophils will exit the capillary through these gaps in a process called **diapedesis**. Once the neutrophils enter the tissue, they will follow the cytokines to the source of the tissue damage by a process called **chemotaxis**. At the site of the injury, the neutrophils will attack any pathogens that have entered through the injury.

  Symptoms of Inflammation include pain due to activation of the nearby nerves by cytokines, swelling due to fluid escaping dilated capillaries, redness caused by the dilated capillaries being more visible through the skin, and heat due to increased blood flow to the area.

- **Immune Proteins** are proteins that are normally found in the blood, but can be activated by the immune system to attach to pathogens, attract immune cells, and puncture cell membranes to destroy pathogens.
  An example of these are the **complement proteins**, a series of proteins that can be activated by antibodies or chemicals released into the blood during periods where the body is fighting infection. The complement proteins will bind to the pathogen, attract immune cells (**opsonization**), cause inflammation, and form structures to damage the cell membranes of bacteria (**membrane attack complex**).
  Interferons are proteins released by cells infected by viruses. These proteins signal neighboring cells to prepare defenses against viruses, and help immune cells target the infected cells.

- **Immune surveillance** involves innate immune cells roaming through tissues searching for signs of infection or cancer. **Macrophages** are found in the epidermis and other tissues, and search for signs of pathogens. **Natural Killer cells** are a type of innate immune cell that specializes in recognizing and destroying cells that are cancerous or infected by viruses.

Third Layer - Adaptive Defenses

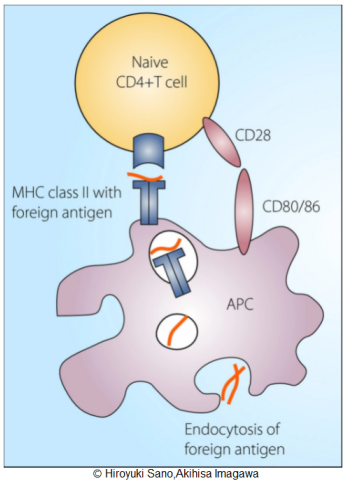
The third layer of defense is based around adaptive immunity. In order for this layer to be activated, an innate immune cell must locate a pathogen and collect a sample of its antigen in order to provide a target for the adaptive response. The cells capable of doing this are called **Antigen Presenting Cells (APCs)**.

Major Histocompatibility Complexes

There are two types of MHC proteins produced in the body. All cells with a nucleus will produce **Major Histocompatibility Complex Type 1** (**MHC1**) proteins over their life cycle. These proteins will float through the cytoplasm to the cell membrane, and grab any proteins they brush into on the way. Once these proteins reach the cell membrane, they are attached to the outer surface, displaying the proteins found inside the cell. If any foreign proteins are present, it means the cell has been invaded by a pathogen and needs to be destroyed by the immune system.

Major Histocompatibility Complex Type 2 (**MHC2**) proteins are found only on certain immune cells. These proteins are used to transport foreign antigens to activate the cells of the adaptive immune system.

Antigen Processing and Presentation



Antigen presenting cells are phagocytes such as macrophages, which will ingest and destroy foreign cells. The residue of those cells contains antigens which can be used to identify those pathogens by the adaptive immune system.

To pass these antigens on to the adaptive immune system, the APC will attach these antigens to a MHC2 protein, and release chemicals to attract cells to transport the protein.

T-Helper lymphocytes (CD4 cells) will bond to the MHC2 protein, while also going through a process called **costimulation**, where a protein on the CD4 cell interacts with a protein from the APC.

After collecting the antigen, the T-helper cell will scan the structure of the antigen before entering a period of rapid division. This process is called **clonal selection**, and allows the T-helper cell to produce copies of itself with the antigen, as well as **T-cytotoxic cells** which will search for and destroy any cell that has the antigen that was delivered to the T-helper cell. Some of these cytotoxic cells will remain inactive as **T-memory cells**, which will be activated in the future if this pathogen is found again.

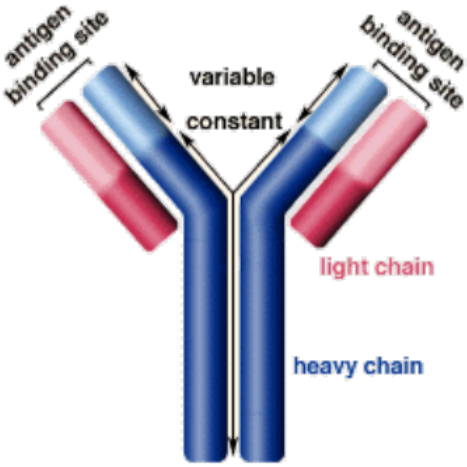
The T-helper cells will migrate to the lymph nodes and locate **B-Lymphocyte** cells to deliver the antigens to. If this antigen has not been found in the past, it will cause the B-cell to first design a targeted antibody before undergoing clonal selection. When the B-cell divides, it will produce

Plasma cells that specialize in mass producing antibodies, as well as B-memory cells that will produce antibodies if this antibody is encountered in the future.

Antibody Structure and Types

Antibodies are immune proteins produced by B-cells that are designed to bond to foreign antigens. The monomer form of an antibody is a Y-shaped protein, made of two heavy protein chains and two light protein chains.

The two tips of the Y shape are the areas that are designed to match the antigen they are targeting. These are called the **antigen binding site**. As each antibody is targeted against a different antigen, the antigen binding sites of different antibodies will be different from each other, while the rest of the structure is identical.



Types of Antibodies

The immune system produces several types of antibodies, tailored to the needed function.The protein structure of antibodies are referred to as **immunoglobulins (Ig)**. The type of antibody is usually indicated by adding a letter after Ig.

IgA is primarily found in secretions such as tears, breast milk, nasal mucous, and saliva. Structurally it is a dimer (two monomers attached to each other), allowing it to bond to up to 4 antigens per antibody. IgA from breast milk temporarily protects breastfeeding infants from gastroenteric infection.

IgG is the most common antibody found in the blood. It is associated with long term immunity, and is found in people suffering from chronic (long term) infections. IgG is able to cross the placenta, and provides protection to the infant for approximately 6 months.

IgM is the first antibody produced by B-cells during acute (new) infection. Structurally IgM is a pentamer (five monomers arranged in a star shape), providing it with 10 antigen binding sites, and allowing it to affect multiple pathogens at once.

IgD is a surface protein on B-cells, and is suspected to be involved in antibody production

IgE is a surface protein found on basophils and mast cells, and is involved in inflammation and allergic reactions.

Immune Function of Antibodies

Antibodies are able to bond their antigen binding sites to the antigens of their targeted pathogens. Monomer antibodies such as IgG are capable of attaching up to two pathogens together, while the pentamer IgM is capable of attaching up to ten pathogens together. This ability to bind pathogens together is known as **agglutination**.

When antibodies bond to an antigen, it will activate nearby immune proteins in the blood, activating the complement protein system.

Types of Immunity

Immunity is when the body has sufficient protection to prevent pathogens from causing harm to the body before they can be destroyed. Some types of immunity provide long term protection, while others only provide temporary protection.

Passive immunity is achieved by receiving antibodies from another person. These antibodies will protect an individual until they break down and leave the blood. **The individual's body does not gain the ability to produce its own antibodies** however, as it does not receive a copy of the antigen.

Active immunity is achieved by receiving an antigen and producing your own antibodies. **This allows the body to produce new antibodies** when the number of antibodies circulating in the blood drops below a useful number.

These two types of immunity can be achieved in two ways, **Natural immunity** and **Artificial immunity**.

Passive natural immunity occurs in infants, where IgG acquired from the mother through the placenta, and IgA acquired from breast milk provides some protection against infection.

Passive artificial immunity occurs when a person has been injected with antibodies collected from another individual.

Active natural immunity occurs after recovering from an infection, as your body acquires the antigen during the process of fighting the infection.

Active artificial immunity occurs through vaccination. Vaccines contain antigen proteins designed based on the target pathogen. Using these antigens, a person will be able to create their own antibodies in the future

Respiratory System

The respiratory system is responsible for many processes in the body, including providing for oxygen and carbon dioxide exchange with the blood, allowing for vocalization, providing the sense of smell, assisting in pH control of the blood, and controlling pressures in the thorax that assist in movement of venous blood and lymph.

Respiratory Anatomy

The structures in the respiratory system are usually divided into the **conducting division** and the **respiratory division**, based on their function. The conducting division is designed to move air through the respiratory passageways, enabling speech and the sense of smell. The respiratory division is responsible for gas exchange.

Nose

The nose serves to warm, filter, and humidify inhaled air. It is also the site of the olfactory receptors that provide the sense of smell as air moves past them. Finally the hollow spaces in the nasal cavity allow for resonance and amplification of the voice.
Air enters the nose through the **nares** (nostrils), then passing into the nasal cavity where hairs and mucous membranes will help capture particles floating in the air. The **nasal conchae** causes turbulence in the inhaled air that helps ensure that most of the air comes in contact with the mucous membranes.

Pharynx

The pharynx is a funnel shaped passageway that extends downwards from behind the nasal cavity, behind the oral cavity, and connects to the larynx. The upper portion is called the **nasopharynx**, and is the site where the eustachian tubes from the middle ear connect to equalize pressures in the ear. Below the nasopharynx is the **oropharynx**, located posterior to the oral cavity. The oropharynx is the site where the palatine tonsils are located. Both the nasopharynx and oropharynx are composed of pseudostratified epithelium. Below the oropharynx is the **laryngopharynx**, which receives food from the oral cavity as well as air. To prevent aspiration of food or liquids, the laryngopharynx has a structure called the **epiglottis**, which seals the entry to the larynx when swallowing. The laryngopharynx is composed of stratified squamous epithelium.

Larynx

The larynx is sometimes referred to as the voice box, as it is the site of the **vocal folds** that are used to produce speech. The superior edge of the larynx is anchored to the **hyoid bone** by the thyrohyoid ligament. The larynx is composed of multiple pieces of hyaline cartilage, as well as several muscles used to manipulate the vocal folds and to seal the larynx during swallowing.

Trachea

The trachea is a rigid tube that collects air from the larynx downward, anterior to the esophagus. The trachea is supported by “C” shaped pieces of hyaline cartilage. The interior of the trachea is lined by pseudostratified columnar epithelium. At the lungs, the trachea will divide, forming the **primary bronchi** that carry air into the lungs.

Lungs and Bronchial Tree

The lungs are large conical organs with a broad, flat base that rests on the diaphragm, a broad **costal surface** that rests against the rib cage, and a flattened **apex** that extends just above the clavicles. The **hilum** is the location on the medial surface of the lung where the primary bronchi, blood vessels, nerves, and lymphatic vessels enter.
Inside the lung, the primary bronchi are responsible for supplying air to each of the lungs, before branching to form the **secondary (lobular) bronchi**. The secondary bronchi will spread to each of the **lobes** of the lungs to supply air. The right lung contains three lobes, while the left lung contains two lobes. In the lobes, the secondary bronchi will branch to form the **tertiary (segmental) bronchi**, which will continue to branch into **bronchioles**, **terminal bronchioles**, and finally **respiratory bronchioles**.
The respiratory bronchioles are the first portion of the respiratory system where gas exchange can occur, being the beginning of the respiratory division. Each respiratory bronchiole supplies air to multiple **alveolar ducts**, which carry air to the **alveolar sacs**. To enable gas exchange, these structures are composed of simple squamous epithelium. These cells are called **Type I alveolar cells** in the alveoli. **Type 2 alveolar cells** are responsible for creating **surfactant**, a substance that reduces surface tension in water that prevents the alveoli from sticking shut due to their moist surfaces.

Ventilation

Air moves due to differences in pressure between two areas, moving from areas of higher pressure to areas of lower pressure. In order to move air in (**inspiration**) or out (**expiration**), the body needs to be able to alter the pressures in the lungs.

Boyle’s Law

In physics, Boyle’s law describes the relationship between pressure and volume in gas as being inversely proportional. This means that when one of these properties changes, the other property will have the opposite reaction. This would mean that as the volume of a gas increases, the pressure of that gas will decrease.
In order to cause air to enter the body, the pressure in the lungs must be lower than that of the surrounding air. Using Boyle’s law, we can reduce the pressure in the lungs by causing the volume of the lungs to increase. To cause air to exit the body, the pressure in the lungs must be higher than the surrounding air. This can be done by reducing the volume of the lungs to increase the pressure.

Dalton's Law

Dalton's law describes how pressures of gasses are found in a mixture of gas. This is important, because the air in the atmosphere is actually a mixture of several different gasses. The air we breathe is composed of 78% nitrogen, 21% oxygen, and 1% other gasses, including argon, carbon dioxide, and water vapor. Overall atmospheric pressure is normally 760mmHg, or 1atm.

Dalton's law states that the total pressure of a gas is equal to the sum of the individual (partial) pressures of the gas. This also allows us to say that the partial pressure of a gas can be found by taking the percentage that gas makes of the atmosphere, multiplied by the atmospheric pressure.

> Ex: If normal atmospheric pressure is 760mmHg, and oxygen makes up 21% of the atmosphere, then 760*21/100 = 160mmHg of that pressure comes from oxygen.

This concept of partial pressure is important to understand, as the movement of the individual gasses will be based on the difference in partial pressure of those gasses in different locations.

Henry's Law

Henry's law describes the relationship between pressure and the amount of gasses that can dissolve into a liquid. Henry's law states that the amount of dissolved gas in a liquid is directly proportional to the partial pressure of the gas surrounding that liquid. This means that as the pressure of the gas around a liquid changes, the amount of the gas in the liquid will be forced to change as well, with either gas entering the liquid or being forced to leave the liquid.

In the blood, there is a low concentration of oxygen, while in air at the lungs, there is a high partial pressure of oxygen,which causes the movement of oxygen into the blood. At the same time, there is a high concentration of carbon dioxide in the blood, while the partial pressure of carbon dioxide in the lungs is very low. This will make it so that carbon dioxide cannot stay dissolved in the blood, and instead releases the CO_2 gas out into the lungs.

Respiratory Muscles

In order to change the volume of the lungs, we rely on muscles to cause movement in the thoracic cavity. The primary muscle that causes this change is the **diaphragm**, which forms the inferior border of the thoracic cavity. When the diaphragm contracts, it moves downward into the abdominal cavity, causing the volume of the thoracic cavity to increase. Secondary muscles that assist in ventilation include the i**nternal and external intercostal muscles**, which will cause the ribs to rise and move outward when they contract, increasing the volume of the thoracic cavity.

While there are other muscles that can assist in ventilation, such as the sternocleidomastoid, scalences, pectoralis minor, rectus abdominis, and external abdominal obliques, these muscles are not normally used. Usage of these muscles indicates respiratory distress.

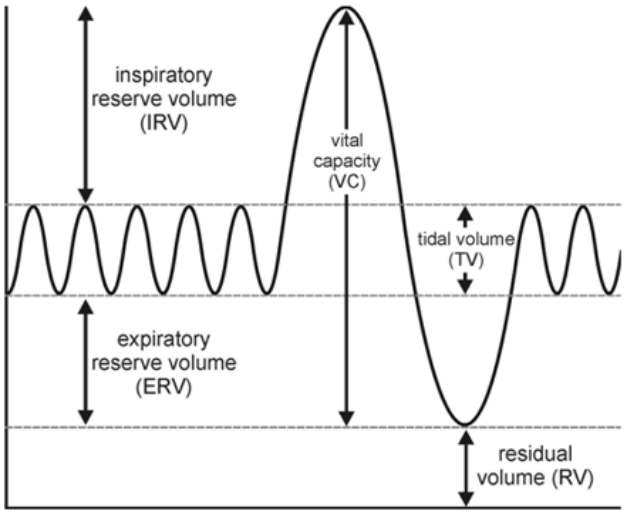
Process of Ventilation

Inspiration begins when the diaphragm and intercostal muscles contract, expanding the thoracic cavity. This causes the pressure in the thoracic cavity to decrease. Due to the decreased surrounding pressure, the pleural cavities containing the lungs will then expand to relieve the pressure in the thoracic cavity. As the lungs expand, pressure in the lungs will decrease, causing air to be forced into the body due to higher pressure in the surrounding atmosphere.

Expiration is caused when the respiratory muscles relax and return to their original positions, reducing the volume of the thoracic cavity. This causes pressure inside the thoracic cavity to increase, which forces the pleural cavity to contract. As the lungs contract, pressure increases, forcing air out toward the lower air pressure in the surrounding atmosphere.

Respiratory Volumes

Spirometry is a method used to measure the volume of air moved in or out of the lungs. Using this, we can quantify how much air is present in the lungs, how much air normally moves during ventilation, and how much air can be moved through forced inspiration or expiration.



Tidal volume refers to the quantity of air moved by a normal inspiration and expiration

Expiratory reserve volume refers to the quantity of air that can be moved by forcefully exhaling after a normal expiration.

Inspiratory reserve volume refers to the quantity of air that can be forcefully inhaled after a normal inspiration
Residual volume is the quantity of air that remains in the lungs after a forceful expiration

Gas exchange

Gas exchange is the process of exchanging oxygen and carbon dioxide in the blood with air in the lungs (**external respiration**), or with tissues of the body (**internal respiration**). The need for gas exchange is due to the required materials and waste products of the process the cells use to produce energy

Cellular Respiration

Cellular respiration is a series of chemical reactions that allows sugars to be converted into energy, which is used to make ATP. This process occurs in the mitochondria of the cells.

$$\underset{\text{glucose}}{C_6H_{12}O_6} + \underset{\text{oxygen}}{6O_2} \rightarrow \underset{\text{carbon dioxide}}{6CO_2} + \underset{\text{water}}{6H_2O} + \text{energy}$$

One sugar molecule will require six oxygen molecules to perform the reaction. The waste products of the reaction are six water, and six carbon dioxide. Due to this, the cells are constantly using up oxygen and producing carbon dioxide.

Oxygen Transport

In the blood, oxygen is primarily carried inside of red blood cells, due to the hemoglobin molecule. 98.5% of oxygen will bond to the hemoglobin inside of the RBCs, leaving 1.5% that is carried dissolved in solution with the plasma of the blood.

Oxygen Unloading

Hemoglobin can be triggered to release oxygen due to an increase in temperature, or a decrease in pH (**Bohr effect**). These are commonly found near metabolically active cells that are rapidly consuming oxygen to produce energy. Once oxygen is unloaded from hemoglobin, it will diffuse into tissues that have a lower oxygen concentration.

Carbon Dioxide Transport

Due to an enzyme (**carbonic anhydrase**) found in RBCs, the majority of the carbon dioxide in the blood will be converted into bicarbonate in a series of chemical reactions.

$$\underset{\text{carbon dioxide}}{CO_2} + \underset{\text{water}}{H_2O} \rightarrow \underset{\text{carbonic acid}}{H_2CO_3} \rightarrow \underset{\text{Hydrogen Ion}}{H^+} + \underset{\text{Bicarbonate Ion}}{HCO_3^-}$$

In the first step of this reaction, carbon dioxide and water are combined by the enzyme to form carbonic acid. Carbonic acid will then break down and form a hydrogen ion and a bicarbonate ion.

Approximately 70% of the carbon dioxide in the blood will be converted into bicarbonate and be carried in the blood plasma.
After it has released oxygen, hemoglobin is able to bond to and transport 23% of the carbon dioxide released by the tissues (**Haldane effect**).
The final 7% of the carbon dioxide is carried as a dissolved gas in solution with the plasma.

Respiratory Control of pH

Due to the enzyme carbonic anhydrase, carbon dioxide is converted into an acid in the blood, causing the blood pH to decrease based on the concentration of the carbon dioxide. Carbon dioxide concentration is inversely related to the respiratory rate, as respiratory rate increases, carbon dioxide concentrations will decrease.

Based on this, as respiratory rate increases, carbon dioxide levels will decrease, and pH will increase. Otherwise, if respiratory rate decreases, carbon dioxide levels will increase, and pH will decrease.

This means that there is a direct relationship between respiratory rate and blood pH. When the body needs to increase the blood pH, respiratory rates will increase, and if the body needs to decrease blood pH, respiratory rates will decrease.

Neural Control of Breathing

The **ventral respiratory group (VRG)** of the medulla oblongata creates a regular rhythm of breathing, at a rate of about 12 breaths per minute. This can be modified by signals from the **pontine respiratory group (PRG)** of the pons. The PRG receives signals from the hypothalamus, limbic system, and cerebral cortex, and modifies the respiratory rate, depth, and rhythm for vocalization, emotional responses,or based on activity levels. The **dorsal respiratory group (DRG)** of the medulla can also alter the respiratory rhythm based on input from chemoreceptors in the major arteries and stretch and irritant receptors in the airways.

Chemoreceptors

The body uses special receptors in the aortic arch and carotid arteries to monitor the chemical composition of the gasses in the blood. Carbon dioxide is the easiest of these gasses to monitor, as 77% of the carbon dioxide is present in the plasma as bicarbonate or dissolved gas, compared to 1.5% of the total oxygen, with the remainder inside the RBCs where it cannot be detected.
The body estimates the quantity of oxygen in the blood based on the carbon dioxide levels. When carbon dioxide levels increase, the body assumes the level of oxygen is deceased, and will cause increased respiration in order to replenish the oxygen levels.

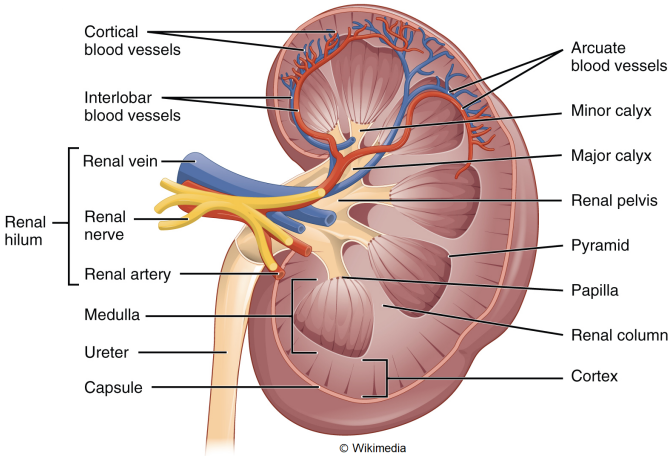
Urinary System

The urinary system is the main method to remove wastes and harmful materials from the body. It is also responsible for maintaining pH, fluid, and electrolyte balance in the body. The urinary system also plays an important role in maintaining blood pressure in the body.

Anatomy of the Urinary system

Kidneys

The kidneys are the primary organ of filtration for the urinary system. They filter fluid from the blood, removing wastes and producing urine. The kidneys are located retroperitoneally, at the posterior of the abdominal cavity at the level of rib 12.



The kidneys are surrounded by a fibrous capsule, with their internal structure divided into the **cortex**, **medulla**, and **renal pelvis**. Blood vessels and the ureters connect to the kidney on their medial surface at an opening called the **hilum**.

The cortex is the site where the **nephrons**, which filter the blood, are located.

The medulla contains the renal pyramids, which carry urine toward the pelvis, and protrusions of the cortex called the renal columns.

The renal pelvis contains the calyxes, which collect urine that was produced by the nephrons of the kidney and converge to form the ureter.

Ureters

The ureters are muscular tubes that carry urine from the kidney to the urinary bladder. The ureters will produce a peristalsis-like wave to help transport urine down to the urinary bladder.

Urinary bladder

Located on the floor of the pelvic cavity, posterior to the pubic symphysis. The urinary bladder has a muscular layer called the **detrusor muscle** which is responsible for putting pressure on the contents, enabling it to be propelled out of the body. The inner surface of the urinary bladder is covered by a layer of transitional epithelial tissue, allowing the bladder to expand its capacity as it fills with urine.

Urethra

The urethra is a tube that connects the urinary bladder to the outside of the body at the external urethral orifice. The female urethra runs for about 3-4cm, while the male urethra is about 18cm long. The male urethra is separated into the **prostatic urethra**, which connects the bladder to the prostate gland, the **membranous urethra** which passes through the muscular floor of the pelvic cavity, and the **spongy urethra** which passes through the penis.
The urethra contains an internal sphincter muscle at the point where it joins with the urinary bladder, and an external sphincter muscle when it passes through the muscular floor of the pelvis. The internal sphincter operates under the **micturition reflex**, which opens the internal sphincter and contracts the detrusor muscle when stretch receptors in the urinary bladder are activated. The external sphincter operates under conscious control, except in small children and those with nerve degradation.

Renal Circulation

Due to their function of filtering wastes from the blood, the kidneys require a large supply of blood. Each kidney receives blood from the **renal artery**, which branches off of the abdominal aorta. At the hilum, the renal artery branches to form the **segmental arteries**. The segmental arteries will branch to form the **interlobar arteries** at the renal pelvis. The interlobar arteries will branch to form the **arcuate arteries** in the medulla. At the border of the cortex and medulla, the arcuate arteries will branch out into the cortex, forming the **interlobular arteries**. The interlobular arteries are the source of the **afferent arterioles**, which supply blood to each nephron

When blood is returning from the nephron, it will enter the **interlobular vein**, which converges to form the **arcuate veins** in the medulla, and the **interlobar** veins in the pelvis. Unlike the arteries, there is no segmental vein, with the interlobar veins converging to form the **renal vein**.

Nitrogenous Wastes

As a byproduct of metabolism, our cells produce many chemical wastes that are harmful if allowed to build up in the body. To prevent this, these wastes are removed from the blood by the kidneys, and excreted in urine.
In this chapter we focus on four primary wastes, but the kidneys are also capable of removing other harmful substances such as drugs and medications. These are referred to as **nitrogenous wastes**, as they are nitrogen based compounds (while most other compounds in the body are carbon based). The quantity of these wastes in the blood can be checked by the **Blood Urea Nitrates** (**BUN**) test. The wastes are:

- Ammonia (NH_3) is produced by **deamination**, a process that removes the amino group from an amino acid. Ammonia is a base that will raise the pH, and can easily cause damaging chemical reactions in the body.

- Urea is formed by combining two ammonia molecules with carbon dioxide, producing water and urea. This process occurs in the liver, to protect the body from ammonia by changing it into a less harmful chemical.
- Uric Acid is created by the breakdown of purines. Purines are normally used in the body to produce the nitrogenous bases adenine and guanine for DNA and RNA, while excess purines are broken down to uric acid and excreted.
- Creatinine is created when creatine phosphate is used by the muscles as a source of phosphate to produce ATP.

Nephron

The nephron is sometimes called the functional unit of the kidney. This is because the nephron is the structure responsible for filtering wastes from the blood. In the kidney there are two types of nephrons, **cortical nephrons** and **juxtamedullary nephrons**.

Cortical nephrons are located entirely within the cortex of the kidney. These nephrons are best able to remove non-waste materials from the filtered fluid and return them to the blood. Juxtamedullary nephrons are located on the border between the cortex and the medulla, and specialize in returning fluid from the filtrate to the blood, reducing the amount of water lost to urine.

Anatomy of the Nephron

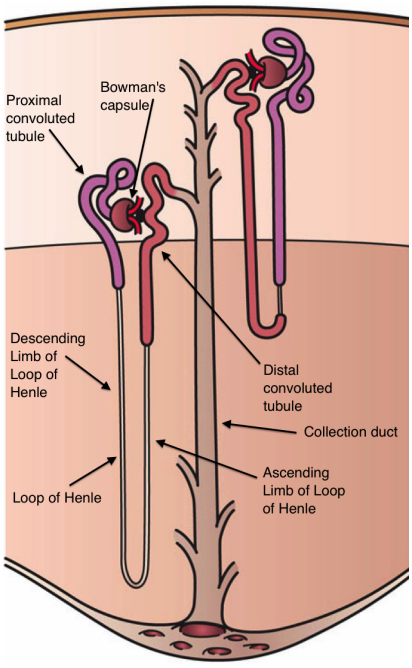
The nephron has a capillary bed called the **glomerulus**, which receives blood from the **afferent arteriole**, and returns blood to the **efferent arteriole**.

Fluid is removed from the blood in the capillary bed and absorbed by the surrounding **bowman's capsule**.

Fluid will then flow into the **proximal convoluted tubule (PCT)**, which is surrounded by the **peritubular capillaries**.

After the PCT, fluid will flow through the **Nephron loop** and **Loop of Henle**, which is surrounded by a capillary bed called the **vasa recta**.

Finally, the fluid will enter a set of tubes called the **distal convoluted tubule (DCT)**, which is also surrounded by the peritubular capillaries.



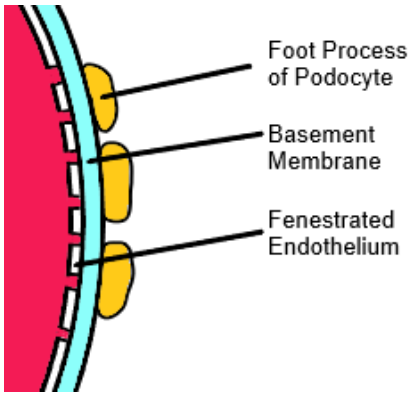
Any fluid that remains in the tubules at this point will be delivered to the **collecting duct**, which will carry the fluid to the renal pelvis for transport to the urinary bladder.

Glomerular Filtration

The first stage of urine formation is glomerular filtration, where blood plasma is filtered and enters the nephron.

Filtration membrane

The **fenestrated capillaries** of the glomerulus are covered in small pores on their surfaces that allow some of the fluid from the plasma to escape. After passing through these pores, the fluid passes through the **basement membrane** that surrounds the capillary. Surrounding the capillaries are specialized cells called **podocytes** which wrap **foot processes** around the capillaries, leaving small gaps called **filtration slits** that allow fluid to pass through before entering into the capsule.



Each of these stages forces the fluid to pass through progressively smaller spaces, trapping large solutes and preventing them from leaving the capillary. Additionally, the foot processes of the podocytes are negatively charged, preventing positively charged ions from passing through them.

Filtration Pressure

Similar to capillary exchange, fluid movement in the glomerulus depends on the balance of forces acting on the fluid of the blood.

Blood Hydrostatic Pressure
The pressure within the capillary is the main force pushing fluid out into the nephron capsule. As blood pressure increases, more fluid will be forced out of the capillary, while if blood pressure drops, less fluid will exit.

Osmotic Pressure
As fluids leave the capillary, the plasma remaining behind becomes more concentrated. This causes osmosis to exert pressure that works to reduce the amount of fluid leaving the capillary. If the concentration of the blood is higher than normal, less fluid will leave the capillary, while if the concentration of the blood is reduced, more fluid will exit.

Capsule Hydrostatic Pressure
This is the pressure exerted by the fluid already within the capsule that resists the movement of fluid leaving the capillary, reducing the amount of filtration

Regulation of Glomerular Filtration

The nephron requires a certain rate of filtration in order to properly function. As glomerular filtration decreases, the flow of filtrate through the nephron drops, allowing wastes to diffuse back into the blood, while nutrients and electrolytes can diffuse back into the nephron. If the flow of filtrate increases, there may not be time for the structures of the nephron to reabsorb nutrients and electrolytes.

Since the largest factor of the glomerular filtration rate is the blood pressure within the glomerulus, there are several mechanisms that function to keep it at the proper levels. This is called **renal autoregulation**.

Myogenic mechanism
As blood pressure in a blood vessel increases, the blood vessel will be forced to expand. The afferent arteriole, which supplies the glomerulus with blood, has a layer of smooth muscles. When the blood vessel expands, it causes the smooth muscle cells to contract, causing vasoconstriction and reducing blood flow into the glomerulus.

Tubuloglomerular Feedback
This feedback mechanism is caused by a set of cells located in what is called the **juxtaglomerular apparatus**. This is a structure created by cells of the DCT, cells surrounding the afferent arteriole, and cells within the glomerulus. The **macula densa** cells are capable of detecting the presence of sodium ions, which are the most common electrolyte found in plasma. By measuring the concentration of sodium, these cells can estimate the rate of glomerular filtration. When filtration rates change, they stimulate the **juxtaglomerular** cells and **mesangial** cells. The mesangial cells surround the capillaries and podocytes, and when glomerular filtration increases, they will constrict, reducing the amount of filtrate that can exit the capillaries. Juxtaglomerular cells are specialized smooth muscle cells that surround the afferent arteriole. If glomerular filtration has increased, these cells will contract, reducing blood flow in the afferent arteriole to reduce filtration. If the glomerular filtration rate decreases, they will first dilate to increase blood flow and if glomerular filtration does not increase, they will release the hormone **renin**.

Renin/Angiotensin/Aldosterone system

When it is secreted, renin will start a reaction within the blood that will create a hormone designed to increase blood pressure systemically. Renin will activate **angiotensinogen**, which is produced by the liver, converting it into **angiotensin I**. Angiotensin I will then react with an enzyme produced in the lungs, **angiotensin converting enzyme (ACE)**, which forms the hormone **angiotensin II**.

Angiotensin II is a powerful hormone that causes systemic vasoconstriction, triggers the sense of thirst, and causes the release of **aldosterone**. Aldosterone acts on the DCT of the nephron, and causes more fluid to be reabsorbed into the blood, reducing urine production. All of these actions will cause blood pressure to be increased.

Tubular Reabsorption and Secretion

Once filtrate enters the nephron, materials that are useful for the body are removed from the nephron and returned to the blood by a process called tubular reabsorption. At the same time, additional wastes are removed from the blood and sent into the nephron by tubular secretion.

Proximal Convoluted Tubule

The majority of tubular reabsorption and secretion occur within the PCT. The PCT is relatively long, and the epithelium lining it is lined with microvilli that increase their surface area, allowing for additional transport. These cells will utilize active transport proteins to transport sodium, glucose, and chloride out of the tubules. This will cause the concentration of the cells to increase, causing water to enter the cells through water channels called **aquaporins** due to osmosis.

These cells will then actively transport sodium, potassium, glucose, and chloride into the peritubular capillaries that surround the PCT. The peritubular capillaries are fed blood from the efferent arteriole, which collects the highly concentrated blood that leaves the glomerulus. This highly concentrated solution will draw additional fluid out of the tubule through the gaps in the epithelium of the PCT in what is called the **paracellular route**. As fluid leaves the tubule in this way, it will carry solutes such as electrolytes with it in a process called **solvent drag**.

The cells of the PCT will also actively transport wastes from the blood into the tubules. Depending on blood pH, these cells will also secrete hydrogen ions or bicarbonate ions in order to regulate pH balance.

Nephron Loop

After exiting the PCT, the filtrate will enter the nephron loop. The initial descending portion of the nephron loop is impermeable to water, preventing water transport. As the nephron loop descends deeper into the kidney, the surrounding tissues become more concentrated. At the bottom of the nephron loop, the tubule thins and aquaporins are present in the epithelium, allowing water to leave the loop to enter the more concentrated tissues surrounding the loop. Due to this, the fluid within the loop becomes more concentrated. As the loop begins to ascend again, the walls of the tubule become impermeable to water while proteins will actively transport sodium, potassium, and chloride ions out of the tubule. Removing these electrolytes will cause the concentration of the filtrate to decrease.

Distal Convoluted Tubule

Tubular reabsorption and secretion in the DCT relies on the presence of hormones**.** Aldosterone will activate sodium/potassium pumps in the tubular epithelium, causing sodium and water to be reabsorbed while secreting potassium. Parathyroid hormone will cause the DCT to reabsorb calcium.

Water Conservation

The final stage of urine production is to ensure that the maximum amount of water has been reclaimed from the filtrate in the tubules. This portion will describe how mechanisms in the nephron increase the amount of water that is removed from the tubules.

Countercurrent Multiplier

The countercurrent multiplier refers to the mechanism that causes the tissues around the nephron loop to become more concentrated, which allows them to remove additional water from the tubule.

These tissues will receive salt and electrolytes from the PCT, which causes them to become more concentrated than the fluid in the tubules. This difference in concentration causes water to be pulled out of the tubule by osmosis, while leaving electrolytes behind in the tubule. In the ascending limb of the nephron loop, these excess electrolytes are transported out of the tubules into the tissue surrounding the tubules, causing them to become more concentrated.

This forms a positive feedback loop where the high concentration surrounding the loop allows both more water to be extracted, as well as more electrolytes to maintain the high concentration.

Countercurrent Exchange System

The countercurrent exchange system refers to how water and electrolytes enter and exit the capillaries of the vasa recta that surround the nephron loop. The capillaries of the vasa recta are arranged in parallel sets, with one vessel carrying blood downward being next to another vessel carrying blood upward.

As blood travels downward, water will leave the capillary, while salt enters the capillary. As blood travels upward, salt will exit the capillary, while water enters the capillary. This creates a system where the two capillaries are exchanging water and salt with each other. Similarly to the peritubular capillaries, the vasa recta originates from the efferent arteriole, causing the blood inside to have higher than normal concentration. This higher initial concentration means that the ascending capillaries of the vasa recta are able to reabsorb more water than was lost in the descending capillaries.

Collecting Duct

Collecting ducts will collect filtrate from multiple nephrons, carrying it down towards the renal pelvis. When **Antidiuretic Hormone (ADH)** is released from the posterior pituitary, it will cause aquaporins to form in the collecting duct. Due to the concentration of the tissues surrounding the collecting ducts water will be drawn out by osmosis, causing less water to enter the urine and retaining water in the body.

Fluid, Electrolyte, and pH Balance

In addition to removing wastes from the body, the urinary system is also responsible for helping maintain the correct amounts of fluid and electrolytes in the body. It will also work with the respiratory system to help maintain the correct pH balance in the blood.

Fluid Homeostasis

Fluid Compartments

Water in the body is distributed in different portions of the body areas, separated by selectively permeable membranes that prevent easy movement from one area to another.

Intracellular fluid
This is the fluid found inside the different cells of the body, and makes up about 65% of the water in the body.
Extracellular fluid
This all of the fluid found outside of the cells.and makes up the remaining 35% of the water in the body. This is usually separated into the **interstitial fluid**, which is the fluid found in various tissue spaces, and **blood** which circulates within the cardiovascular system.

When fluid imbalances occur, they tend to affect the blood first due to its direct connection to the urinary and digestive systems, before influencing the fluid in tissues, and finally the fluid in the cells.
As blood volume decreases, its concentration increases which will cause additional fluids to be drawn out of the tissue spaces during capillary exchange. This in turn will cause fluid to be drawn out of the cells into the tissue spaces. As fluid balance increases, water first enters the blood from the digestive system, and is then drawn into the tissue spaces and finally into the cells.

Intake and Output

To prevent fluid imbalances, intake and output of water from the body must be balanced. In an average adult, 2500mL of water is gained and lost every day.

Water gains
Approximately 1600mL of water is gained through drinking, 700mL of water is recovered from food that is eaten, and 200mL of water is produced by the cells of the body when performing cellular respiration.

Water losses
Approximately 1500mL of water is lost due to urination. 400mL of water is lost by **cutaneous transpiration**, which is when water diffuses through the epidermis and evaporates (as opposed to being secreted by sweat glands). 300mL of water is lost due to exhaled water vapor from respiration. 200mL of water is lost in feces. 100mL of water is lost through secreted sweat.

Regulation of intake
Water intake is primarily regulated by thirst. The sensation of thirst is triggered by the hypothalamus either due to increased blood concentration, or due to the release of angiotensin II due to low blood pressure. Under these influences, the hypothalamus will decrease saliva production, which will cause dry mouth and contribute to the sensation of thirst.

Regulation of output
Water output is primarily achieved through alteration of urine production.
When there is excess water volume in the body, the increased water volume will cause blood pressure to increase. This will lead to the suppression of hormones that cause water reabsorption in the nephron and increase urine production.
When there is deficient water volume, blood pressure will decrease. This will cause the renin/angiotensin/aldosterone system to be activated and the hypothalamus will trigger the release of antidiuretic hormone from the posterior pituitary, with all of these hormones acting to reduce urine production.

Electrolyte Balance

Electrolytes plan an important role in the body due to their ability to affect muscles, nerves, and other electrically excitable cells.

Electrolytes of the Intracellular and Extracellular Fluid

The five most common electrolytes in the body fluids are sodium, potassium, calcium, chloride, and phosphate.

Intracellular fluid
Potassium and phosphate are the major electrolytes found in the intracellular fluid. Potassium is a common intracellular electrolyte due to the active transport of potassium into cells by the sodium/potassium pump. Phosphate in the intracellular fluid is created by the breakdown of ATP, creating an ADP and a phosphate.

Extracellular fluid
In the extracellular fluid, sodium and chloride are the most common electrolytes. Sodium is present due to the actions of the sodium/potassium pump actively transporting sodium out into the extracellular fluid. Chloride is common in the extracellular fluid due to ionic attraction to sodium ions.

Sodium Homeostasis

The primary method of maintaining sodium levels in the body is the hormone aldosterone, which increases renal reabsorption of sodium. Low sodium concentration in the blood (**hyponatremia**) causes decreased blood concentration, which inhibits the release of ADH and increases urine production. The loss of water to urine causes the concentration of sodium in the remaining body fluids to become higher (due to becoming less diluted by fluid). High sodium concentration

(**hypernatremia**) usually causes increased blood pressure due to fluid retention. This will trigger the release of **atrial and brain natriuretic peptides**, which inhibit sodium and water reabsorption, as well as inhibiting renin and aldosterone release. This causes a loss of both sodium and water to the urine, decreasing sodium concentrations.

Potassium Homeostasis

Potassium homeostasis is closely linked to sodium homeostasis due to the effect of aldosterone, which causes potassium excretion. Low potassium concentration (**hypokalemia**) will reduce the amount of potassium lost to urine, reducing losses and allowing them to be made up for from diet. High potassium concentration (**hyperkalemia**) will increase blood concentration causing the secretion of aldosterone, and increasing the amount of potassium excreted into the urine.

Chloride Homeostasis

Chloride homeostasis is directly linked to sodium homeostasis. When sodium ions are retained, they will draw chloride ions along with them. When sodium ions are excreted, chloride ions will follow them and be excreted as well.

Calcium Homeostasis

Calcium homeostasis is regulated by Parathyroid hormone(PTH) and calcitriol. Low blood calcium levels (**hypocalcemia**) will trigger the release of PTH. PTH will cause bone tissue breakdown, releasing calcium to the blood, as well as increasing calcium reabsorption in the kidneys. High blood calcium levels (**hypercalcemia**) will inhibit the release of PTH, increasing renal excretion of calcium.

Phosphate Homeostasis

Phosphate levels are primarily regulated through the balance of diet and loss through urine. When PTH is released, it will increase the amount of phosphate excreted through urine.

pH Balance

pH balance is vital for the function of the body. When pH levels go beyond normal levels, enzymes needed for chemical reactions in the body cease functioning. Normal pH levels in the blood are between 7.35-7.45. pH higher than 7.45 is referred to as alkalosis, while a pH below 7.35 is acidosis. Death will occur if blood pH drops below 6.8, or exceeds 8.0

Buffers

A buffer is a mixture of an acid and a base that do not neutralize each other. This means that if any acids are added, some of the bases from the buffer will be able to neutralize them. Similarly if any bases are added, the acids from the buffer will be able to neutralize those. Neutralizing acids and bases will prevent them from changing the pH.

Bicarbonate Buffer System

$$H_2CO_3 \leftrightarrows \underset{\text{acid}}{H^+} + \underset{\text{base}}{HCO_3^-}$$

This buffer system uses the carbonic acid and bicarbonate created by combining water and carbon dioxide in the blood as sources of acid and bases that can be used to neutralize changes in pH. This is the most common buffer system found in the extracellular fluid.

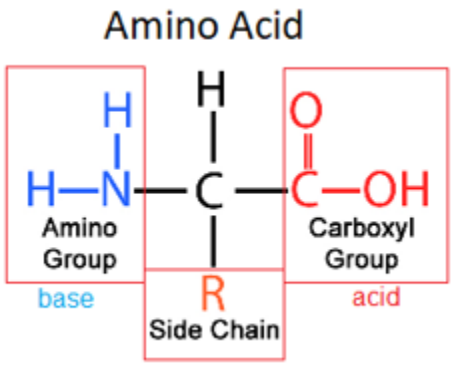
Phosphate Buffer System

$$H_2PO_4^- \leftrightarrows \underset{\text{acid}}{H^+} + \underset{\text{base}}{HPO_4^{2-}}$$

This buffer system uses phosphoric acid which is created by reacting phosphate with water. As phosphate is most commonly found in the intracellular fluid, this buffer system is the most common buffer system found in the intracellular fluid.

Protein Buffer System

This buffer system uses the structure of amino acids as a source of acids and bases used to neutralize other substances



The amino group of an amino acid acts as a base, binding to acids to neutralize them.

The carboxyl group of an amino acid acts as an acid, binding to bases to neutralize them.

This buffer system is found throughout the body, as proteins are widely present in both the intracellular and extracellular fluids.

Renal Control of pH

The kidneys are able to affect the long term balance of acid and base levels in the body through production and excretion of acids and bases in the urine. Renal control is also known as **metabolic control** of pH. Renal control of pH works alongside respiratory control, but where respiratory control is best suited to short term, low duration changes in pH, renal control is best suited to long term, long duration changes.

When the blood pH changes, the kidneys will combine carbon dioxide and water to produce basic bicarbonate and acidic hydrogen ions.

- If the blood pH is low, the kidney will release the basic bicarbonate ion into the blood to increase the pH, while excreting the acidic hydrogen ion into the urine in order to reduce the amount of acid in the body.
- If the blood pH is high, the kidney will release the acidic hydrogen ion into the blood to lower the pH, while excreting the basic bicarbonate in the urine.

Reproductive System

The reproductive system is responsible for the production of sex cells (**gametes**) in both males and females, as well a providing an environment for fetal development, birth, and nourishing of children in females.

Gametes

Gametes are the sex cells produced by the male and female reproductive system. These cells have half the number of chromosomes as a normal cell (**haploid cells**). When a male and female gamete combine, it creates an embryo with a normal number of chromosomes (**diploid cell**),which may develop into a fetus.Gametes are produced by Meiosis

Meiosis

Meiosis and Mitosis are closely related. Meiosis follows the same steps as mitosis, prophase, metaphase, anaphase, and telophase. Unlike mitosis, the cell undergoing meiosis undergoes two consecutive divisions. The steps of the first division are labeled with (I), and the second with (II) ex. Metaphase II.
Due to having two sets of cell division, after meiosis each parent cell will produce a total of four daughter cells. As there is no interphase or DNA synthesis in between the divisions, each of the daughter cells will only receive one set of chromosomes compared to normal cells which have two sets of chromosomes, causing them to be called haploid daughter cells.
During Prophase I, a process called crossing over occurs. Chromosomes will overlap their edges and exchange pieces with neighboring chromosomes, changing the locations where genes are placed

Male Reproductive system

The male reproductive system is focused on the development and delivery of sperm to the female reproductive system.

Male Reproductive Anatomy

Penis

Sexual organ used for depositing semen in the vagina. Consists of an internal root, and external shaft and glans. Contains three sets of erectile tissue:on the dorsal side of the penis are two corpus cavernosum, while on the ventral side of the penis is the corpus spongiosum

Accessory glands

Produce the fluids that when mixed with the sperm to form semen

- **Seminal Vesicles** produce about 60% of the fluids
- **Prostate Gland** produces about 30% of the fluids
- **Bulbourethral Glands** secrete fluid into the urethra prior to intercourse, neutralizing acids and lubricating the head of the penis

Spermatic Ducts

Carry sperm from the testes to the urethra
Efferent Ductules → Duct of the epididymis → Ductus Deferens → Ejaculatory Duct

Testes

Produce male sex hormones and Sperm. Each of the testes contains 250-300 Lobules with each lobule containing one to three seminiferous tubules

Scrotum

Pouch of skin, muscle, and connective tissue that contains the Testes. Helps maintain a temperature of 35°C in the Testes, which is necessary for sperm production

Spermatogenesis

In the seminiferous tubules, testosterone and androgen binding protein activate **Type A spermatogonium**, which will perform mitosis and form a **Type B spermatogonium**. The type B spermatogonium will enlarge and develop into a **primary spermatocyte**. The primary spermatocyte will undergo meiosis I, forming two **secondary spermatocytes**. Each of the spermatocytes will undergo meiosis II, creating a total of four **spermatids**. These spermatids will migrate to the lumen of the seminiferous tubule and then undergo **spermiogenesis**, transforming into a mature **sperm** cell

Hormonal Regulation of Sperm Production

1. **GnRH** is released from the hypothalamus
2. In the anterior pituitary, GnRH causes **FSH** and **LH** to be released
3. In the testes, FSH acts on **sustentacular cells**, causing them to release **androgen binding protein (ABP)**. LH acts on **interstitial cells**, causing them to release **testosterone**
4. ABP+testosterone will trigger spermatogenesis in the seminiferous tubules.
5. Testosterone forms a negative feedback loop with GnRH, inhibiting the release of GnRH and reducing the effect it has on the pituitary.
6. Sustentacular cells also produce Inhibin, which reduce FSH secretion from the anterior pituitary

Female Reproductive system

The female reproductive system is complementary to the male reproductive system, including accommodations for receiving the male gametes, as well as producing its own gametes. In addition to this, the female reproductive system is designed to house a developing fetus, birth it, and provide sustenance for it after birth

Female Reproductive Anatomy

External genitalia

Clitoris
Contains erectile tissue similar to the corpus cavernosum in the penis. The clitoris is primarily a sensory organ associated with sexual excitement and stimulation.

Labia Majora
Pair of thick folds of skin and adipose tissue located laterally to the entrance of the vagina, The outer surface of the labia majora is covered by pubic hair, and acts to protect the access to the urinary and reproductive tracts.

Labia Minora
Thin folds of skin medial to the Labia Majora and adjacent to the entrance of the vagina.

Internal genitalia

Vagina
Tubular organ that connects the uterus to the external genitalia. Allows intercourse, the passage of semen, the discharge of menstruation, and the delivery of children.
Uterus
Thick, muscular organ where the fetus can develop and later be propelled out of. The Uterus has three layers: the **perimetrium** is the outer fibrous layer, the **myometrium** is a thick layer of smooth muscle, and the **endometrium** is a thinner mucous membrane that a fertilized embryo will implant into.
The structure of the uterus forms three regions. The **fundus**, which forms the superior, curved portion of the uterus. The **body** is the largest portion of the uterus. The **cervix** is the inferior portion of the uterus that connects to the vagina

Uterine tubes (Fallopian tubes)
The uterine tubes collect Ova that have been released from the ovaries, and transport them to the uterus. These tubes are separated into three segments. The **infundibulum** makes up the flared end that is closest to the ovary. It is responsible for receiving the ova after ovulation occurs. The **ampulla** is the middle portion of the uterine tube, and is responsible for using smooth muscle and ciliated cells to propel the ova toward the uterus. The **isthmus** is the narrowed end of the uterine tube that forms the connection to the uterus

Ovaries
These are the primary sexual organ of the female reproductive system. The ovaries produce sexual hormones and releases matured ova. The ovary is separated into two layers, with the Cortex containing the germ cells (reproductive cells) and the medulla containing the major arteries and veins of the ovary. The ovary is surrounded by a capsule called the Tunica Albuginea

Oogenesis

The production of ova, or **oogenesis** begins in utero in female fetuses. **Oogonia** will develop in the ovaries starting 5-6 weeks after fertilization. These cells will multiply until the 5th month of pregnancy, before going dormant until slightly before birth. By the age of 6 months, the oogonia will change into **primary oocytes**, and begin meiosis I, but pause before completing it. Over time, primary oocytes will break down in a process called **atresia**, which lasts until puberty, leaving a female with around 400,000 ova. After puberty, follicle stimulating hormone (FSH) will trigger the development of sets of ova and their surrounding supporting (**folicular**) cells. When stimulated by FSH, these ova will complete meiosis I, producing a **secondary oocyte** and the **first polar body**, which is a non-viable cell. The secondary oocyte will begin meiosis II, but pause at metaphase II. If the ova is fertilized, meiosis II will complete, forming the **second polar body** and the **zygote**.

Folliculogenesis

The development of the follicle cells surrounding the ova are necessary in order to enable the ova to be released from the ovary through ovulation.
When primary oocytes form, they are surrounded by a single layer of squamous cells that form the **primordial follicle**. As the follicle develops into a **primary follicle**, the cells surrounding the ova expand, becoming cuboidal cells. **Secondary follicles** have multiple layers of cells surrounding the ova, and will create a layer of glycoprotein around the ova that is called the **zona pellucida**. In a tertiary follicle, the follicular cells begin secreting a fluid into the space around the ova, forming a fluid filled cavity called the **antrum**. The ova is suspended within the antrum, connected to the wall of the follicle by a layer of cells called the **cumulus oophorus**. The final stage of follicular development is the **graafian follicle**, in which the cumulus oophorus first thins, and then completely breaks down, leaving the ova floating in the antrum.

Hormonal Regulation of Ovarian and Menstrual Cycles

1. GnRH is released by the hypothalamus
2. In the anterior pituitary, GnrH causes the release of FSH and LH
3. In the ovaries, FSH causes development of follicular cells
4. As follicular cells develop, they secrete estrogen
5. Estrogen stimulate Hypothalamus and Pituitary, increasing levels of FSH and LH release
6. High levels of LH cause the release of the ovum from **graffian(tertiary) follicle** (ovulation)
7. After ovulation, the graafian follicle becomes the corpus luteum

8. The corpus luteum will secrete progesterone, causes development of **stratum functionalis** of uterus
    - Corpus luteum will live for ~10 days, at which time it undergoes involution and becomes the corpus albicans (no longer secretes hormones)
9. Without progesterone, stratum functionalis breaks down, then separates and causes menstruation

Human Development

This chapter describes the changes that occur between conception and delivery of a child. At this point in the life cycle, there is a transition from being a single cell, differentiation of tissues, and development of the human form.

Major Stages

First Trimester

The first trimester of development spans from fertilization until week 12. This stage is the most dangerous for the developing fetus, as it either does not yet have, or is first developing the structures that will support it. The fetus is especially vulnerable to stress, nutritional deficiency, and drugs at this point in the life cycle.

Second Trimester

The second semester runs from week 13 until week 24. During this stage of development, the fetus will nearly complete the development of most of its organs. The fetus will also take on the final human form during this period. By the end of this trimester, the fetus will be barely capable of surviving premature birth if it receives critical care.

Third Trimester

The third trimester runs from week 25 until birth. During this stage, the fetus grows rapidly and its organs will be completely developed, allowing the fetus to survive without outside assistance after birth. The brain, liver, and kidneys will require additional development after birth to achieve full function.

Preembryonic Stage

The preembryonic stage describes the steps from just after fertilization until the development of the embryo. It lasts for approximately 10 days. During this stage, the developing cells are sometimes referred to as the **conceptus**.

Cleavage

Cleavage is a series of rapid divisions that the original **zygote** starts after fertilization. The first division will usually occur 30 hours after fertilization, before continuing through a 4-cell, 8-cell,and finally the 16-cell **morula** stage by day three. At this point the cluster of cells has not

had time to grow, so the 16 vells of the morula are the same size as the original zygote. At this time, the morula will have exited the uterine tubes and entered into the uterus.
Over the next four to five days, the cells will continue to divide, forming a hollow sphere of cells called a **blastocyst**

Implantation

The blastocyst will attach itself to the endometrium of the uterus, usually in the fundus (the superior portion of the uterus). The process of attachment is called **implantation**. Inside of the blastocyst, cells will accumulate on one side of the hollow inner portion, forming the **embryoblast**. The cells on the surface of the blastocyst will separate into two layers, with the superficial layer's cells fusing with the cells of the endometrium, forming the **syncytiotrophoblast**, while the inner layers of the blastocyst will form the **cytotrophoblast**. The syncytiotrophoblast will grow deeper into the endometrium, which will respond to the damage by growing over and covering the conceptus.
The trophoblast cells will begin to secrete **Human Chorionic Gonadotropin (HCG)**, which will stimulate the corpus luteum to secrete estrogen and progesterone, suppressing menstruation. As the conceptus develops further, HCG levels will increase over time. Most pregnancy test kits react to the presence of HCG to indicate pregnancy.

Embryogenesis

During Implantation, the cells within the conceptus begin to differentiate, forming new tissues. During this process, the embryoblast will separate from the wall of the blastocyst, creating an empty space called the **amniotic cavity**. The embryoblast will flatten out, forming the **embryonic disc**. On one side of the embryonic disc will be the amniotic cavity, and the cells on the other side will develop into a space called the **yolk sac**. The side of the embryonic disc facing the amniotic cavity is called the **epiblast**, while the side facing the yolk sac is called the **hypoblast**.
By day 15, the embryonic disc continues to grow, with a layer of thickened cells called the **primitive streak** forming along the epiblast, with a small groove running down the middle called the **primitive groove**. In a process called **gastrulation**, the multiplying cells in the epiblast move downward through the primitive groove, and replace the cells in the hypoblast. These new cells form a layer called the **endoderm**. As epiblast cells continue to move downward they will form a new layer in between the endoderm and the epiblast, called the **mesoderm**. From this point, the remaining epiblast is referred to as the **ectoderm**. These three layers, the ectoderm, mesoderm, and endoderm are known as the **primary germ layers**, as all of the tissues and organs of the fetus will develop from them.

Derivatives of the Primary Germ Layers

The Ectoderm gives rise to the epidermis, sweat glands, hair follicles, and sensory receptors; epithelial lining of mouth and anus; cornea and lens of the eye, the nervous system, adrenal medulla, tooth enamel, and the epithelium of pineal and pituitary glands.

The Mesoderm gives rise to the skeletal system; muscular system; muscularis of the digestive system; circulatory and lymphatic systems; reproductive system; dermis of skin; fibrous linings of body cavities; and the adrenal cortex.
The Endoderm gives rise to the epithelial lining of the digestive, respiratory, urinary, and reproductive systems; and produces the liver, pancreas, thymus, thyroid, and parathyroid glands.

Embryonic Stage

The embryonic stage starts once the primary germ layers are developed, and will last for about six weeks. During this period, the placenta will form around the embryo and the germ layers will differentiate into organs and organ systems.
At the fourth week of development, the embryonic disc will begin to fold inward around the yolk sac.The folding occurs both laterally and longitudinally, with the lateral folds creating a tube that runs down the length of the embryo, called the **primitive gut**. As the folding continues, the ectoderm, which was on the side opposite of the yolk sac, now covers the entire surface of the embryo, with the endoderm lining the inner cavity of the embryo (the **coelom**). At this point, the embryo will resemble a cylinder that has been bent into a “C” shape.
By the fifth week, the inner cavities will divide, forming the thoracic and peritoneal cavities. By the end of the fifth week, the thoracic cavity will divide further, forming the pleural and pericardial cavities.
During this period, the **neural tube** will continue to develop into what will become the central nervous system. The neural tube originated with the folding over of the **neural groove**, where a section of the ectoderm is drawn down into the mesoderm and folded over, forming a tube.
In the mesoderm, **somites** form. These are a type of tissue that will further develop and become the bones of the vertebrae, the muscles of the abdominal trunk, and the dermis of the skin.

As the embryo develops, a set of membranes will develop surrounding the embryo. The **amnion** is a growth from the epiblast, and forms a transparent sac filled with **amniotic fluid** that the fetus will float in.This fluid will protect the fetus, prevent adhesion between body parts during development, and aid in development of the lungs and muscles.
The **yolk sac** develops from the hypoblast cells. It is suspended from the ventral side of the embryo, outside the amnion. The yolk sac is involved in the development of the digestive system, blood, and the development of the cells that will produce gametes.
The **alantosis** begins as a part of the yolk sac, but develops to become the start of the umbilical cord, and contributes to the development of the urinary bladder.
The **chorion** is the outermost membrane that wraps around all of the other membranes and forms the border with the uterus. The chorion is lined with villi which extend into the endometrium, to gain better access to maternal blood vessels, and exchange gasses and nutrients.

Fetal Development

Fetal development starts from the ninth week, and continues until birth. During this stage, the organs and tissues that were initially created in the embryonic period will continue to develop

and improve in function. Most of the organs are able to function in the way that they will after birth, with the exception of the circulatory system.

The fetal circulatory system undergoes adaptations, as its source of oxygenated blood becomes the umbilical arteries, rather than the lungs. The umbilical arteries provide oxygen to the blood carried in the inferior vena cava, which then carries it to the right atrium. In the fetal heart, there is an opening in the interventricular septum, called the foramen ovale, which allows some of the oxygenated blood to move from the right ventricle into the left ventricle before being sent out to the body. Additionally, there is a connection between the pulmonary trunk and the aorta, which allows oxygenated blood to bypass the lungs and be directed out to the body.

These adaptations quickly revert during and shortly after birth, allowing the fetus to transition to obtaining oxygenated blood from the lungs.

Major Events of Prenatal Development

Week	Length, Weight	Developmental Events
4	0.6cm, <1g	Vertebral column and central nervous system begin to form; limbs represented by small limb buds: heart begins beating around day 22, no visible eyes, nose, or ear
8	3cm, 1g	Eyes form, eyelids fused shut; nose flat, nostrils evident but plugged with mucus; head nearly as large as the rest of the body; brain waves detectable; bone calcification begins; limb buds form paddlelike hands and feet with ridges called digital rays, which then separate into distinct fingers and toes; blood cells and major blood vessels form; genitals present but sexes not yet distinguishable
12	9cm, 45g	Eyes well developed, facing laterally; eyelids still fused; nose develops bridge; external ears present: limbs well formed, digits exhibit nails; fetus swallows amniotic fluid and produces urine: fetus moves, but too weakly for mother to feel it; liver is prominent and produces bile; palate is fusing; sexes can be distinguished
16	14cm, 200g	Eyes face anteriorly, external ears stand out from head, face looks more distinctly human; body larger in proportion to head; skin is bright pink, scalp has hair; joints forming; lips exhibit sucking movements; kidneys well formed; digestive glands forming and meconium (fetal feces) accumulating in intestine; heartbeat can be heard with a stethoscope
20	19cm, 460cm	Body covered with fine hair called lanugo and cheese like sebaceous secretion called vernix caseosa, which protects it from amniotic fluid; skin bright pink; brown fat forms and will be used for postpartum heat production; fetus is now bent forward into “fetal position” because of crowding; quickening occurs-mother can feel fetal movements
24	23cm, 820g	Eyes partially open; skin wrinkled, pink, and translucent; lungs begin producing surfactant; rapid weight gain
28	27cm, 1.3kg	Eyes fully open; skin wrinkled and red; full head of hair present; eyelashes formed; fetus turns into upside down vertex position; testes begin to descend into scrotum; marginally viable if born at 28 weeks
32	30cm, 2.1kg	Subcutaneous fat deposition gives fetus a more plump, babyish appearance, with lighter, less wrinkled skin; testes descending; twins usually born at this stage
36	34cm, 2.9kg	More subcutaneous fat deposited, body plump; lanugo is shed; nails extend to fingertips; limbs flexed; firm hand grip
38	36cm, 3.4kg	Prominent chest, protruding breasts; testes in inguinal canal or scrotum; fingernails extend beyond fingertips