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Blood

I. Functions

a. Transportation

- i. Gasses : oxygen, Carbon dioxide
- ii. Nutrients
- iii. Waste products
- iv. Hormones

b. Regulation

- i. Temperature (body)
- ii. Ph
- iii. Electrolyte balance
- iv. Maintain Fluid Balance

c. Protection

- i. Clot – helps from losing blood
- ii. Preventing infection (mostly white blood cells)

II. Composition (blood temp is 100.4 F)

- i. Ph 7.35 – 7.45
- ii. Comprises 7 – 8% of body weight
- iii. Average person has 5 – 5.5 liters
- iv. Slightly more in males due to increased blood production from testosterone
- v. Physical description
 1. Opaque
 2. Salty
 3. Metallic taste
 4. Scarlet to Dark red color depending on oxygen and CO2 concentration
 5. Viscus (5X more viscus than water)
- vi. Connective tissue with high percent of non-living matrix (55% plasma)
- vii. Formed elements (living part) 45%
 1. Hematocrit : test for formed elements vs Plasma

A. Plasma: Composition: 92% water, 7% Plasma proteins, 1% other solutes. NON

LIVING

a. Plasma Proteins (7%)

- i. **Albumins 60%** (made by liver)
 1. Helps regulate osmotic pressure, Transports lipids, steroids, hormones.
 2. Osmotic pressure pulls the fluid leaking from the small capillaries back into the vessels due to the amount of solute (albumins) in the vessels.
- ii. **Globulins 35%**
 1. Alpha & Beta are made in the liver
 2. Gamma is made by plasma cells

3. Transport globulins bind to small ions, hormones and compounds so they are not filtered out by the liver.
4. These include immunoglobulin's (antibodies)
- iii. **Enzymes**, proenzymes, hormones <1%
- iv. **Fibrinogens 4%**
 1. Clotting proteins – most produced by the liver
 2. Essential component of clotting, can be converted to insoluble fibrin.

** Sufex "ogen" represents the nonsense section of the protein. Enzyme cleaves off "ogen" and attached fibrin (sticky fibers like a meshwork).

Serum – liquid left after whole blood clots. This differs from Plasma. Serum has no clotting proteins

B. Formed Elements

- a. Red Blood Cells – erythrocytes
- b. White Blood Cells – Leukocytes
- c. Platelets – Thromocytes
- d. ALL formed elements come from Hemocytoblasts (Stem Cells)
 - i. Then most become Myeloid stem cells which eventually become erythrocytes, platelets, and white blood cells **except for Lymphocytes.**
 - ii. Some become Lymphoid stem cells which become lymphocytes
 - iii. Formation of all blood formed elements is called Hemopoiesis
 1. **Thrombopoiesis** – platelet formation
 2. **Erythropoiesis** – RBC formation
 3. **Leukopoiesis** – WBC formation

RED BLOOD CELLS – far outnumber all other blood cells and comprise 1/3rd of all cells in the body

- i. 5 million RBCs fit in 1 cubic mm
- ii. Lifespan is about 120 days
- iii. Structure: Bi-concave disc 7.5 microns wide by 2 microns high
 1. Benefit – shape provides more surface area which facilitates faster diffusion
 2. Benefit – shape allows cell to fold and travel through capillaries narrower than the cell itself.
 3. Benefit – shape allows them to stack like dimes in the small vessels. (**Rouleau**). Keeps them from banging into each other and the vessel walls. Keeps them from jamming up in vessels.
- iv. Cell contents
 1. Cytoplasm
 2. NO nucleus – *cannot divide*
 3. NO ribosome – *no protein synthesis*
 4. NO mitochondria – *no aerobic* ATP production (only anaerobic ATP production, 2 ATP for every sugar molecule)
 5. 95% hemoglobin (a protein)
 - a. Quadrinary structure (two or more tertiary structures bound together)
 - i. Four tertiary structures, Alpha 1 & 2, Beta 1 & 2
 - b. In the middle of each chain (tertiary group) is a heme.
 - i. Heme – nitrogen containing pigment, holds a molecule of Iron the 4 nitrogen molecules.

- c. Each hemoglobin has 4 hemes, therefore 4 Fe molecules.
- d. Each Fe molecule holds a molecule (O^2) of Oxygen
- e. When the first oxygen bonds to the first heme, the shape changes, pushing out the next heme making it easier for the next oxygen to attach.
- f. Each cell has about 250 million hemoglobin and therefore can hold about 1 billion molecules of oxygen.
- g. Oxyhemoglobin – when Hgb carries oxygen
- h. Deoxyhemoglobin – when Hgb has no oxygen
- i. CO₂ is carried on the Globin part (protein part)
 - i. Called Carbamino Hgb (about 20%)
- v. Hemoglobin Recycling (End of RBC's life)
 - 1. 10% hemolyze and get filtered out by the kidney, then excreted in the urine (partly why urine is yellow).
 - 2. 90% gets phagocytized by macrophage
 - a. Globins part broken down to amino acids – these go into the blood stream and picked up by bone marrow or other organs that need it.
 - b. Heme – Iron ion pulled out, put into blood stream, bound to **transferrin** (protein). This is stored in bone marrow and liver. Stored as **Ferritin** and **hemosiderin** in the liver.
 - c. Nitrogen: Macrophage turns the nitrogen into **Biliverdin**, a greenish compound, then into **unconjugated bilirubin**. Some travels to the liver where it is turned into **conjugated bilirubin**, a yellowish brown substance. This bilirubin is then excreted into large intestine where bacteria break it down and it is eliminated in feces. Some travels to the kidney where it is eliminated in the urine. Nitrogen is toxic to the body.

Jaundice: Yellow coloring in the whites of eyes from excess unconjugated bilirubin, indicates poor or non functioning liver.

Erythropoiesis: Production of RBCs : made in the RED bone marrow. In adults this is located in the proximal epiphysis of long bones, especially femur, humerus and in the flat bones, especially the hip.

Liver and spleen also make RBCs

Needs: Amino Acids, Iron, Vit B12, Vit B6

1. **Myeloid Stem Cells**: become red blood cells and white blood cells **except for Lymphocytes**
 - a. RBC production regulated by hormone EPO – made in kidney. [When kidney detects less oxygen or decrease in BP it makes EPO] The hormone's target is in bone marrow.
 - i. EPO causes increase rate of mytosis (faster division) and increase rate of maturation.
 - ii. Normally it takes 5-7 days for a RBC to get into the bloodstream and mature. EPO makes it go faster.
2. Diseases related to RBCs
 - a. **Anemia**: a decreased oxygen carrying capacity of the blood. Two ways this occurs: ¹decrease in number of RBCs and ² Something wrong with the hemoglobin. PLUS there are some genetic issues.
 - i. Decreased RBC problems:
 1. **Hemorrhagic Anemia** – blood loss
 2. **Hemolytic Anemia** – RBCs are breaking apart (lycing).
 - a. Transfusion reaction

- b. Certain types of bacteria
 - c. Parasites that use RBC as a host
- 3. **Aplastic Anemia** – destruction of bone marrow. Can be due to cancer, radiation, bacteria or toxin.
- ii. Hemoglobin Cause
 - 1. **Iron deficiency Anemia**
 - 2. **Pernicious Anemia** – Cells will not divide if there is not enough B12. Stomach makes intrinsic factor needed to absorb B12. A severe stomach problem may make B12 absorption poor.
- iii. Genetic Issues
 - 1. **Thalassemia** – a pre-disposed condition of Mediterranean people that causes a reduced rate of synthesis of one of the globin chains and therefore causes abnormal hemoglobin. The effect is an underproduction of normal hemoglobin. This disease could be classified as a decreased RBC Anemia
 - a. The name comes from the Greek word *Thalassa* meaning sea and the Greek word *Haema*, which means blood.
 - 2. **Cycle Cell Anemia** – predominant in the black population.
 - a. 1 amino acid is switched in the sequence.
 - b. Triggered when Oxygen is low (Hypoxia), this can occur in times of stress, physical or even emotional.
 - c. Hemoglobin changes shape for the worse and therefore changes the shape of the RBC.
- b. **Polycythemia** – too many red blood cells
 - i. Causes
 - 1. Can be caused by something wrong with the bone marrow
 - 2. Blood Doping
 - a. Physical by injecting RBCs
 - b. Chemically by injecting synthesized EPO (Blood Doping)
 - ii. Complications
 - 1. Increased blood pressure
 - 2. Blood thickens – raises the possibility of a thrombus
 - 3. Hematocrit rises beyond normal

White Blood Cells

5 types of WBCs:

Basophil Eosinophil

Neutrophil

Monocyte

Lymphocyte



White Blood Cells average 7-10 thousand per cubic mm.

About 7,500 per mm³

All have a nucleus and can divide.

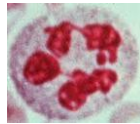
Many WBCs spend most of their time out in the tissue (macrophage, which is a monocyte after it gets out of the bloodstream).

1. Common to all WBCs
 - a. **Diapedesis** – can crawl out of the vascular system into the tissue
 - i. Amoeboid motion
 - b. **Positive Chemotaxis** – ability to respond or attracted to certain chemicals (like when a vessel breaks).
2. Only 3 can do phagocytosis
 - a. Neutrophils
 - b. Monocytes
 - c. Eosinophils
3. Lifespan: from a few hours (neutrophils) to decades depending on their job (lymphocytes live for decades giving us immunity to certain diseases)

WHITE BLOOD CELL TYPES: Nice Little Monkey Eats Bananas

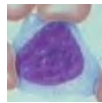
Neutrophils

- a. Most prevalent (50-70%)
- b. Phagocytic for bacteria
- c. Survive minutes to days



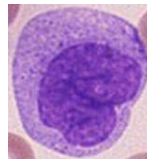
Lymphocytes

- a. 20-30%
- b. Give you specific immunity
- c. Survive for months to decades



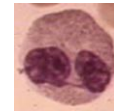
Monocytes

- a. 2-8%
- b. Phagocytic – crawl out into tissue
- c. Can absorb large debris



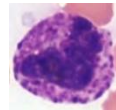
Eosinophils

- a. 2-4%
- b. Phagocytic – mostly allergic and parasitic, like things with antibodies



Basophils

- a. <1%
- b. Granules contain histamine and heparin
 - a. Turns on swelling and prevents clotting



Leukopoeisis – production of White Blood Cells

1. Regulated by hormones of the immune system called **cytokines**. Known as Colony Stimulating Factor or **CSF**.

White Blood Cell Disorder:

Leukemia – Cancer of bone marrow

- a. White blood cell production goes WAY up and the WBCs becomes less effective.
- b. 7500 / mm³ normal 11,000+ abnormal

[Differential Count] – This is a breakdown by type and may help point a diagnosis in a certain direction.

Blood Type United States:

O is the most popular, AB the least. Most Americans are Rh+ (85%)

Platelet formation:

Megakaryocyte : an offshoot of a myeloid stem cell. Very large cell (160 microns in diameter).

Cytoplasmic fragments break off and live about 10 days. They are phagositized in the spleen. Normal amount of platelets is about 350,000 mm³.

Platelet functions

1. Transport chemicals important in the clotting process
2. Can become “sticky” and form platelet plugs and patch small holes in vessels
3. Slightly contractile (have actin and myosin)
 - a. Allows them to pull the edges of a wound closer together promoting healing

Too few platelets: **Thrombocytopenia** (below 80,000 mm³)

Too many: starts to make blood harder to push around (**thrombocytosis**)

Hemostasis : Prevention of blood loss through breaks in blood vessels

Phases of Hemostasis

** = main event of that phase

1. Vascular Phase
 - a. **Vascular Spasm (immediate response)
 - i. Lasts about 30 minutes
 - ii. Most important in tiny vessels
2. Platelet Phase
 - a. Exposed collagen fibers and chemicals associated cause the platelets to get sticky to each other and the vessel.
 - b. ** Forms a Platelet Plug – 15 seconds
3. Coagulation Phase
 - a. Starts 30 seconds to 2 minutes
 - b. GOAL – produce a protein called fibrin (remember – fibrinogen is one of the five plasma proteins)
 - c. ** Creates a clot (fibrin, platelets, and RBCs)
 - i. Cascade mechanism (if one step does not occur, the process stops)
 - ii. Clotting needs:
 1. Clotting factors (most made in liver, NEED VIT. K)
 2. Calcium
 3. Chemical signals from damaged tissue
 4. Chemical signals from platelet
 - d. 2 Pathways Extrinsic and Intrinsic
 - i. Extrinsic Pathway – Faster – less clotting factors
 1. Turned on by tissue damage
 - a. Tissue releases “tissue factors”
 - b. Clotting factor VII
 2. End Product -- TTP (Tissue Thrombin Plastin)

- ii. Intrinsic Pathway – Slower but better clot
 - 1. Turned on by platelets getting exposed to collagen fibers, they release platelet factor
 - 2. Needs Calcium, Factor VIII, Factor IX
 - 3. End Product -- PTP (Platelet Thrombo Plastin)
 - iii. Then – Either PTP or TTP react with Factor X to form Prothrombinase
 - 1. Prothrombinase catalyzes Prothrombin to form Thrombin
 - 2. Thrombin acts as an enzyme to Catalize Fibrinogen into Fibrin
 - 3. FIBRIN = CLOT
 - iv. Intrinsic can occur inside a vessel (BAD)
 - 1. Where there is plak damage intrinsic clotting can be triggered and create a clot on the plak.
 - 2. This clot could break loose and become an embolus.
 - 3. Embolus can clog an artery and cause infarction to tissue beyond it.
 - v. Factor VIII – Hemophelia Factor
 - 1. Hemophelia – genetic disease where there is a lack of clotting factor VIII
 - a. Only the Extrinsic clotting pathway works.
 - b. These people need blood clotting factors when they have bleeding problems
4. Clot retraction Phase
 - a. After a clot is in place for ½ to 1 hour
 - b. Actin and myosin in platelets in the clot begin to contract and begins to pull the wound together.
 5. Fibrinolysis Phase(breakdown phase)
 - a. Breaks down fiber
 - b. In the Plasma is a protein called Plasminogen
 - c. Plasminogen is catalyzed by Thrombin and TPA (Tissue plasminogen Activator) into **Plasmin**
 - d. Plasmin breaks down Fibrin
 - e. TPA is a CLOT BUSTER

D.I.C. Disseminated intravascular coagulation: Fatal side effect of platelet, factors and blood infusion, once it starts it is FATAL

Bleeding Disorders

1. Hemophelia – Genetic lack of Factor VIII
2. Liver Problems – lack of clotting factors
3. Thrombocytopenia : too few platelets – too little intrinsic pathway

Manipulators:

1. AntiCoagulants
 - a. Heperin (Intrinsic(produced by Basophils))
 - b. Coumadin – blocks vitamin K (ties up clotting factors that need Vitamin K)
 - c. Aspirin – inhibits platelet enzymes (inhibits platelet plug formation)
2. Clot Busters
 - a. TPA – plasmin breaks down fibers

- b. Urokinase – synthetic clot buster
- c. Streptokinase – synthetic clot buster

The Heart

Weight: less than 1 lb.

Contained within the pericardial cavity, inside the mediastinum

Posterior to the sternum

Between ribs 2 and 6

Rests on the diaphragm

Pericardium consists of the

Parietal pericardium (defines the pericardial cavity)

Two layers

Outer layer is dense fibrous connective tissue

Inner layer is simple squamous epithelium tissue

Visceral pericardium (surface of the heart, synonymous with the epicardium)

Single layer of simple squamous epithelium tissue

An infection of the pericardium – pericarditis (can see blood spots in the nail beds)

A trip through the heart:

Three entrances to the heart:

1. Superior vena cava, 2. Inferior vena cava, 3. Coronary sinus

Blood enters the right atrium

Exits down through the tricuspid valve into the right ventricle

Exits right ventricle medial and superior through the pulmonary semi lunar valve

Goes through the pulmonary trunk out to the lungs via the pulmonary artery (3R, 2L)

Back from the lungs through 4 veins into the left atrium

Through the Bicuspid Valve (mitral valve) into the left ventricle.

Exits medial and superior through the aortic semi lunar valve into the aorta

Coronary Sinus – drains the coronary system

Layers of the heart

1. Epicardium (visceral pericardium)
2. Myocardium (middle)
3. Endocardium (inside edge) - simple squamous epithelium that rolls out over everything and is continuous throughout the circulatory system. Any irritation of this can stimulate the intrinsic pathway of hemostasis. (clots)

Cardiac Muscle:

1. Single cells can have branches
2. Uni nucleated
3. Intercalated disc – kind of cell junction

- a. Desmosomes give strength (spot welds)
 - b. Gap Junctions allow rapid fusion of channel proteins
4. Each cell is covered with dense connective tissue made of elastin and collagen. This fibrous connective tissue is connected to the next cell and the next Forms the FIBRO SKELETON

Fibro Skeleton – anchored into:

1. Valves
2. Plate of fibrous connective tissue that runs across the valves and anchors the great vessels.
3. Helps the heart keep its shape
 - a. Distribution of force of every contraction over the entire heart
4. Helps to maintain the position of the heart in the thorax – the connection to the great vessels keeps it from jumping around as it beats.
5. Non conductive – electrically isolates the atriums from the ventricles.

CHAMBERS

Atria (plural) Atrium (singular)

1. Interatrial septum – wall that separates the left and right atrium.
2. Auricle – ear like flap (expansion chamber)
3. Left and right same size, shape and wall thickness.

Ventricle

1. Right ventricle wall is thin, Left is thick
2. When the left ventricle contracts it also contracts apex to base.
3. It pushes into the right ventricle space which helps the right ventricle push blood out
4. As the ventricle contracts, blood flowing superiorly will close the cuspid valves
5. The cordea tendinea keep the valve flaps from over extending
6. Semi lunar valves open from the pressure caused by contraction and close by the backflow of blood during systole

Valve Problems

1. Incompetent valve: valve that leaks
 - a. Murmur – non smooth flow in the heart.
2. Stenosis – narrowing of an opening.
 - a. Bacteria loves to grow on valves, causes incrustations
 - b. Heart murmur when blood is going from atrium to ventricle with an incompetent valve

Cardiac nervous system connections

Terms:

Inervation - connective to nervous system

Intrinsic – beats on its own

The heart is connected to the autonomic nervous system.

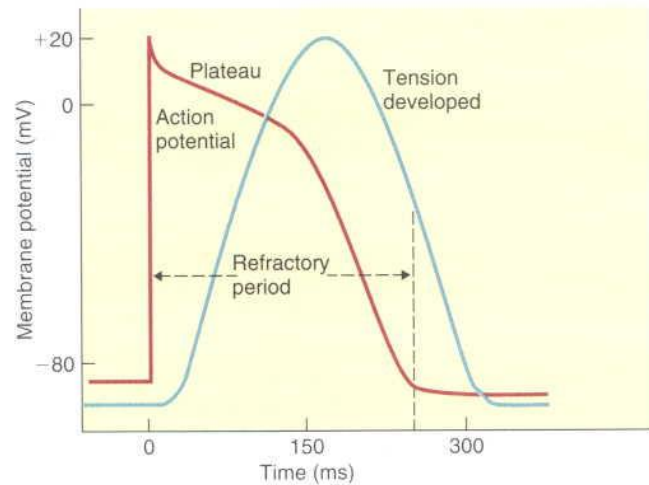
Both the sympathetic and parasympathetic systems

Sympathetic + Rate AND + Strength

Parasympathetic - Rate

Cardiac Muscle Physiology

Beginning and end of the cycle look much the same as a normal muscle cell BUT the use of Ca^{++} keeps the membrane potential high for an extended period until the Ca^{++} gates close. The resting potential of the cardiac cell is -90mV . The absolute refractory period is 250ms , and lasts almost as long as the contraction, therefore tetanus is impossible.



There are two specialized types of cardiac muscle cells:

1. Nodal Cells
 - a. These are auto rhythmic cells or pacemaker cells.
 - b. They spontaneously depolarize because they are always leaking some sodium
2. Conducting Fibers
 - a. These distribute the action potential stimulus over the rest of the myocardium (referred to as bunches or branches.)

NODAL

1. Sinoatrial Node (SA Node)
 - a. The pacemaker of the heart
 - b. Located in the right atrium, on the posterior and superior wall just inferior to the entrance of the superior vena cava
 - c. Action potential spreads over both atria, from cardiac cell to cardiac cell.
 - d. SA node generates a "Sinus Rhythm"
 - e. Average heart rate is 75bpm , normal range $60\text{-}90\text{bpm}$
2. Atrio Ventricular Node (AV Node)
 - a. Located on the floor of the right atrium, medially next to the opening of the coronary sinus.
 - b. Can spontaneously depolarize
 - c. Slower than the SA node
 - d. Action potential from the SA node causes the AV node to reach action potential
 - e. When the SA node fails, the AV node will generate a heart rate about $40\text{-}60\text{bpm}$
 - f. This is called a "junctional rhythm"
3. AV node is connected to conducting fibers called the Atrioventricular Bundle.
 - a. These conductive fibers connect the AV node to the Myocardium interventricular septum, there the fibers split into two branches called bundle branches
 - b. These bundle branches run down parallel along the septum toward the apex of the heart
 - c. Near the Apex, side branches called Purkinje fibers send the action potential to the rest of the myocardium.

- d. In this conduction system of the ventricles, the purkinje fibers start the action potential at the apex. The contraction begins there and moves superiorly which not only pumps the blood, but pumps it superiorly.

EKG is the electrical signature of the heart

P – atrial depolarization

QRS – Ventricle depolarization

T – ventricle re-polarization

DEFINITIONS

Arrhythmia – pattern of heartbeats becomes irregular

Ectopic Focus: place in heart that has spontaneously depolarized that is not a node

Causes: Alcohol, Drugs, Lack of Sleep, Caffeine

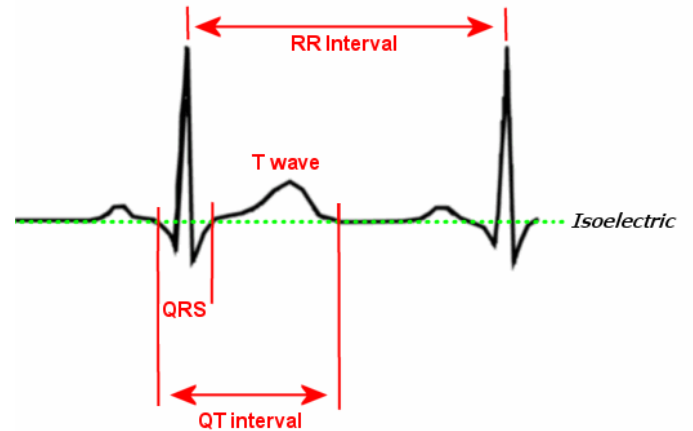
Flutter – 200-300 beats per minute

Fibrillation – 300+ and lack of sync. – Fatal arrhythmia

Tachycardic – fast heart rate

Bradycardic – slow heart rate

Heart blocks – blockage through the conductive fibers.



For illustration only.

Cardiac Cycle

Time between start of one heartbeat and the beginning of the next

Pressure gradient: reason why blood does not stop between heart beats.

1. Atrial Systole
 - a. Ventricles are already filled 70% before atria contract. Atrial systole fills the remaining 30%
2. Ventricle Systole
 - a. As pressure builds, AV valves close.
 - b. At this point all four valves are closed and the ventricle is contracting this is **Isovolumetric Contraction**. (No blood moving as the ventricle builds pressure)
 - c. Semi Lunar valves open and blood leaves the ventricle.
3. Ventricle Diastole
 - a. Ventricle begins to relax
 - b. Blood begins to fall back and closes the semi lunar valves.
 - c. Ventricles still losing pressure and all 4 valves are closed, this is **Isovolumetric Relaxation**.
 - d. After pressure lowers enough the AV valves open.
4. Atrial Diastole
 - a. Blood falls into the ventricles passively filling the 70% of the ventricle
5. Back to Atrial Systole

Heart Sounds: 1st Sound AV valves closing, 2nd Sound Semi Lunar valves

1. Energy for Heart Contraction

2. K⁺ : Both reduce force of contractions
 - a. Hyperkalemia: Causes weak contractions AND irregular heartbeats.
 - b. Hypokalemia: Hyperpolarizes cell and makes it harder to produce an action potential.
- b. Afterload: how much PRESSURE the ventricle needs to open the semi lunar valve.
 - i. As BP increases the amount of pressure needed increases (higher afterload). The ventricle spends more time opening the valve than pushing blood through it, therefore causing a lower EDV, higher ESV and lower SV.
3. VOLUME
 - a. Filling time (Rate)
 - b. Venous return (to atrium) an increase in EDV
4. Temperature
 - a. Increase in Temp causes increase in heart rate
 - b. Decrease in Temp causes decrease in heart rate

Venus return has an effect on the heart rate

1. Atrium Stretches (increased pre-load): stretches the SA node causing it to depolarize faster thereby increasing the heart rate.
2. In the wall of the Right atrium are stretch receptors. These receptors are connected to the Cardio Acceleratory center in the Cardio Regulatory Center of the Medulla Oblongata.
 - a. This center triggers the sympathetic part of the autonomic nervous system and tells the heart to increase its rate.
 - b. Starlings law: More in, More out
Starling's law or the Frank-Starling mechanism) states that the greater the volume of blood entering the heart during diastole ([end-diastolic volume](#)), the greater the volume of blood ejected during systolic contraction ([stroke volume](#)).
 - c. The Cardio Regulatory Center in the medulla Oblongata is divided into two equal sections, the cardio acceleratory center and the cardio inhibitory center.

Pulmonary Edema: When blood backs up from the left ventricle through the left atrium and into the lungs, plasma comes out of the blood vessels in the lung and around the cell. Patients will have an unproductive cough, be tired and will be short of breath.

Congestive Heart Failure: Blood backs up from the right side of the heart through the right atrium into the systemic circulatory system. Symptoms include distended jugular veins, and, when backed up into the liver, it will push fluid into the peritoneal cavity (abdomen)

Blood Vessels

Tunica Media: Muscle layer in the wall of a vessel

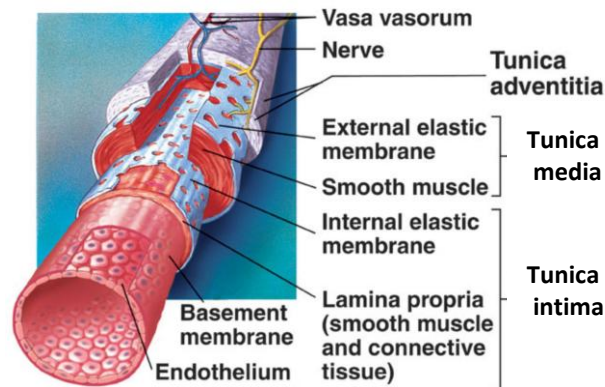
Pulmonary circuit: Right side of heart to Lungs to Left side of heart

Systemic circuit: Left side of heart to Body to Right side of heart

Coronary circuit: Left side of heart to coronary arteries to coronary veins to right side of heart.

General Structure of Blood Vessel Walls: Three Major Layers

1. Tunica Intima
 - a. Innermost layer (lumen) Endothelium connective tissue (simple squamous)
 - b. Basement membrane
 - c. A little bit of smooth muscle and connective tissue called lamina propria
 - d. Could have an internal elastic membrane
2. Tunica Media
 - a. Some smooth muscle (main area of smooth muscle)
 - b. External elastic membrane
3. Tunica Adventitia (Tunica Externa)
 - a. Dense irregular connective tissue (structural strength)

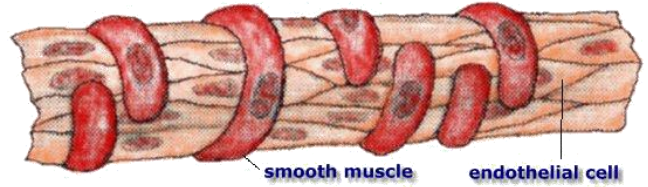


Nerves connect smooth muscles of the vessels to the autonomic nervous system. A system of small blood vessels called the **Vasa Vasorum** feeds the smooth muscles of larger blood vessels.

Arteries

1. Elastic Arteries (biggest arteries like the Aorta, Pulmonary Trunk)
 - a. Have all three layers
 - b. Within the Tunica Interna have all four
 - i. Has internal elastic layer
 - c. Tunica Media
 - i. Has LOTS of elastic
 - ii. Compared to other vessels, has more elastic than smooth muscle
 - d. Tunica Externa
 - i. VERY THICK
 - ii. Has more elastic than smooth muscle
2. Muscular Arteries (about .5mm in diameter)
 - a. Most named arteries are muscular arteries (brachial artery)
 - b. Tunica Interna: everything but the elastic membrane
 - c. Tunica Media: almost no elastic but lots of muscle
 - d. Tunica Externa: Fairly thick
 - e. These arteries control the amount of flow to an area by controlling their diameter
3. Arteriole (30 μm or less)

- a. These are the most numerous vessels in the body
- b. Tunica Interna
 - i. Only has the endothelium and the basement membrane
- c. Tunica Media
 - i. Few smooth muscle cells, not a complete layer
- d. Poorly defined Tunica Externa
- e. Major control vessel directing blood flow to an area (because there are so many of them)



Veins

1. Largest (up to 2.5 cm: Superior and Inferior Vena Cava)
 - a. **No elastic membranes**
 - b. Tunica Interna
 - i. Has endothelium, basement membrane and a tiny bit of smooth muscle: *lamina propria*
 - c. Tunica Media – slender
 - d. Tunica Externa
 - i. A bit thicker than expected compared to other layers.
2. Medium Size Veins (about .6 cm) – looks like large veins but smaller
 - a. Tunica Externa – thinner
 - b. Has everything that the Large veins have
3. Small veins : Venules (average about 20µm up to 50 µm)
 - a. NO Tunica Media
 - b. Basically just endothelium with connective tissue

Capillaries

Connection between the arterioles and the venules

- Exists as capillary beds (multiple capillaries)
- Run directly next to and around cells
- Deliver and pick up products (oxygen, CO₂, nutrients, waste)
- Very thin
- Mostly simple squamous endothelium and basement membrane.
- **ALL CAPILLARIES LEAK FLUID TO SOME EXTENT**

1. Continuous capillaries – most capillaries
 - a. **Least leaky**
 - b. Leak between the endothelial cell junctions
2. Fenestrated capillaries *fenestra – latin word for window*
 - a. Simple squamous endothelium
 - b. **Pores or fenestrations** – more leaky
 - c. Found in the kidney
3. Sinusoid capillary
 - a. Distance between cell junctions of squamous endothelium is large. Large enough for cells to crawl out of. **Most leaky**. WBCs can move through the endothelium cells here (diapedesis).
 - b. Found in spleen, liver and other places
 - c. The basement membrane holds it together.

4. Usually 1 capillary is called the preferred channel (a thoroughfare channel)
 - a. When needed, the capillary, **on the arterial end**, closes (pre-capillary sphincter, small piece of smooth muscle) that cuts down flow from that capillary bed **except for the preferred channel**. This is caused by the conditions in the interstitial fluid.

In larger arteries the endothelium looks like it is a little rippled. In arteries there is a lot of elastic and muscle tissue. Arteries have less stretch in the Tunica Media.

Veins have more stretch in the Tunica Media.

Cardiovascular Physiology

1. Systolic Pressure – Pressure in LARGER arteries measured at the time of systole (120 mm Hg)
2. Diastolic Pressure – Pressure in the LARGER vessels measured at the time of diastole (80 mmHg)

**** most of the pressure in the vascular system is throughout the arterioles and is less than 35mm Hg
This is because there are more arterioles than any other vessel.

** Than there is a large pressure loss in the capillary beds (down about 18mm Hg)

On the **venus** side, pressure starts at about **18mm Hg** and ends at about **2mm Hg** where it pours into the right atrium.

Pressures through the System:

- a. Right Atrium at systole generates about 15mm Hg
- b. Right Ventricle at systole generates about 30mm Hg
 - i. Blood goes through the pulmonary artery, through lung, through the pulmonary vein and dumps into the Left Atrium at about 2mm Hg
- c. Left Atrium at systole generates about 15mm Hg
- d. Left Ventricle at systole generates about 120mm Hg
- e. Majority of pressure loss is between the arterioles and the capillaries.
- f. Second major pressure loss is between the capillary beds and the R atrium.

FLOW RATES (Arterial Side) Influenced by :

1. Pressure – flow rate is DIRECTLY proportional to changes in pressure. $F \sim P$
 - a. Increased pressure = increased flow rate
 - b. The greater the change in pressure, the greater the change in flow rate.
2. Resistance – flow rate is INVERSLY proportional to resistance. $F \sim \frac{1}{R}$
3. THEREFORE $F \sim \frac{P}{R}$
4. If the resistance is impeding flow, the pressure must increase to overcome resistance.

*** The arterial side begins at the Aorta and ends at the Arterioles.

** Total **peripheral resistance** (TPR) = All resistance that occurs on the Arterial side.

Three factors: 1 Vascular resistance 2 Viscosity 3 Turbulance

1. Vascular resistance:
 - a. Velocity of blood in the center of the blood is faster than blood that touches the vessel walls

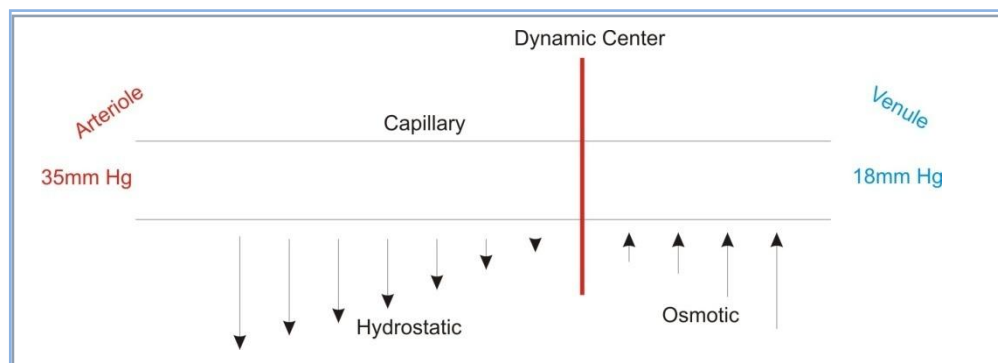
- b. If 2 vessels are the same diameter but one is twice as long, the resistance in the longer vessel will be 2X the resistance. (can be caused by weight gain)
 - c. If 2 vessels are the same length but one is half the diameter, the resistance of the smaller vessel will be 16X the resistance. (remember, pressure will increase to overcome resistance : **Resistance ~ BP**)
 - d. **ARTERIOLES** have the most effect on flow and pressure.
2. Viscosity: The higher the viscosity, the higher the resistance
 - a. Increased in formed elements (blood doping)
 - b. Decreased plasma (dehydration)
 - c. Generally, viscosity will not change. Certain diseases will have an effect (Leukemia)
 3. Turbulence
 - a. Blood flows in straight lines, BUT, at a bifurcation some turbulence occurs (eddy currents)
 - b. Can be caused by buildup of cholesterol in the vessel walls
 - c. Can be caused by a thrombus in the vessel
 - d. You can hear non smooth flow (this is what you cause to take a blood pressure)

10/6/08

Lecture exam sched. 10/20

Hemodynamics : pressure and resistance

Capillary Dynamics



Hydrostatic Pressure: Pressure that forces fluid out of the vessels

Osmotic Pressure: Pushes fluid back into the vessels.

Dynamic Center: Theoretical point where hydrostatic pressure and osmotic pressure are equal

Interstitial fluid is caused because there is more hydrostatic pressure than osmotic pressure, so some fluid is always in the tissue.

Some Associated Problems:

1. Chronic increase in BP – dynamic center will shift toward the venule side. Increased BP creates more hydrostatic pressure causing more fluid to lead into the tissue. Fluid comes out of the vessels: Leads to **edema (excess interstitial fluid)**.
2. Chronic decrease in protein intake: Poor diet.

- a. Blood proteins (Albumins) regulate osmotic pressure. A decrease in Albumins changes decreases osmotic pressure, therefore hydrostatic pressure increases. (the dynamic center shifts toward the venule. Fluid comes out of the vessels.
- b. This edema will be seen in the peritoneal cavity (belly). Called "ascites"
3. Hemorrhaging – decrease in BP = decrease in hydrostatic pressure, therefore the osmotic pressure rises. Fluid goes into the vessels.

Local bruising:

Proteins go to the cut (to create the clot), osmotic pressure goes down (locally), hydrostatic pressure goes up, local dynamic shift toward the venule, fluid comes out of the vessel (local swelling).

Perfusion: *Blood Flow to the Tissues*

Perfusion is effected by

1. Cardiac Output
 - a. Local factors
 - i. Venus Return (starlings law)
 - ii. Autonomic nervous system
 - iii. Hormones
2. Peripheral Resistance
 - a. Closing pre-capillary sphincters = increased resistance (cardiac output goes down)
 - b. Hormones (indirect) – vasoconstrict – increases resistance, CO goes down
3. Blood Pressure
 - a. Blood pressure is directly proportional to Cardiac Output [$BP \approx C.O.$]
 - b. Increased resistance causes increased BP [$BP \approx R$]
 - c. Therefore $BP \approx BV$ (venus return)

Regulation of Blood Pressure

Short term – regulated by the nervous system

- I. Baroreceptors (stretch receptors) located in the ascending aorta, carotid sinus
 - a. Hooked up to the Medulla Oblongata
 - i. Cardio regulatory Center
 1. Cardio acceleratory center
 2. Cardio inhibitory center
 - ii. Vasomotor center (sympathetic nervous system to regulate the diameter of blood vessels.
- II. Chemoreceptors - Receptors that monitor H^+ ion concentration in the plasma (pH). Increase in CO_2 leads to more H^+ which causes pH to go down.
 - a. Carbon dioxide + water \rightarrow Carbonic Acid \rightarrow Hydrogen + Bicarbonate
 $CO_2 + H_2O \rightarrow H_2CO_3 \rightarrow H^+ + HCO_3^-$
 - pH shift $\leftarrow + 7 - \rightarrow$ more acidic
 - b. Chemoreceptors located in the Aortic Arch (aortic bodies) and Carotid Sinus are hooked up to the Medulla Oblongata and the PONS
 - i. These influence the cardio regulatory and vasomotor centers
 - ii. Influence the respiratory regulatory center in PONS
 - iii. CO_2 up = HR up + vasodialate + increased respiration

- iv. CO₂ down = HR down

Long term blood pressure regulation- Regulated by the endocrine system (hormones)

When blood pressure is low:

- I. ADH – anti diuretic hormone (water retention)
 - a. Also called “vasopressin”
 - b. Released by the posterior pituitary
 - c. Made by the hypothalamus
 - d. In high concentration will cause vasoconstriction
 - e. Increased BP
- II. Angiotension II – made by plasma protein called angiotensin I
 - a. Very powerful vasoconstrictor
 - b. Increases BP
 - c. Makes you thirsty (take on more fluids)
 - d. Will call for ADH
 - e. Will call for Aldosterone
 - f. Converted by Angiotensin Converting Enzyme (ACE)
 - i. ACE inhibitors are a type of high BP medication
- III. Aldosterone – made by the adrenal gland in response to Angiotension II
 - a. Causes the retention of sodium
 - i. Tells the kidney to hold on to sodium
 - ii. Water follows sodium
 - b. Increases BP
- IV. EPO – Erythropoietin
 - a. Increases RBC production
 - i. This increases blood viscosity and thereby increases BP

When Blood Pressure is High

- I. ANP – Atrial natriuretic peptide
 - a. Produced by the cardiac muscle cells of the right atrium
 - b. Triggered by too much venus return
 - c. Tells the kidney to get rid of H₂O
 - d. Decreases thirst
 - e. Decreases angiotension II and ADH

Low blood pressure is much more dangerous under normal circumstances and therefore the body has more mechanisms to correct low BP.

Shock – acute circulatory crisis marked by low blood pressure (hypotension, **inadequate perfusion**)

Circulatory Shock – 35% loss of blood volume

Symptoms:

1. Hypotension – systolic <90
2. Clammy skin, pale, moist, cool
3. Confusion, disorientation
4. Rapid, weak pulse
5. Cessation of urination
6. Acidosis – lactic acid generation due to lack of O² in tissue – (anaerobic metabolism)

3 Phases of Circulatory Shock

1. Compensated
 - a. Homeostatic adjustment can cope with problem
 - b. Peripheral blood flow is decreased
 - c. BP ok, HR increased
2. Progressive Stage (35% blood loss)
 - a. Homeostatic mechanism cannot cope
 - b. BP abnormally low
 - c. Cardiac output inadequate
 - d. Low C.O. causes myocardial damage
 - e. When **BP = 50mm** Hg, Cardio sinus baro receptors trigger a massive activation of vasomotor center, called **Central Ischemic Response**. **Without treatment this is fatal.**
3. Irreversible Shock – STAGE III
 - a. When arteriolar smooth muscles and pre-capillary sphincters become unable to contract any more the result is widespread vasodilatation. There is an immediate and FATAL decline in blood pressure.

Varicose Veins

In the **extremities** Veins have valves. These valves are similar to the semi lunar valves in the heart. They are designed to keep blood moving toward the heart. Varicose veins are veins with incompetent valves.

Muscular pump works with the valves in the veins helping to push blood back to the heart. The **respiratory pump** causes enough pressure in the trunk to help push blood back to the heart.

Lymphatic System

10/8/08

-A network of lymphatic vessels that begin in the tissues and end up fusing with the venous system.

Lymph – fluid that resembles plasma but lacks platelets or RBCs

Lymphatic Organs – Tissue connected to lymphatic vessels and contains many lymphocytes.

Organs in the Lymphatic system:

1. Thymus

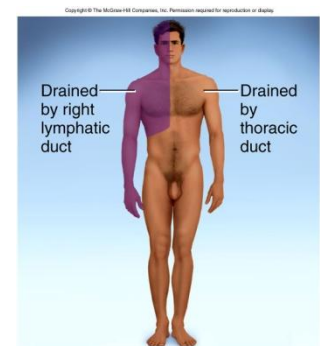
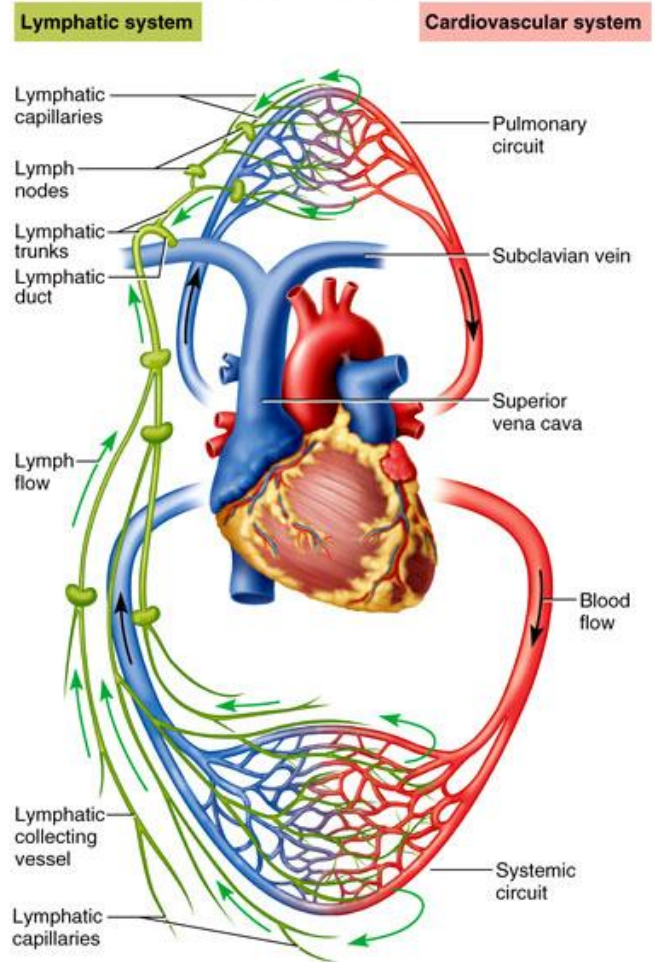
2. Spleen
3. Mucosa Associated Lymphatic Tissue (MALT) :
intestinal tract
4. Tonsils
5. Appendix

Functions

1. Make, distribute and maintain lymphocytes
2. Maintain blood volume (long term control)
3. Travel: distribute hormones
 - a. Some unwanted cells travel here (like cancer)

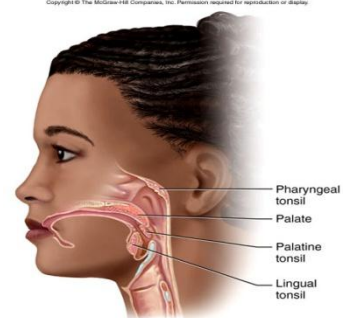
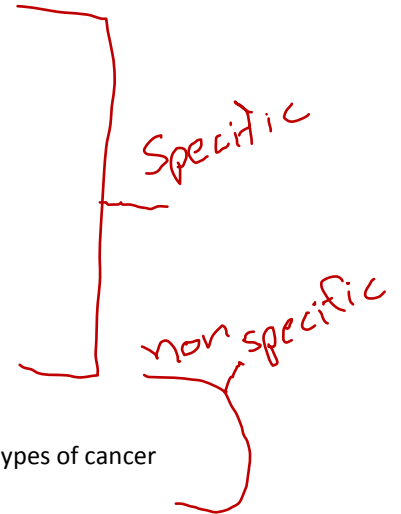
Lymphatic Vessels

1. One way transportation (Tissue to Heart)
2. Vessels begin as Blind end Sacks (lymphatic capillaries)
3. Lymphatic capillaries are larger than regular capillaries
 - a. Walls are thinner, **NO BASEMENT MEMBRANE**
 - i. They stay together due to the tissue around them
 - b. Flattened and irregular shape
 - c. **NO PRESSURE** in this system
4. Endothelial cells are not tightly joined but overlap like shingles (work like valve, letting fluid in)
5. Absent in:
 - a. Cornea of eye
 - b. Bone marrow
 - c. Brain and central nervous system (these are closed system where pressure is a problem)
6. **FLOW** : Lymph flows from lymph capillaries to larger vessels:
 - a. Collecting vessel
 - i. Resemble small veins and have all three tunics, very thin wall and have valves
 - b. Trunks : collecting vessels drain into trunks
 - c. Lymphatic Ducts
 - i. Left Thoracic Duct
 1. All the lymph from below the diaphragm dumps into a collecting area called the **Cisterna Chyli** (at about L2)
 2. The Cisterna Chyli drains into the **Left Thoracic Duct**
 3. Thoracic duct dumps into the left subclavian vein between the left and right external jugular vein
 4. The left thorax, and left upper extremities also dump here.
 - ii. Right Thoracic Duct



(c)

1. Originates near the Right Clavicle
 2. Drains right thorax, right upper extremities, right neck and right head
 3. Dumps into the right subclavian vein
7. Lymphocytes: 20-30% of circulating WBCs
- a. Most are in the lymphatic tissue organs
 - b. T-Cells (80% of WBCs) give **Cellular Immunity**. Three types.
 - i. Cytotoxic T-Cells : brings us Cellular Immunity
 1. Attack foreign cells or body cells infected with viruses
 - ii. Helper T-Cells
 1. Stimulate the activity of other T and B cells
 - iii. Suppressor T-Cells
 1. Suppress T-cell activity
 - c. B-Cells (10-15%) gives us Humoral Immunity
 - i. When properly stimulated they turn into B-Cells.
 - ii. Plasma makes antibodies
 - d. NK cells – (5-10%) natural killers
 - i. Attack foreign cells, body cells infected with viruses and many types of cancer
 - ii. Provide immunological surveillance.
 - e. Lifespan
 - i. These cells are on the mood and depending upon which tissue you are in the T to B cell ratio may vary. THYMUS = T cells, LYMPH NODES = more B Cells, BLOOD = more T cells.
 - ii. These are UNIQUE blood cells: They maintain their ability to divide and create daughter cells.
 - iii. Lifespan is LONG, 80% live longer than 4 years, some 20 years.
8. Lymphopoiesis
- a. Involves
 - i. Bone Marrow
 - ii. Thymus
 - iii. Secondary lymphatic tissue
 - b. Hemocytoblasts in the bone marrow produce lymphocytic stem cells with two distinctive fates.
 - i. One group stay in the bone marrow and mature into B cells and NK cells
 - ii. Other group migrates to the Thymus gland where immature T-cells, under the influence of thymic hormone called thymosins, They develop into mature T-Cells and differentiate.
 1. Then they migrate to the blood stream and other lymphatic tissues
 - iii. Bone marrow is essential.
 - c. ONCE MATURATION PROCESS IS COMPLETE – B&T CELLS HAVE THE ABILITY TO RESPOND TO SPECIFIC ANTIGENS AND NK CELLS RESPOND TO ABNORMAL CELLS.
9. Lymphatic Tissue : reticular connective tissue dominated by lymphocytes and macrophages
- a. Lymphatic nodules – poorly organized area of reticular connective tissue and lymph about 1mm in diameter
 - i. Under endothelium in systems that open to the outside (respiratory, digestive, urinary)
 - b. Tonsils (largest lymphatic tissue) Five tonsils, two sets of two and one singular
 - i. Palatine tonsils (2) – two lumps on sides of uvula
 1. Here “critters” are presented to the lymphocytes. (they build defenses)



- ii. Lingual tonsils (2) - tonsils on the posterior inferior surface of the tongue
- iii. Pharyngeal tonsil (1) – In the upper part of the pharyngeal pharynx.
 - 1. When enlarged it is called the **adenoids**.

Lymphatic Tissue has small crypts that trap bacteria. This is where lymphatic tissue destroys them.

Tonsils function: guard against infection.

Lymphatic tissue: can be very concentrated as in the Spleen, or very diffuse as in the digestive tract (MALT). Peyer's patches in the intestine.

Lymphatic organs: Well defined

- 1. Primary – produce and mature lymph cells
 - a. Red bone marrow
 - b. Thymus gland (central, like the fort)
- 2. Secondary
 - a. Lymph nodes
 - b. Spleen

Lymph Nodes

- 1. Most numerous
- 2. Filters lymph – main function. 99% of antigens are cleaned or filtered here. This is the site of B and T cell activation.
- 3. Lymph flows from node to node, filtered at each node (well purifies lymph)
- 4. Lymph node as **efferent (outflow)** and **afferent (inflow)** vessels. (more in than out)
- 5. Resemble Kidneys
 - a. Have a Cortex (both T and B cells here)
 - b. Have a Medulla (predominantly B cells and plasma cells)
 - c. Traveculae
 - d. Hylus – this is there the vessels come out.
- 6. Major nodes are in the Groin, Axilla, Neck
- 7. Lymphatic Flow
 - a. Afferent vessel
 - b. Subscapular Sinus (dendrite cells)
 - c. Outer cortex
 - d. Deep cortex (this is where actual filtration takes place)
 - e. Medulla (filtration)
 - f. Efferent vessel
- 8. When things go wrong
 - a. Lymphadenopathy – chronic but not severe swelling
 - b. Lymphedema – significant (severe) swelling of lymphatic vessels
 - i. Factors include excessive weight (gross obesity)

Thymus – In mediastinum

As we get older this organ gets smaller – peak grown at age 1 to 2, increases slowly until puberty

Structure: is well defined, has an outer capsule made of dense connective tissue. HAS LOBES, cortex and medulla

Cortex – immature T cells come in and divide

Site of maturation, then they go to the medulla

Has a barrier inside and out

Medulla does not have a big barrier

Function: Houses developing lymphocytes

Spleen (upper left quadrant) - largest lymph organ.

1. Encapsulated (spleen thymus, lymph nodes)
2. Located between the 9th and 11th ribs
3. Abuts the kidney, stomach and diaphragm
4. Has a hilus (where vessels enter)
5. Functions [spleen does for blood what the thymus does for lymph]
 - a. Filters blood
 - b. Initiation of immune response
 - c. Blood reservoir
 - d. RBC disposal
 - e. Blood cell production
6. Functional regions
 - a. Red pulp – lymphocytes
 - i. RBC graveyard
 - ii. Very permeable
 - b. White pulp – macrophages
 - i. Sleeves of lymphocytes and macrophages
 - ii. Monitors blood for foreign agents

Defense against Pathogens

1. 1st line of defense
 - a. External defense (chemical, physical)
 - b. Nonspecific defense
 - c. Present at birth
 - d. Skin (tough, dry and nutrient poor, peptides), hair, mucus membranes (stickiness), etc.
2. 2nd line of defense
 - a. Nonspecific defense
 - b. First line of cellular defense
 - c. White blood cell response (antimicrobial proteins)
 - i. Neutrophils, eosinophils
 - ii. Phagocytes “see” bacteria
 1. Microphages (neutrophils and eosinophils) mainly in blood
 2. Macrophages – fixed or free
 - a. Derived from monocytes – everywhere
 - b. Fixed – cannot move (CNS- macroglia)
 - c. Free – move through body and arrive at site of injury
 - iii. Work by Diapedis (penetrate cell wall)

1. Chemotaxis attractions
 2. Phagocytosis – receptors bind to receptor site on pathogen (adhesion)
 - d. NK cells (immunological surveillance)
 - i. Large lymphocytes
 - ii. Attack and destroy foreign agents in the **peripheral**
 - iii. Differ
 1. Respond more rapidly
 2. Less selective about target
 3. Process:
 - a. Adheres to target
 - b. Golgi apparatus positions itself and releases secretory vesicle into target cell.
 - c. Vesicle disrupts the plasma membrane of target cell.
 - d. Target cell can no longer maintain its cell wall
 - e. Interferons (cytokines – *chemical that coordinates action between cells* [messenger]) Help protect body (cellular response)
 - i. Small protein secreted by activated WBC when invaded by a virus
 - ii. Protein goes to a NON Infected cells
 - iii. Stops cell from replicating virus
 - iv. Alerts neighboring cells
3. 3rd line of defense
 - a. Specific defense
 - b. Many develop after birth, when exposed to antigens

Complement System- non-specific

11 proteins that function together to compliment antibodies

2 pathways: Classical and Alternate

1. C1 binds to antibody and stimulates activation of other proteins
2. Initiates a cascade of activity
3. The most important function is activating C3 to become C3b
 - a. C3b attracts phagocytes (chemotaxis)
 - b. C3b stimulates phagocytic activity
 - c. Stimulation of inflammation**
4. Inflammation: good thing
 - a. Damage cells lyse and break down, chemically attract mast cells, histamine – protoglandin
 - b. Limits the spread of pathogens.
 - c. Edema – any tissue, Effusion-Joints
 - d. Redness, heat pain
5. Fever: Body temp above 99 degrees
 - a. Benefits within limits
 - b. Promotes interferon activity
 - c. Increase in metabolic rate, tissue repair
 - d. Decrease in bacteria, virus production

3rd Specific resistance

Performed by coordinated activities of B and T cells

T cell = cell mediated immunity

B cell = humoral mediated immunity

1. Properties
 - a. Specific
 - b. Systemic action
 - c. Memory (creates specific and memory cells)
 - d. Tolerance – does not respond to everything, only responds when needed.
2. MHC proteins (B and T cells cannot work without them) Antigens bind to them
 - a. T and B cells cannot respond immediately
 - b. Respond to antigen when it is combining with glycoprotein
 - c. Class I – produced by nucleated cells
 - d. Class II – only in antigen presenting cells.

Immunity

1. Cellular (cell mediated)
 - a. T cells
 - b. Lymphocytes – directly attack
2. Antigen is recognized – T cells binds to it
3. Activation of cytotoxic T cells
 - a. CD8 T cells
 - i. Binds to MHC to activate
 - ii. Cell division to make memory cells
 - iii. Cell lyses, releases lymphotoxin – disrupts cell metabolism, releases cytotoxin
 - b. CD4 T cells
 - i. Enhances cytotoxic T cell maturation
 - ii. Promotes B cell division
 - iii. Stimulates phagocytosis
4. Humoral mediated immunity (antibody mediated)
 - a. B cell sensitisation
 - i. Exposed to antigen
 - ii. Antigen must match B cell antibody
 - b. B cell activation
 - i. Antigen binds to antibodies in B cell membrane. (Antigen Antibody Complex)
 - ii. Meets up with activated helper T cells and binds to it.
 - iii. Gives signal to B cells which begin to divide into
 1. Activated B cells
 2. Memory cells
5. **Antigen/Antibody Complex**
 - a. **Neutralization**
 - i. Makes bacteria/virus unable to bind to others
 - b. **Agglutination**
 - i. Forms bridges – ties antigens together
 - c. **Precipitation**
 - i. Binding to antibody, too big to stay in solution
 - d. **Compliment activation**
6. Immune response – activation from 1st exposure – peaks in two weeks
 - a. Second exposure, much faster reaction due to memory cells

Auto immune- immune system attacks itself.

Body makes antibodies that attack own tissue

Example: Addison's disease, endometriosis, multiple sclerosis, rheumatoid arthritis.

Respiratory System

Function: Supplies tissue with oxygen, Gets rid of CO₂, Protects body from pathogens, pH regulation, Voice production, Olfaction

Works with cardio vascular system

Works with urinary system (pH balance, which is regulated by the kidney)

Mucosa – respiratory mucosa

Underlying areolar connective tissue

Epithelium

*** ciliated pseudostratified columnar = trachea, larynx, bronchi

Stratified squamous – oropharynx, laryngopharynx

Simple cuboidal – tertiary bronchi

***simple squamous = alveoli

Nose : functions – warms, cleanses, humidifies air, detects odors, voice (resonator)

Nostrils, nasal bone, cartilage, nasal cavity

Pharynx

Nasal pharynx – auditory tubes

Oropharynx = air AND food

Laryngopharynx = air only

Larynx Cartilage

Epiglottis

***Thyroid cartilage – largest (adams apple)

***Cricoid cartilage – connects larynx to trachea.

Trachea – rigid

12cm long, 2.5cm diameter

6-20 C shaped rings

Trachea muscle (behind trachea where the esophagus rests

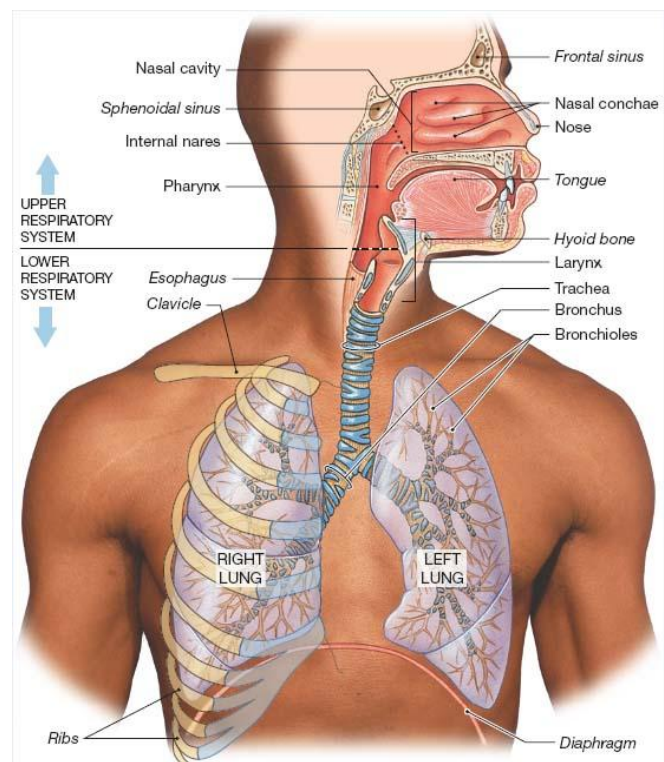
Lined with pseudostratified columnar epithelium

Goblet cells – exocrine glands

Bronchi branches to the **L and R bronchi** at the **Carina**, enters lungs at lung hilus

Secondary bronchi – (lobar), 3 right, 2 left

Tertiary bronchi (segmented bronchi) – 10 right, 8 left
– these constrict and dilate



Bronchioles to Terminal Bronchioles to Respiratory Bronchioles to Alveoli

1500 miles of airways

Left lung – two lobes

Right lung – 3 lobes

Alveoli 300-500 million

1. Small pouches *** site of gas exchange
2. Much lower blood pressure here in the alveoli
3. Osmotic pressure is greater than the blood pressure – oxygen dissolves into the blood in the capillary beds
4. Extensive lymph draining

Alveoli Cells

Type 1 – squamous (coverage) 95%

Type 2 – Great 5%

These repair epithelium, and secrete surfactant

Larger cells

Surfactin decreases surface tension. Without it the alveoli would not be able to open

Macrophages – most numerous – free alveoli of foreign particles

Pulmonary Functions

1. Pulmonary Ventilation
2. Mechanics:
 - a. Boyles Law: the pressure of a gas is inversely proportional to its volume.
 - i. Increased lung volume = decreased intrapulmonary pressure
 - b. Breathing is done by pressure differential
3. Breathing (pulmonary ventilation)
 - a. Oxygen in : Inspiration requires muscles – expiration is passive (not forced)
 - i. *Diaphragm (2/3 – primary mover)
 1. Contracts to compress abdominal organs
 - ii. External internal intercostals & pectorals
 - b. Expiration: passive at rest
 - i. Diaphragm relaxes
 - ii. Forced uses internal intercostals
 - c. Normal respirations occur with very little pressure change (about 1mm Hg)
 - d. Forced respirations occur with up to 30mm Hg change
4. Factors that effect respiration
 - a. Resistance : flow is related to change of pressure/resistance
 - i. Increased flow of air
 - ii. Increased barometric
 - iii. Decreased resistance
5. Alveoli: Surface tension
 - a. Surfactant needed to prevent alveoli collapse
 - b. Maintains decreased surface tension

6. Alveoli ventilation rate
 - a. Amount of air enter alveoli x rate
 - b. Best measure of oxygen in and carbon dioxide out
 - c. Dead air
 - d. Residual volume
7. Gas Exchange : AIR = 76.6 % nitrogen, 20.9% oxygen, .04% carbon dioxide
 - a. **Dalton's law**
 - i. **Total atmospheric pressure – sum of partial pressure of gasses in air**
 - ii. **Partial pressure = pressure gas emits against its environment**
 - iii. Air that gets to the Alveoli has a little more CO₂ and less O₂.
 - b. **Henry's law**
 - i. **Amount of gas in a solution is directly proportional to the partial pressure of that gas. Amount of gas that dissolves in water is determined by its solubility in water and its partial pressure in air.**
 - c. Alveoli Gas exchange: alveoli – blood
 - d. Systemic Gas exchange: blood – tissue
 - e. **Alveoli gas exchange – works by pressure gradient (diffusion)**
 - i. Factors – concentration of gasses
 - f. CO₂ is more soluble but slower than O₂
 - g. Factors effecting gas exchange
 - i. Concentration gradients of gases
 - ii. Gas solubility
 - iii. Membrane thickness
 - iv. Ventilation – perfusion coupling
 1. Ability to match ventilation (amount of air) and perfusion (rate of absorbtion)
 2. Typically .8 (flow 4.2liter air, 5.5liter blood)
 - h. Systemic gas exchange – exchange of gas between blood and tissue
 - i. Pressure gradient (high to low)
 - ii. Capillary has high PO₂ (95mmHg) Tissue low PO₂ (40mmHg)
 - iii. Capillary has low PCO₂ (40mmHg) Tissue higher PCO₂ (45mmHg)
 - i. Transport of Oxygen
 - i. Hemoglobin in RBC transports 97%
 - ii. Blood Plasma 3%
 - iii. *** differences in PO₂ affect O₂ saturation
 - j. Transport of Carbon Dioxide
 - i. Plasma proteins and hemoglobin (5%)
 - ii. Bicarbonate (90%) – primary buffer system
 1. Reacts with water, disassociates with H⁺ (buffer system)
 - k. Oxyhemoglobin disassociation curve
 - i. O₂ binds to hemoglobin rapidly until saturation of Hg
 - ii. At low PO₂ Hg saturates close to 100%
 - iii. Rate of unloading changes under different conditions like exercise
 - iv. Ambient PO₂ – maintains low PO₂ in tissue.
 - l. Respiratory Rhythm – typically rate of tissue O₂ absorbtion / CO₂
 - m. Change in PO₂ or PCO₂ controlled by smooth muscles in body

- n. Increased activity (exercise) decreases PO₂, increases PCO₂ results in increased pressure gradient and therefore increased O₂ to tissue.

2 types of gas exchange: Internal and External

Alveolar Gas Exchange and Systemic Gas Exchange

**Partial pressure of gasses that drives them across the membranes. (Pressure Gradient)

The pressure gradient for O₂ is larger than CO₂, but CO₂ is more soluble.

Respiratory Rhythm : inhalation and exhalation control

NO internal control mechanisms

Autoregulation/Local control and CNS regulation (respiratory centers)

1. Medulla
 - a. Dorsal respiratory group (DRG) – inspiratory center
 - i. Active during inspiration and quiet expiration
 - b. Ventral respiratory group (VRG)
 - i. Active ONLY during forced inspiration and expiration
 - ii. Heavy breathing – forced expiration
2. Pons
 - a. Apneustic center
 - b. Pneumotaxic center
 - i. Regulates the SHIFT from inspiration to expiration
3. Both the Medulla and Pons receive input from
 - a. Limbic system and hypothalamus
 - i. Pain, emotion
 - b. Chemo receptors
 - i. pH, O₂, CO₂ levels of CSF
 - c. Stretch receptors
 - i. Smooth muscles of bronchi, bronchioles
4. Voluntary Control
 - a. Originate in the motor complex of frontal lobe of cerebrum
 - b. Impulses sent to spinal cord (these bypass the BS)
 - c. Limitation
 - i. Blood CO₂ and O₂ limits cause automatic overrides
5. Input from peripheral receptors.
 - a. Chemo receptors (Aortic and Carotid bodies on medulla)
 - i. Blood pH, PCO₂, PO₂
 - b. Results in a respiratory “reflex” response
 - c. 75% of medulla response induced by pH shifts

CO₂

- Normal PCO₂ = 40mm Hg
- Rise in 10% causes Respiratory Rate to double

- Hypercapnia: Increased PCO_2 arterial blood Decreased pH
- Body responds by increasing resp. rate to get rid of CO_2

O_2

- Surprisingly little effect
- Body can withstand changes up to 40%
- Hypocapnia: decreased PCO_2 , increased pH
- Body responds by decreasing resp. rate to conserve CO_2

Disorders of Respiratory System

2 Classes: Restrictive and Obstructive

1. Restrictive: loss of lung compliance (stretch)
 - a. Results in lower lung capacity
 - b. Eg: Pulmonary fibrosis & interstitial lung disease
2. Obstructive
 - a. Narrowing or blocking of the airway
 - b. COPD – irreversible decrease in ability to force air OUT of the lungs
 - c. Emphysema – permanent enlargement of the alveoli sacks
 - d. Cystic Fibrosis, Bronchitis, Asthma

Digestive System

Functions

1. Ingestion : intake of food (body needs nutrients to sustain life)
2. Mechanical process (physical breakdown)
3. Digestion: chemical breakdown of food
4. Secretion: release of substances to aid digestion
5. Absorption: Uptake nutrients into digestive tract
6. Defecation: goes without saying

The digestive tract is a 30 foot tube. Plus accessory organs: Gallbladder, Liver, Pancreas, teeth, tongue

- A. Peritoneum
 - a. Peritoneal cavity – cavity within the abdomen containing digestive organs
 - i. Lined by the parietal peritoneum(outer) and visceral peritoneum (internal) – separated by thin layer of fluid and connective tissue (purpose is to reduce friction)
- B. Mesenteries (BIG COVERINGS)
 - a. Double serous membrane
 - b. Loosely suspends GI organs
 - c. This prevents GI organs from twisting
 - d. Passageway for nutrients, blood vessels, lymph
 - e. Three mesenteries:
 - i. Greater Omentum – greater curvature of stomach to cover small intestine (apron)

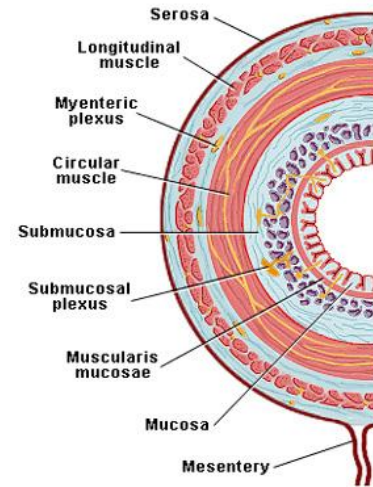
- ii. Lesser Omentum – From stomach to liver – stabilizes stomach and provides a route for nutrients to the liver
- iii. Mesentery proper – connects the small intestine to viscera

C. Retro Peritoneum

- a. Duodenum : beginning of the small intestine
- b. Pancreas
- c. Most of the large intestine

Layers of the GI tract. Innermost to Outer

1. Mucosa – epithelial tissue
 - a. Simple columnar
 - b. Some areas are stratified squamous (esophagus)
 - c. Absorption/secretion
 - d. Lamina propria – thin layer of smooth muscle (basement layer)
2. Submucosa
 - a. Dense, thick, irregular connective tissue
 - b. Contains blood vessels, lymph and nerves
 - c. Submucosa plexus (sensory neurons & sympathetic – parasympathetic nerve fibers)
3. Muscularis externa
 - a. Smooth muscle layers (motility)
 - i. Inner layer is circular
 - ii. Outer layer is longitudinal
 - b. Myenteric plexus
4. Serosa
 - a. Outermost layer
 - b. Thin areolar layer – simple squamous
 - c. In some regions where it is thick : Adventitia – fibrous connective tissue layer. Present in the esophagus, oral cavity, pharynx, rectum.



Movement Processes

1. Peristalsis
 - a. Wave of contraction – push bolus in 1 direction
 - b. Muscularis externa
 - c. In the small intestine, stomach, esophagus
2. Segmentation – occurs in the small intestine
 - a. Cycle of contractions – churning to mix contents with intestinal secretions

PATH of DIGESTION: Mouth – Pharynx – Esophagus – Stomach – Small Intestine – Large Intestine – Rectum – Anus.

Oral Cavity

1. Functions
 - a. Ingestions, taste
 - b. Mastication – mechanical chewing

- c. Lubrication – saliva
- d. Limited digestion – some starch digestion starts here
- 2. Anatomy
 - a. Cheeks/Lips
 - b. Tongue
 - i. Lingual frenulum
- 3. Salivary Glands
 - a. Moistens mouth
 - b. Produce amylase in saliva that breaks down starch
 - c. Inhibits bacterial growth
 - d. pH 6.8 – 7.0
 - i. parotid
 - ii. submandibular
 - iii. sublingual

} glands

Pharynx (throat)

- 1. Two layers of skeletal muscle
 - a. Deep longitudinal
 - b. Superficial circular
- 2. surrounded by adventitia
 - a. fibrous connective tissue

Esophagus 20-30 cm long

- 1. passageway from mouth to stomach
- 2. Sphincter controls rate of flow into stomach (upper, lower, esophageal)
- 3. Esophageal wall:
 - a. Outer adventitia
 - b. Submucosa – secretes mucus
 - c. Muscular externa
 - i. Upper third: skeletal muscle
 - ii. Middle third: both
 - iii. Lower third: smooth
 - d. Coordination of swallowing in the medulla swallowing center
 - i. Buccal phase- tongue forms bolus
 - ii. Pharyngeal phase- bolus moves past epiglottis
 - iii. Esophageal phase – ensures bolus travels down, triggers peristalsis

Stomach – mechanically breaks up food, liquefies food, stores food.

Begins chemical digestion – resulting soupy mixture called **Chyme**

Four regions of stomach:

- i. Cardiac (entrance) – more mucus secretion
 - 1. cardiac glands secrete gastric juices,
 - 2. Parietal cells, HCL made in pancreas, intrinsic factor
 - 3. Chief cells : pepsinogen
 - 4. Pyloric glands: mucus secretions

- ii. Fundis – above cardiac
- iii. Body – most digestion occurs here
- iv. Pyloric (pyloric sphincter)
 - a. Controls exiting into small intestine

Layers of the stomach wall

- i. Mucosa (inner)
 - 1. simple columnar with gastric pits
- ii. Muscular externa – 3 layers (outer longitudinal, middle circular, inner oblique)
- iii. Gastric rugae

Gastric Secretions : 2-3 liters per day

- i. hydrochloric acid
 - 1. high concentration
 - 2. low pH (.8)
 - 3. activates enzymes, breaks down substances
 - 4. kills bacteria
- ii. Pepsin
 - 1. breaks down proteins
- iii. Intrinsic factor
 - 1. needed to absorb B12
 - 2. **indispensible function of the stomach.**

ENTERIC SYSTEM : regulation of digestion.

Autonomic system, only deals with digestion.

Three phases of digestion

- a. Cephalic Phase
 - a. Triggered by smell, sight, thought
 - b. Hypothalamus relays sensory input to medulla
 - c. Activates enteric nervous system
- b. Gastric Phase
 - a. Activates by swallowing food
 - b. 2/3 of gastric secretions activated by stretch receptors, stomach pH and gastric contents.
 - c. Activation carried out by Ach., Histamine, Gastrine (hormone that stimulates gastric stretch and stomach response.)
- c. Intestinal phase
 - a. Begins when food enters small intestine
 - b. Controls gastric activity
 - i. Matches absorption with rate of incoming chyme
 - ii. Coordinates activity with accessory organs: pancreas, Gallbladder
 - iii. Hormones
 - 1. Secretion increases bile production
 - 2. Cholecystikin (CCK)
 - a. Secreted with arrival of lipids and CHO

- b. Inhibits gastric secretions so fats and CHO stay in stomach longer.

- iv. Nerve reflexes

- 1. Enterogastric reflex prevents overfilling of small intestine.

Small Intestine: Chemical digestion (most) and nutrient absorption occurs (6 meters long)

- a. Duodenum (25cm) – retroperitoneal
 - a. Neutralizes stomach acids
 - b. Receives pancreatic juice and bile
- b. Jejunum (next 8feet)- where most of chemical digestion absorption takes place – thicker walls
- c. Ileum (last 12 feet)
 - a. Thin walls
 - b. Peyer patches (lymph nodules)
 - c. Ends at ileocecal junction with LI
- d. TOTAL surface area of SI = 2200 Sq feet
- e. Microscopic Anatomy
 - a. Circular folds – spiral pattern
 - i. Villi – fingerlike projections with microvilli
 - ii. Lymph vessels (lacteal)
 - 1. Transport for protein/lipids
 - iii. Blood vessels
 - iv. Largest in duodenum
 - v. Microvilli – brush border on cell : enzymes for final stage of digestion.
 - vi. Goblet cells – secrete mucus
 - b. Intestinal glands at base of villi
 - i. Produces stem cells
 - ii. Produces enzymes (brush border)

Motility

1. Chyme mixes with intestinal juices in duodenum
2. Slow peristaltic contractions initiated by reflexes in plexus
3. Chyme is churned to increase contact with mucosa for absorption and digestion
4. Moves residue toward large intestine
 - a. Segmentation – constriction – mixes and churns – most common
 - b. Peristalsis begins when major absorption is over
 - i. Overlapping waves of contraction
 - ii. Mixes chyme to colon

Gastroenteric/Gastroileo reflexes

1. Triggered by stretching of stomach
2. Accelerate movement in SI
3. Stimulation relaxation of ileocecal valve

Accessory Organs

1. Pancreas – retroperitoneal

Metabolism

Def: all chemical reactions in the body

Catabolism –

Carbohydrate metabolism know goal, steps, result

1. Glycolysis 2 ATP, pyruvic acid
2. Krebs cycle take pyruvic acid and
 - a. Prep convert pyruvic acid to acetal col A
 - b. 8 successive steps
 - c. End product/ mytoconreal enzymes NADH and FADH2
3. Electron transport chain Goal: final catabolic reactions to form ATP
 - a. Chain reaction
 - b. Enzymes NADH
 - c. Involves transport of electrons through chemical reactions
 - d. Final product: electronpairs meet up with oxygen and this creates ADP and then ATP
4. TOTAL yield 36 ATP
5. Cellular respiration captures 38% of ATP, rest is lot as heat.

Glycogen Metabolism (stored glucose)

- A. Glycogenesis – extra clucose is stored as glycogen
- B. Glycogenolysis
 - a. Release of glucose (through hydrolysis of stored glycogen) between meals
 - b. Stimulated by glucagon and epinephrine

Carbohydrate Loading : CHO best choice for athletes

Increase Complex CHO intake prior to competition

Tricks body into storing more glycogen

Lipid Metabolism

1. Stored as triglycerides (excess fat)
2. LIPIDS give you the most energy per molecules (9kcal/ p/gram)
3. Lipogenesis – synthesis of triglycerieds
4. Lipolysis – breaking down stored fat for fuel
5. Stored in liver and skeletal muscles

Protein Metabolism

1. Some amino acids used as immediate fuel
 - a. Conversion to pyruvic acid or keto acid intermediates of krebs cycle
 - b. Enters kreb cycle

Metabolic states and rates (regulation)

1. Dynamic catabolic-anabolic state
 - a. Molecules continually broken down and rebuilt
2. Metabolic control
 - a. Balance of 2 phases
 - i. Absorptive state
 1. Absorbs nutrients

2. Storing things
3. Insuling
4. Anabolism > Catabolism
- ii. Post absorptive state
 1. Occurs between meals, overnight
 2. Body's energy needs are met through stored fuels
 3. Catabolism > Anabolism
3. Metabolic rate
 - a. Amount of energy used in the body in a given period of time
 - i. Measured directly in calorimeter
 - b. Basal metabolic rate (BMR)
 - i. Measured in a **relaxed state**, after fasting, room comfortable temperature
 - ii. Adult BMR is 66 kcal/hour
 - c. Total metabolic rate (TMR)
 - i. Rate of kilocalorie consumption needed to fuel ongoing activities
 - ii. BMR account for large portion of this (70%)
4. Nutrition
 - a. FAT contains 9 kcal/g (most)
 - b. Carbohydrates: 4 kcal/gram (quickest) 45-55% intake
 - i. Requirements
 1. 130 – 175 g/d
 2. 45%-55%
 - c. Lipids 30% of daily intake
 - d. Proteins 12-15% daily intake

Urinary System

Composition

1. Kidneys
2. Ureters
3. Urinary Bladder
4. Urethra

Urinary System works with most other systems

1. Helps control pH – alters what it absorbs or secretes, buffer systems
2. Function: Filtration, elimination of waste (kidneys)

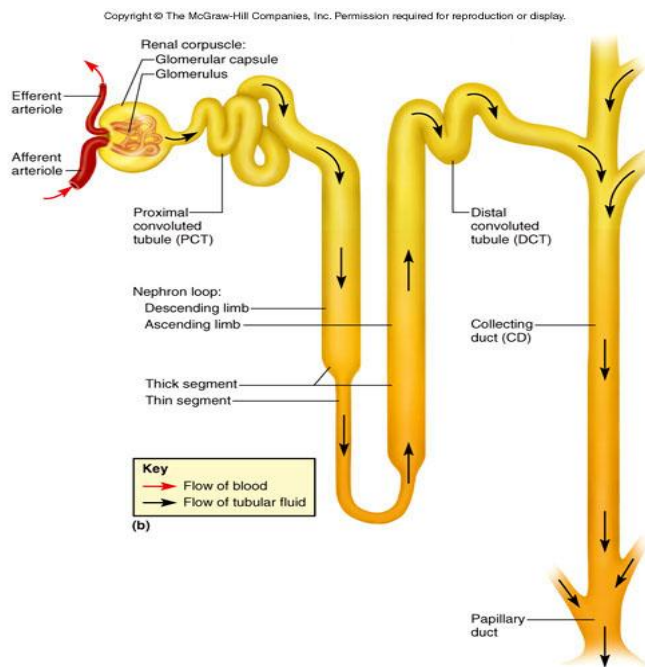
Homeostasis

1. Maintain fluid volume and concentration
2. pH, blood volume, RBC concentration
3. Ion concentration
4. Glucose concentration
5. Elimination of waste
 - a. Respiratory system - CO₂
 - b. Integumentary system – water, salts, lactic acid

Kidneys

1. Right is lower than left
2. Both are retroperitoneal
3. Kidney shape
4. Outer layer is renal fascia (connects to wall)
5. Adipose capsule
6. Renal capsule – encloses kidney like cellophane wrap
7. Anatomy of Kidney
 - a. Functional unit : nephron (1.2 million)
 - b. Renal cortex – outer region (1cm)
 - c. Renal medulla – inner portion
 - i. Renal pyramids – divisions (6-10)
 - ii. Renal columns (in between pyramids)
 - iii. Renal Papilla – point of pyramid
 1. Major and Minor calyx – ducts urine travels through
 - iv. Renal pelvis – funnel like passageway (big, after major calyx) for urine leading into and out of medulla
 - d. Renal sinus – space inside
8. Blood supply
 - a. Kidneys receive about 25% of Cardiac output
 - b. Kidneys 0.4% of body weight
 - c. 1200ml of blood flow per minute
 - d. Renal Artery
 - i. Segmental artery
 - ii. Interlobar arteries (between lobes)
 - iii. Arcuate arteries (around the outside)
 - iv. Interlobular (into cortex)
 - v. Afferent arterioles into nephron
 - vi. Interlobular veins
 - vii. Arcuate vein
 - viii. Interlobar vein
9. Nephron – functional units 2 parts
 - a. Renal corpuscle
 - i. Filters blood and plasma
 1. Glomerulus – network of blood capillaries
 2. Glomerular capsule (bowman's) – cup shaped capsule
 - a. Lined with 2 layers of epithelium
 - i. Parietal, visceral (simple squamous)
 - ii. Visceral epithelium contains **podocytes**
 1. Large cells ("feet") that wrap around glomerular capillaries
 3. Capsular space – chamber continuous with renal tubules
 4. **BLOOD INTO GLOMERULUS – FORCED THROUGH CAPSULAR- INTO RENAL TUBULE FOR FILTRATION BLOOD IN – FILTRATE OUT**
 - 5.
 - ii. **ONLY IN CORTEX**
 - b. Renal Tubule

- i. Process filtrate into urine
- ii. Found in renal cortex and medulla
- iii. Four regions
 1. Proximal convoluted tubule (PCT)
 - a. Longest, most coiled, absorption
 2. Nephron Loop (loop of Henle)
 - a. Thick and thin segments
 3. Distal convoluted tubule (DCT)
 - a. Shorter coil, less convoluted, in cortex
 - b. Reabsorbs useful substances
 4. Collecting duct
 5. Filtrate now called tubular fluid
 6. After tubules is called urine



Juxtaglomerular
 apparatus: junction between
 afferent and efferent arterioles (DCT)

1. Macula Densa – cells in the DCT
 - a. Region of tall epithelial cells on DCT – have a role in movement of smooth muscle of afferent arteriole.
 - b. Way to stabilize and monitor blood pressure in the nephron

Types of nephrons

1. Cortical nephron
 - a. About 85%
 - b. Almost all in the cortex
2. Juxtamedullary nephron
 - a. Long loops of Henle extend deep into medulla
 - b. Concentrates urine

Nephron Blood supply

Urine Storage and Elimination

Ureters

1. Retroperitoneal, muscular tube
2. Receives urine from renal pelvis
3. Pass behind bladder, enter it from below

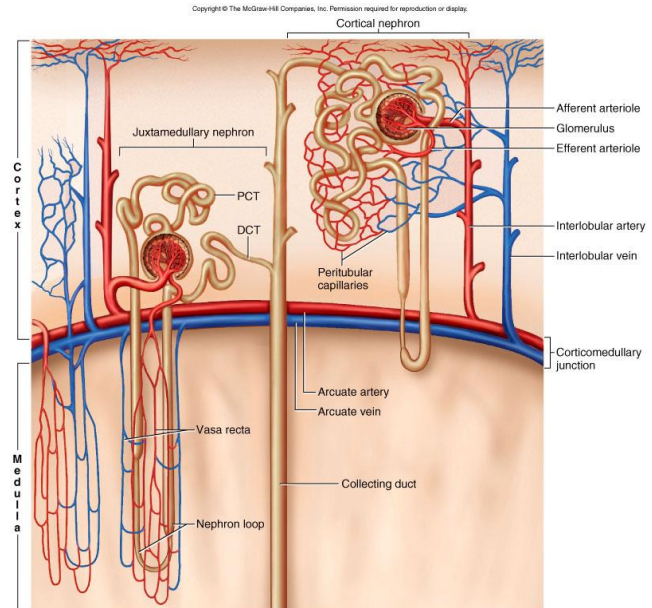
1. Bladder

- a. Muscular sac
- b. 3 layers of smooth muscle in its wall
- c. Walls contain rugae
- d. As it distends rugae flatten out
- e. Moderately full 500ml
- f. Maximum capacity 700-800 ml

2. Ureter Orifice

3. Urethra

- a. Carries urine out of the body
- b. Structure different between woman and men
- c. Detrusor muscle thickens, forms internal urethral sphincter
- d. External urethral sphincter: skeletal muscle



Urine Formation

Goals: Maintain homeostasis of blood volume and composition

Every 24 Hours, kidneys filter 150 – 180 liters of blood.

Concentrates this down to 1 liter of urine.

Three Steps

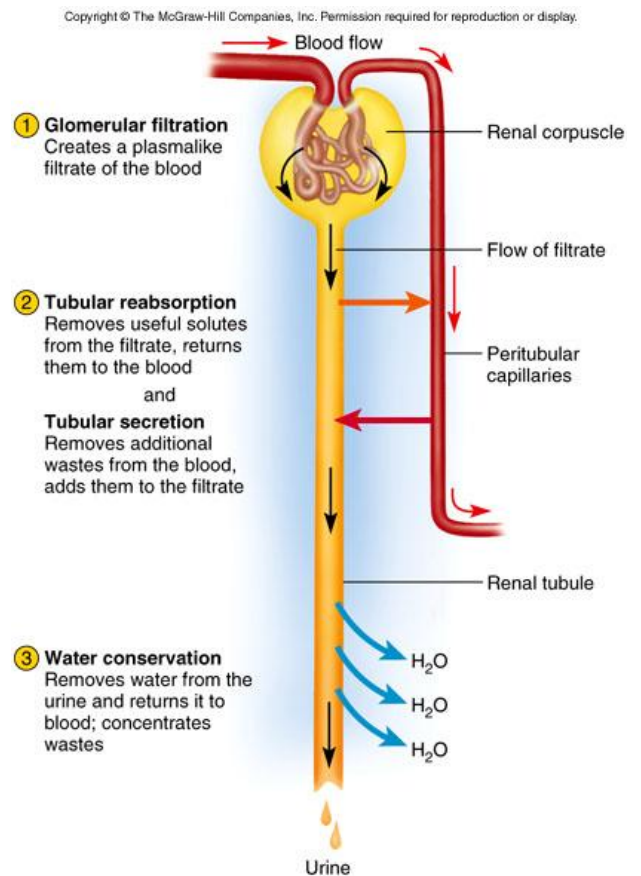
Overview: filtration, reabsorption, secretion

HOW: membrane permeability, Net filtration pressure

1. Glomerular Filtration

1. Blood enters glomerulus (has layered membrane that allow small things through)
2. Filtration: Done through pressure
 - i. Blood hydrostatic pressure 35mm Hg
 - ii. Osmotic pressure – pressure 25mm Hg
 - iii. Net Filtration Pressure **10mm Hg**
OUT OF CAPILLARIES

2. Tubular reabsorption: useful substances reabsorbed back into the bloodstream



1. PCT reabsorbes 65% of glomerular filtrate, Also removes some substances from the blood.
 2. Reabsorbed fluid returns to bloodstream via peritubular capillaries
 3. Transport Maximum
 - i. Transport proteins can become saturated.
 4. Tubular Secretion
 - i. Removal of toxins, etc. from blood
 - ii. Returns them to tubular fluid
 - iii. Waste removal: urea, uric acid, bile salts, ammonia, catecholamine, many drugs
 - iv. Acid-Base balance: secretion of hydrogen and bicarbonate ions regulates pH of body fluids
 - v. Mostly in PCT, Nephron Loop : function – water conservation.
3. Water Conservation
1. In addition to filtering blood . . Kidneys help to regulate blood volume, maintain body's fluid balance
 2. Maintains fluid balance by PREVENTING excess fluid loss.

Endocrine Control

Aldosterone: "salt-retaining" hormone, indirectly helps to regulate bp

3. Atrial Natriuretic Peptide (ANP)

1. Glomerular Filtration Rate (GFR)

- a. Volume of filtrate formed each minute by the kidney
- b. Normal GFR in adults: 120-125 ml/min
- c. Why is it important?
 - i. Maintain kidney function
- d. Influenced by:
 - i. Surface area available (typically high)
 - ii. Filtration membrane permeability (typically high)
 - iii. Net filtration pressure (NFP)
 - iv. GFR is directly proportional to NFP
- e. Increased permeability and increased surface area allow for Large amounts of filtration production
- f. Small drops (18%) in NFP(net filtration pressure) can STOP filtration
- g. Regulation of GFR is therefore VERY important
- h. If GFR is too high:
 - i. Needed substances cannot be reabsorbed
 - ii. Are lost in urine
- i. If GFR is too low
 - i. Everything is reabsorbed
 - ii. Including waste products usually lost in urine.

2. Regulation

- a. Intrinsic Control – this prevails under normal conditions
 - i. Act locally (within kidneys)
 - ii. Functions to maintain GFR in kidneys
 1. Renal autoregulation
 - a. Maintains constant GFR in normal body conditions
 - b. Adjust vascular resistance of afferent arterioles

2. 2 mechanisms
 - a. Myogenic mechanism (pressure triggered – dilatation)
 - b. Tubuloglomerular feedback mechanism (inhibit release of constrictor, better dilatation). Based on NaCl level
- b. Extrinsic Controls
 - i. Act outside kidney
 - ii. Functions to maintain bp
 - iii. Activates under stress
 - iv. Neural controls
 1. Under stress, sympathetic system is activated.
 2. Shuts blood away from kidney to vital organs
 3. Norepinephrine released – constrict vessels that feed glomerulus decreasing GFR
 4. Indirectly stimulates the Renin-angiotensin mechanism (extrinsic control)
 - a. Triggered by bp below 80mm Hg (hemorrhage, dehydration)
 - b. Activation of macula densa cells
 - c. Stimulated by sympathetic nervous system
 - d. Renin starts the reaction in which angiotensin is released
 - e. Angiotensin 2 stabilizes blood pressure and volume
 - f. Angiotensin 2 constricts arterioles
 - i. Stimulates reabsorption of Na⁺
 - ii. Stimulates hypothalamus, activates thirst center
 - g. End result
 - i. Systemic and glomerular hydrostatic pressure increase
 - ii. Restored bp and blood volume

Voiding Urine

1. As bladder fills, detrusor muscle relaxes, both sphincters closed
 - a. Sympathetic pathways maintain this
 - b. Micturition – act of urinating
 - c. Bladder filling excites bladder walls

Electrolytes

IMPORTANT

2 primary substances that are integral to body homeostasis

Water Balance

- Total body water for 150lb male = 40 liters
- Water amount in tissues
 - Constant movement (dynamic)
 - If imbalanced, osmosis occurs in one direction to re-balance
- Adipose, bone, skeletal muscle

- Intracellular fluid ICF – 65%
 - Higher concentration of Potassium K⁺
 - Extracellular fluid (interstitial)ECF – 35%
 - Higher concentration of sodium ions Na⁺ extracellular
1. Water Gain
 - a. 2500 ml/day
 - b. Preformed water – ingested
 - c. Metabolic water (air)
 2. Water Loss
 - a. Insensible water loss (not conscious too)
 - i. Breath
 - b. Obligatory water loss
 - i. Urine, feces, breath, sweat
 3. Regulation of intake
 - a. Thirst center
 - b. Hypothalamus respond in dehydration
 - i. Osmoreceptors
 4. Hormone regulation
 - a. Aldosterone: regulates Na⁺ concentration in the ECF (extra cellular fluid)
 - i. Indirectly affects water volume
 - b. Antidiuretic Hormone (ADH)
 - i. When dehydrated hypothalamic osmoreceptors stimulate posterior pituitary to release ADH
 - c. Aquaporins produce channels that allow ↑ diffusion of water into ECF
 - d. Result is ↑ reabsorption of water, ↑ blood volume

	When dehydrated	How?
Aldosterone	Released	Increase Na ⁺ reabsorption Increased fluid retention “Water follows salt”
ADH	Released	In response to ↑ Na ⁺ concentration stimulates water conservation

Regulation of output: Accomplished

Electrolytes:

1. Function
 - a. Chemicals that participate in metabolism
 - b. Determine cell membrane potentials
 - c. Affect osmolarity of body fluids
 - d. Affects body's water content and distribution

Major Cations: Na⁺, K⁺, Ca²⁺, H⁺

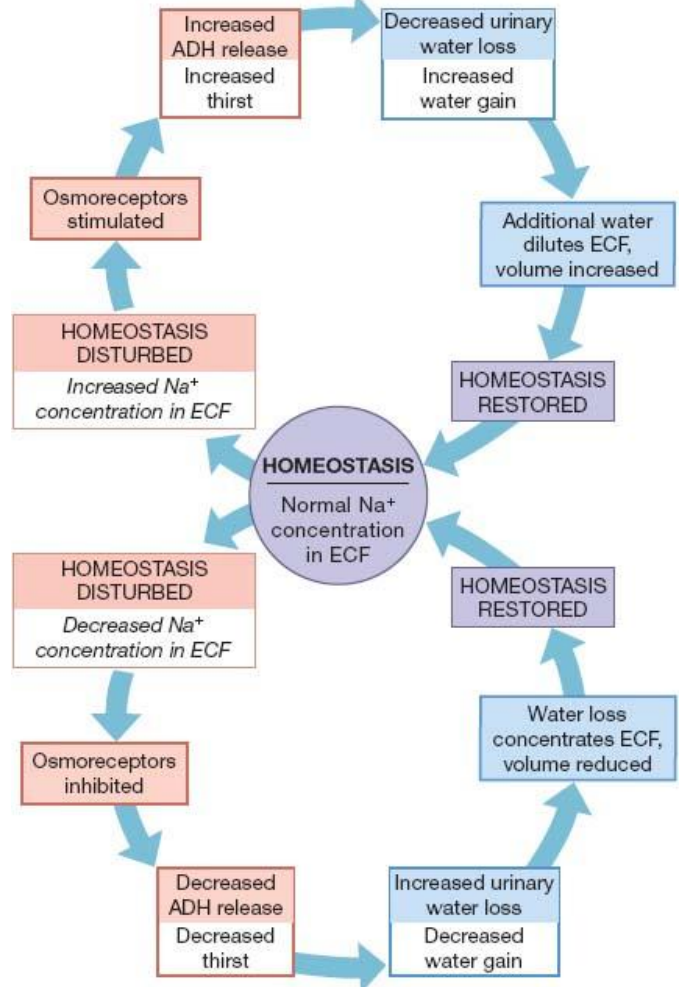
Major anions: Cl⁻, HCO₃⁻, PO₄⁻

Sodium Functions: accounts for 90-95 % of osmolarity of ECF

**Major role in determining body water distribution and volume

Sodium Homeostasis

1. Primary concern – excretion of dietary excess
2. 0.5 g/day needed, typical diet has 3 to 7 g/day
3. Changes in Na⁺ intake / output DO NOT directly affect Na⁺ concentration in ECF (extra cellular fluid)
 - a. If there is a lot of sodium in ECF, body will release fluid from inside the cell.
 - b. As a result with increased Na⁺ in ECF, water volume increased which leads to a high BP
 - c. Body holds more water to maintain the same concentration (retain water)
4. ADH (antidiuretic Hormone): **responds to osmolarity** (concentration of solute)
 - a. Changes amount of water excretion – indirectly affects Na⁺ concentration
 - b. Change in osmolarity sensed by osmoreceptors – ADH released
 - c. Released by hypothalamus
5. ANP : (atrial natriuretic peptide)
 - a. If increased ECF volume (due to increased Na⁺)
 - b. Increased blood volume and bp
 - c. ANP released
 - d. Kidneys reabsorb decrease Na⁺, then water, therefore excretion goes up
6. Aldosterone: **responds to changes in fluid volume**.
 - a. If decreased ECF volume (decreased Na⁺)
 - b. Renin angiotensin mechanism activated
 - c. Aldosterone released (salt retaining hormone)
 - d. ADH (to increase thirst) in response to fluid volume not Na⁺



Hypernatremia

Plasma sodium > 145 mEq/L

Water retention, hypertension and edema

Hyponatremia

Plasma sodium <130 mEq/L

Result of excess body water, quickly corrected by excretion of excess water.

Potassium Functions: Most abundant cation of ICF

1. Closely linked with Na⁺ homeostasis (opposite)
2. Regulated by Aldosterone
 - a. With too much potassium, aldosterone is released, body reabsorbs more Na⁺

b. With too little potassium, aldosterone is inhibited, Increased Na^+ in ECF

3. Imbalances

a. **Hyperkalemia: effects depend on rate of imbalance**

- i. If concentration rises quickly (crush injury), the sudden increase in extracellular K^+ makes nerve and muscle cells abnormally excitable.
- ii. Slow onset, inactivates voltage gated Na^+ channels, nerve and muscle cells become less excitable.

b. Hypokalemia

- i. From chronic sweating, chronic vomiting or diarrhea
- ii. Nerve and muscle cells less excitable.
 1. Muscle weakness, loss of muscle tone, decreased reflexes, arhythmias

Calcium Functions

1. Skeletal mineralization
2. 99% of Ca^{+2} found in bone
3. Muscle contraction
4. Second messenger
5. Exocytosis
6. Only 0.8 – 1.2 mEq/L ingestion needed daily
7. Homeostasis
 - o Parathyroid Hormone
 - o Calcitriol (vitamin D)
 - o Calcitonin (in children)

ACID BASE BALANCE

1. Important part of homeostasis
 - a. Metabolism depends on enzymes, that are sensitive to pH
2. Normal pH of ECF is 7.35 to 7.45
3. Challenges to acid-base balance

Strong Acid/Base – substances that dissociate completely

Weak Acid/Base – substances that do not dissociate completely

Disassociation – separates and breaks down ions completely and evenly

- Substances in body most often are dissolved in water ($\text{H}_2\text{O} \rightarrow \text{H}^+$ and OH^-)
- When base is added to a solution, part of it breaks free (OH^-) to form H_2O and in the process takes (removes) H^+

BUFFER SYSTEMS - Systems within body that resist changes in pH

Chemical buffers and Physiological buffers

Chemical Buffer System

1. How do they work?
 - a. Able to resist change because chemical can act as wither an acid or base depending on what is needed to bring pH back to normal
 - b. Converts strong acids/bases into weak ones
 - c. Weak acids/bases can give or accept H⁺ ions because dissociation not complete
 - d. All buffer systems have
 - i. Weak acid (H⁺ donor)
 - ii. Weak base (H⁺ acceptor)
 - iii. H⁺ ions
 - e. ** these systems do have limits to how much they can buffer.
2. Carbonic Acid – Bicarbonate Buffer System
 - a. Most important in ECF
 - b. Most of CO₂ generated by cells is converted into carbonic acid (H₂CO₃)
 - c. Increased carbonic acid results in decreased pH, so body constangtly trying to buffer this.
 - d. HOW?
 - i. Reversible reactions where carbonic acid can disassociate into H⁺ and bicarbonate ion (HCO₃⁻)
 - ii. $[\text{CO}_2 + \text{H}_2\text{O} \leftrightarrow \text{H}_2\text{CO}_3 \leftrightarrow \text{HCO}_3^- + \text{H}^+]$

pH↑ — pH↓
 - iii. System seldom used to buffer high pH
 - iv. If needed, reaction will shift to the right as weak acid dissociates slightly and H⁺ ions are added
3. Phosphate buffer System
 - a. Works similarly to bicarbonate system
 - b. Important in **the ICF and urine**
 - i. System functions to lower pH
4. Protein buffer System
 - a. ¾ of all chemical buffering in the body
 - b. Regulation of pH in ECF and ICF
 - c. Always interacting with other chemical systems
 - d. How?
 - i. Aminio acids have the ability of accepting or release H⁺ to increase or decrease pH
5. Chemical buffers are good SHORT TERM
6. Released and accepted H⁺ ions remain in body, howeber.
7. Respiratory and urinary systems only way body can remove or replace H⁺ as needed

Physiological Buffers

1. Respiratory
 - a. Works with bicarbonate buffer system
 - b. Addition removal of CO₂ to alter pH
 - c. Able to neutralize 2-3 more times as much acid as chemical buffer alone.
 - d.

Endocrine System

Function

1. Works with nervous system to regulate body functions
2. Communicates through hormones
3. Hormones have specific and direct effect on many body processes

Composed of

1. Endocrine /exocrine glands
2. Hormones
3. Target cells

Cell communication

-gap junctions – pores in cell membrane allow signaling chemicals to move from cell to cell

Paracrine (local) hormones

1. Use of chemical messengers to transfer info from cell to cell within same tissue
2. Chemicals enter bloodstream , but only have local effects
3. Prostaglandins (remain in same tissue), Growth factors
4. Many of these go on to have secondary effects to distant cells

Hormones

- Chemical messengers that travel through bloodstream to alter activities of distant tissues
- Produced only in specialized areas

(endocrine glands)

Endocrine compared to Nervous system

- Endocrine system works slower
- Endocrine has widespread effects, Nervous system has localized effects
- Endocrine gives prolonged response compared to the nervous system quick, short lasting
- Communicates through hormones (only chemicals)
- Similarities:
 - Several chemicals function as both hormones and neurotransmitters (norepinephrine)
 - Some hormones are secreted by neurons (oxytocin and catecholamines)
 - Overlapping effects on same target cells (NE and glucagon cause glycogen hydrolysis in liver)
- System regulates each other

Control of endocrine secretion

1. No “master control center
2. Hypothalamus
 - a. Highest level of endocrine control
 - b. Greatest influence on other glands
3. Endocrine reflexes
 - a. Changes in ECF, hormone levels, neural stimuli
 - b. Response- release of hormone to reduce intensity of stimuli
4. Most function lie a negative feedback mechanism

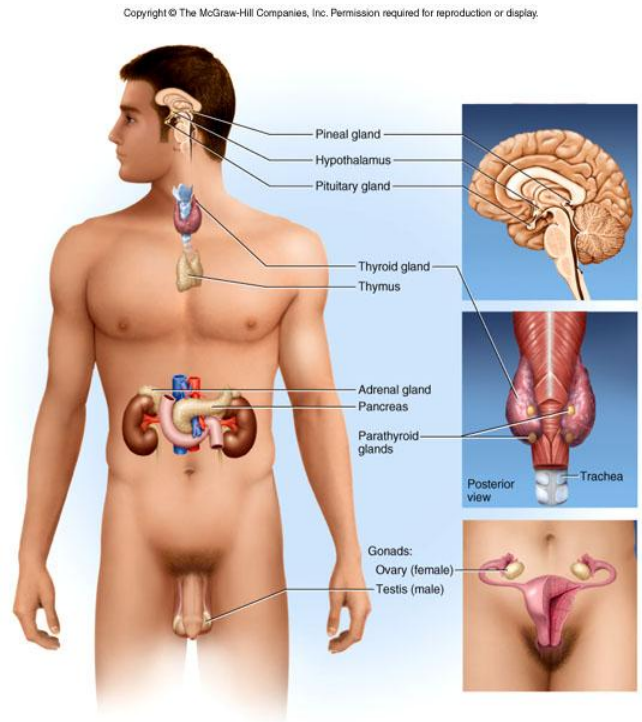
5. Complex endocrine reflexes
 - a. Involve many steps, 2 or more hormones
 - b. Integrates nervous and endocrine systems
6. Control works in three ways
 - a. Hypothalamus secretes regulatory hormones – act on pituitary gland – eventually control thyroid, adrenal cortex, reproductive organs
 - b. Hypothalamus itself produces hormones (ADH, oxytocin)
 - c. Hypothalamus controls adrenal medulla – regulates autonomic responses

General Anatomy

- Endocrine glands
 - Produce hormones
 - Specialized tissue that produces hormones
 - Have no ducts, secrete their product into the bloodstream
 - Extracellular effects, alter target cell metabolism
- Exocrine glands have a duct

Types of Hormones (3, most are peptide)

- Peptide
 - Long amino acid chains
 - OT, ADH; all releasing and inhibiting hormones of hypothalamus; most of anterior pituitary hormones
- Monoamines (Amino acid)
 - derived from amino acids
 - catecholamines (norepinephrine, epinephrine, dopamine) and thyroid hormones
- Steroid (Lipid)
 - Eicanooids – Leukotrienes Prostaglandins
 - Steroid hormones (**testosterone, estrogen**)



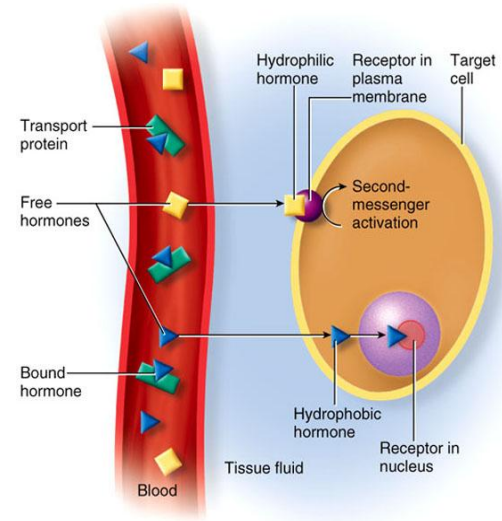
Hormones are most abundant near capillaries. They circulate freely, or are bound to carrier proteins
 Freely circulating hormones don't last as long as bound hormones.

Transport

1. Monoamines and peptides
 - a. Hydrophilic
 - b. Mix easily with blood plasma
2. Steroid and thyroid hormone
 - a. Hydrophobic
 - b. Must bind to transport protein

Hormone receptors

- Specific to hormone
- Made up of protein or glycoprotein
- Found in plasma membrane, or inside cell
- Similar to enzyme-substrate interactions
 - Specificity, Saturation
 - Receptors do NOT change chemical structure of substance
- First Messenger
 - Hormones that bind to plasma membrane
 - Needs intracellular mediary to exert effects inside the cell
- Second Messenger (this has the effect inside the cell)
 - Appears due to 1st messenger
 - Carries effect of hormone
 - Cyclic – AMP (*cAMP*) , cyclic- GMP
 - Amplification – presence of small # of 1st messengers can lead to thousands of 2nd messengers
- G proteins – usually needed as link between 1st and 2nd messengers



1. Hormone Clearance

- a. Hormone signals must be turned off
- b. Take up and degraded by liver and kidney
- c. Excreted in bile or urine
- d. Half life – time required to clear 50% of the hormone

- Endocrine Glands (must know these)

Hypothalamus

- Location: Diencephalon Controls secretions of the pituitary glands
- Hormones – many travel to pituitary gland
- Anterior pituitary (7 hormones)
 - Releasing (5)
 - Inhibiting (2)
- Posterior pituitary (2)

Pituitary

- Suspended from hypothalamus by stalk (infundibulum)
- Hormones
 - Anterior lobe (6)
 - Posterior lobe (2)
- Portal system (between the hypothalamus and the anterior pituitary)
 - Hormones are secreted by the anterior pituitary
- Anterior Pituitary Gland
 - 7 hormones in total, Know these
 - Follicle stimulating
 - Stimulates eggs / sperm
 - Luteinizing

- Stimulates ovulation, secretion of estrogen, progesterone
- Stimulates cells of testes to secrete testosterone
- **Thyroid stimulating hormone (TSH)**
 - Stimulates growth of thyroid gland
 - Secretion of thyroid hormone - Metabolism!
- ***Growth Hormone (GH)**
 - Most secreted by anterior pituitary
 - Widespread targets - bone, cartilage, muscle, fat
 - Indirect & Direct effects
 - *Promotes tissue growth
- Posterior Pituitary
 - **Oxytocin (OT)**
 - Stimulates uterus contractions
 - Muscles of lactation
 - **Antidiuretic hormone (ADH)**
 - *Acts on kidneys
 - ↑ water retention, ↑ solute concentration, ↓ urine volume
 - Vasopressin
 - Vasoconstriction – of peripheral bv, can ↑ bp

Pineal

- Location: roof of 3rd and 4th ventricle of the brain
- Hormone:
 - **Serotonin (day)** – mood
 - **Melatonin (night)** – biological clock

Thymus

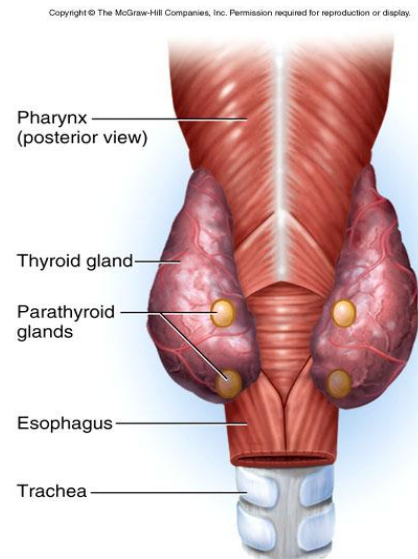
- Location – in mediastinum
- Hormone:
 - **Thymosins** – regulate the development and activation of T lymphocytes

Thyroid

- Largest endocrine gland
- Surrounds trachea
- Hormones
 - **Thyroxin** – helps regulate metabolism
 - Secreted in response to TSH from pituitary
 - Helps with growth/repair of tissue
 - **Calcitonin**
 - Regulates blood Ca⁺ levels
 - Works with parathyroid
 - Stimulates osteoblasts

Parathyroid

- Hormones
 - ***Parathyroid hormone (PTH)**
 - Works with thyroid to regulate blood Ca⁺ levels



- Secreted when blood Ca^{+} ↓, stimulates Ca^{+} absorption, indirectly stimulates osteoclasts
- **Calcitonin** stimulates calcium salt deposit in bone
 - Calcitonin ↑ blood Ca^{2+} levels trigger the thyroid to release calcitonin

Adrenal

- Hormones
 - From Adrenal Medulla
 - **Epinephrine (EPI) (85%)**
 - **Norepinephrine**
 - Both work to mobilizes glucose, inhibits insulin, decreases activity of GI
 - From Adrenal Cortex
 - **Alosterone** – acts on kidney to maintain electrolyte balance
 - **Cortisol** – Helps body adapt to stress and repair damaged tissues, stimulates fat/protein metabolism, anti-inflammatory effects.

Pancreas (85%)

- Hormones
 - **Insulin**
 - Secreted after eating, ↑ blood glucose
 - Stimulates glucose absorption
 - Stimulates muscle & fat cells to store (& liver)
 - **Glucagon**
 - Secreted when blood glucose ↓
 - Stimulates release of glucose into blood

Gonads

- Ovary
 - Hormones
 - ***Estrogen**
 - Stimulates female repro development, regulates menstrual cycle
 - ***Progesterone**
 - Regulates menstrual cycle, prepares mammary glands
- Testes
 - Hormones
 - ***Testosterone**
 - development of male reproductive system and physique
 - sustains sperm production and sex drive
 - **Estrogen**
 - Also secrete inhibin - suppresses FSH secretion which stabilizes sperm production rates

Stress and Adaptation

1. Stress- situation that upsets homeostasis
2. Mediated mostly by SNS and Endocrine system
3. General adaptation syndrome – way body reacts to stress (three stages)
 - a. **Alarm reaction**

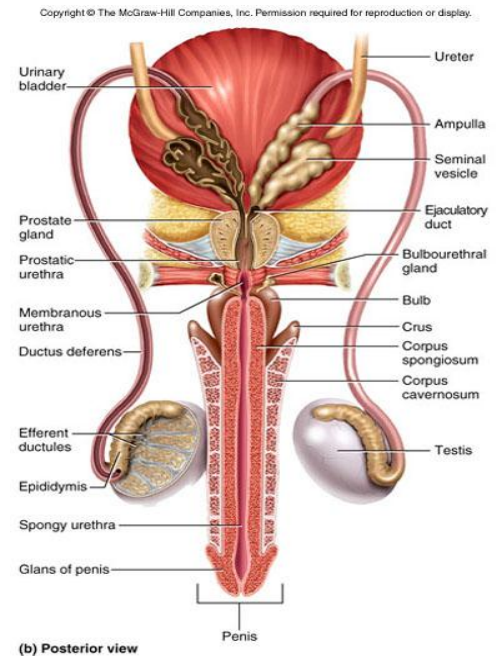
- i. Initial response, prepare body (Epi, Ne, hr up, bp up)
- b. Stage of resistance**
 - i. Glucose stores exhausted
 - ii. Body turns to alternate fuels (cortisol, pituitary secretions (stimulate fat metabolism))
- c. Stage of Exhaustion**
 - i. Occurs after very long term stress
 - ii. Fat stores exhausted, body turns to protein
 - iii. Effects
 1. Muscle breakdown, weakness
 2. Alkalosis, hypokalemia
 3. Tissue death

Reproduction

- Primary sex organs
 - Gonads (testes or ovaries)
 - Produce gametes
- Gametes
 - Sex cells (sperm, egg)
 - Secrete sex hormones
 - Complete development - initiate zygote/reproduction

Testes – primary sex organs (produce sperm)

- Seminiferous tubules
 - Tightly coiled
 - “sperm factories”
- Interstitial Cells
 - Produce testosterone
- Scrotum
 - Pouch holding testes
 - Divided into 2 compartments by median septum
 - Spermatic cord travels up from the scrotum to pass through inguinal canal
- Route of sperm
 - Efferent ductules
 - 12 small ciliated ducts collecting sperm from rete testes and transporting it to epididymis
 - Epididymis
 - 6 m long coiled duct adhering to posterior of testis
 - site of sperm maturation and storage
 - Ductus deferens



- muscular tube 45 cm long passing up from scrotum through inguinal canal to posterior surface of bladder
 - Ejaculatory duct
 - 2 cm duct formed from ductus deferens and seminal vesicle and passing through prostate to empty into urethra
 - Male Urethra
 - Longer in male
 - Carries sperm and urine (at different times)
1. Accessory Glands
 2. Seminal Vesicles (2)
 - a. 60% of the semen comes from seminal vesicle (transport medium)
 - b. Function : secrete fluid, activate sperm, provide fluid as a transport medium
 3. Prostate Gland
 - a. Secretes fluid that activates sperm
 - b. More acidic, kills bacteria and unwanted things
 - c. 30% of the semen
 4. Bulbourethral glands
 - a. Near bulb of penis
 - b. Thick, mucus fluid
 - c. Fluid neutralizes acidic urine in urethra
 - d. Empties into penile urethra
 - e. Lubricates
- 1) Spermatogenesis – sperm production
 - a. Process starts at an early age, but process does not complete itself until the hormones needed
 - 2) Semen – mixture of sperm and accessory gland secretions
 - a. Milky white
 - b. Contains substances that suppress woman's immune system

Female Reproductive System

Primary Organ: Ovary

- Tunica Albuniginea
 - External, fibrous covering
- Cortex
 - Outer region - houses gametes
- Medulla
 - Inner region - blood vessels, nerves
- Follicles**
 - Small, sac-like structures
 - Contain oocytes (immature egg)

Named at different times based on external structure (primary, secondary, vesicular)

Uterine Tubes

Infundibulum

Open, funnel shaped structure inferior to ampulla

Fimbriae

- Ciliated finger-like projections off of Infundibulum - drape over ovary

Cervix: outlet into Vagina

Uterine Wall

- 1) Perimetrium – outermost layer
- 2) Myometrium
 - a. Middle smooth muscular layer
 - b. Produce labor contractions
 - i. Very thick layer
- 3) Endometrium
 - a. Innermost layer
 - b. If egg fertilized, it will implant here.

Vagina

- 1) Distensible muscular tube
 - a. Discharge of menstrual fluid, receipt of penis, birth canal
 - b. Three layers of wall
 - c. Tilted posteriorly between rectum and urethra

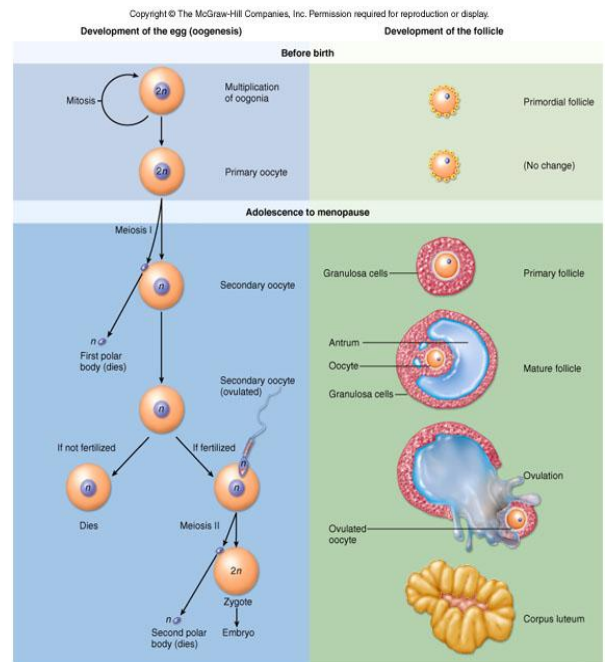
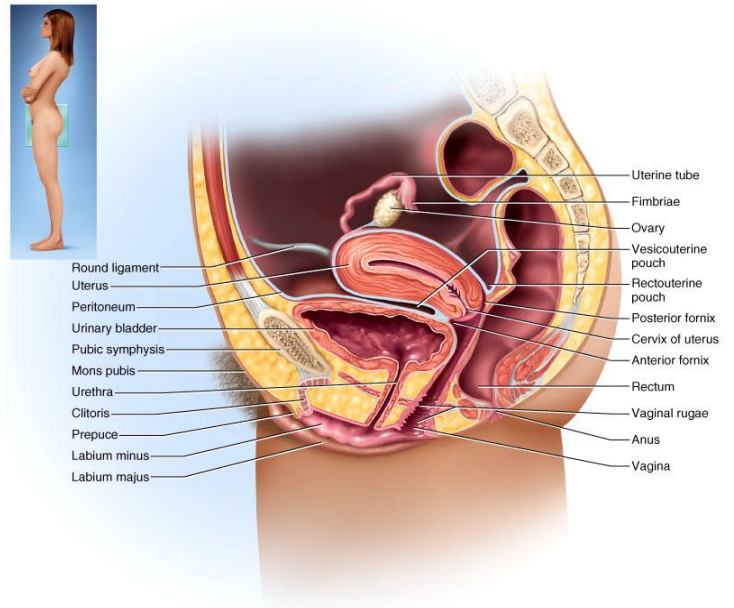
Mammary Glands

Present in both sexes, normally only functional in females

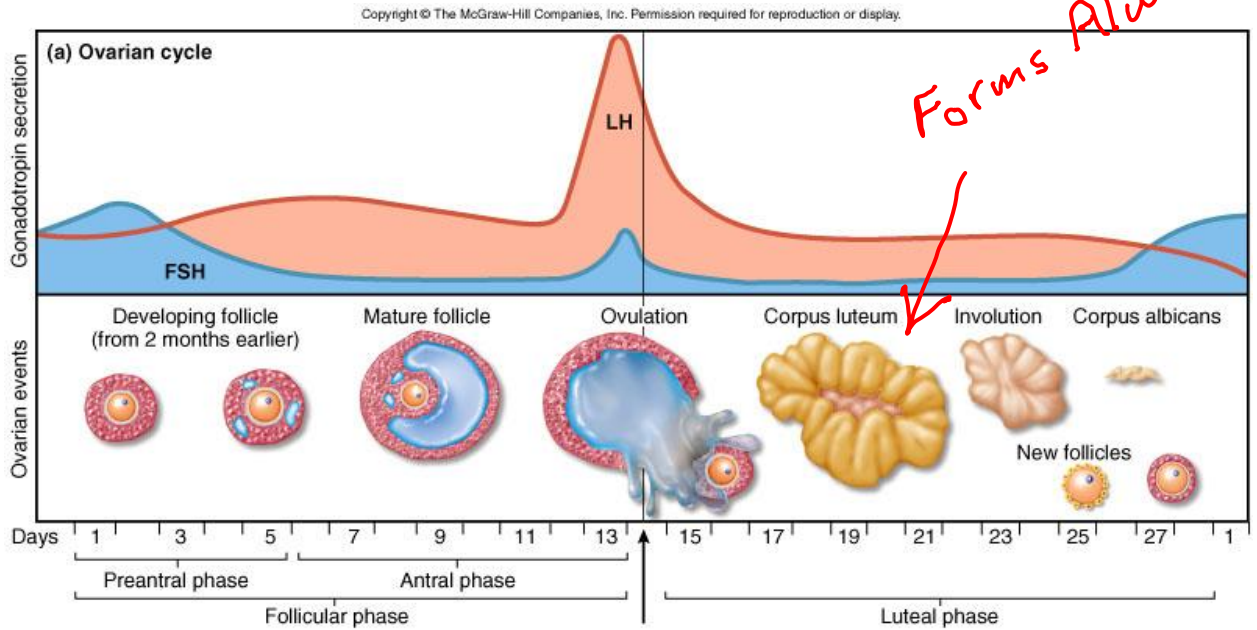
Structure: modified sweat glands

Oogenesis : production of female sex eggs: **occurs in the ovary**

- 1) Monthly event of production/maturation of egg
- 2) Males - gamete production begins at puberty, continues throughout life
- 3) Females -
 - a. Total supply of eggs determined by birth
 - b. Released only from puberty until menopause
 - c. Takes years to complete



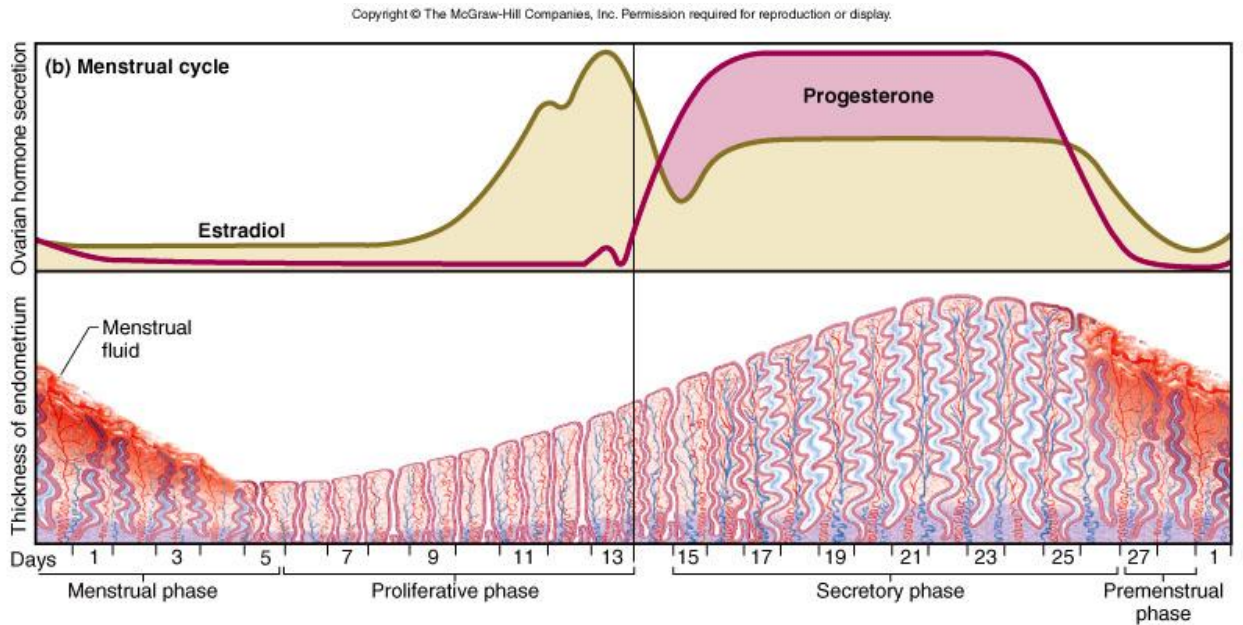
Sexual Cycle



Sex hormones are secreted from the Anterior Pituitary Gland

Onset of puberty in females triggered by message from adipose tissue

Menstrual Cycle –



END OF TESTABLE INFORMATION