

Ministry of Higher Education and Scientific Research  
Technical Education Commission  
Department of Nursing  
First stage

# PHYSIOLOGY



( 1) week

## COMPOSITION AND FUNCTION OF THE BLOOD

### **FUNCTIONS:**

1. Transports oxygen and nutrients to cells
2. Removes carbon dioxide and wastes from cells
3. Immunity (protects from disease)
4. Temperature regulation (cold, constricts; hot, dilates)
5. Helps prevent loss of blood by clotting
6. Transports hormones
7. Erection of the penis

### **COMPONENTS OF CIRCULATORY SYSTEM**

1. Blood
2. Heart
3. Blood vessels (arteries, capillaries, veins)
4. Lymph and lymph vessels

### **1. BLOOD**

Blood is not an epithelial tissue, and it's not loose or dense connective tissue; it's classified as a "special connective tissue". You have about 5 liters of blood, but that is only half of the body fluid. The other half includes fluid around each cell, and joint fluids, etc.

Blood consists of the following:

- A. Plasma
- B. Red blood cells
- C. White blood cells
- D. Platelets

### **A. PLASMA**

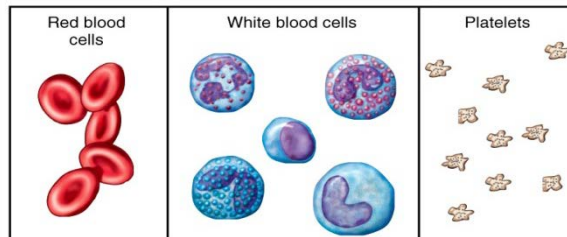
Plasma is what the blood cells float around in. If you spin a blood sample in a test tube, the red blood cells sink to the bottom, and you'll see the yellow plasma on top. Some people who need blood just need the packed RBCs, others need the plasma, and some need whole blood,

which is both plasma and RBCs. The plasma also carries around the platelets and some white blood cells.



### PLASMA CONTENTS

1. Water (90%)
2. Dissolved substances (10%)
  - a. Proteins
    - i. Antibodies
    - ii. Clotting factors
    - iii. Lipoproteins (move fats through blood: HDL, LDL)
  - b. Nutrients
    - i. Glucose (main energy source)
    - ii. Amino Acids (builds proteins)
  - c. Wastes (urea)
  - d. Gases (O<sub>2</sub>, CO<sub>2</sub>, Nitrogen)
  - e. Electrolytes = ions (Na<sup>+</sup>, K<sup>+</sup>, Cl<sup>-</sup>, Ca<sup>++</sup>)



### RED BLOOD CELLS (ERYTHROCYTES)

**These are small red biconcave discs.** They are among the smallest cells in the body. There are about 5 million of them in each of us. Their structure is simple; like a doughnut with the hole not fully cut out.

- a. They have no nucleus
- b. Filled with a red pigment called **hemoglobin, which carries O<sub>2</sub> throughout the body**. Oxygenated Hb is bright red, deoxy Hb is dull red. Blood in the veins only looks blue because you are seeing the dull red color through a yellow fat layer in the skin and subdermal tissue.

- c. Average life span is 120 days. They are made in the red bone marrow, and **the old ones are destroyed in the spleen and liver**, and Hb is recycled. During your lifetime, about 250 billion of these cells are destroyed, and 250 billion are made.

**Blood volume**

is the volume of blood (both red blood cells and plasma) in the circulatory system of any individual.

A typical adult has a blood volume of approximately between 4.7 and 5 litres, with females generally having less blood volume than males. Blood volume is regulated by the kidneys.

Blood volume (BV) can be calculated given the hematocrit (HC; the fraction of blood that is red blood cells) and plasma volume (PV):

$$BV = \frac{PV}{1 - HC}$$

Diagnostic technologies are commercially available to measure human blood volume. A recent radionucleotide study called BVA-100, Blood Volume Analysis is the only FDA approved instrument that provides a measure of Red Blood Cells and Plasma with 98% accuracy.

Blood volume measurement is indicated for the diagnosis and treatment patients suffering from Congestive Heart Failure, Chronic hypertension, Renal Failure and Critical Care.

Normal red blood cells values at various ages are:

- **Newborns: 4.8 - 7.2 million**
- **Adults: (males): 4.6 - 6.0 million**
- **(Females): 4.2-5.0 million**
- **Pregnancy: slightly lower than normal adult values**
- **Children: 3.8 – 5.5 million**

## **Red Cell Production**

- † Erythropoiesis is the production of red blood cells. After birth, red cells are produced in the red bone marrow. Until age 5 years, almost all bones produce red cells to meet growth needs. After this period, bone marrow activity gradually declines.
- † After 20 years of age, red cell production takes place mainly in the membranous bones of the vertebrae, sternum, ribs, and pelvis. With this reduction in activity, the red bone marrow is replaced with fatty yellow bone marrow.
- † Erythropoiesis is governed for the most part by tissue oxygen needs. Any condition that causes a decrease in the amount of oxygen that is transported in the blood produces an increase in red cell production. The oxygen content of the blood does not act directly on the bone marrow to stimulate red blood cell production. Instead, the decreased oxygen content is sensed by the kidneys, which then produce a hormone called *erythropoietin*.
- † Normally, the kidneys produce approximately 90% of erythropoietin, with the remaining 10% being released by the liver. In the absence of erythropoietin, as in kidney failure, hypoxia has little or no effect on red blood cell production.

## **Red Cell Destruction**

- † Mature red blood cells have a life span of approximately 4 months or 120 days. As the red blood cell ages, a number of changes occur. Metabolic activity in the cell decreases, and enzyme activity decreases; adenosine triphosphate (ATP) decreases, and the cell membrane becomes more fragile. Once the red cell membrane becomes fragile, the cell ruptures during passage through narrowed places in the circulation.
- † The destruction of red blood cells is facilitated by a group of large phagocytic cells found in the spleen, liver, bone marrow, and lymph nodes. These phagocytic cells ingest the hemoglobin from the ruptured cells and break it down in a series of enzymatic reactions. During these reactions, the amino acids from the globulin chains and

iron from the heme units are salvaged and reused. The bulk of the heme unit is converted to bilirubin, the pigment of bile, which is insoluble in plasma and attaches to the plasma proteins for transport.

- † Bilirubin is removed from the blood by the liver and conjugated with glucuronide to render it water soluble so that it can be excreted in the bile. The plasma-insoluble form of bilirubin is referred to as *unconjugated bilirubin*; the water-soluble form is referred to as *conjugated bilirubin*.

### **Catabolism of Hemoglobin**

When old red blood cells are destroyed in the tissue macrophage system, the globin portion of the hemoglobin molecule is split off, and the heme is converted to biliverdin. The enzyme involved is a subtype of heme oxygenase . and CO is formed in the process. CO may be an intercellular messenger, like NO .

In humans, most of the biliverdin is converted to bilirubin and excreted in the bile . The iron from the heme is reused for hemoglobin synthesis.

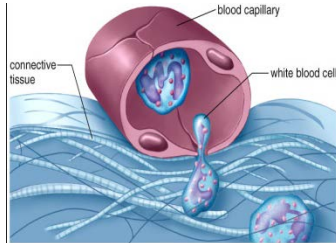
Exposure of the skin to white light converts bilirubin to lumirubin, which has a shorter half-life than bilirubin.

Phototherapy (exposure to light) is of value in treating infants with jaundice due to hemolysis. Iron is essential for hemoglobin synthesis; if blood is lost from the body and the iron deficiency is not corrected, iron deficiency anemia results.

(2 )Week

## WHITE BLOOD CELLS (LEUKOCYTES)

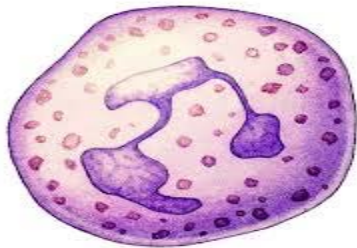
There are different kinds; **all fight infection**. They seep out of the blood vessels whenever they sense bacteria nearby.



The immune system is a complex network of cells, tissues and organs working together to defend the body against foreign invaders. The workhorse cells of the immune system are the white blood cells (WBC). They consist of both specific and non-specific defense cells that have the capability of recognizing self vs. non-self cells and microbes. The many different types of white blood cells can be found maturing in the lymph nodes and bone marrow, or traveling the bloodstream in search of potentially harmful outside organisms.

### **Neutrophils**

Neutrophils are non-specific immune cells and comprise approximately 55 to 70 percent of the total white blood cells. Neutrophils are the first line of defense against invading antigens and are first to arrive at the site of infection or injury. Chemical signals released by damaged cells attract neutrophils, which stick to blood vessel walls and engulf any foreign particles before they enter the bloodstream. Neutrophils are short lived and self-destruct after engulfing harmful antigens.





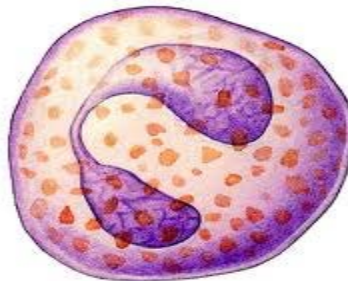
## **Monocytes**

Monocytes comprise 2 to 8 percent of the total population of circulating white blood cells. Monocytes originate in the bone marrow and develop into large macrophages in the bloodstream. Macrophages are the largest of the white blood cells and are responsible for engulfing cell debris, waste and harmful bacteria. Macrophages attack microbes by extending pseudopodia (feet-like extensions) around the cells and then destroy the microbe by releasing enzymes from inside the macrophage.



## **Eosinophils**

Sometimes referred to as acidophils, eosinophils defend the body against multicellular parasites and moderate allergic reactions. Eosinophils develop in the bone marrow before migrating out into the bloodstream. Eosinophils combat foreign parasites and particles by releasing chemical mediators in a process called degranulation. During degranulation, small granules inside the eosinophils are released to destroy the foreign invaders. These harmful chemicals are reactive proteins such as peroxides, nucleases and lipases.

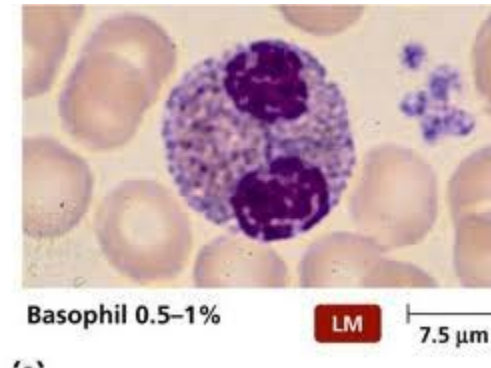


## **Basophils**

Comprising less than 1 percent of the total white blood cell count, basophils play an integral role in promoting blood flow and preventing coagulation. Basophils circulate the bloodstream and release two important chemicals at the tissue site: heparin and histamine. Heparin is an [anti-coagulant](#) that prevents blood cells from clotting too quickly and histamine is a vasodilator

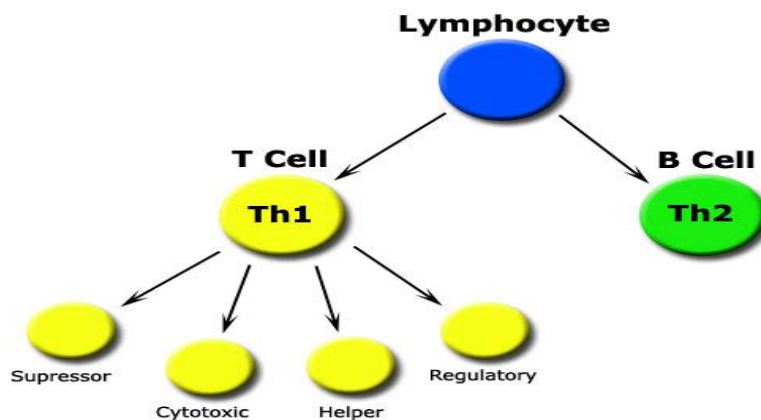


commonly released during allergic reactions to increase blood flow. These two molecules work together to quickly increase the availability of other immune system cells at the site of infection or inflammation.



## Lymphocytes

Lymphocytes refer to a group of cells consisting of B cells, T cell and natural killer (NK) cells, which comprise 25 to 33 percent of the total white blood cell count. B cells and T cells are the major components of the body's adaptive immunity. The B cells are primarily responsible for producing antibodies against foreign particles, which remember and specifically bind to foreign particles more quickly to be presented to and destroyed by T cells. T cells serve many functions but primarily are involved in destroying cells identified by antibodies. NK cells are not as specific as T cells but also function in destroying cells by releasing granules, like eosinophils. All three cells work together too quickly and efficiently rid the body of harmful, invading particles but are also implicated in autoimmune disorders in which the immune cells attack cells of the human body.



### (3) Weeks

#### A. PLATELETS

When a platelet encounters a broken blood vessel it releases a substance that clots blood. **Platelets are responsible for clot formation.**

**HEMOPHILIA** is a hereditary disease of males, where they are unable to clot properly. When they get even a slight bump or bruise they have to have an intravenous infusion of clotting factors or they will bleed to death. This is probably the disease that was in the genes of Henry VIII, which caused all of his male children to become weak and die in infancy.

Platelet production is regulated by :

1. **colony- stimulating factors** that control the production of megakaryocytes.
2. **thrombopoietin**, a circulating protein factor. This factor, which facilitates megakaryocyte maturation

#### **Thrombocytopenic purpura**

When the platelet count is low, clot retraction is deficient and there is poor constriction of ruptured vessels. The resulting clinical syndrome (thrombocytopenic purpura) is characterized by easy bruisability and multiple subcutaneous hemorrhages. Purpura may also occur when the platelet count is normal, and in some of these cases, the circulating platelets are abnormal (thrombasthenic purpura). Individuals with thrombocytosis (increased number of platelets) are predisposed to thrombotic events

#### **Hemostasis (stoppage of blood flow after damage)**

Steps of hemostasis:

1. Vascular spasms (vasoconstriction at injured site)
2. Platelet plug formation (plugging the hole)
3. Coagulation (blood clotting - complex mechanism)

**Vascular Spasms:** first response to vascular injury - vasoconstriction is stimulated by:

- a. compression of vessel by escaping blood
- b. injury "chemicals" released by injured cells
- c. reflexes from adjacent pain receptors

#### **Formation of a Platelet Plug**

1. damage to endothelium of vessel
2. platelets become spiky and sticky in response
3. platelets attach to damaged vessel wall to plug it
4. platelets produce thromboxane A<sub>2</sub> - granule release

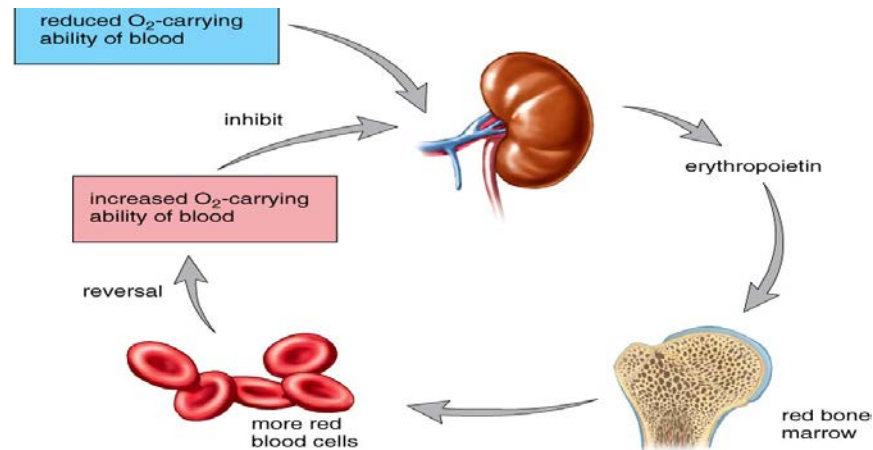
5. serotonin release enhances vascular spasm
6. ADP - attracts and stimulates platelets at site
7. prostacyclin - inhibits aggregation at other sites

Platelet aggregation: When a blood vessel wall is injured, platelets adhere to the exposed collagen and von Willebrand factor in the wall via the receptors on the platelet membrane. Binding produces platelet activations which release the contents of their granules. The released ADP acts on the ADP receptors in the platelet membranes to produce further accumulation of more platelets

### **BONE MARROW**

Most blood cells mature in the red bone marrow. When they are mature, they are released into the bloodstream. When they are old, they are destroyed in the spleen.

#### ( 4) Weeks



### Anemia

- † Anemia is defined as an abnormally low hemoglobin level, number of circulating red blood cells, or both, resulting in diminished oxygen-carrying capacity of the blood. Anemia usually results from excessive loss (*i.e.*, bleeding) or destruction (*i.e.*, hemolysis) of red blood cells or from deficient red blood cell production because of a lack of nutritional elements or bone marrow failure.
- † Anemia is not a disease, but an indication of some disease process or alteration in body function. The manifestations of anemia can be grouped into three categories: (1) impaired oxygen transport and recruitment of compensatory mechanisms; (2) alterations in hemoglobin levels and red cell number and appearance; and (3) signs and symptoms associated with the pathologic process that is causing the anemia.
- † Manifestations of anemia are caused by the decreased presence of hemoglobin in the blood (pallor), tissue hypoxia due to deficient oxygen transport (weakness and fatigue), and recruitment of compensatory mechanisms (tachycardia and palpitations) designed to increase oxygen delivery to the tissues.

### Blood Loss Anemia

- † With anemia caused by bleeding, iron and other components of the erythrocyte are lost from the body. Blood loss may be acute or chronic.

- ‡ Acute blood loss is accompanied by a loss of vascular volume and carries with it a risk of hypovolemia and shock. The red cells are normal in size and color. Hemodilution caused by movement of fluid into the vascular compartment produces a fall in red blood cell count, hemoglobin, and hematocrit.
- ‡ The hypoxia that results from blood loss stimulates red cell production by the bone marrow. If the bleeding is controlled and sufficient iron stores are available, the red cell concentration returns to normal within 3 to 4 weeks.
- ‡ Chronic blood loss does not affect blood volume but instead leads to iron-deficiency anemia when iron stores are depleted. Because of compensatory mechanisms, patients commonly have no symptoms until the hemoglobin level is less than 8 g/dL. The red cells that are produced have too little hemoglobin, giving rise to microcytic hypochromic anemia.

### **Hemolytic Anemia**

- ‡ Hemolytic anemia is characterized by the (1) premature destruction of red cells, (2) retention in the body of iron and the other products of hemoglobin destruction, and (3) marked increase in erythropoiesis within the bone marrow.
- ‡ Because of the red blood cell's shortened life span, the bone marrow usually is hyperactive, resulting in an increase in the number of reticulocytes in the circulating blood. As with other types of anemias, the person experiences easy fatigability, dyspnea, and other signs and symptoms of impaired oxygen transport. The person may also have an increase in serum bilirubin and mild jaundice.

### **Sickle Cell Disease (Anemia)**

- ‡ Persons with sickle cell disease experience problems associated with severe hemolytic anemia, chronic hyperbilirubinemia, and vaso-occlusion. Chronic hemolysis produces rather severe anemia, with hematocrit levels ranging from 18% to 30%.
- ‡ Vaso-occlusion accounts for the most severe complications of sickle cell disease. An acute pain episode results from vessel occlusion and can affect almost any part of the body. Common sites obstructed by sickled cells include the abdomen, chest, bones, and joints. Multiple areas are frequently involved simultaneously,

### **Thalassemias**

- ‡ In contrast to sickle cell anemia, the thalassemias result from absent or defective synthesis of the  $\alpha$  or the  $\beta$  chains of hemoglobin. The  $\beta$ -thalassemias represent a defect in  $\beta$ -chain synthesis, and the  $\alpha$ -thalassemias represent a defect in  $\alpha$ -chain synthesis.
- ‡ The defect is inherited as a mendelian trait, and a person may be heterozygous for the trait and have a mild form of the disease or be homozygous and have the severe form of the disease.

### **Anemias of Deficient Red Cell Production**

Anemia may result from the decreased production of erythrocytes by the bone marrow. A deficiency of nutrients for hemoglobin synthesis (iron) or DNA synthesis (cobalamin or folic acid) may reduce red cell production by the bone marrow.

### **Iron-Deficiency Anemia**

- ‡ Iron deficiency is a common worldwide cause of anemia affecting persons of all ages. The anemia results from dietary deficiency, loss of iron through bleeding, or increased demands. Because iron is a component of heme, a deficiency leads to decreased hemoglobin synthesis and consequent impairment of oxygen delivery.
- ‡ Iron balance is maintained by the absorption of 0.5 to 1.5 mg daily to replace the 1 mg lost in the feces.
- ‡ The usual reason for iron deficiency in adults is chronic blood loss because iron cannot be recycled to the pool. In men and postmenopausal women, blood loss may occur from gastrointestinal bleeding because of peptic ulcer, intestinal polyps, hemorrhoids, or cancer. Excessive aspirin intake may cause undetected gastrointestinal bleeding.
- ‡ The manifestations of iron-deficiency anemia are related to lack of hemoglobin and impaired oxygen transport. Depending on the severity of the anemia, fatigability, palpitations, dyspnea, angina, and tachycardia may occur.
- ‡ The treatment of iron-deficiency anemia is directed toward controlling chronic blood loss, increasing dietary intake of iron, and administering supplemental iron. Ferrous sulfate, which is the usual

oral replacement therapy, replenishes iron stores in several months.  
Parenteral iron (iron dextran) therapy

### **Cobalamin (Vitamin B12)-Deficiency Anemia**

- ‡ Vitamin B12 is found in all foods of animal origin. Dietary deficiency is rare and usually found only in strict vegetarians who avoid all dairy products as well as meat and fish. It is absorbed by a unique process. After release from the animal protein, vitamin B12 is bound to intrinsic factor, a protein secreted by the gastric parietal cells
- ‡ An important cause of vitamin B12 deficiency is pernicious anemia, resulting from a hereditary atrophic gastritis.
- ‡ Other causes of vitamin B12 deficiency anemia include gastrectomy, ileal resection, & malabsorption syndromes in which vitamin B12 and other vitamin B compounds are poorly absorbed.

### **Aplastic Anemia**

- ‡ Aplastic anemia (*i.e.*, bone marrow depression) describes a primary condition of bone marrow stem cells that results in a reduction of all three hematopoietic cell lines—red blood cells, white blood cells, and platelets—with fatty replacement of bone marrow. Pure red cell aplasia, in which only the red cells are affected, rarely occurs.
- ‡ Anemia results from the failure of the marrow to replace senescent red cells that are destroyed and leave the circulation, although the cells that remain are of normal size and color. At the same time, because the leukocytes, particularly the neutrophils, and the thrombocytes have a short life span, a deficiency of these cells usually is apparent before the anemia becomes severe.
- ‡ Among the causes of aplastic anemia are exposure to high doses of radiation, chemicals, and toxins that suppress hematopoiesis directly, or through immune mechanisms. Chemotherapy and irradiation commonly result in bone marrow depression.

### **Chronic Disease Anemias**

- ‡ Anemia often occurs as a complication of chronic infections, inflammation, and cancer. Chronic diseases commonly associated with anemia include AIDS, osteomyelitis, rheumatoid arthritis, and Hodgkin's disease. It is theorized that the short life span, deficient red



cell production, and low serum iron are caused by actions of macrophages and lymphocytes in response to cell injury.

- ‡ Chronic renal failure almost always results in a normocytic, normochromic anemia, primarily because of a deficiency of erythropoietin. Uremic toxins also interfere with the actions of erythropoietin and red cell production.
- ‡ They also cause hemolysis and bleeding tendencies, which contribute to the anemia. Until recently, dialysis and red cell transfusions constituted the only therapy.

### **Polycythemia**

- ‡ Polycythemia is an abnormally high total red blood cell mass with a hematocrit greater than 54% in males and 51% in females. It is categorized as relative, primary, or secondary. In relative polycythemia, the hematocrit rises because of a loss of plasma volume without a corresponding decrease in red cells.
- ‡ This may occur with water deprivation, excess use of diuretics, or gastrointestinal losses. Relative polycythemia is corrected by increasing the vascular fluid volume.
- ‡ In polycythemia vera, the manifestations are related to an increase in the red cell count, hemoglobin level, and hematocrite with increased blood volume and viscosity. Commonly reported symptoms include headache, dizziness, and some difficulty with hearing and vision because of decreased cerebral blood flow. Hypertension is common, the result of an increase in blood viscosity.
- ‡ The goal of treatment in primary polycythemia is to reduce blood viscosity. This can be done by withdrawing blood by means of periodic phlebotomy to reduce red cell volume.

**LEUKEMIA:** Cancer of the blood is called leukemia. It actually only involves the white blood cells. Something goes wrong in one stem cell, and it starts making huge amounts of clones of itself which don't work right and not enough normal white blood cells are made. Therefore, the body cannot fight infection. There are many types of leukemias.

## **BLOOD TYPING: The ABO SYSTEM**

Blood typing is the technique for determining which specific protein type is present on RBCs.

Only certain types of blood transfusions are safe because the outer membranes of the red blood cells carry certain types of proteins that another person's body will think is a foreign body and reject it.

These proteins are called antigens (something that causes an allergic reaction). There are two types of blood antigens: Type A and Type B.

A person with Type A antigens on their blood cells have Type A blood.

A person with Type B antigens have Type B blood.

A person with both types has type AB blood.

A person with neither antigen has type O blood.



If a person with type A blood gets a transfusion of type B antigens (from Type B or Type AB), the donated blood will clump in masses (coagulation), and the person will die.

The same is true for a type B person getting type A or AB blood.

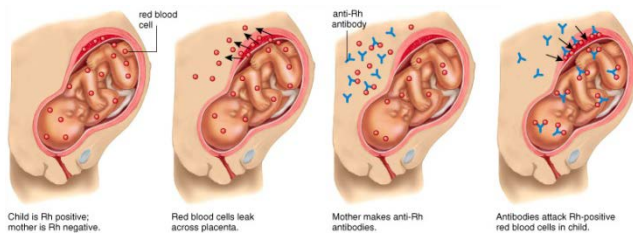
Type O blood is called the universal donor, because there are no antigens, so that blood can be donated to anyone. Type AB blood is considered the universal acceptor, because they can use any other type of blood. This blood type is fairly rare.

## **RH FACTOR**

There is another term that follows the blood type. The term is “positive” or “negative”. This refers to the presence of another type of protein, called the Rh factor. A person with type B blood and has the Rh factor is called B-positive.

A person with type B blood and no Rh factor is called B-negative.

The reason this is so important is that if an Rh- mother has an Rh+ fetus in her womb (from an Rh+ father), her antibodies will attack the red blood cells of the fetus because her body detects the Rh protein on the baby's red blood cells and thinks they are foreign objects. This is called Hemolytic Disease of the Newborn (HDN).



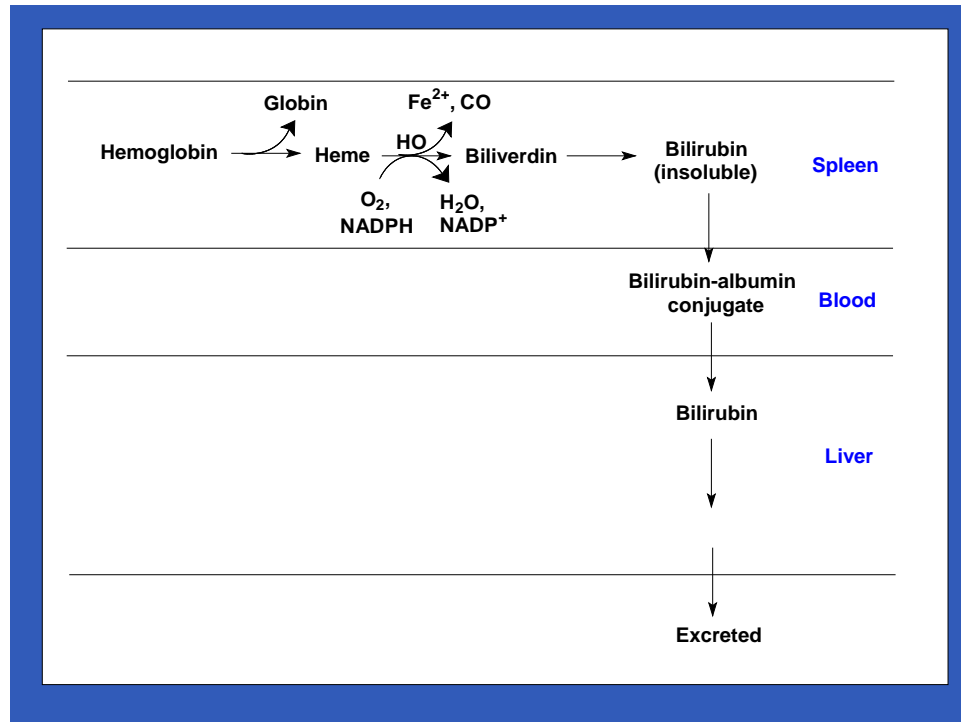
This can be prevented if the doctor knows the mother is Rh- and the father is Rh+, because that means the baby has a 50% chance of being Rh+ like the father. Therefore, anytime a mother is Rh-, they will ask if the father is Rh-. If so, they will give her an injection of a medicine that will prevent her immune system from attacking the baby.

( 5 ) weeks

### Bilirubin

- **Bilirubin** is a yellow breakdown product of normal heme catabolism. Its levels are elevated in certain diseases and it is responsible for the yellow colour of bruises and the brown colour of feces.
- Bilirubin reduction in the gut leads to a product called urobilinogen, which is excreted in urine.
- It is thought to be a toxin because it is associated with neonatal jaundice, possibly leading to irreversible brain damage due to neurotoxicity.
- Like these other pigments, bilirubin changes its conformation when exposed to light. This is used in the phototherapy of jaundiced newborns: the illuminated version of bilirubin is more soluble than the unilluminated version.

## Metabolism



- Erythrocytes (red blood cells) generated in the bone marrow are destroyed in the spleen when they get old or damaged. This releases hemoglobin, which is broken down to heme, as the globin parts are turned into amino acids.
- The heme is then turned into unconjugated bilirubin in the macrophages of the spleen.
- Bilirubin is bound to albumin and transported in plasma from the reticuloendothelial system to the liver, as unconjugated bilirubin.
- In the liver, bilirubin is made water soluble by hepatocytes which conjugate bilirubin with glucuronic acid to form conjugated bilirubin (BC). This process requires the enzyme uridine diphosphate-glucuronosyltransferase (UPD-GT) and produces bilirubin diglucuronide.
- BC is secreted from hepatocytes to the bile canaliculi of the liver and is transported from the liver via the gall bladder and common bile duct to the gastrointestinal tract.
- In the ileum and colon, bacteria converts bilirubin into stercobilinogen.

- Stercobilinogen is oxidized to stercobilin, which is excreted in the feces.
- While most bilirubin is excreted as stercobilin, a small amount of stercobilinogen is reabsorbed into the blood, modified by the kidneys, and excreted as urobilinogen in the urine.

### **Function**

- Bilirubin is created by the activity of biliverdin reductase on biliverdin. Bilirubin, when oxidized, reverts to become biliverdin once again. This cycle, in addition to the demonstration of the potent antioxidant activity of bilirubin, has led to the hypothesis that bilirubin's main physiologic role is as a **cellular antioxidant**.

### **Toxicity**

- Unconjugated hyperbilirubinaemia in the neonate can lead to accumulation of bilirubin in certain brain regions, a phenomenon known as kernicterus, with consequent irreversible damage to these areas manifesting as various neurological deficits, seizures, abnormal reflexes and eye movements.
- Aside from specific chronic medical conditions that may lead to hyperbilirubinaemia, neonates in general are at increased risk since they lack the intestinal bacteria that facilitate the breakdown and excretion of conjugated bilirubin in the feces (this is largely why the feces of a neonate are paler than those of an adult). Instead the conjugated bilirubin is converted back into the unconjugated form by the enzyme b-glucoronidase and a large proportion is reabsorbed through the enterohepatic circulation.

### **Benefits**

Reasonable levels of bilirubin can be beneficial to the organism. Evidence is accumulating that suggests bilirubin can protect tissues against oxidative damage caused by free radicals and other reactive oxygen species. Statistical analysis of people with high normal or slightly elevated bilirubin levels in blood shows that they have a lower risk of developing cardiovascular diseases

### **Jaundice:**

Jaundice may be noticeable in the sclera (white) of the eyes at levels of about 30-50  $\mu\text{mol/l}$ , and in the skin at higher levels. Jaundice is classified depending upon whether the bilirubin is free or conjugated to glucuronic acid into:

- *Conjugated jaundice*
- *Unconjugated jaundice*

Jaundice also can be classified into three categories, depending on which part of the physiological mechanism and the pathology affects. The three categories are:

- *Pre-hepatic: The pathology is occurring prior the liver*
- *Hepatic: The pathology is located within the liver*
- *Post-Hepatic: The pathology is located after the conjugation of bilirubin in the liver*

### **Pre-hepatic**

- **Pre-hepatic** jaundice is caused by anything which causes an increased rate of hemolysis (breakdown of red blood cells).
- In tropical countries, malaria can cause jaundice in this manner. Certain genetic diseases, such as sickle cell anemia, spherocytosis and glucose 6-phosphate dehydrogenase deficiency can lead to increased red cell lysis and therefore hemolytic jaundice. Commonly, diseases of the kidney, such as hemolytic uremic syndrome, can also lead to coloration. Defects in bilirubin metabolism also present as jaundice. Jaundice usually comes with high fevers.

### **Hepatic**

- **Hepatic** jaundice causes include acute hepatitis, hepatotoxicity and alcoholic liver disease, whereby cell necrosis reduces the liver's ability to metabolise and excrete bilirubin leading to a buildup in the blood.
- Less common causes include primary biliary cirrhosis, Gilbert's syndrome (a genetic disorder of bilirubin metabolism which can result in mild jaundice, which is found in about 5% of the population) and metastatic carcinoma.
- Jaundice seen in the newborn, known as neonatal jaundice, is common, occurring in almost every newborn as hepatic machinery for

the conjugation and excretion of bilirubin does not fully mature until approximately two weeks of age.

### **Post-hepatic**

- **Post-hepatic** jaundice, also called obstructive jaundice, is caused by an interruption to the drainage of bile in the biliary system.
- The most common causes are **gallstones** in the common bile duct, and pancreatic cancer in the head of the pancreas. Also, a group of **parasites** known as "liver flukes" live in the common bile duct, causing obstructive jaundice. Other causes include strictures of the common bile duct, biliary atresia, ductal carcinoma, pancreatitis and pancreatic pseudocysts. A rare cause of obstructive jaundice is Mirizzi's syndrome.
- The presence of pale stools and dark urine suggests an obstructive or post-hepatic cause as normal feces get their color from bile pigments.
- Patients also can present with elevated serum cholesterol, and often complain of severe itching or "pruritus".



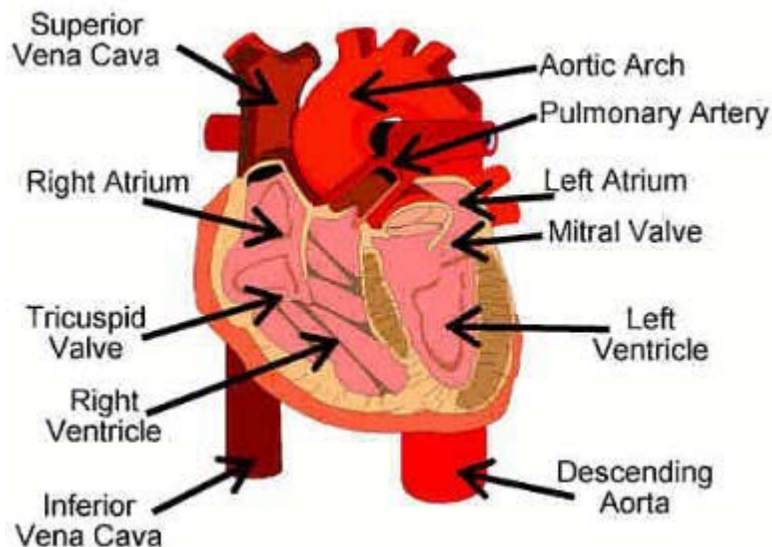
( 6 – 7 ) Weeks

### **The cardiovascular system**

The cardiovascular system is one of the major body systems. It transports oxygen, carbon dioxide, waste products, nutrients and hormones to and from various parts of the body. The cardiovascular system is made up of the heart, the blood vessels (arteries and veins and capillaries) and blood. The heart has major vessels that supply it with deoxygenated blood (travels back to the heart from the body), and major vessels that carry oxygenated blood away from the heart to all the parts of the body.

The major vessels that carry blood to and from the heart are:

- inferior vena cava conveys deoxygenated blood (blood low in oxygen) from the lower extremities of the body to the heart
- superior vena cava conveys deoxygenated blood from the upper extremities of the body to the heart
- aorta conveys oxygenated blood (blood high in oxygen) away from the heart



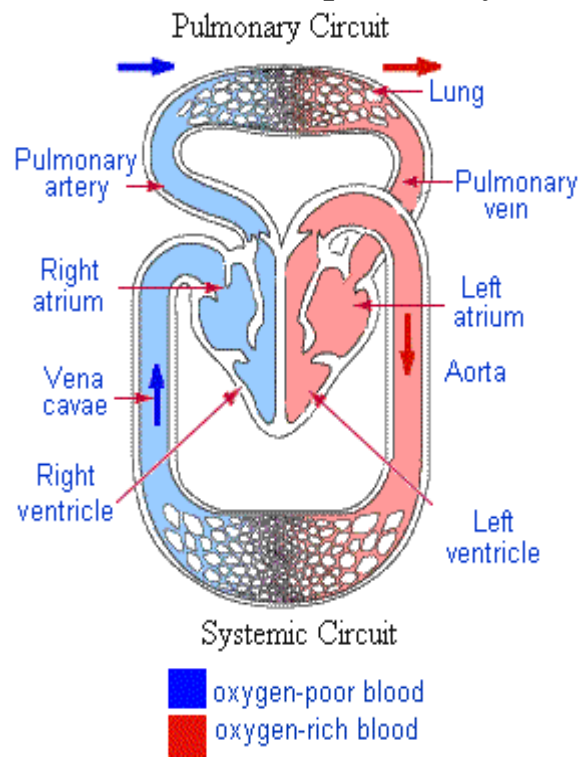
#### **The heart**

The heart is a muscular organ enclosed in a fibrous sac (the pericardium). The pericardial sac contains watery fluid that acts as a lubricant as the heart moves within the sac. The wall of the heart is composed of cardiac muscle cells, termed the myocardium. The inner surface of the wall

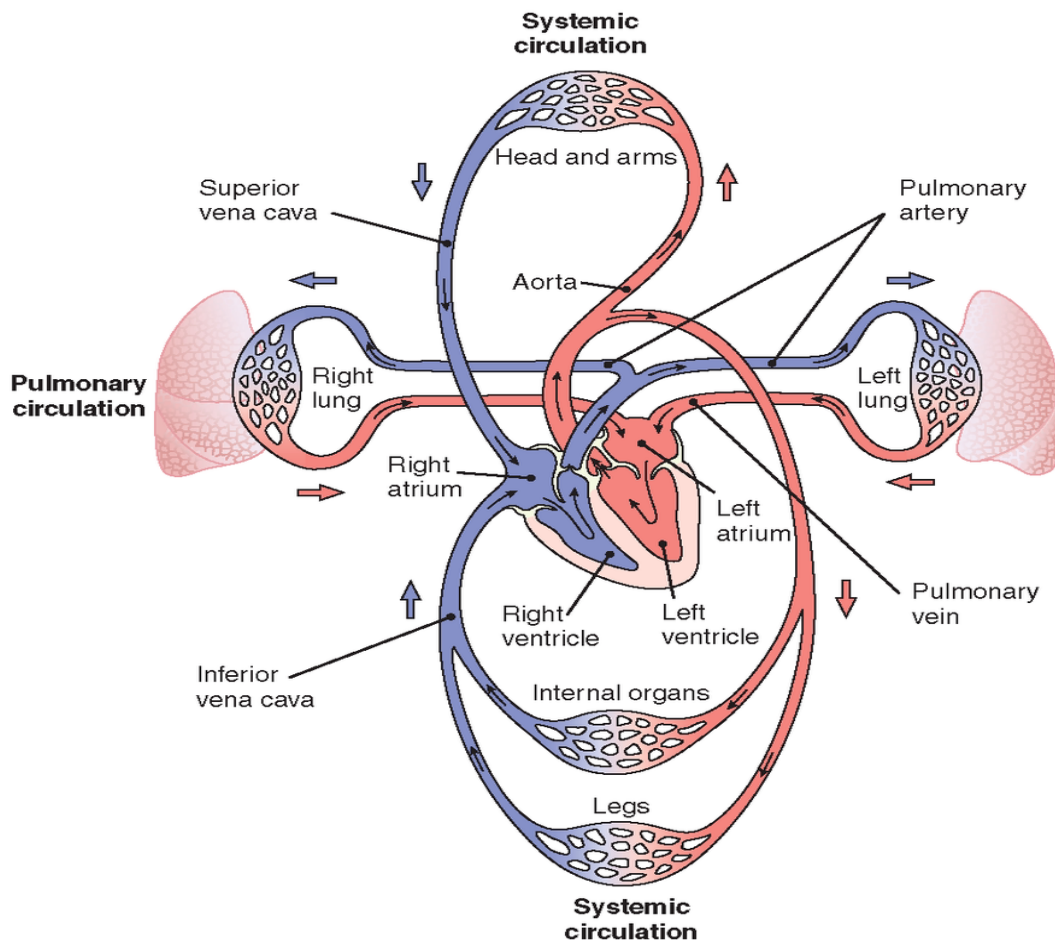
is lined by a thin layer of endothelial cell; the endothelium. The heart is actually two separate pumps; a right heart which pumps blood through the pulmonary artery into the lung, and a left heart which pumps blood through the aorta into the peripheral organ. Each of these two pumps consists of two chambers, an atrium and a ventricle, separated by atrioventricular valve (left; mitral valve and right; tricuspid valve). Blood exists from the right ventricle through the pulmonary valve to the pulmonary trunk, and from the left ventricle through the aortic valve into the aorta.

### **Pulmonary and Systemic Circulations**

Blood whose oxygen content has become partially depleted and carbon dioxide content has increased as a result of tissue metabolism returns to the right atrium. This blood then enters the ventricle, which pumps it into the pulmonary trunk and pulmonary arteries. The pulmonary arteries branch to transport blood to the lungs, where gas exchange occurs between the lung capillaries and the alveoli of the lungs. Oxygen diffuses from the air to the capillary blood; while carbon dioxide diffuses in the opposite direction. The blood that returns to the left atrium by way of the pulmonary veins is therefore enriched in oxygen and partially depleted of carbon dioxide. The blood that is ejected from the right ventricle to the lungs and back to the left atrium completes one circuit: called **the pulmonary circulation**.



Oxygen-rich blood in the left atrium enters the left ventricle and is pumped into a very large, elastic artery; the aorta. The aorta ascends for a short distance, makes a U-turn, and then descends through the thoracic and abdominal cavities. Arterial branches from the aorta supply oxygen-rich blood to all of the organ systems and are thus part of the systemic circulation. As a result of cellular respiration, the oxygen concentration is lower and the carbon dioxide concentration is higher in the tissues than in the capillary blood. Blood that drains into the systemic veins is thus partially depleted of oxygen and increased in carbon dioxide content. These veins empty into two large veins; the superior and inferior venae cavae that return the oxygen-poor blood to the right atrium. This completes **the systemic circulation**; from the heart (left ventricle), through the organ systems, and back to the heart (right atrium)



### Cardiac cycle

The cardiac events that occur from the beginning of one heartbeat to the beginning of the next are called the cardiac cycle. Each cycle is initiated by spontaneous generation of an action potential in the sinus node which

travels rapidly through both atria and then through the A-V bundle into the ventricles.

Because of this special arrangement of the conducting system from the atria into the ventricles, there is a delay of more than 0.1 second during passage of the cardiac impulse from the atria into the ventricles. This allows the atria to contract, pumping blood into the ventricles before the strong ventricular contraction begins. Thus, the atria act as primer pumps for the ventricles, and the ventricles in turn provide the major source of power for moving blood through the body's vascular system.

In a normal heart, cardiac activity is repeated in a regular cycle. At a normal heart rate of about 72 beats/minute; for the atria, the cycle lasts for about 0.15 second in systole and 0.65 second in diastole. For the ventricles, the duration of each cardiac cycle lasts about 0.8 second. If the heart rate increases, the diastole decreases, which means that the heart beating very fast may not remain relaxed long enough to allow complete filling of the ventricles before the next contraction.

For the ventricles, the two major phases of the cardiac cycle are:

- The diastole; a period of ventricular relaxation in which the ventricles fill with blood and it last for about 0.5 second.
- The systole; a period of ventricular contraction and blood ejection, lasting about 0.3 second.

### **The function of the heart valves**

The atrioventricular valves (AV valves) are composed of thin membranous cusps (fibrous flaps of tissue covered with endothelium), which hang down in the ventricular cavities during diastole. After atrial contraction and just before ventricular contraction, the AV valves begin to close and the leaflets (cusps) come together by means of backflow of the blood in the ventricles towards the atria.

The AV valves include:

- The mitral valve; the left AV valve; bicuspid valve, which consists of two cusps (anterior and posterior), located between left atrium and left ventricle.
- The tricuspid valve; the right AV valve, which consists of three cusps, located between right atrium and right ventricle.

The function of AV valves is to prevent backflow (prevent regurgitation; leakage) of blood into the atria during ventricular contraction. Normally they

allow blood to flow from the atrium to the ventricle but prevent backward flow from the ventricle to the atria. The atrioventricular valves contain and supported by papillary muscles.

The aortic and pulmonary valves each consist of three semilunar cusps that resemble pockets projecting into the lumen of aorta and pulmonary trunk. They contain no papillary muscle. During diastole the cusps of these valves become closely approximated to prevent regurgitation of blood from aorta and pulmonary arteries into the ventricles. During systole the cusps are open towards arterial wall, leaving a wide opening for ejection of blood from the ventricles. In other words, the pulmonary and aortic valves allow blood to flow into the arteries during ventricular contraction (systole) but prevent blood from moving in the opposite direction during ventricular relaxation (diastole).

\*All valves close and open passively. That is, they close when a backward pressure gradient pushes blood backward, and they open when a forward pressure gradient forces blood in the forward direction.

\*There are no valves at entrance of superior, inferior vena cava and pulmonary veins into the atria. What prevents the backflow of blood from the atria toward the veins is the compression of these veins by the atrial contraction. However little blood is ejected back into veins, this represents the venous pulse seen in the neck veins (jugular veins) when the atria contracting.

( 8) weeks

## **ELECTROCARDIOGRAM**

### **INTRODUCTION**

Both electrical activity and sound accompany the beating of the heart. The pattern of electrical activity produced by each heart beat cycle is called the electrocardiogram (ECG). The aim of this session is for students to record and analyze an ECG from a student volunteer and to examine the relationship between the ECG and the characteristic sounds of the heart.

The cardiac cycle involves a sequential contraction of the atria and the ventricles. The combined electrical activity of the different myocardial cells produces electrical currents that spread through the body fluids. These currents are large enough to be detected by recording electrodes placed on the skin. A typical regular pattern of peaks produced by each heart beat cycle can be shown below.

The components of the ECG can be correlated with the electrical activity of the atrial and ventricle muscle

### **Components of Normal ECG complex**

#### **P wave-**

Represents the spread of electrical activity (wave of negativity) over the atria after the initial depolarization of the SA node.

#### **QRS complex**

Represents the spread of the negativity wave (depolarization) through the ventricular musculature. A small amount of atrial repolarization also occurs at the same time.

#### **PR interval**

Time from the beginning of the P wave to the beginning of the QRS complex, interval between activation of the SA node and the beginning of ventricular depolarization. Any abnormal lengthening of this interval suggests some interference with conduction of the impulse through the atria, atria-ventricular (AV) node, bundle of His and Purkinje fibres.

### **T wave**

Represents the repolarization of the ventricular musculature. It is of longer duration and lower amplitude than the depolarization wave (QRS complex), which indicates that the ventricular repolarization process is less synchronized and slower than the depolarization process.

### **QT interval**

Represents the time from the beginning of the QRS complex to the end of the T wave that is from the beginning of ventricular depolarization to the end of ventricular repolarization. The QT interval varies with the heart rate, becoming shorter as the heart rate increases.

### **PR segment**

From the end of the P wave to the beginning of the QRS complex. During this time the impulse is travelling through the AV node, AV bundle and the Purkinje fibres. These structures are within the heart myocardium; therefore during this time there is no change in the negativity of the surface of the heart, and we say that the record is isoelectric (no change in potential is occurring).

### **ST segment**

From the end of the S wave to the beginning of the T wave. During this time the heart is completely depolarized, and therefore the record is isoelectric. The position and the shape of the ST segment are important in diagnosis.

### **Normal values for Duration and Voltage of Different Phases of ECG Complex**

<b>Phase of Complex</b>	<b>Duration (seconds)</b>	<b>Voltage (mV)</b>
<b>P wave</b>	0.1	0.2
<b>QRS complex (Lead II)</b>	0.08-0.12	1
<b>T wave</b>	0.16-0.27	0.2-0.3
<b>PR interval</b>	0.13-0.16	-
<b>QT interval</b>	0.3-0.34	-
<b>PR segment</b>	0.03-0.06	-
<b>ST segment</b>	0.08	-



The PR interval greater than 0.2 second is abnormal and indicates first degree heart block. In second degree heart block there are P waves that are not followed by QRS waves; this may occur regularly or irregularly. Third degree heart block is a complete AV dissociation in which P waves occur quite regularly but have no relation to R waves. The normal duration of the QRS complex is 0.08 to 0.12 sec. A duration of more than 0.12 sec indicates bundle branch block or that the beat has arisen in one of the ventricles-a so called ventricular beat or extra systole.

Variations in the T wave are quite numerous and require an expert cardiologist for proper diagnosis. Elevation of the ST segment by more than 2mm is associated with acute injury or anoxia.

### **Einthoven's Law**

Einthoven, the father of the electrocardiograph, originated many of the conventions used in the recording of ECG. He visualized the three standard limb leads as enclosing the heart in a triangle, often referred to as **Einthoven's triangle**. Einthoven also found a relationship between the amplitude of the QRS complexes in each lead, such that:

$$\text{Lead I and Lead III} = \text{Lead II} \\ (\text{Einthoven's Law}).$$

### **Bipolar standard limb leads (I, II, III):**

These leads record the differences between the potentials in 2 limbs, by applying electrodes usually at the wrist and ankle. The 3 standard bipolar limb leads include:

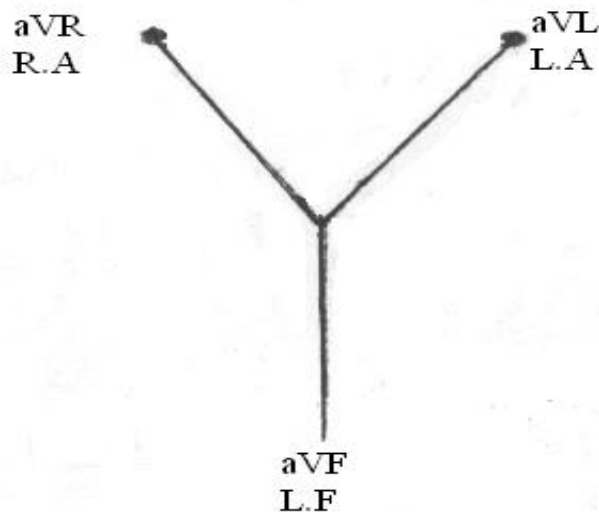
- Lead I: This records the difference between the potential in the left arm (LA) and that in the right arm (RA).
- Lead II: This records the difference between the potential in the right arm (RA) and that in the left leg (LL).
- Lead III: This records the difference between the potential in the left leg (LL) and that in the left arm (LA).

Einthoven's triangle: This is an equilateral triangle, the sides of which represent the 3 bipolar standard limb leads while the heart lies at its centre.

### **Unipolar limb leads (aVR, aVL, aVF):**

These measure the absolute (actual) potential at a certain point. This is carried out by applying one electrode from the electrocardiograph to the desired point (it is active, +ve or exploring electrode) while the other electrode represents a common reference point inside the instrument; it is the -ve electrode (0 potential) i.e. the unipolar leads measure the potential differences between active electrodes and zero potential.

They are augmented unipolar limb leads that have magnified amplitudes by about 50 % without any change in their configuration, so they are called aVR, aVL and aVF (a = augmented).



### **Unipolar chest leads:**

Unipolar leads (precordial or chest leads) record the absolute potential at 6 standard points on the anterior chest wall designated as V1 to V6, the locations of which are as follows:

- V1: At the right margin of the sternum in the 4th right intercostal space.
- V2: At the left margin of the sternum in the 4th left intercostal space.
- V3: Midway between V2 and V4.
- V4: At the left midclavicular line in the 5th intercostal space.
- V5: At the left anterior axillary line in the 5th intercostal space.
- V6: At the left midaxillary line in the 5th intercostal space.

The precordial leads look at the heart in a horizontal plane from the front & left sides. Leads V1 & V2 look at the right ventricle and reflect its activity, V3 & V4 look at the interventricular septum and reflect its activity, while leads V5 & V6 look at the left ventricle and reflect its activity.

### **Cardiac output**

The amount of blood the heart pumps through the circulatory system in a minute. The amount of blood put out by the left ventricle of the heart in one contraction is called the [stroke](#) volume. The stroke volume and the heart rate determine the cardiac output. A normal adult has a cardiac output of 4.7 liters (5 quarts) of blood per minute.

## **Heart Sounds**

When the stethoscope is placed on the chest wall over the heart, two sounds are normally heard during each cardiac cycle (1st & 2nd heart sounds). Heart sounds are associated with closure of the valves with their associated vibration of the flaps of the valves and the surrounding blood under the influence of the sudden pressure changes that develop across the valve. That is, heart sound does not produced by the opening of the valve because this opening is a slow developing process that makes no noise.

1-The first heart sound ( $S_1$ ): is caused by closure of the AV valves when ventricles contract at systole. The vibration is soft, low-pitched lub.

2-The second heart sound ( $S_2$ ): is caused by closure of the aortic and pulmonary valves when the ventricles relax at the beginning of diastole. The vibration is loud, high-pitched dup. It is rapid sound because these valves close rapidly and continue for only a short period i.e., rapid, short and of higher pitch dup.

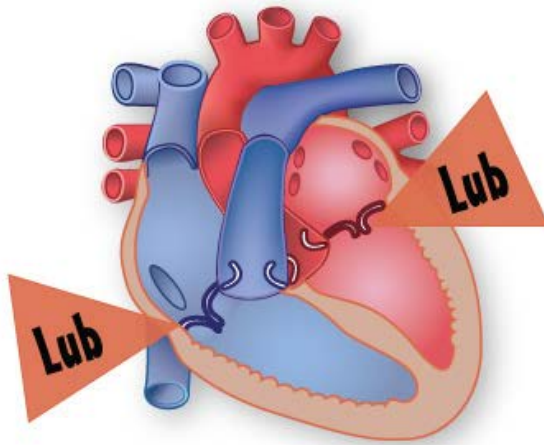
3-The third heart sound ( $S_3$ ): is caused by rapid filling of the ventricles, by blood that flow with a rumbling motion into the almost filled ventricles; at the middle one third ( $1/3$ ) of diastole i.e., it is caused by the vibrations of the ventricular walls during the period of rapid ventricular filling that follows the opening of AV valves. It is a low-pitched sound and can be heard after the  $S_2$ . It is heard in normal heart; in children and in adult during exercise. It is also heard in anemia, and AV valve regurgitation.

4-The fourth heart sound ( $S_4$ ): it is an atrial sound when the atria contract (at late diastole). It is a vibration sound (similar to that of  $S_3$ ) associated with the flow of blood into the ventricle. It is not heard in normal hearts but occurs during ventricular overload as in severe anemia, Thyrotoxicosis (hyperthyroidism) or in reduced ventricular compliance and in hypertension. If present, it is heard before  $S_1$ . ( $S_4$ ,  $S_1$ ,  $S_2$ ,  $S_3$ ).

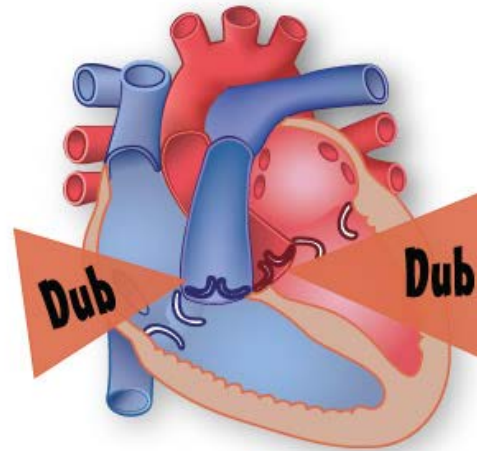
## **Heart murmurs**

They are abnormal sounds, can be produced by blood flowing rapidly in the usual direction but through an abnormally narrowed valve (stenosis), by blood flowing backward through a damaged, leaky valve (incompetent, regurgitant valve) or by blood flowing between the two atria or two ventricles through a small hole: ASD (atrial septal defect), VSD (ventricular septal defect).

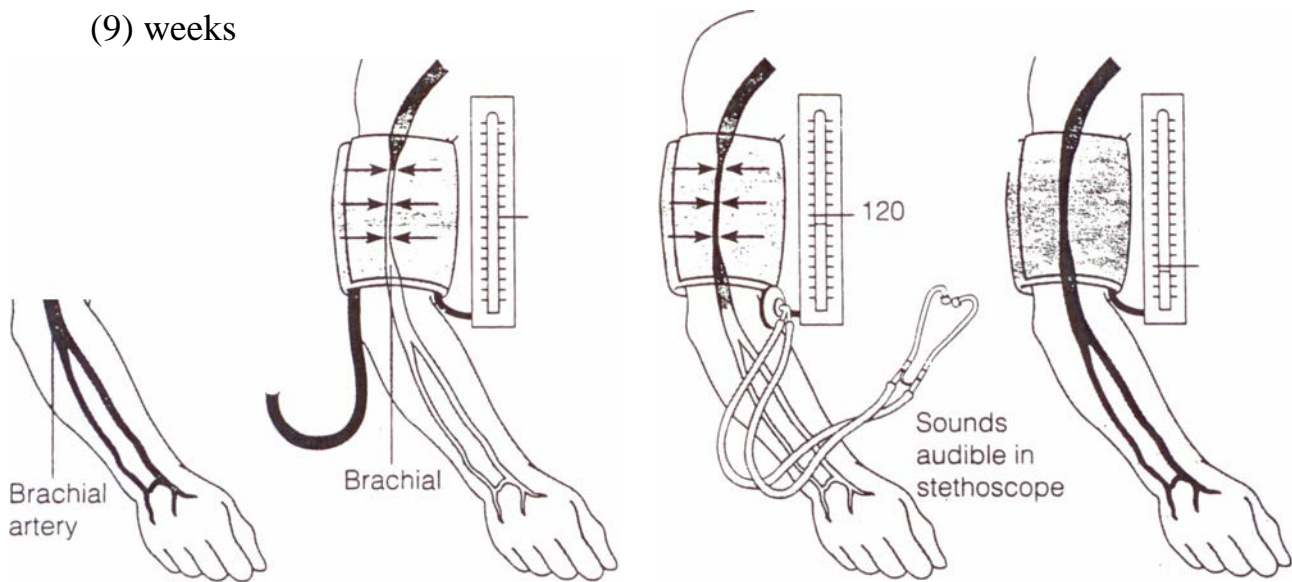
**Normal Heart "Lub"**



**Normal Heart "Dub"**



(9) weeks



## **BLOOD Pressure**

**Procedure for measurement of blood pressure. (Assume a blood pressure of 120/70.)**

**Blood pressure** is the pressure the blood exerts against the inner blood vessel walls; it is generally measured in the arteries. Because the heart alternately contracts and relaxes, the rhythmic flow of blood into the arteries causes the blood pressure to rise and fall during each beat. Thus you must take two blood pressure readings: the systolic **pressure**, which is the pressure in the arteries at the peak of ventricular ejection. and the **diastolic pressure**, the pressure during ventricular relaxation. Blood pressures are reported in millimeters of mercury (mm Hg). with the systolic pressure appearing first; 120/80 translates to 120 over 80, or a systolic pressure of 120 mm Hg and a diastolic pressure of 80 mm of Hg. However, normal blood pressure varies considerably from one person to another.

Using a Sphygmomanometer to Measure Arterial Blood Pressure Indirectly  
The sphygmomanometer, commonly called a blood pressure cuff, is an instrument used to measure blood pressure by the auscultatory method (It consists of an inflatable cuff with an attached pressure gauge. The cuff is wrapped snugly around the arm just above the elbow and inflated until the cuff pressure exceeds systolic pressure to stop blood flow to the forearm. As cuff pressure is gradually released, the examiner listens with a stethoscope over the brachial artery for characteristic sounds called the sounds of Korotkoff, which indicate the resumption of blood flow into the forearm. The pressure at which the first soft tapping sounds are heard is recorded as the systolic pressure. As the pressure is reduced further, blood flow becomes more turbulent, and the sounds become louder. Below the diastolic pressure, when the artery is no longer compressed, blood flows freely and the sounds of Korotkoff can no longer be heard. The pressure at which the sounds disappear is recorded as the diastolic pressure.

1. Work in pairs to obtain radial artery blood pressure readings. Obtain a stethoscope, alcohol swabs, and a sphygmomanometer. Clean the earpieces of the stethoscope with the alcohol swabs, and check the cuff for the presence of trapped air by compressing it against the laboratory table. (A partially inflated cuff will produce erroneous measurements.)
2. The subject should sit in a comfortable position with one arm resting on the laboratory table (approximately at heart level if possible). Wrap the cuff around the subject's arm, just above the elbow, with the inflatable area on the medial arm surface. The cuff may be marked with an arrow; if so, the arrow should be positioned over the brachial artery (Figure 22.3). Secure the cuff by tucking the distal end under the wrapped portion or by bringing the Velcro areas together.
3. Palpate the brachial pulse, and lightly mark its position with a felt pen. Don the stethoscope, and place its diaphragm over the pulse point. The cuff should not be kept inflated for more than 1 minute. If you have any trouble obtaining a reading within this time, deflate the cuff, wait 1 or 2 minutes, and try again. (A prolonged interruption of blood flow can cause fainting. )
4. Inflate the cuff to approximately 160 mm Hg pressure, and slowly release the pressure valve. Watch the pressure gauge as you listen for the first soft thudding sounds of the blood spurting through the partially blocked artery. Make a mental note of this pressure (systolic pressure), and continue to release the cuff pressure. You will notice first an increase, then a muffling of



the sound. Record as the diastolic pressure, the pressure at which the sound disappears. Make two blood pressure determinations and record your results.

## **(10) weeks**

### **Observing the Effect of Various Factors on Blood Pressure a Heart Rate**

Arterial blood pressure is directly proportional to cardiac output (amount of blood pumped out of the left ventricle per minute) and peripheral resistance, that is: **BP = CO X PR**

Peripheral resistance is increased by constriction of blood vessels (most importantly the arterioles), by an increase in blood viscosity or volume, and by a loss of elasticity of the arteries (seen in arteriosclerosis). Any factor that increases either the cardiac output or the peripheral resistance causes an almost immediate reflex rise in blood pressure. The influence of two factors that alter blood pressure-posture and exercise-are investigated here.

To do the following tests efficiently, one student should act as the subject and two as examiners (one taking the radial pulse and the other auscultating the brachial blood pressure). A fourth student collects and records the data. The sphygmomanometer cuff should be left on the subject's arm throughout the experiments (in a deflated state, of course) so that, at the proper times, the blood pressure can be taken quickly. In each case, take the measurements at least twice. To monitor circulatory adjustments to changes in position, take blood pressure and pulse measurements under the conditions noted in Chart 1. Also record your results on that chart.

Investigate the effects of exercise on blood pressure, pulse, and cardiovascular fitness.

Changes in blood pressure and pulse during and after exercise provide a good yardstick for measuring overall cardiovascular fitness. Although there are more accurate tests to evaluate fitness, the *Harvard Step Test* described here is a quick way to compare the relative fitness level of a group of people. You will be working in groups of four. duties assigned as indicated above. except that student 4, in addition to recording the data. will act as the timer and call the cadence (rhythm). ***Any student with a known heart problem should refuse to be the subject.*** All four students may act as the subject in turn, if desired. but the bench stepping is to be performed *at least twice* in each group-once with a well-conditioned person acting as the subject, and once with an individual that does not exercise on a regular basis.

Bench stepping is the following series of movements repeated sequentially:

1. Place one foot on the step.
2. Step up with the other foot so that both feet are on the platform. Straighten the legs and the back.
3. Step down with the other foot.
4. Bring the other foot down.

The pace for the stepping will be set by the "timer" (student 4), who will repeat "Up-2-3-4. up-2-3-4" at such a pace that each "up-1-2-3" sequence takes 2 sec (so there are 30 cycles/min).

1. Student 4 should obtain the step (20-in. height for male subject. or 16 in. for a female subject) while baseline measurements are being obtained on the subject.
2. Once the baseline pulse and blood pressure measurements have been recorded on Chart 2. the subject is to stand quietly at attention for 2 min to allow his or her blood pressure to stabilize before beginning to step.
3. The subject is to bench step for as long as possible, up to a maximum of 5 min, according to the cadence called by the timer. Watch the subject for crouching (posture must remain erect). If he or she is unable to keep the pace up for 15 sec, stop the test.
4. When the subject is stopped by the pacer, stops voluntarily because he or she is unable to continue, or has completed 5 min of bench stepping, he or she is to sit down. At this point, record the duration of exercise (in seconds), and measure the blood pressure and pulse immediately and thereafter at 1-min intervals for 3 min post-exercise.
5. The subject's *index of physical fitness* is to be calculated using the following formula:

$$\text{Index} = \frac{\text{duration of exercise in seconds} \times 100}{2 \times \text{sum of the 3 pulse counts in recovery}}$$

Scores are interpreted according to the following scale:

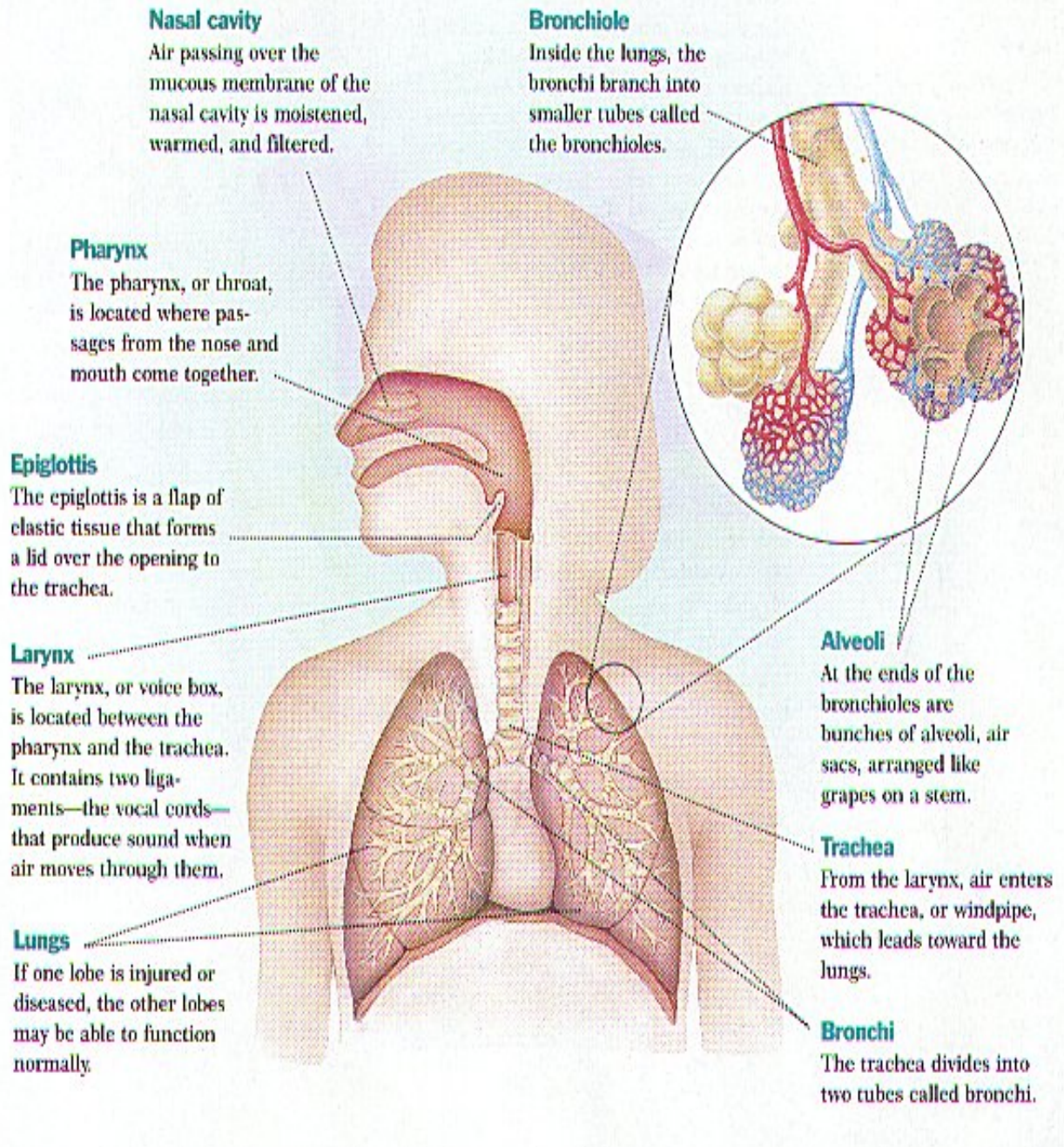
below 55	poor physical condition
55 to 62	low average
63 to 71	average
72 to 79	high average
80 to 89	good
90 and over	excellent

5. Record the test values on Chart 2, and repeat the testing and recording procedure with the second subject. Answer the question.

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(11 – 12 – 13 - 14) weeks

## **THE RESPIRATORY SYSTEM**

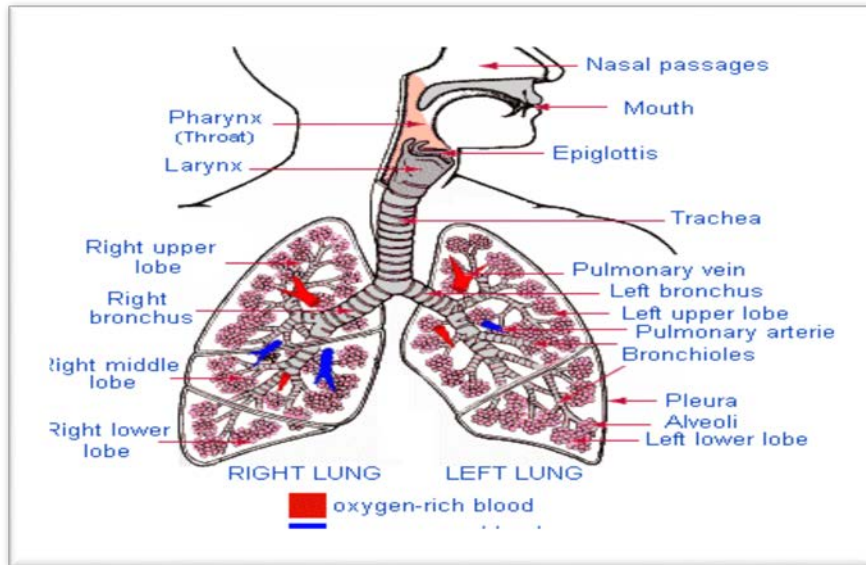


## **THE RESPIRATORY SYSTEM**

You have read how the blood transports oxygen from the lungs to cells and carries carbon dioxide from the cells to the lungs. It is the function of the respiratory system to transport gases to and from the circulatory system. The respiratory system involves both External and Internal respiration.

**External Respiration** is the exchange of gases between the atmosphere and the blood. **Internal Respiration** is the exchange of gases between the blood and the cells of the body. **Cellular Respiration** or **Aerobic Respiration** involves the use of oxygen to break down glucose in the cell. We will examine the structures and mechanisms that carry oxygen to the cells for use in aerobic respiration and that eliminate the carbon dioxide that is produced by the

same process.



1. **NOSE:** This is made of cartilage. Nose jobs involve taking a mallet, breaking the nasal bone and shaving the cartilages.
  - a. **NASAL CAVITY:** This is where the nostrils are. They have hairs which filter large particles in the respiratory tract. (insects, etc).

The functions of the nasal cavity is for the air you breathe:

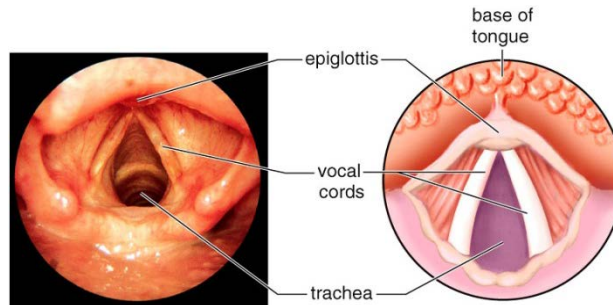
1. Warm (cold air can freeze lungs); warmed by superficial veins
2. Clean (dirty air can clog lungs); mucous is sticky, and cilia will move that dirt down the back of the throat, then it's swallowed.
3. Humidify (dry lungs can crack). The fluid secreted by glands makes the moisture, even on windy days the air goes to 100% humidity by the time it gets to the lungs.

## LARYNX

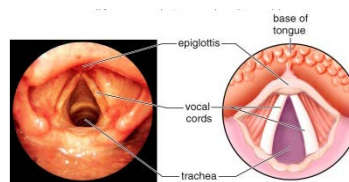
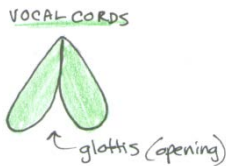
This is a very complex structure (show overhead). Made up of cartilages  
It has two functions:

1. Produce sounds (vocal cords are located in the larynx)
2. Prevent food from entering lungs





**A. EPIGLOTTIS** closes when you swallow so nothing will go into the trachea and lungs. When you get hiccoughs, it's from a sudden movement of air into the lungs, so the epiglottis closes to prevent more air from going in. It's unknown why you get hiccoughs. All the treatments you can try involve interrupting the normal breathing patterns.



**B. GLOTTIS** is the opening.

### **C. VOCAL CORDS**

Vocal cords are attached to cartilage. If these cartilages move, the vocal cords open.

The type and pitch of sounds you make depend on how far apart the vocal cords are.

Way open = no sound (like when breathing)

Mostly closed = sounds

Men: their thyroid cartilage is larger, so their vocal cords are longer = deeper voice.

**LARYNGITIS**: inflamed vocal cords (↓ sound production).

Singers can get scar tissue nodules, requires surgery.

The number one sign that a person is lying is voice irregularities.

**4. TRACHEA** This is a tube that carries air from the larynx to the lungs.  
(See model)

It's fairly rigid from about 16 rings of cartilage.

The purpose of the cartilage rings is to keep the trachea open like a hollow tube. Otherwise, when you inhale, the trachea would collapse like when you suck hard on a straw. That's why your vacuum cleaner has rings on the hose.



The trachea is lined with epithelium interspaced with goblet cells, which are the cells that produce mucous to trap dirt. The epithelial cells also have little hairs on them called cilia which sweep dirt to larynx → swallowed. In this way, the respiratory passage is filtered. Therefore, the cilia have several functions: they move the mucus, remove debris and harmful organisms, and circulate the air.

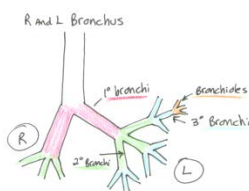
The trachea branches out into smaller tubes called **BRONCHI**.

Bronchi branch out into smaller tubes called **BRONCHIOLES**.

Bronchioles branch out into smaller tubes that empty into a sack =

**ALVEOLI** (overhead picture). This sac is like a balloon surrounded by a capillaries. The alveoli are where the gas exchange occurs: oxygen goes from the air in the lungs into the red blood cells passing by there, and carbon dioxide diffuses out of the cells and into the air in the lungs where it is exhaled. Therefore, inspired air (breathe in) contains oxygen, and expired air (breathe out) contains more carbon dioxide than oxygen.

By the time these air tubes are this small, they don't have any more cilia, so any particle that gets down that far has to be eaten by macrophages or just stay there. Therefore, within the alveoli are macrophages to eat the foreign object.



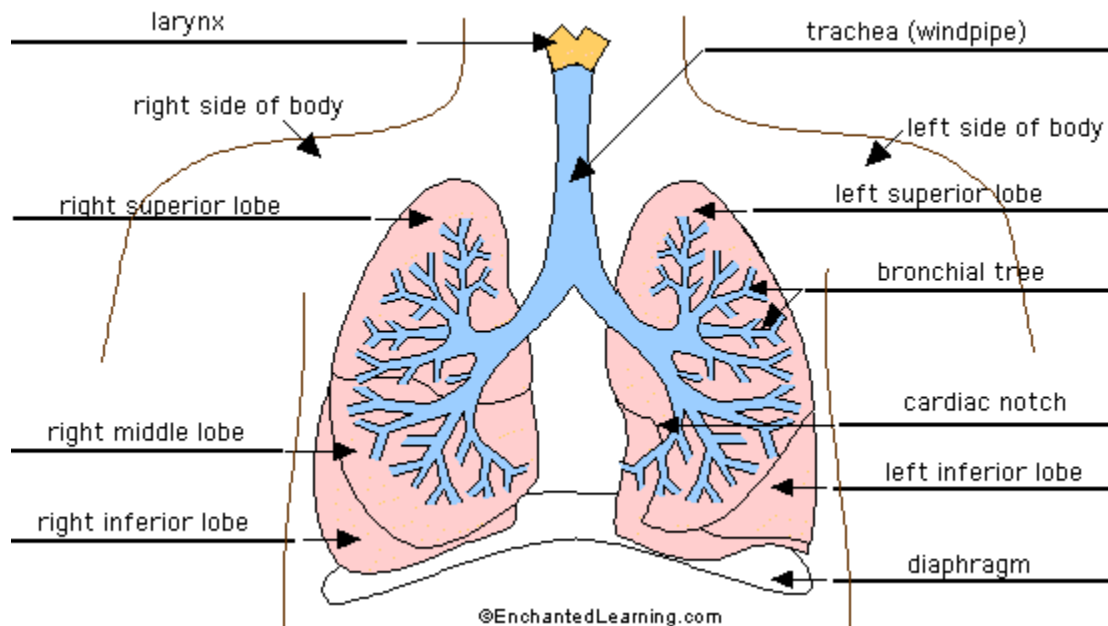
A cough can be expelled at 60 mph.

**DIAPHRAGM** is a muscle on the floor of the chest cavity. It is involved in breathing.

## Lung

The lungs are respiratory organs -- we use them to breathe. We breathe in order to get oxygen ( $O_2$ ) and to get rid of carbon dioxide ( $CO_2$ ). We breathe in through the nose or mouth. The air then goes through the larynx and the trachea (also called the windpipe) and into the lungs. We breathe by using the diaphragm, a muscular membrane under the lungs. When the diaphragm contracts and pulls downwards, the lungs expand and air enters the lungs (inhalation). When the diaphragm relaxes, air is exhaled from the lungs. When the air is in the lungs, it comes enters capillary-lined alveoli (singular alveolus). In the hollow alveoli, gas exchange occurs [oxygen ( $O_2$ ) is absorbed by blood in the capillaries and carbon dioxide ( $CO_2$ ) is gotten rid of].

People have two lungs -- they are located on either side of the heart within the rib cage. The two lungs are not identical; the right lung has three lobes and the left lung has two lobes.



## Breathing

In mammals, the diaphragm divides the body cavity into the



- **abdominal cavity**, which contains the viscera (e.g., stomach and intestines) and the
- **thoracic cavity**, which contains the heart and lungs.

The inner surface of the thoracic cavity and the outer surface of the lungs are lined with **pleural membranes** which adhere to each other. If air is introduced between them, the adhesion is broken and the natural elasticity of the lung causes it to collapse. This can occur from trauma. And it is sometimes induced deliberately to allow the lung to rest. In either case, reinflation occurs as the air is gradually absorbed by the tissues. Because of this adhesion, any action that increases the volume of the thoracic cavity causes the lungs to expand, drawing air into them.

- During inspiration (inhaling),
  - The external intercostal muscles contract, lifting the ribs up and out.
  - The diaphragm contracts, drawing it down .
- During expiration (exhaling), these processes are reversed and the natural elasticity of the lungs returns them to their normal volume. At rest, we breath 15–18 times a minute exchanging about 500 ml of air.
- In more vigorous expiration,
  - The internal intercostal muscles draw the ribs down and inward
  - The wall of the abdomen contracts pushing the stomach and liver upward.

Under these conditions, an average adult male can flush his lungs with about 4 liters of air at each breath. This is called the **vital capacity**. Even with maximum expiration, about 1200 ml of **residual air** remain.

(12) weeks

## LUNG VOLUMES ( respiratory size )

### a. **primary lung volumes**

- i. RV Residual Volume
- ii. ERV Expiratory Reserve Volume
- iii. TV Tidal Volume
- iv. IRV Inspiratory Reserve Volume

### b. **secondary derived capacities**

- i. TLC Total Lung Capacity
- ii. VC Vital Capacity
- iii. IC Inspiratory Capacity
- iv. FRC Functional Residual Capacity

A person's vital capacity can be measured by a spirometer which can be a wet or regular spirometer. In combination with other physiological measurements, the vital capacity can help make a diagnosis of underlying lung disease.

### **Residual Volume**

**Def'n:** the volume of gas in the lung at the end of maximal expiration determined by the balance of expiratory muscle activity and the resistance to volume decrease by the lungs and chest wall

### **Vital Capacity**

**Def'n:** the maximum volume that can be exhaled following a maximal inspiration

$$VC = IRV + TV + ERV$$

VC and its components are measured by *spirometry*, either bell (Benedict-Roth), or wedge

variations in VC occur with,

1. height, weight and surface area - VC roughly proportional to **height**
2. age - ↓ VC with increasing age
3. sex - M > F

### **Functional Residual Capacity**

**Def'n:** the volume of gas left in the lungs at the end of normal tidal expiration

FRC is the lung volume in which gas exchange is taking place

small fluctuations of alveolar and arterial gas tensions occur with each tidal breath as fresh gas

mixes with alveolar air

FRC therefore acts as 4. posture - less when supine, cf. sitting or standing

Total lung capacity (TLC) is the maximum volume to which the lungs can be expanded with the greatest possible inspiratory effort; it is equal to the vital capacity (VC) plus the residual volume (RV) and is approximately 5800 ml.

Also given as:  $TLC = TV \text{ (tidal volume)} + IRV \text{ (inspiratory reserve volume)} + ERV \text{ (expiratory reserve volume)} + RV \text{ (residual Volume)}$

**Expiratory reserve volume (ERV)** :- refers to the extra volume of air that can be exhaled with maximum effort beyond the level reached at the end of a normal, passive exhalation.

**Tidal volume** is the lung volume representing the normal volume of air displaced between normal inspiration and expiration when extra effort is not applied. In a healthy, young adult, tidal volume is approximately 500 ml per inspiration or 7 ml/kg of body weight.

( 14) weeks

**The walls of alveoli** are coated with a thin film of water & this creates a potential problem. Water molecules, including those on the alveolar walls, are more attracted to each other than to air, and this attraction creates a force called surface tension. This surface tension increases as water molecules come closer together, which is what happens when we exhale & our alveoli become smaller (like air leaving a balloon). Potentially, surface tension could cause alveoli to collapse and, in addition, would make it more difficult to 're-expand' the alveoli (when you inhaled). Both of these would represent serious problems: if alveoli collapsed they'd contain no air & no oxygen to diffuse into the blood &, if 're-expansion' was more difficult, inhalation would be very, very difficult if not impossible. Fortunately, our alveoli do

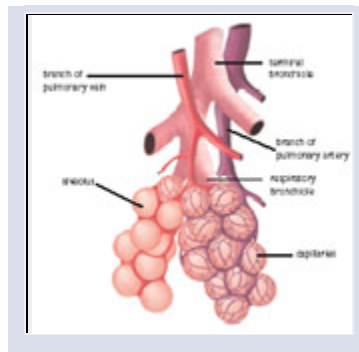
not collapse & inhalation is relatively easy because the lungs produce a substance called surfactant that reduces surface tension.

### **Role of Pulmonary Surfactant**

- Surfactant decreases surface tension which:
  - increases pulmonary compliance (reducing the effort needed to expand the lungs)
  - reduces tendency for alveoli to collapse

### **Structure and function of the alveoli**

At the end of each alveolar duct there are a number of sac-like structures called alveoli, it is within these structures that surfactant is produced. The alveoli are grouped together like a lot of interlinked caves, rather than existing as separate individual sacs.



Gas exchange of oxygen and carbon dioxide takes place in the alveoli. Oxygen from the inhaled air diffuses through the walls of the alveoli and adjacent capillaries into the red blood cells. The oxygen is then carried by the blood to the body tissues. Carbon dioxide produced by the body's metabolism returns to the lung via the blood. It then diffuses across the capillary and alveolar walls into the air to be removed from the body with expiration. The alveoli have a structure specialised for efficient gaseous exchange:

- Walls are extremely thin.
- They have a large surface area in relation to volume.
- They are fluid lined enabling gases to dissolve.
- They are surrounded by numerous capillaries.

## **Acidic blood**

Ventilation also plays a major role in maintaining pH balance. The respiratory system can activate changes in pH within 1 to 3 minutes and can eliminate or conserve  $\text{CO}_2$  (which directly affects acid-base status) more quickly and efficiently than all the buffer systems combined. As discussed, when a strong acid is present in the body, the bicarbonate-carbonic acid buffer pair is activated to buffer the acid. This results in a net increase of carbonic acid, which dissociates into  $\text{CO}_2$  and  $\text{H}_2\text{O}$ . Carbon dioxide is then eliminated by the lungs (Fig. 9-2). An increase in  $\text{H}^+$  concentration in the blood stimulates the breathing center in the medulla to increase the respiratory rate, which facilitates  $\text{CO}_2$  elimination. If, on the other hand, pH is elevated secondary to an increase in  $\text{HCO}_3^-$ , the respiratory center is inhibited, and the respiratory rate decreases. This results in  $\text{CO}_2$  retention, which then becomes available to form carbonic acid, which buffers the excess bicarbonate. The respiratory system is thus able to compensate for changes in pH related to metabolic disorders (e.g., diabetic ketoacidosis) by regulating  $\text{PcO}_2$ , which alters the bicarbonate-carbonic acid ratio. The respiratory system cannot, however, produce any loss or gain of hydrogen ions. Respiratory compensation is activated within minutes and is usually fully functional within 1 to 2 days.

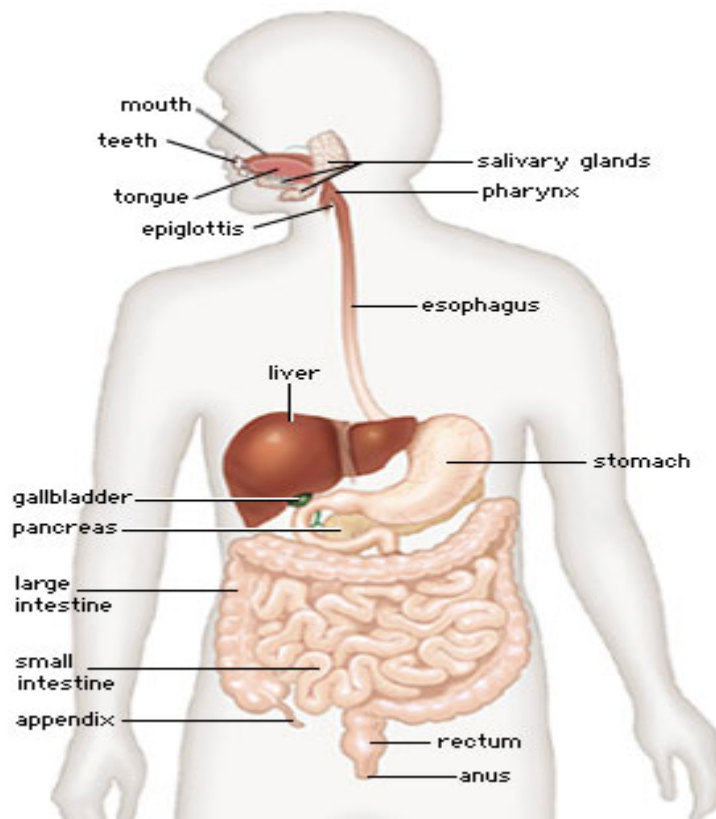
( 15 – 16 -17 ) weeks

**Digestive system**

Digestion is necessary to break a complex mixture of proteins, carbohydrates, lipids, and other substances into small molecules, which can move through cell g from the mouth to the anus.

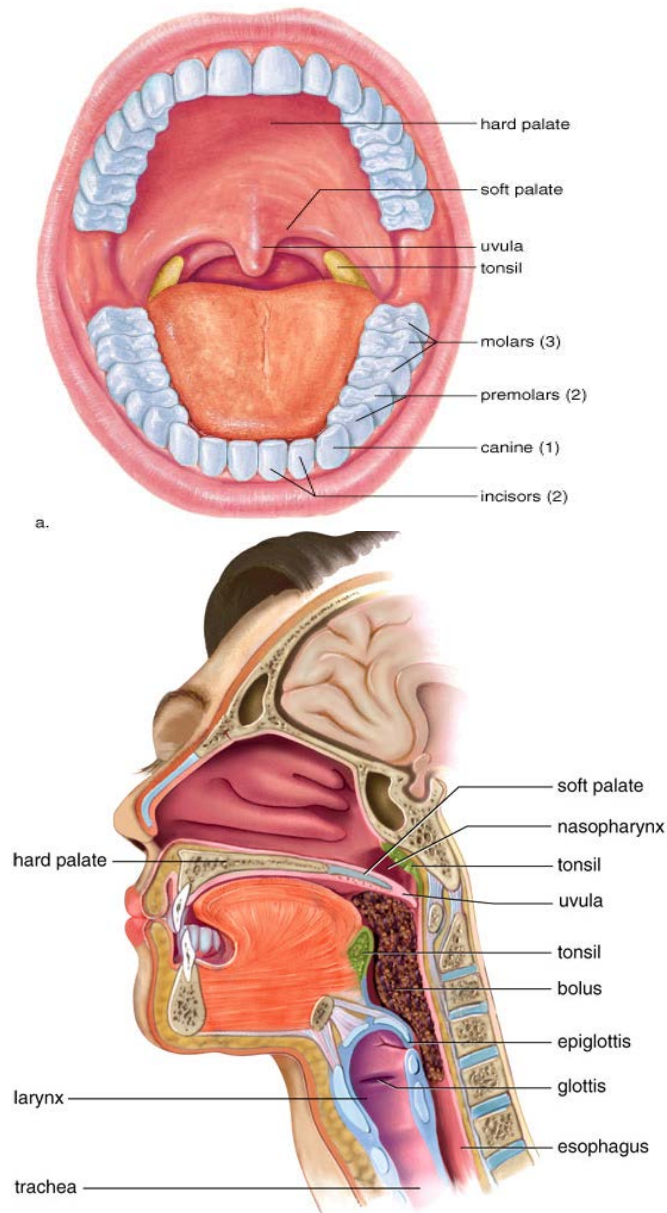
Digestion is both mechanical and chemical. Chemical digestion is the breakdown of larger molecules into smaller ones. Proteins, carbohydrates, and lipids can be broken down by combining them with water. This is called hydrolysis. Proteins are hydrolyzed into amino acids. Polysaccharides are hydrolyzed into simple sugars (glucose). Triglycerides (complex fats) are hydrolyzed into fatty acids and glycerol (simple parts of fat molecules). Mechanical digestion is the physical breakdown of food into smaller particles. This involves chewing and muscular churning. These processes expose more surface area to the enzymes, therefore, it speeds up chemical digestion.

As you read about the following parts of the digestive system, find these parts in the diagram:



Parts of The Digestive System

Teeth - cut, tear, and grind food. A variety of types of teeth indicates adaptation to an omnivore (organism that eats both plants and animals).



Mucus - from cells lining the mouth; it makes food easier to swallow.

Saliva - from three pairs of salivary glands; lubricates food and adds the enzyme amylase which breaks down starch.

two functions:

- 1) To moisten food so you can swallow, especially crackers.
- 2) To inhibit growth of bacteria (which like dark, warm, moist areas). What does this are the antibodies and enzymes in the saliva.

Tongue- muscular organ; keeps food where it can be chewed and pushes food to the back of the mouth to be swallowed. Also contains sensory organs for taste.

Pharynx- large area at the back of the mouth; food passes from here, past the epiglottis (which prevents food from entering the lungs).

Esophagus - takes food from the pharynx and carries it to the stomach. The hollow interior of the esophagus is the lumen. The cells that line the lumen, and secrete mucus are the mucosa. Beneath the mucosa are two layers of muscle. In the innermost layer, muscle fibers wrap around the esophagus. Fibers of the outer layer run lengthwise along the esophagus. These layers alternately contract and relax causing waves of constriction. These waves push food along ahead of them. This rhythmic muscular contraction is called peristalsis. It moves food in the esophagus, and the rest of the alimentary canal.

Stomach- the opening is controlled by a muscular sphincter, which opens and closes the tube. The stomach is J-shaped; one of its primary functions is food storage (about 2L). It too, is lined with mucosa. There are three kinds of cells in the stomach mucosa (one secretes mucus; one secretes enzymes; one secretes hydrochloric acid and water). The enzymes, water and hydrochloric acid combine to form gastric juice. The pH of gastric juice is about 1.0. It helps break up connective tissue and cell membranes; it also kills harmful bacteria.

Chemical digestion is aided by mechanical digestion in the stomach. Peristalsis of the stomach wall churns food for several hours. Mucus in the stomach is resistant to attack by gastric juice; this protects the stomach cells. Sheets of fat molecules resist digestion because they digest so slowly. Digestive enzymes are only activated by an acidic environment. When these factors are out of balance, stomach cells are attacked. The result is an ulcer; this may require a change in diet, or surgery. The other end of the stomach



also has a sphincter. When it relaxes, partially digested food moves into the small intestine.

Function of stomach :-

1. Store Food, so it can be slowly released into a small intestine. Your whole

Thanksgiving dinner can take your stomach diameter from 2" to 8" diameter.

2. Churn food. Secretions from the stomach turns everything gooey, called CHYME.

3. Kill bacteria. The stomach is very acidic (pH 1) like battery acid. Chyme will even eat through clothing.

4. Some digestion: of proteins.

5. Some absorption: of water, alcohol (alcohol is absorbed in the mouth, too!)

Food takes four hours to completely leave the stomach.

It is folded over into RUGAE, to allow for expansion of the stomach.

Small Intestine- Food from the stomach enters the first 30 cm of the small intestine, called the duodenum; this is where bile and pancreatic juice enter. Cells of the intestinal lining also produce digestive enzymes.

The next several metres of small intestine are called the jejunum. Many small molecules are absorbed here. The last half of the small intestine is called the ileum. By now, most chemical digestion is complete. The ileum is primarily responsible for absorption of nutrients.

Blood from the small intestine moves to the liver where excess glucose and some broken down proteins are removed.

Stretched out, the small intestine measures about 6 meters.

Large Intestine- Also known as the colon, it is about two meters long, but larger in diameter than the small intestine (about 2X). Where the small and large intestines join, there is a small projection known as the appendix. It has no known function in humans, but in some plant eating species it helps digest the tough outer part of plant cells. Appendicitis results when bacteria lodge, grow, and secrete toxins in the appendix. It is more common in children, because the opening is much larger.

(18) weeks

enzymes and digestion in humans.

### enzymes

different enzymes are required for the digestion of different food substances.

for example amylase can only digest starch. it cannot digest protein, carbohydrates or lipids.

this is because each type of food substance has a particular shape. since enzymes can only function if they have a particular shape, the type of substance they act on depends on which substance has a complementary shape to the enzyme.

hence, a different enzyme is required for each type of food substance molecule. i.e

- lipases- for the digestion of lipids. lipids are hydrolysed to fatty acids and glycerol aka monoglycerides.
- proteases – for the digestion of proteins and polypeptide chains. particular proteases hydrolyse the peptide bonds within proteins, and break down their tertiary structures, creating long polypeptide chains. other proteases hydrolyse the peptide bonds between the individual units forming these polypeptide chains and the chains are broken down into amino acids.
- amylases – for the digestion of starch. amylase acts upon starch, by hydrolysing the glucoside bonds between the individual units of glucose which for the polysaccharide starch, hence converting it to its simpler form maltose, which is a disaccharide.

digestion in the stomach

- the walls of the stomach contain layers of muscle. the functions of which include:
  - churning, mechanical digestion, mixing, and peristalsis.
  - the gastric glands in the stomach wall secrete endopeptidase pepsin. however, it is secreted in its inactive form, pepsinogen. hcl in the stomach activates the enzyme.

- the enzyme is secreted in its inactive form in order to prevent it from digesting the walls of the stomach, while it is in storage in the gastric glands.
- once the enzyme has been activated, mucus, which coats the stomach walls, prevents them from being digested, and also protects the walls from acid.
- hcl in the stomach kills bacteria which are ingested along with food, and also created a low ph environment in which stomach enzymes work at their optimum rate.
- endopeptidases digest proteins into polypeptide chains
- exopeptidases digest polypeptide chains to amino acids.
- both endo and exopeptidases are required for efficient digestion of polypeptides and proteins because:
- endopeptidases act on the centre of polypeptide chains within proteins and hydrolyse them to smaller chains.
- this means that more 'ends' are created for the exopeptidases to act upon, in order to break down polypeptide chains to amino acids.
- food is released from the stomach by periodic relaxation of the pyloric sphincter muscle at the lower end of the stomach.
- after being released from the stomach, food enters the first part of the small intestine, known as the duodenum.

#### digestion in the duodenum.

- the duodenum contains the following enzymes:
- lipase – for the digestion of lipids. lipids are hydrolysed to fatty acids and glycerol.
- nucleases – for the digestion of nucleic acids. these are hydrolysed to nucleotides.
- maltases – the small intestine contains maltase as part of the intestinal fluid which forms a secretion which coats the walls of the small intestine epithelial cells. maltase acts on the disaccharide sugar maltose and hydrolyses the glycoside bonds between the units of glucose. the sugar is broken down to its simplest form glucose, and can then be absorbed.
- trypsin – for the digestion of proteins. these are hydrolysed to polypeptides.

- enzymes in the duodenum are secreted from the pancreas, and are carried to the duodenum by the hepato-pancreatic duct which also brings bile from the liver.
- the duodenum is the main site of absorption of all components of digestion, except water.
- food is moved along the duodenum by peristalsis (rhythmic contraction of the muscles of the intestinal wall, cause food to be pushed along the duodenum)
- segmentation in the duodenum is co-ordinated by the auerbach's plexus. it produces a to and fro movement that causes mixing of the contents of the gut and digestive juices. causing acid chyme which has a creamy consistency to be converted to chyle which is alkaline with a watery consistency.
- segmentation also aids digestion by bringing products into contact with the mucosa –hence enabling absorption to occur.

#### the role of the liver in digestion

- bile is a biological detergent, which is produced in the liver.
- bile reduces the surface tension of the contents of the gut and increases the surface area. this allows enzymes to work. e.g lipase.
- in order for lipids to act upon triglycerides, the triglycerides must first be broken down into minute droplets to enable them to mix with lipases present in the pancreatic juice within the duodenum.
- in order to do this bile is secreted from the gall bladder.
- bile reduces the surface tension and increases the surface area /volume ratio. i.e, fats are emulsified.
- therefore, lipases act on a larger volume of material in a shorter time, ensuring that enzymes operate at their optimum rate.
- bile also neutralises stomach acid, and provides the optimum pH for pancreatic digestive enzymes to work.

#### the role of the pancreas in digestion

- produces pancreatic juice.
- pancreatic juice is rich in sodium hydrogencarbonate, which:
- neutralises acid chyme from the stomach.
- raises the pH to enable enzymes in the pancreatic juice to work.

The major role of the large intestine is water absorption. The volume of water in the human body must remain relatively constant. A great deal of water enters the stomach as gastric juice. The only food residue left at the end of the colon is indigestible waste, called feces.

Feces is about 75% water and 25% solid matter. Of the solid matter, about 30% is dead bacteria, 10-20% inorganic matter, 2-3% protein, and 30% undigested fiber. Feces also contains epithelial cells (cells that line and cover body parts) and bile pigments.

The last 20-30 cm of the colon is called the rectum. Feces is stored here until eliminated from the body.

#### LARGE INTESTINE (Colon, or large bowel)

This is 5 feet long and 4" diameter

The large intestine is important for several reasons:

1. Absorbs a LOT of water from the food
2. Absorbs electrolytes (Na, K, etc) out of the food
3. Stores feces for defecation
4. Contains bacteria (*E. coli*), about 3 pounds of it! These bacteria have functions:
  - a. Make vitamins (B12, K)
  - b. Allow material to move through large intestine easier
  - c. Keep out harmful bacteria
  - d. They eat things you can't digest
    - i. Fiber
    - ii. Some sugars that we don't have enzymes for

**(19 – 20 ) weeks**

Pancreas/Liver- These are not part of the alimentary canal, but they are very important to digestion.

The pancreas produces hormones that regulate homeostasis (fairly constant level) of blood glucose. It also produces pancreatic juice which neutralizes the acidic stomach contents before they enter the small intestine. Pancreatic juice also contains a number of digestive enzymes, including many different proteases (chemical enzymes that break down protein that you eat). Pancreatic juice reaches the small intestine via the pancreatic duct.

The liver takes glucose from the blood and converts it to glycogen. It stores the glycogen until it is needed by the body. The liver also produces bile. Bile contains no enzymes, but does aid in the digestion of fats and oils in the intestine, breaking them down into tiny droplets (fats are not water soluble).

Bile travels through ducts to the gall bladder for storage. During digestion, it is released through the common bile duct into the small intestine. Gallstones develop from insoluble materials in the bile. They can block the bile duct and cause bile to accumulate in the gallbladder. In serious cases, the gall bladder may be surgically removed with no serious long-lasting effects.

### **Functions of the liver:**

The liver regulates most chemical levels in the blood and excretes a product called bile, which helps carry away waste products from the liver. All the blood leaving the stomach and intestines passes through the liver. The liver processes this blood and breaks down the nutrients and drugs into forms that are easier to use for the rest of the body. More than 500 vital functions have been identified with the liver. Some of the more well-known functions include the following:

- Production of bile, which helps carry away waste and break down fats in the small intestine during digestion
- Production of certain proteins for blood plasma
- Production of cholesterol and special proteins to help carry fats through the body

- Conversion of excess glucose into glycogen for storage (glycogen can later be converted back to glucose for energy)
- Regulation of blood levels of amino acids, which form the building blocks of proteins
- Processing of hemoglobin for use of its iron content (the liver stores iron)
- Conversion of poisonous ammonia to urea (urea is an end product of protein metabolism and is excreted in the urine)
- Clearing the blood of drugs and other poisonous substances
- Regulating blood clotting
- Resisting infections by producing immune factors and removing bacteria from the bloodstream

When the liver has broken down harmful substances, its by-products are excreted into the bile or blood. Bile by-products enter the intestine and ultimately leave the body in the form of feces. Blood by-products are filtered out by the kidneys, and leave the body in the form of urine.

**CARBOHYDRATES** are organic compounds (substances that contain the element carbon) that are used primarily as a source of energy for living things. They are also one of the main building blocks that make up the bodies of living things. For example, the walls of plant cells are made up of cellulose, a substance made up of carbohydrates.

Simple carbohydrates (monosaccharides) are often referred to as sugars and taste sweet. When two simple sugars link up, they form disaccharides. Some of these taste sweet and some do not. Complex carbohydrates made up of more than two simple ones linked together are called polysaccharides and do not taste sweet.

An important complex carbohydrate to humans is starch. Starch is a polysaccharide found in plants. Foods like potatoes contain starch. When you take starch into the body, the chemical enzyme amylase (present in the mouth and small intestine) breaks it down into smaller parts. After further digestion, many glucose units, smaller carbohydrates, are released from the starch and can be absorbed into the bloodstream and used by cells as fuel.

Another important polysaccharide is glycogen. As you may remember, glycogen found in the liver and the muscles and is made up of excess glucose molecules linked together. When the body is low on glucose, some

of the glycogen can be converted back to glucose for the body's cells to use as energy. Glycogen is often referred to as 'animal starch.'

**LIPIDS** are commonly known as fats, oils and waxes. They are a second type of organic compound that are non-polar (do not dissolve in water). Because of this, lipids serve valuable functions. These include acting as a barrier between the cell and its watery environment, acting as insulation in animals and acting as a water repellent on the feathers of birds, like ducks. Lipids also store a lot of energy and therefore are a source of energy for us!

building blocks of an important group of lipids are fatty acids. These molecules are long chains of carbon atoms with a carbon, oxygen and hydrogen bonded to the end. If the carbon chain has a maximum number of hydrogen atoms attached, it is said to be saturated. These are usually solid at room temperature and are known as fats. Lipids with a double bond, and therefore not the maximum number of hydrogen atoms are unsaturated. These are usually liquid at room temperature, come from plants and are known as oils. The majority of fat in organisms consists of molecules called triglycerides. These are made up of three fatty acid molecules plus a glycerol molecule. If the fatty acids of a triglyceride have more than two double bonds, they are polyunsaturated.

Energy released from a triglyceride is more than twice that released from a equal amount of carbohydrate. Humans can store less than a day's worth of glycogen (a carbohydrate) but can store three month's worth of energy in the form of triglycerides (lipids).

Since lipids store a lot of energy, they give us a lot of energy when eaten. If you consume more lipids than necessary, your body converts the excess to triglycerides. This is then stored in the fatty tissues of your body.

**PROTEINS** are the third kind of organic compound. There are many different kinds of proteins. For example, hair, spider webs, feathers and turtle shells are all very different, but are all made up of proteins!

Proteins serve as the raw material for the creation of new body parts. They also serve as a source of energy for the cell when supplies of carbohydrates and lipids are low. Eating other animals is a great way to get proteins, but soybeans and beans are also an excellent source. Proteins are made up of amino acids. Each amino acid has four parts bonded to it. Each has a



hydrogen atom, an amino group and a carboxyl group (made of C, H and O). A fourth part is different in every amino acid. All organisms are composed of combinations of the same 20 amino acids.

Amino acids are linked together by peptide bonds. When two amino acids join, the molecule that forms is called a dipeptide. The bonding of more than two forms a polypeptide. Proteins are long polypeptide chains averaging 200 or more amino acids. The sequence of the amino acids is what makes every protein unique. The protein is also twisted and folded before it begins to function. Every protein made by a cell has a specific function. This function is due to its unique 3 dimensional shape, caused by the folding and twisting. If even one amino acid is out of order, the entire protein can fold differently. This will change its function.

For each of the three organic compounds research:

- what sources of food contain each
- why each organic compound is important in the diet
- what ethnic foods that you may eat fall into each category

**(21) weeks**

**Here are some conditions which an Enzymes Deficiency can Lead to:**

- Heartburn/Indigestion
- Gas/flatulence
- Bloating
- Cardiovascular problems
- Hypertension/high blood pressure
- Constipation
- Weight Gain
- Slow Healing
- Inflammation
- Fibromyalgia
- Fatigue
- Chronic Fatigue Syndrome/CFS
- Arthritis
- Crohn's Disease

## **Diabetes mellitus**

or simply **diabetes**, is a group of metabolic diseases in which a person has high **blood sugar**, either because the **pancreas** does not produce enough **insulin**, or because cells do not respond to the insulin that is produced.<sup>[2]</sup> This high blood sugar produces the classical symptoms of **polyuria** (frequent urination), **polydipsia** (increased thirst) and **polyphagia** (increased hunger). There are three main types of diabetes mellitus (DM).

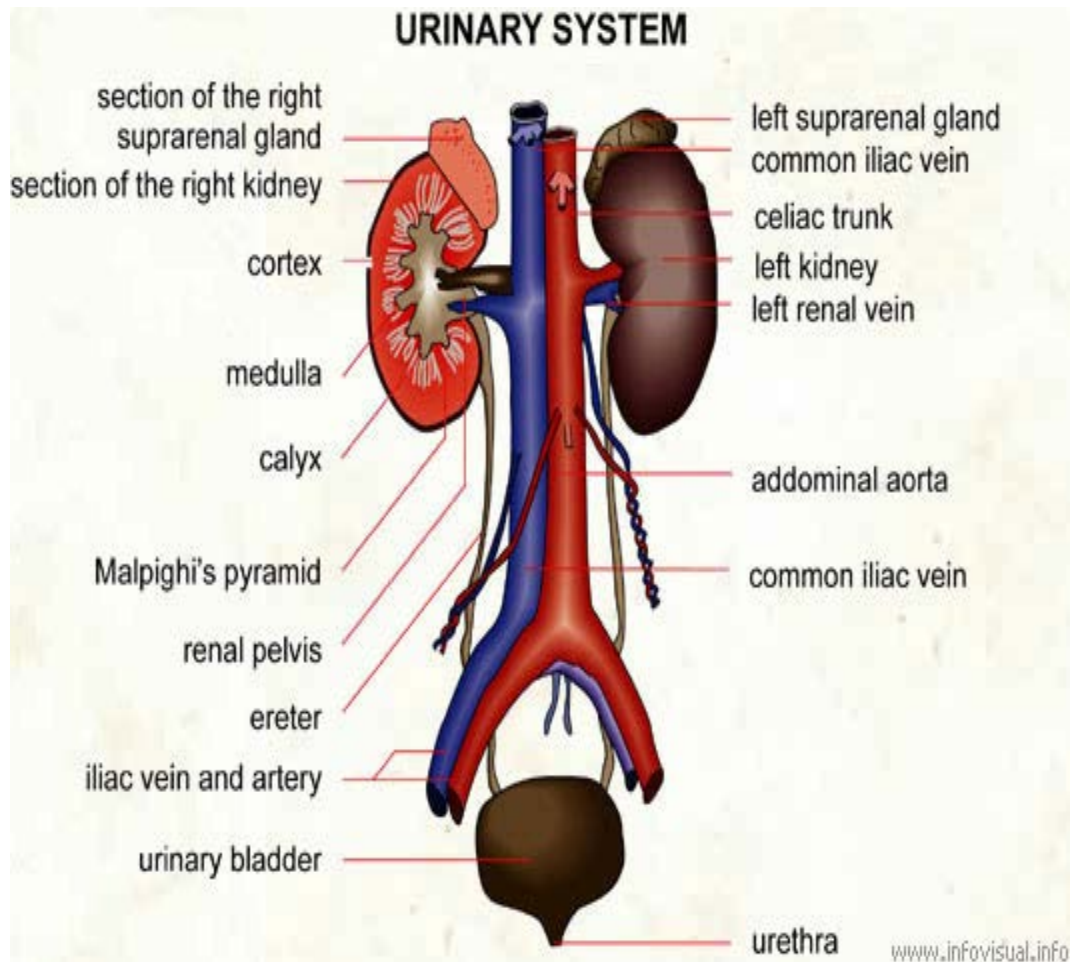
- **Type 1 DM** results from the body's failure to produce insulin, and currently requires the person to inject insulin or wear an insulin pump. This form was previously referred to as "insulin-dependent diabetes mellitus" (IDDM) or "juvenile diabetes".
- **Type 2 DM** results from **insulin resistance**, a condition in which cells fail to use insulin properly, sometimes combined with an absolute insulin deficiency. This form was previously referred to as non insulin-dependent diabetes mellitus (NIDDM) or "adult-onset diabetes".
- The third main form, **gestational diabetes** occurs when pregnant women without a previous diagnosis of diabetes develop a high blood glucose level. It may precede development of type 2 DM.

Other forms of diabetes mellitus include congenital diabetes, which is due to **genetic** defects of insulin secretion, **cystic fibrosis**-related diabetes, steroid diabetes induced by high doses of **glucocorticoids**, and several forms of **monogenic diabetes**.

Untreated, diabetes can cause many complications. **Acute** complications include **diabetic ketoacidosis** and **nonketotic hyperosmolar coma**. Serious long-term complications include **cardiovascular disease**, **chronic renal failure**, and **diabetic retinopathy** (retinal damage). Adequate treatment of diabetes is thus important, as well as **blood pressure** control and lifestyle factors such as stopping **smoking** and maintaining a healthy **body weight**. All forms of diabetes have been treatable since **insulin** became available in 1921, and type 2 diabetes may be controlled with medications. Insulin and some oral medications can cause **hypoglycemia** (low blood sugars), which can be dangerous if severe. Both types 1 and 2 are **chronic** conditions that cannot be cured.<sup>[3]</sup> **Pancreas transplants** have been tried with limited success in type 1 DM; **gastric bypass surgery** has been successful in many with **morbid obesity** and type 2 DM. Gestational diabetes usually resolves after delivery.

(22) weeks

## Urinary SYSTEM



### INTRODUCTION

The urinary system is responsible for the removal of wastes and harmful chemicals from the body. Some wastes are removed from the body by fecal elimination (exhalation gases) and others by sweating, but the filtering process of the kidneys removes the large majority.

When foods are eaten they are broken down into carbon, hydrogen, oxygen, nitrogen, and other small compounds and elements. The body will remove most of these through the kidney's filtering systems. Sometimes, like in diabetes, some of the foods are inadequately broken down and the body will not remove them well. When protein foods are broken down they form

nitrogen compounds, which are excreted by the kidneys as urea. This is an important part of the function of a kidney because if they are not removed, they become very toxic causing damage to tissue and severe pain, as in gout.

The kidney has the function of maintaining the correct amounts of the body's electrolytes, water, and other chemicals found in body fluids. These are important in the equilibrium of the body's chemistry. The body's electrolytes are responsible for the correct functioning of nerve and muscle tissue. Water is important in bathing of the cells, movement of substances throughout the body, and the maintenance of body temperature. The secretion of chemicals into the urine that maintain and exactly balance these in the body's tissues controls the amount of water and electrolytes.

The kidneys have one more important function, the secretion of hormones into the bloodstream that react with the body to help provide for homeostasis. One of the most important hormones secreted by the kidneys is renin, used in the control of blood pressure. A second one is erythropoietin that regulates the production of red blood cells. A third is vitamin D that reacts with the parathyroid hormones and provides for correct calcium absorption. Finally, hormones like insulin are acted upon and removed from the body by the kidney.

This system consists of the **KIDNEYS, URETERS, URETHRA**, and **BLADDER**.

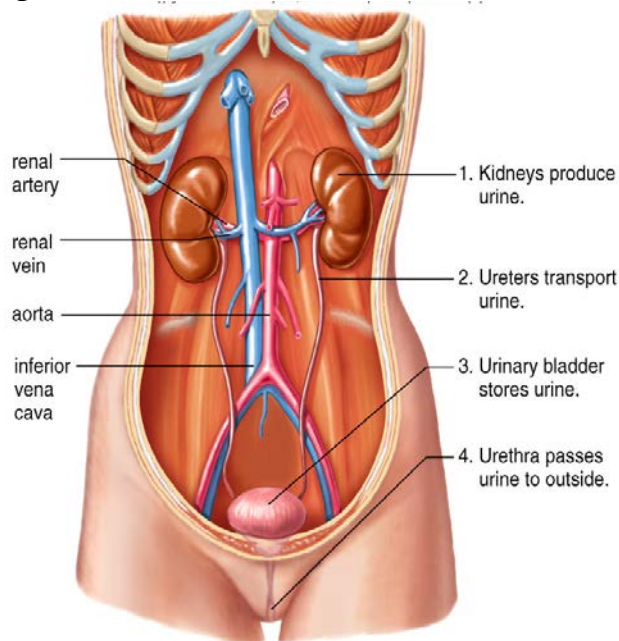
Not many structures, but very important.

### **Functions:**

1. Regulate electrolytes (K, Na, etc) in body
2. Regulate pH in blood
3. Regulate blood pressure
4. Regulate blood volume
5. Removing metabolic wastes (chemicals produced by chemical reactions in the body are excreted). This is the least important of the kidney's functions. You can survive for a few weeks without excreting waste products in the urine, but hour by hour, the other functions are more important.

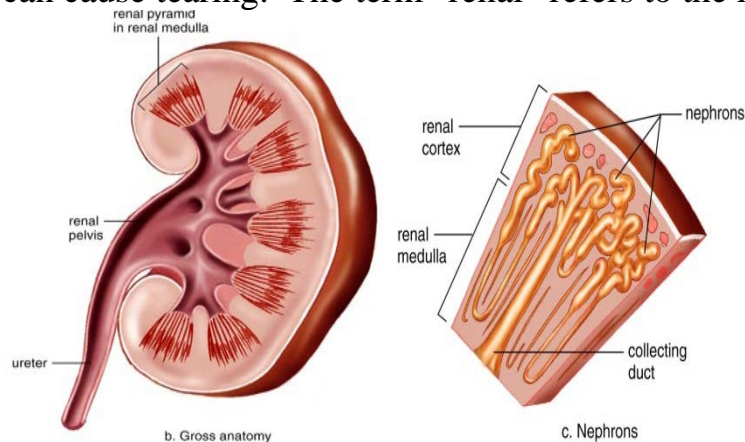
## **LOCATION OF THE KIDNEYS**

They are toward the back side of the body, partly protected by the lower border of the ribcage.

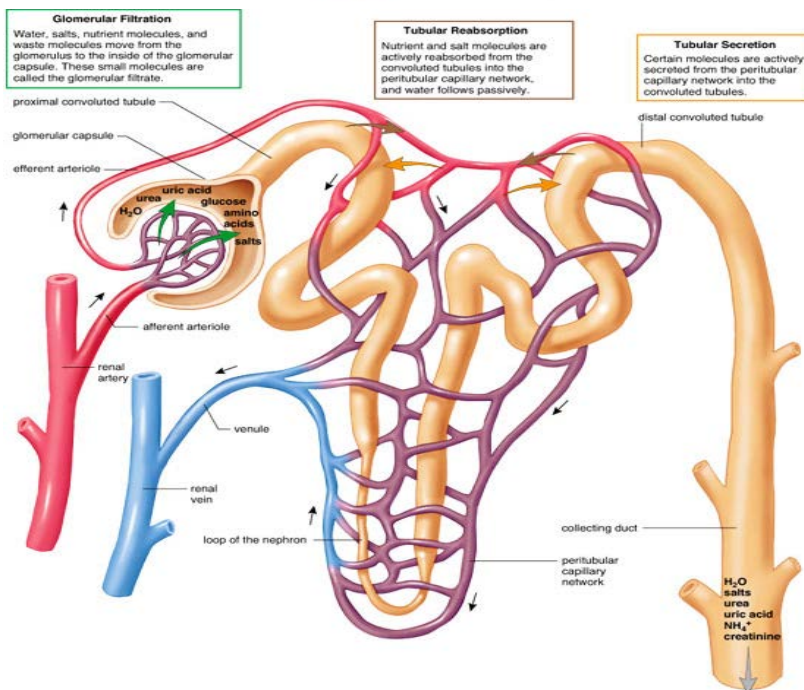
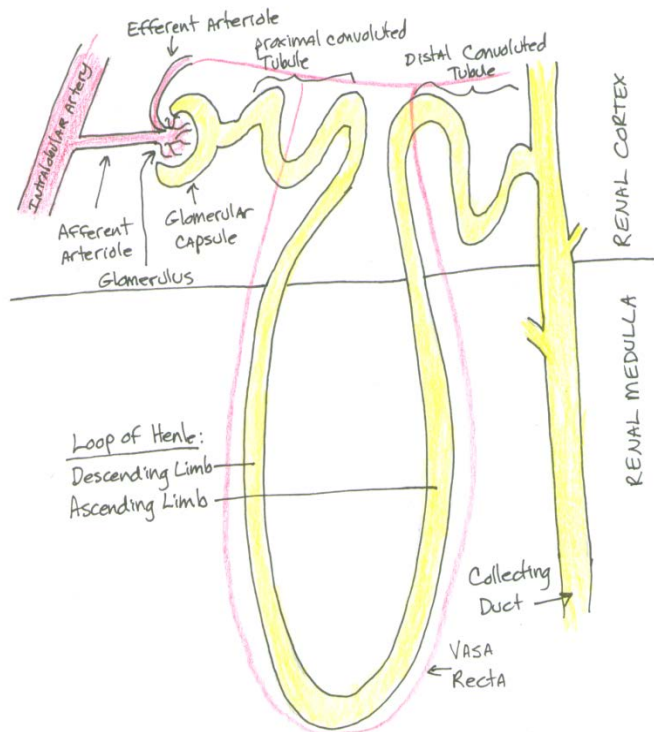


## STRUCTURES WITHIN THE KIDNEY

The kidney is surrounded by a capsule and some loose connective tissue which anchors the kidney to the abdominal wall. Not very strong. Jumping up and down can cause tearing. The term “renal” refers to the kidney.







## **FUNCTION OF THE NEPHRON**

Blood comes into the capillary bed, and plasma leaks out and enters the glomerulus. The plasma contains good stuff like nutrients, and bad stuff like waste products. As the plasma moves through the convoluted tubules and Loop of Henle, all of the nutrients, and most of the water, are absorbed back into the blood. Everything that is not reabsorbed (the waste products) goes into the collecting duct and is excreted as urine. This is also how the water-salt balance is maintained, as well as the acid-base balance.

Diuretics are medicines that increase the amount of urine that is produced. People who have high blood pressure might be prescribed diuretics to decrease the blood volume. **Alcohol is a diuretic and this is what contributes to the symptoms of a hangover. Caffeine is also a diuretic, so coffee and regular Coca-cola are diuretics.**

### **UREA**

Urea is a waste product of amino acid metabolism. Remember, proteins are made of amino acids, so when you break down proteins, you break down amino acids, and the waste product left over is urea. This is the main waste product in urine.

### **URETERS**

These are long tubes that transport urine from the kidney to the urinary bladder. It comes in at the base of the urinary bladder, not the top. As the bladder fills, it presses down on the ureters to prevent urine from backing up into the kidneys.

### **URINARY BLADDER**

The function is to store urine to permit controlled urination. The structure has folds =

**RUGAE** which allow for expansion. You can hold up to one liter of urine, although at 500ml, you'll be dancing. The function of the urinary bladder is just to store urine. There is a sphincter that keeps the urine in, and it's made of skeletal muscle, so it is under voluntary control.

The **URETHRA** connects the urinary bladder to the outside of the body. Don't get urethra and ureters mixed up!

The length differs from males to females:

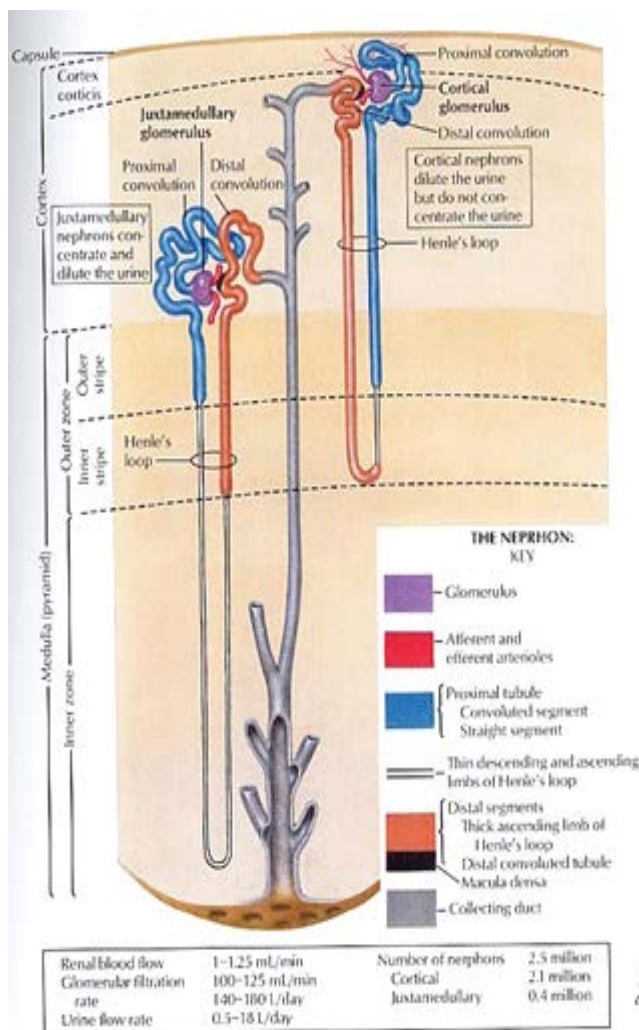
Females: 4cm

Males 20 cm (varies with mood)

**Because females have a much shorter urethra, they are more susceptible to bladder infections.**

**URETHRITIS** = infection of the urethra

**CYSTITIS** = infection of the urinary bladder.



### Mechanism of urine production in the nephron:

#### **Filtration:**

- Blood passing through glomerulus is filtered
- Filtrate consists of all components with less than 50000 molecular weight

#### **Reabsorption:**

- Material to be retained is reabsorbed in proximal convoluted tubule
- Includes ions, glucose, amino acids, small proteins and water

#### **Creation of hyper-osmotic extracellular fluid:**

- Main function of the loop of henle and vasa recta

- Countercurrent mechanism

#### **Adjustment of ion content of urine:**

- Occurs at distal convoluted tubule and collecting duct



- Controls amounts of  $\text{Na}^+$ ,  $\text{K}^+$ ,  $\text{H}^+$ ,  $\text{NH}_4^+$  excreted

### Concentration of urine:

- Occurs at collecting duct
- Movement of water down osmotic gradient into extracellular fluid
- Controlled vasopressin

### Components:

- Bowman's capsule contains basement membrane, parietal epithelium and visceral epithelium (surrounds the glomerulus and high pressure of blood forces ions to filter into glomerulus)
- Glomerulus (capillaries)
- Podocytes (visceral epithelial cells)
- Mesangial cells

### Blood supply:

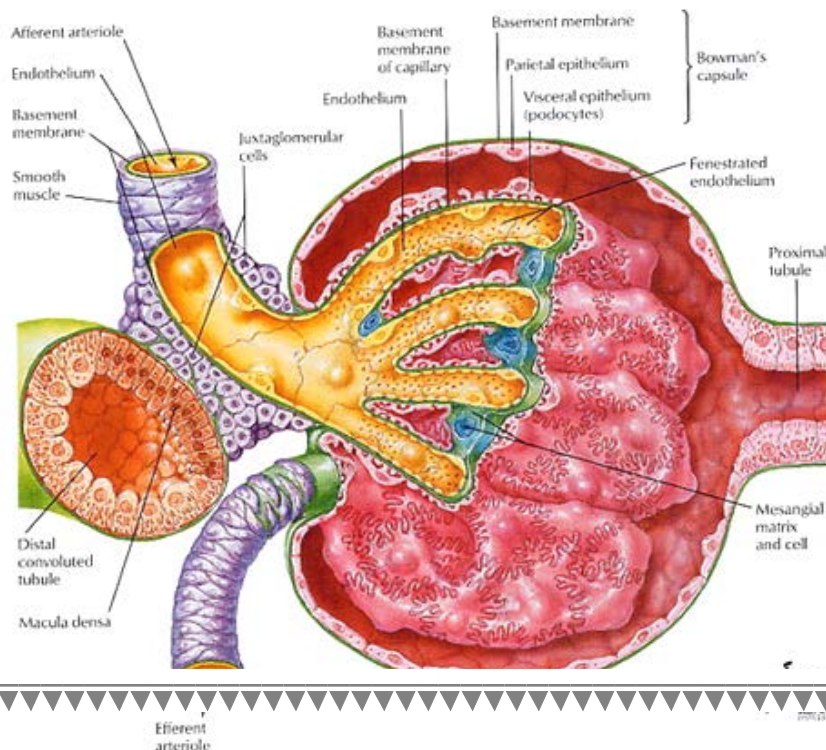
- Enters at vascular pole of corpuscle into afferent arteriole
- Filters through capillary network at high pressure
- Exits at efferent arteriole

### Filtration barrier:

- Fenestrae in capillary endothelium
- Specialised basal lamina
- Filtration slits between foot processes of podocytes
- Slits allow passage of ions and molecules < 50000 molecular weight

### Drainage of filtrate:

- To proximal convoluted tubule, at urinary pole



### **Proximal convoluted tubule:**

#### **Function:**

- Reabsorption of 70% of glomerular filtrate
- Na<sup>+</sup> movement by Na<sup>+</sup> pump
- Na<sup>+</sup> movement causes water and anions (-ve) to follow
- Glucose is taken up by Na<sup>+</sup>/glucose co transporter (movement of Na<sup>+</sup> into cell also moves glucose in)
- Amino acids by Na<sup>+</sup>/amino acid co-transporter
- Protein uptake by endocytosis

#### **Structure:**

- Cuboidal epithelium
- Tight junctions
- Membrane area increased to maximise rate of reabsorption
- Brush border at apical surface
- Interdigitations of basolateral membrane
- Contains aquaporin proteins to mediate water diffusion
- Prominent mitochondria (high energy requirement)

### **Loop of Henle – the countercurrent mechanism**

#### **Descending thin tubule:**

- Passive osmotic equilibrium
- Aquaporins present
- Simple squamous epithelium

#### **Ascending thick limb:**

- Na<sup>+</sup> and Cl<sup>-</sup> actively pumped out of tubular fluid
- Membranes lack aquaporins
- Therefore, low permeability to water
- Therefore, hypoosmotic tubular fluid, hyperosmotic extracellular fluid

- [Creates a countercurrent mechanism - high extracellular ion conc. - that allows water to passively move out of apparatus later on if water needs to be reabsorbed]
- Cuboidal epithelium, few microvilli
- High energy requirement – prominent mitochondria

Vasa recta:

- Blood vessels also arranged in loop
- Blood in rapid equilibrium with extracellular fluid
- Loop structure stabilises hyper-osmotic

### **Distal convoluted tubule/cortical collecting duct**

- Adjustment of  $\text{Na}^+/\text{K}^+/\text{H}^+/\text{NH}_4^+$
- Controlled by **aldosterone**
- Cuboidal epithelium, few microvilli
- Complex lateral membrane interdigitations with  $\text{Na}^+$  pumps
- Numerous large mitochondria
- Specialisation of macula densa, part of juxtaglomerular apparatus

### **Juxtaglomerular apparatus**

- Endocrine specialisation
- Secretes renin to control blood pressure via **angiotensin**
- Senses stretch in arteriole wall and  $\text{Cl}^-$  in tubule
- Cellular components are:
  - Macula densa of distal convoluted tubule
  - Juxtaglomerular cells of afferent arteriole

### **Medullary collecting duct**

- Completes ion adjustment and controls urine osmolarity
- Passes through medulla – hyperosmotic extracellular fluid
- Water moves down osmotic gradient to concentrate urine
- Rate of water movement is due to aquaporin-2 in apical membrane
  - Content varied by exo/endocytosis mechanism
  - Under control of vasopressin (neurohypophysis)
- Basolateral membrane has aquaporin-3, not under control
- Duct has simple cuboidal epithelium, single cilium per cell
- Cell boundaries don't interdigitate
- Smooth muscle wall for peristalsis ( 2 layers)
- Cells contain organelles associated with secretory activity

- Little active pumping (therefore few mitochondria)
- Drains into minor calyx at papilla of medullary pyramid
- Minor and major calyces and pelvis have urinary epithelium

### **Ureters**

- Drain urine from the kidneys
- Peristalsis movement towards the bladder
- Urinary epithelium resists damage by urine

### **Bladder**

- Urine storage organ (capacity of approx. 500ml)
- 2 ureters enter posterior wall, urethra leaves inferiorly
- Urinary epithelium resists damage and allows expansion
- Smooth muscle wall (detrussor muscle)
- Autonomic innervation
- Sphincter vesicae at urethral exit

### **Urinary epithelium – a.k.a. urothelium, transitional epithelium**

- Specialised form of epithelium – only found in urinary tract
- Found in part of kidney, ureters, bladder, part of urethra
- All cells contact basal lamina (but looks stratified)
- Epithelium is resistant to urine and able to stretch

### **Kidney stone**

A **kidney stone**, also known as a **renal calculus** (from the Latin *rēnēs*, "kidneys" and *calculus*, "pebble") is a solid concretion or crystal aggregation formed in the kidneys from dietary minerals in the urine.

Urinary stones are typically classified by their location in the kidney (nephrolithiasis), ureter (ureterolithiasis), or bladder (cystolithiasis), or by

their chemical composition (calcium-containing, struvite, uric acid, or other compounds). About 80% of those with kidney stones are men.

Mostly unknown, sometimes it runs in families and the marker to watch out for is whether members of the same family have an out-of-range hyperuricaemia, that is a high Uric Acid level in their blood. Dietary factors that increase the risk of stone formation include low fluid intake and high dietary intake of animal protein, sodium, refined sugars, fructose and high fructose corn syrup, oxalate, grapefruit juice, apple juice, and cola drinks.<sup>[citation needed]</sup>



X-ray with bilateral kidney stones

## Calcium

Calcium is one component of the most common type of human kidney stones, calcium oxalate. Some studies suggest people who take supplemental calcium have a higher risk of developing kidney stones, and these findings have been used as the basis for setting the recommended daily intake for calcium in adults.<sup>[7]</sup> In the Women's Health Initiative, postmenopausal women who consumed 1000 mg of supplemental calcium and 400 international units of vitamin D per day for seven years had a 17% higher risk of developing kidney stones than subjects taking a placebo. The Nurses' Health Study also showed an association between supplemental calcium intake and kidney stone formation.

Unlike supplemental calcium, high intakes of dietary calcium do not appear to cause kidney stones and may actually protect against their development. This is perhaps related to the role of calcium in binding ingested oxalate in the gastrointestinal tract. As the amount of calcium intake decreases, the amount of oxalate available for absorption into the bloodstream increases; this oxalate is then excreted in greater amounts into the urine by the kidneys. In the urine, oxalate is a very strong promoter of calcium oxalate precipitation, about 15 times stronger than calcium. In fact, current evidence suggests the consumption of diets low in calcium is associated with a higher overall risk for the development of kidney stones. For most individuals, other risk factors for kidney stones, such as high intakes of dietary oxalates and low fluid intake, would play a greater role than calcium intake.

### **Other electrolytes**

Aside from calcium, other electrolytes appear to influence the formation of kidney stones. For example, by increasing urinary calcium excretion, high dietary sodium may increase the risk of stone formation. Fluoridation of drinking water may increase the risk of kidney stone formation by a similar mechanism, though further epidemiologic studies are warranted to determine whether fluoride in drinking water is associated with an increased incidence of kidney stones. On the other hand, high dietary intake of potassium appears to reduce the risk of stone formation because potassium promotes the urinary excretion of citrate, an inhibitor of urinary crystal formation. High dietary intake of magnesium also appears to reduce the risk of stone formation somewhat, because like citrate, magnesium is also an inhibitor of urinary crystal formation.

### **Animal protein**

Diets in Western nations typically contain a large proportion of animal protein. Urinary excretion of excess sulfurous amino acids (e.g., cysteine and methionine), uric acid and other acidic metabolites from animal protein acidifies the urine, which promotes the formation of kidney stones.<sup>[citation needed]</sup> The body often balances this acidic urinary pH by leaching calcium from the bones, which further promotes the formation of kidney stones. Low urinary citrate excretion is also commonly found in those with a high dietary intake of animal protein, whereas vegetarians tend to have higher levels of citrate excretion.

## **Vitamins**

Despite a widely held belief in the medical community that ingestion of vitamin C supplements is associated with an increased incidence of kidney stones, the evidence for a causal relationship between vitamin C supplements and kidney stones is inconclusive. While excess dietary intake of vitamin C might increase the risk of calcium oxalate stone formation, in practice this is rarely encountered. The link between vitamin D intake and kidney stones is also tenuous. Excessive vitamin D supplementation may increase the risk of stone formation by increasing the intestinal absorption of calcium, but there is no evidence that correction of vitamin D deficiency increases the risk of stone formation.

## **Other**

There are no conclusive data demonstrating a cause-and-effect relationship between alcohol consumption and kidney stones. However, some have theorized that certain behaviors associated with frequent and binge drinking can lead to systemic dehydration, which can in turn lead to the development of kidney stones. The American Urological Association has projected that increasing global temperatures will lead to an increased incidence of kidney stones in the United States by expanding the "kidney stone belt" of the southern United States-

(23) weeks

## **NERVOUS SYSTEM**

### **Three Parts of the Nervous System**

1. Central Nervous System (CNS): brain and spinal cord.

2. Peripheral Nervous System (PNS): nerves of the body
3. Autonomic Nervous System (ANS): has parts of the CNS and PNS. Controls automatic functions (blood pressure, digestion)
  - a. Sympathetic division
  - b. Parasympathetic division

Before we talk about these three parts, let's talk about the nerve cells.

The brain has about a trillion nerve cells.

**NEURON** (main cell of the nervous system)

All neurons do three things:

1. Receive a signal.
2. Transmit a signal to another location.
3. Stimulate another cell
  - a. Another neuron transmit signal
  - b. Muscle contraction
  - c. Gland secretion

There are hundreds of different types of neurons, each one is specialized for a particular task (e.g. sense light, smell, tell muscles to contract, etc). They all share certain characteristics.

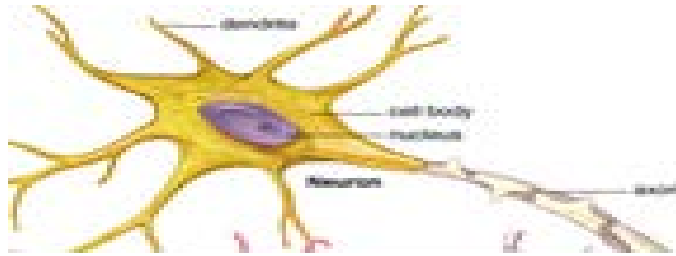
**DENDRITES** receive the signal

**CELL BODY** is where the nucleus, ribosomes, and most organelles are located

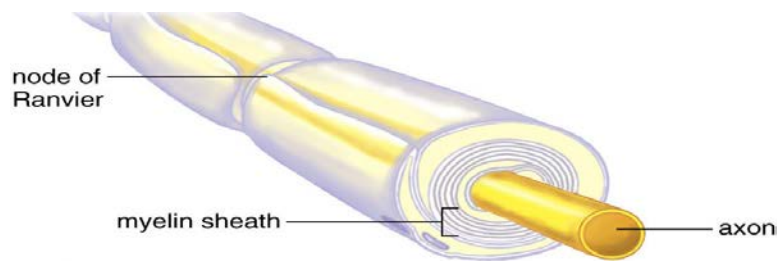
**AXON** sends the signals. Some cells have many axons, some have one, some are short, and some are long.



SYNAPTIC KNOBS function to stimulate another cell.

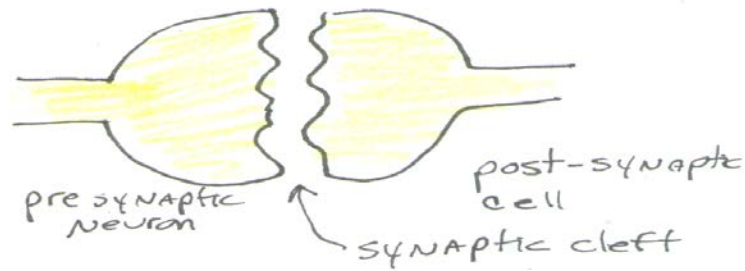


MYELIN SHEATH is a coating of lipids around certain types of neurons. It is like the plastic coating around wires we use around the house. It functions to transmit the signals faster. This is important because in a fetus, the only fat in the body is on the myelin sheaths of neurons. Therefore, excess vitamins A, D, E, and K will tend to lodge there and interfere with nerve transmission.



**MULTIPLE SCLEROSIS** is an autoimmune disease where the sheaths of the neurons are destroyed, interfering with the neuron functions in the CNS and brain. Starts to manifest in late teens and early 20's. It progresses to paralysis and sometimes death. There are treatments, but no cure.

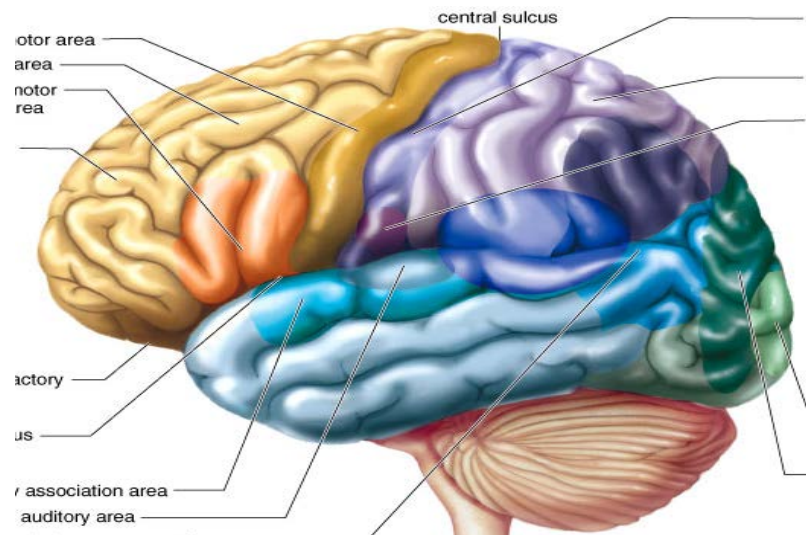
**PRE-SYNAPTIC NEURON SYNAPTIC CLEFT POST SYNAPTIC CELL**



Now let's talk about the three parts of the nervous system.

## 1. CENTRAL NERVOUS SYSTEM: The brain and spinal cord

### THE BRAIN : ANATOMICAL REGIONS



The brain is divided into parts. The largest portion is the **CEREBRUM**, which makes up 80% of the brain. It's responsible for consciousness and all the complex behaviors, sensations, etc. The cerebrum is divided into 2 halves called **CEREBRAL HEMISPHERES**. In general, the left side controls the right half of the body, and the right side of the brain controls the left half of the body. These two halves of the brain communicate with each other.

Since the brain is so important, it is protected by the skull, cerebrospinal fluid which cushions it, and meninges which are membranes that surround the brain and only let certain substances cross through to the brain. The brain is one of the few organs that can only use glucose to get ATP as its energy source. Therefore, without some sugar in our bloodstream, the brain will die. That's one reason why proper nutrition is so important.

By the way, geniuses have the same size brain as everyone else; they are just more efficient at forming synapses. We don't use 10% of our brains, we use 100%.

## MENINGES

These are tissues that cover the entire CNS. They have fluid between them (CSF) and serve to protect and cushion the brain.

## CEREBRAL SPINAL FLUID

CSF is similar to plasma because it is derived from plasma.

1. Allows the brain to float. The brain has the consistency of Jell-O, and weighs three pounds. Its weight would crush the inferior structures if it didn't float.
2. It cushions. In sudden movement, like riding a bike into a tree, and hitting the head on the tree, the brain hits inside the skull in the front, and then in recoil it hits the back of the skull = closed head injury, not necessarily with a fracture.

## MENINGITIS

This is when the meninges become infected. Can be caused from virus (not that bad) or bacteria (can be fatal). The main symptom is a headache, so when this occurs in an infant, they can't say where they hurt.

So when an infant presents with a high fever of 104° with no other symptoms, they will usually test for meningitis, because if they miss

it, it's fatal. The test is a SPINAL TAP, where a needle is inserted in the low back below the level of the spinal cord. They draw the CSF to look at.

## SPINAL CORD

Really, this is just a continuation of the brain. The primary functions of the spinal cord are for simple reflexes and to be a link between brain and body. The spinal cord can also use a SIMPLE REFLEX ARC. They process information without the brain. So if you touch a hot stove, the sensory input comes into the spinal cord, a special neuron there immediately tells your muscles to contract, and you take your hand off the stove before your brain even knows it.

### **(24) weeks**

## 2. PERIPHERAL NERVOUS SYSTEM

These are the nerves of the body outside of the spinal cord and brain.

### Cut nerves

If a small nerve is cut, it will regenerate. Large nerves are harder to re-grow, but you can still stitch the ends together and you may get healing.

### Pinched nerves

When a nerve gets pinched (e.g. herniated vertebral disc), it damages the nerve by interfering with its signal transmission, causing weakness, pain, or paralysis.

### Blood supply interfered with

When a body part “falls asleep”, the region is lacking blood flow, impairing the nerve signals as well. Unlike the CNS, when blood is restored, the nerves recover. Damage to the CNS tends to be permanent, but damage to the PNS tends to heal.

### 3. AUTONOMIC NERVOUS SYSTEM

These are the nerves supplying things we don't have voluntary control over, such as digestion, blood flow, urination, defecation, glandular secretion. The autonomic nervous system has two divisions: sympathetic and parasympathetic.

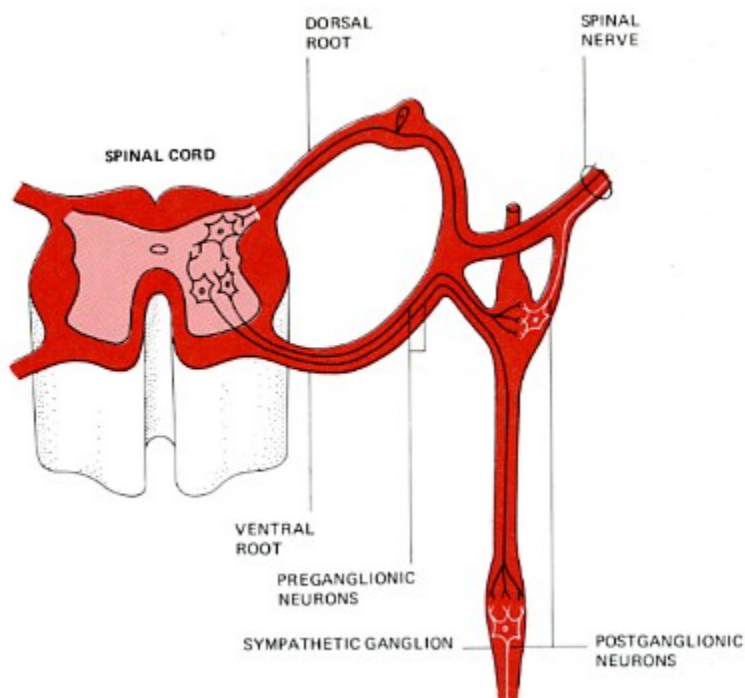
#### a) SYMPATHETIC DIVISION

This is involved in ↑heart rate and sweating, ↓digestive system. E.g. when running, ↑heart rate = sympathetic. When hot ☐ sweat = sympathetic. The term “Fight or Flight” refers to the reaction you get when you are scared and need to run.

#### b) PARASYMPATHETIC DIVISION

The function of this division is the opposite of the sympathetic; it is “rest and digest”. It ↓heart rate, activates digestive system, and causes salivation, urination, and defecation.

### The Sympathetic Nervous System



The **preganglionic** motor neurons of the sympathetic system (shown in black) arise in the spinal cord. They pass into sympathetic **ganglia** which are organized into two chains that run parallel to and on either side of the spinal cord.

The preganglionic neuron may do one of three things in the sympathetic ganglion:

- synapse with **postganglionic** neurons (shown in white) which then reenter the spinal nerve and ultimately pass out to the sweat glands and the walls of blood vessels near the surface of the body.
- pass up or down the sympathetic chain and finally synapse with postganglionic neurons in a higher or lower ganglion
- leave the ganglion by way of a cord leading to special ganglia (e.g. the solar plexus) in the viscera. Here it may synapse with postganglionic sympathetic neurons running to the smooth muscular walls of the viscera. However, some of these preganglionic neurons pass right on through this second ganglion and into the **adrenal medulla**. Here they synapse with the highly-modified postganglionic cells that make up the secretory portion of the adrenal medulla.

The neurotransmitter of the preganglionic sympathetic neurons is **acetylcholine (ACh)**. It stimulates action potentials in the postganglionic neurons.

The neurotransmitter released by the postganglionic neurons is **noradrenaline** (also called **norepinephrine**).

The action of noradrenaline on a particular gland or muscle is excitatory in some cases, inhibitory in others. (At excitatory terminals, **ATP** may be released along with noradrenaline.)

#### The release of noradrenaline

- stimulates **heartbeat**
- raises **blood pressure**
- dilates the pupils
- dilates the **trachea and bronchi**
- stimulates glycogenolysis — the conversion of liver **glycogen** into glucose
- shunts blood away from the skin and viscera to the skeletal muscles, brain, and heart
- inhibits peristalsis in the gastrointestinal (GI) tract
- inhibits contraction of the bladder and rectum
- and, at least in rats and mice, increases the number of **AMPA receptors** in the hippocampus and thus increases **long-term potentiation (LTP)**.

In short, stimulation of the sympathetic branch of the autonomic nervous system prepares the body for emergencies: for "**fight or flight**" (and, perhaps, enhances the memory of the event that triggered the response).

Activation of the sympathetic system is quite general because

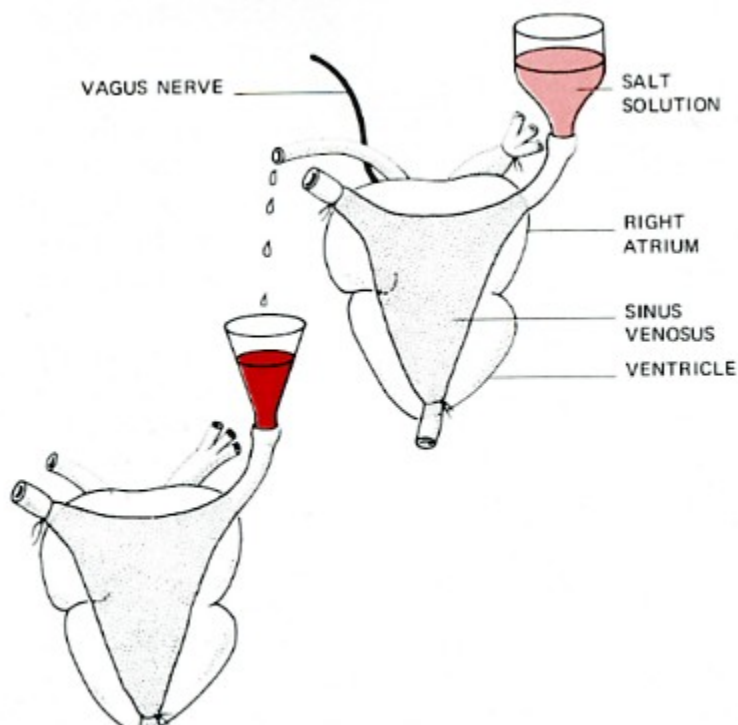
- a single preganglionic neuron usually synapses with many postganglionic neurons;
- the release of **adrenaline** from the **adrenal medulla** into the blood ensures that all the cells of the body will be exposed to sympathetic stimulation even if no postganglionic neurons reach them directly.

### The Parasympathetic Nervous System

The main nerves of the parasympathetic system are the tenth cranial nerves, the **vagus nerves**. They originate in the **medulla oblongata**. Other preganglionic parasympathetic neurons also extend from the brain as well as from the lower tip of the spinal cord.

Each preganglionic parasympathetic neuron synapses with just a few postganglionic neurons, which are located near — or in — the effector organ, a muscle or gland. **Acetylcholine (ACh)** is the neurotransmitter at all the pre- and many of the postganglionic neurons of the parasympathetic system. However, some of the postganglionic neurons release **nitric oxide (NO)** as their neurotransmitter.

The Nobel Prize winning physiologist Otto Loewi discovered (in 1920) that the effect of both sympathetic and parasympathetic stimulation is mediated by released chemicals. He removed the living heart from a frog with its sympathetic and parasympathetic nerve supply intact. As expected, stimulation





of the first speeded up the heart while stimulation of the second slowed it down.

Loewi found that these two responses would occur in a second frog heart supplied with a salt solution taken from the stimulated heart. Electrical stimulation of the vagus nerve leading to the first heart not only slowed its beat but, a short time later, slowed that of the second heart also. The substance responsible was later shown to be acetylcholine. During sympathetic stimulation, adrenaline (in the frog) is released.

In short, the parasympathetic system returns the body functions to normal after they have been altered by sympathetic stimulation. In times of danger, the sympathetic system prepares the body for violent activity. The parasympathetic system reverses these changes when the danger is over.

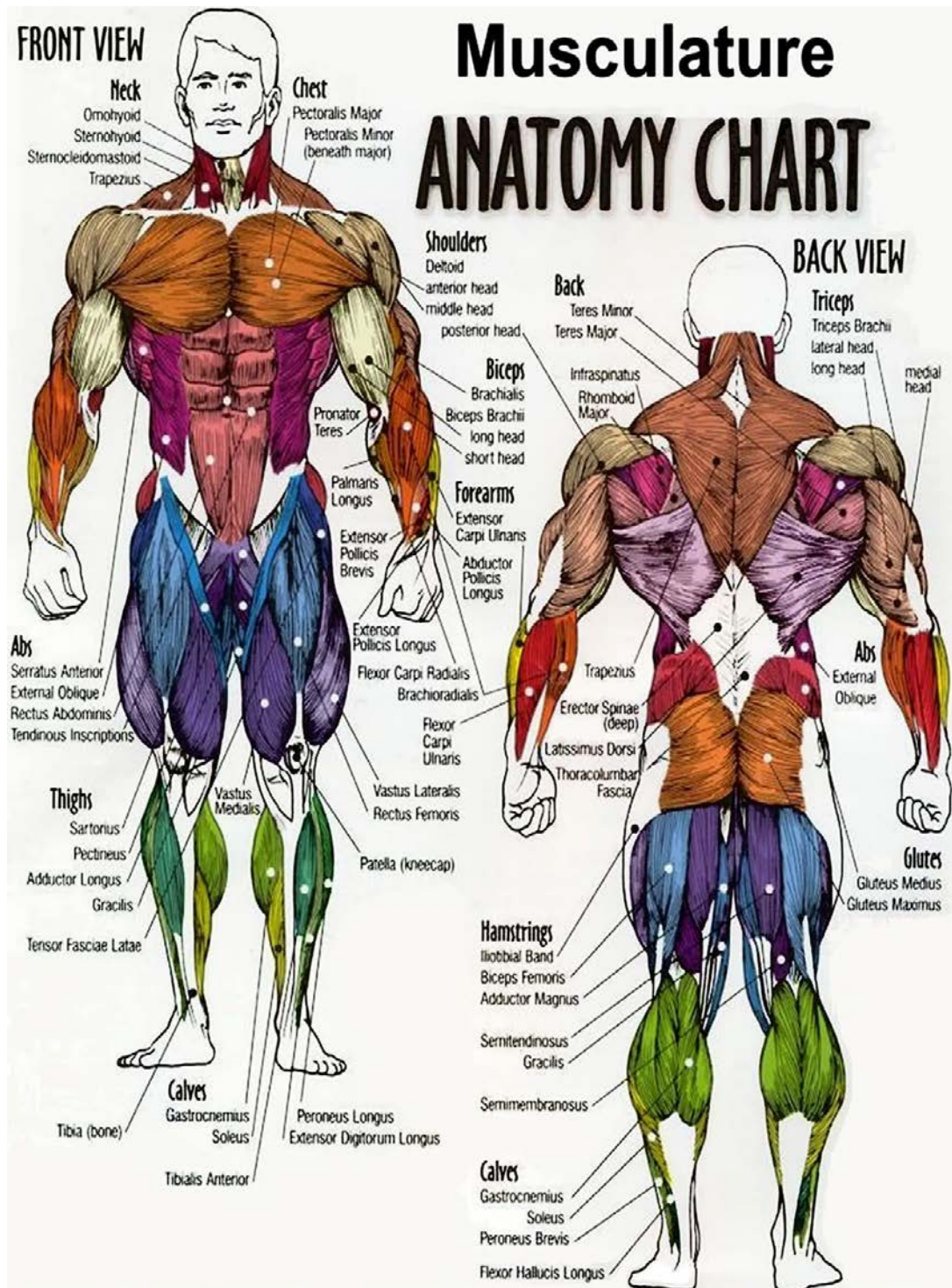
The vagus nerves also help keep [inflammation](#) under control. Inflammation stimulates nearby sensory neurons of the vagus. When these nerve impulses reach the medulla oblongata, they are relayed back along motor fibers to the inflamed area. The acetylcholine from the motor neurons suppresses the release of inflammatory cytokines, e.g., [tumor necrosis factor](#) (TNF), from macrophages in the inflamed tissue.

Although the autonomic nervous system is considered to be involuntary, this is not entirely true. A certain amount of conscious control can be exerted over it as has long been demonstrated by practitioners of Yoga and Zen Buddhism. During their periods of meditation, these people are clearly able to alter a number of autonomic functions including heart rate and the rate of oxygen consumption. These changes are not simply a reflection of decreased physical activity because they exceed the amount of change occurring during



(25) weeks

## Muscular system



Muscle is composed of many elongated cells, called muscle fibres, which are all able to contract and relax. Each has its own nerve supply.

Histologically (histology - study of tissues and cells at microscopic level)

### 3 distinct types:

1 **Skeletal** (striated, striped, voluntary)

Attached to bone. Concerned with locomotion. Contract quickly and fatigue quickly. Innervated by voluntary nervous system.

2 **Smooth** (unstriated, unstriped, plain, involuntary)

Found walls of tubular organs, e.g. intestines, blood vessels, and concerned with movement of materials through them. Contract slowly and fatigue slowly. Innervated by autonomic nervous system.

3 **Cardiac** (myogenic)

Contracts spontaneously, without fatigue. Innervated by autonomic NS

- **Skeletal muscle contractions**

Skeletal muscles contract according to the *sliding filament model* see also *Excitation-contraction coupling*

1. An action potential originating in the CNS reaches an alpha motor neuron, which then transmits an action potential down its own axon.
2. The action potential propagates by activating voltage-gated sodium channels along the axon toward the neuromuscular junction. When it reaches the junction, it causes a calcium ion influx through voltage-gated calcium channels.
3. The  $\text{Ca}^{2+}$  influx causes vesicles containing the neurotransmitter acetylcholine to fuse with the plasma membrane, releasing acetylcholine out into the extracellular space between the motor neuron terminal and the neuromuscular junction of the skeletal muscle fiber.
4. The acetylcholine diffuses across the synapse and binds to and activates nicotinic acetylcholine receptors on the neuromuscular junction. Activation of the nicotinic receptor opens its intrinsic sodium/potassium channel, causing sodium to rush in and potassium to trickle out. Because the channel is more permeable to sodium, the charge difference between internal and external surfaces of the muscle fiber membrane becomes less negative, triggering an action potential.

5. The action potential spreads through the muscle fiber's network of T-tubules, depolarizing the inner portion of the muscle fiber.
6. The depolarization activates L-type voltage-dependent calcium channels (dihydropyridine receptors) in the T tubule membrane, which are in close proximity to calcium-release channels (ryanodine receptors) in the adjacent sarcoplasmic reticulum.
7. Activated voltage-gated calcium channels physically interact with calcium-release channels to activate them, causing the sarcoplasmic reticulum to release calcium.
8. The calcium binds to the troponin C present on the actin-containing thin filaments of the myofibrils. The troponin then allosterically modulates the tropomyosin. Under normal circumstances, the tropomyosin sterically obstructs binding sites for myosin on the thin filament; once calcium binds to the troponin C and causes an allosteric change in the troponin protein, troponin T allows tropomyosin to move, unblocking the binding sites.
9. Myosin (which has ADP and inorganic phosphate bound to its nucleotide binding pocket and is in a ready state) binds to the newly uncovered binding sites on the thin filament (binding to the thin filament is very tightly coupled to the release of inorganic phosphate). Myosin is now bound to actin in the strong binding state. The release of ADP and inorganic phosphate are tightly coupled to the power stroke (actin acts as a cofactor in the release of inorganic phosphate, expediting the release). This will pull the Z-bands towards each other, thus shortening the sarcomere and the I-band.
10. ATP binds to myosin, allowing it to release actin and be in the weak binding state (a lack of ATP makes this step impossible, resulting in the rigor state characteristic of rigor mortis). The myosin then hydrolyzes the ATP and uses the energy to move into the "cocked back" conformation. In general, evidence (predicted and *in vivo*) indicates that each skeletal muscle myosin head moves 10–12 nm each power stroke, however there is also evidence (*in vitro*) of variations (smaller and larger) that appear specific to the myosin isoform.
11. Steps 9 and 10 repeat as long as ATP is available and calcium is present on thin filament.
12. While the above steps are occurring, calcium is actively pumped back into the sarcoplasmic reticulum. When calcium is no longer present on the thin filament, the tropomyosin changes conformation back to its

previous state so as to block the binding sites again. The myosin ceases binding to the thin filament, and the contractions cease.

The calcium ions leave the troponin molecule in order to maintain the calcium ion concentration in the sarcoplasm. The active pumping of calcium ions into the sarcoplasmic reticulum creates a deficiency in the fluid around the myofibrils. This causes the removal of calcium ions from the troponin. Thus, the tropomyosin-troponin complex again covers the binding sites on the actin filaments and contraction ceases.

### Smooth muscle contraction

The interaction of sliding actin and myosin filaments is similar in smooth muscle. There are differences in the proteins involved in contraction in vertebrate smooth muscle compared to cardiac and skeletal muscle. Smooth muscle does not contain troponin, but does contain the thin filament protein tropomyosin and other notable proteins – caldesmon and calponin. Contractions are initiated by the calcium-activated phosphorylation of myosin rather than calcium binding to troponin. Contractions in vertebrate smooth muscle are initiated by agents that increase intracellular calcium. This is a process of depolarizing the sarcolemma and extracellular calcium entering through L-type calcium channels, and intracellular calcium release predominately from the sarcoplasmic reticulum. Calcium release from the sarcoplasmic reticulum is from Ryanodine receptor channels (calcium sparks) by a redox process and Inositol triphosphate receptor channels by the second messenger inositol triphosphate. The intracellular calcium binds with calmodulin, which then binds and activates myosin light-chain kinase. The calcium-calmodulin-myosin light-chain kinase complex phosphorylates myosin on the 20 kilodalton (kDa) myosin light chains on amino acid residue-serine 19, initiating contraction and activating the myosin ATPase. The phosphorylation of caldesmon and calponin by various kinases is suspected to play a role in smooth muscle contraction.

Phosphorylation of the 20 kDa myosin light chains correlates well with the shortening velocity of smooth muscle. During this period, there is a rapid burst of energy utilization as measured by oxygen consumption. Within a few minutes of initiation, the calcium level markedly decreases, the 20 kDa myosin light chains' phosphorylation decreases, and energy utilization decreases; however, force in tonic smooth muscle is maintained. During contraction of muscle, rapidly cycling crossbridges form between activated

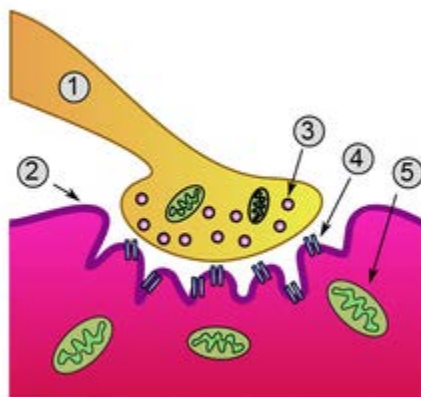
actin and phosphorylated myosin, generating force. It is hypothesized that the maintenance of force results from dephosphorylated "latch-bridges" that slowly cycle and maintain force. A number of kinases such as Rho kinase, Zip kinase, and Protein Kinase C are believed to participate in the sustained phase of contraction, and calcium flux may be significant

### **motor unit**

is made up of a motor neuron and the skeletal muscle fibers innervated by that axon.<sup>[1]</sup> Groups of motor units often work together to coordinate the contractions of a single [muscle](#); all of the motor units within a muscle are considered a [motor pool](#).

All muscle fibers in a motor unit will be of the same [fiber type](#). When a motor unit is activated, all of its fibers contract. In [vertebrates](#), control of muscle contraction force is accomplished by controlling how many motor units are activated for a given motion.

The number of muscle fibers within each unit can vary within a particular muscle and still more widely from muscle to muscle; the muscles that act on the largest body masses have motor units that contain most of the muscle fibers whereas smaller muscles consist of less muscle fibers in each unit.<sup>[1]</sup> For instance, [thigh](#) muscles can have a thousand fibers in each unit, while [extraocular muscles](#) might have ten. Additionally, muscles which possess more motor units are thus able to control force output more finely.





### **neuromuscular junction**

connects the nervous system to the muscular system via synapses between efferent nerve fibers and muscle fibers, also known as muscle cells. As an action potential reaches the end of a motor neuron, voltage-dependent calcium channels open allowing calcium to enter the neuron. Calcium binds to sensor proteins on synaptic vesicles called synaptotagmin triggering vesicle fusion with plasmamembrane and subsequent neurotransmitter release from the motor neuron into the synaptic cleft. In vertebrates, motor neurons release acetylcholine (ACh), a small molecule neurotransmitter, which diffuses through the synapse and binds nicotinic acetylcholine receptors (nAChRs) on the plasma membrane of the muscle fiber, also known as the sarcolemma. nAChRs are ionotropic, meaning they serve as ligand gated ion channels. The binding of ACh to the receptor can depolarize the muscle fiber, causing a cascade that eventually results in muscle contraction.

(27) weeks

### **Fever**

A temperature setpoint is the level at which the body attempts to maintain its temperature. When the setpoint is raised, the result is a fever. Most fevers are caused by [infectious disease](#) and can be lowered, if desired, with [antipyretic](#) medications.

An early morning temperature higher than 37.2°C (>98.9°F) or a late afternoon temperature higher than 37.7°C (>99.9°F) is normally considered a fever, assuming that the temperature is elevated due to a change in the hypothalamus's setpoint.<sup>[1]</sup> Lower thresholds are sometimes appropriate for elderly people.<sup>[1]</sup> The normal daily temperature variation is typically 0.5°C (0.9°F), but can be greater among people recovering from a fever.<sup>[1]</sup>

An organism at optimum temperature is considered *afebrile* or *apyrexia*, meaning "without fever". If temperature is raised, but the setpoint is not raised, then the result is [hyperthermia](#).

## **Hyperthermia**

Hyperthermia occurs when the body produces or absorbs more heat than it can dissipate. It is usually caused by prolonged exposure to high temperatures. The heat-regulating mechanisms of the body eventually become overwhelmed and unable to deal effectively with the heat, causing the body temperature to climb uncontrollably. Hyperthermia at or above about 40 °C (104 °F) is a life-threatening medical emergency that requires immediate treatment. Common symptoms include headache, confusion, and fatigue. If sweating has resulted in dehydration, then the affected person may have dry, red skin.

In a medical setting, mild hyperthermia is commonly called *heat exhaustion* or *heat prostration*; severe hyperthermia is called *heat stroke*. Heat stroke may come on suddenly, but it usually follows the untreated milder stages. Treatment involves cooling and rehydrating the body; fever-reducing drugs are useless for this condition. This may be done through moving out of direct sunlight to a cooler and shaded environment, drinking water, removing clothing that might keep heat close to the body, or sitting in front of a fan. Bathing in tepid or cool water, or even just washing the face and other exposed areas of the skin, can be helpful.

With fever, the body's core temperature rises to a higher temperature through the action of the part of the brain that controls the body temperature; with hyperthermia, the body temperature is raised without the consent of the heat control centers.

## **Hypothermia**

In hypothermia, body temperature drops below that required for normal metabolism and bodily functions. In humans, this is usually due to excessive exposure to cold air or water, but it can be [deliberately induced as a medical treatment](#). Symptoms usually appear when the body's core temperature drops by 1-2 °C (1.8-3.6 °F) below normal temperature.

## **Basal body temperature**

Basal body temperature is the lowest temperature attained by the body during rest (usually during sleep). It is generally measured immediately after awakening and before any physical activity has been undertaken, although the temperature measured at that time is somewhat higher than the true basal body temperature. In women, temperature differs at various points in the [menstrual cycle](#), and this can be used in the long-term to track ovulation both for the purpose of aiding conception or avoiding pregnancy. This process is called [fertility awareness](#)

the body automatically regulates the amount of heat that it gives off. However, the body's ability to adjust to varying environmental conditions is limited. Furthermore, although the body may adjust to a certain (limited) range of atmospheric conditions, it does so with a distinct feeling of discomfort. The discussion that follows will help you understand how atmospheric conditions affect the body's ability to maintain a heat balance.

### **Body Heat Gains**

The body gains heat by radiation, by convection, by conduction, and as a by-product of physiological processes that take place within the body. The heat gain by radiation comes from our surroundings. However, heat always travels from areas of higher temperature to areas of lower temperature. Therefore, the body receives heat from those surroundings that have a temperature higher than body surface temperature. The greatest source of heat radiation is the sun. Some sources of indoor heat radiation are heating devices, operating machinery, and hot steam piping

### **Mechanisms of Heat Loss**

In order to design appropriate clothing and sleep systems, we must first understand the primary mechanisms of heat loss.

### **Conduction**

Conduction is defined as the transfer of heat from a warmer object to a cooler object when the two objects are in direct contact with each other. Backpackers experience conductive heat loss anytime the body is in direct contact with cold ground. While hiking, the primary source of conductive heat loss is out of the feet via soles of your footwear. While at rest, conductive heat loss occurs while sitting or lying on the cold ground surface.



Conduction is also a major source of heat loss in wet clothing, due water's excellent conductive properties.

## **Convection**

Convective heat loss occurs in response to movement of a fluid or gas. In outdoor clothing systems, convective heat loss occurs when warm air next to the body and in the clothing is displaced by cool air from the outside environment. The biggest factor contributing to convective heat loss, of course, is wind.

In addition to wind-induced or "forced" convection, "passive" convection occurs via the "chimney effect" that draws cool, dense air into our clothing system from pants cuffs and waist hems, displacing warm, light air that exits out of our neck hems and other vents.

## **Radiation**

Radiative heat loss from the human body occurs primarily due to infrared emission. Radiative heat loss occurs primarily on cold, clear nights, and is readily noticeable after sunset. Cloud cover dampens the effects of radiative heat loss somewhat, by reflecting a significant portion of radiant heat back to the earth's surface. A backpacker carrying a properly designed cold weather clothing system will not experience a significant amount of radiative heat loss unless he is thinly clothed.

## **Evaporation**

Evaporative heat loss is a desert hiker's best friend and a winter traveler's worst enemy.

Evaporation occurs when a liquid (such as sweat) changes phase to a vapor (sweat vapor). This phase change requires heat. Unfortunately, your body heat drives this phase change. Evaporative heat loss may be most noticeable in context of the "flash-off" effect, which occurs after a period of intense physical activity and sweating in cold conditions, followed by rapid evaporation and chill after stopping to rest.

Evaporative heat loss from perspiration can occur in one of two ways. Sensible (or "active") perspiration is caused by the formation of liquid sweat droplets at the skin surface in response to excess heat. This excess heat is

usually a result of being dressed too warmly for a given activity level. Insensible (or “passive”) perspiration is the direct emission of sweat vapor from the skin in response to a humidity gradient (i.e., your skin is “drying out”). Insensible perspiration is most significant while at rest, or while sleeping, while sensible perspiration is most significant during periods of activity.

## **Respiration**

Technically, respiration combines the processes of evaporation (of moisture in the lungs) and convection (displacement of warm air in the lungs by cold air from the outside environment). Because humidity in the lungs is 100%, respiration is an important heat sink in cold, dry conditions.. Significant moisture (and thus, body heat) can be lost when that moist air is exchanged with much drier outside air. In addition, some body heat is lost to the process of warming the cold air entering your lungs.

(29) weeks

## **ENDOCRINE SYSTEM**

### **INTRODUCTION**

The endocrine system is a collection of ductless glands that secrete chemical messages, known as **hormones**.

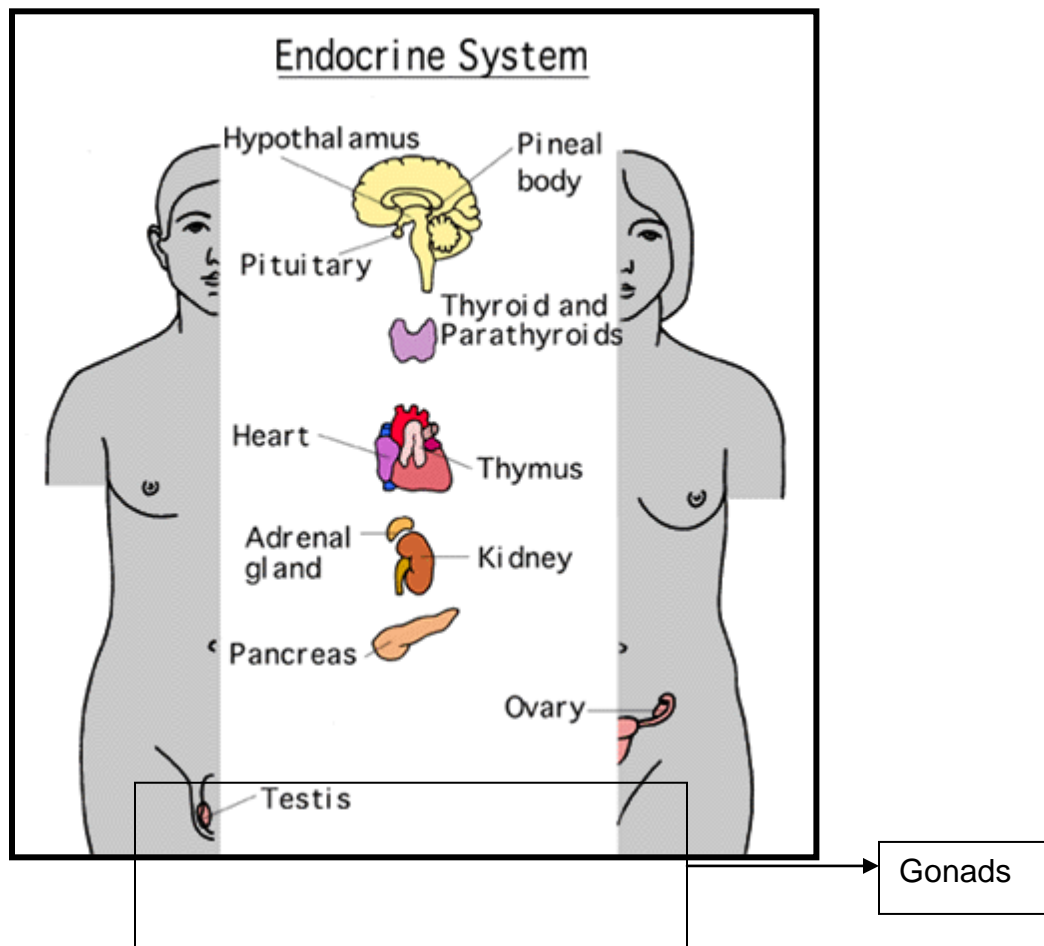
The role of the endocrine system is to maintain homeostasis and long-term control of the human body using chemical signals (the hormones). Also, the endocrine system works in parallel with the nervous system to control growth and maturation along with body homeostasis.

The hormones produced by the glands of the endocrine system are passed through the blood circulation to arrive at a target organ, which possesses a series of cells that bear an appropriate hormone receptor. This receptor binds with the hormone molecule and triggers a series of chemical reactions inside the cell.

As mentioned before, the endocrine system is constituted by the endocrine glands – which secrete hormones.

The major human endocrine glands include:

- the **hypothalamus**
- the **pituitary gland**
- the **thyroid gland**
- the **pancreas**
- the **adrenal glands**
- the **gonads** or sex organs



The endocrine system in females and males

## HORMONES

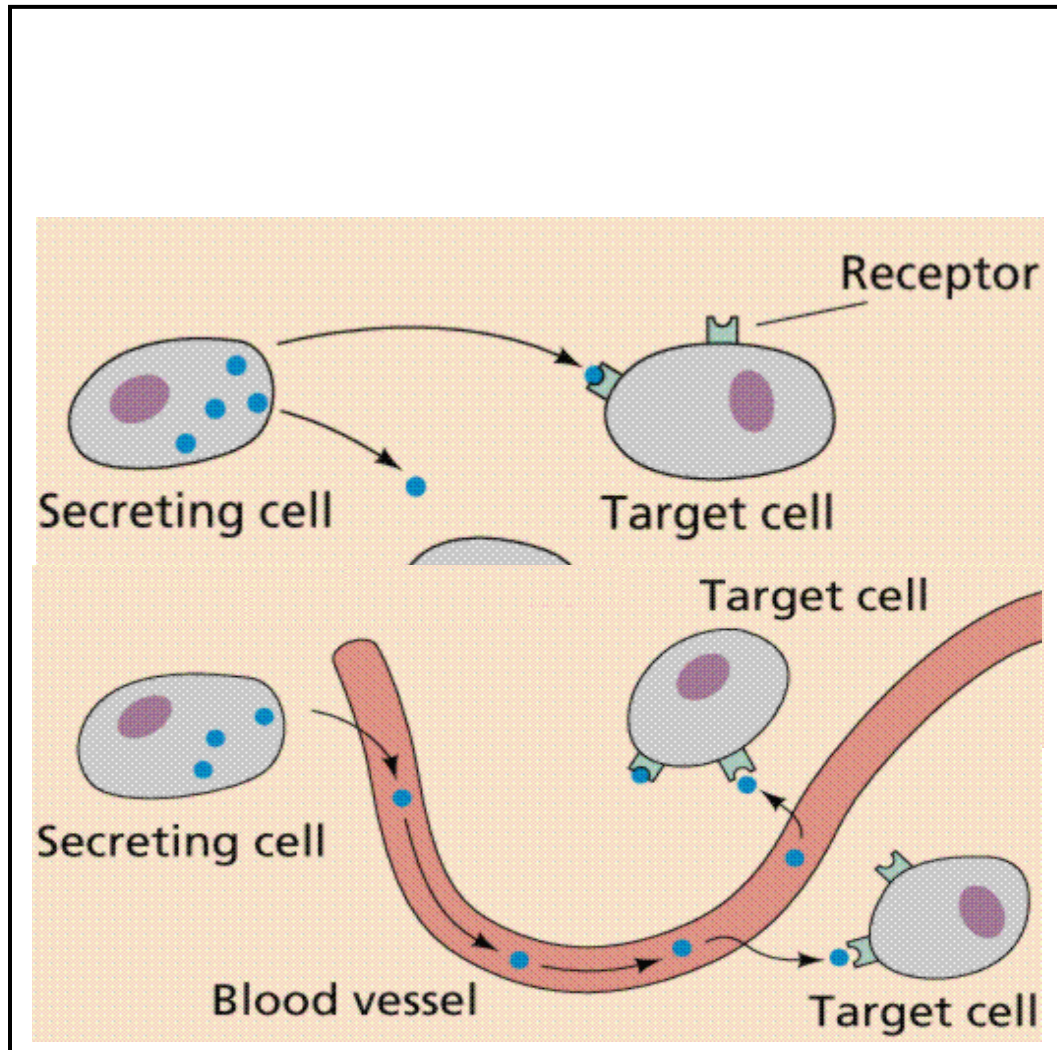
A hormone is a messenger molecule synthesized and secreted by a group of specialized cells that constitute an **endocrine gland**. These glands are **ductless**, which means that their secretions (hormones) are released directly into the bloodstream and travel elsewhere in the body to **target organs**, upon which they act. Note that this is in contrast to the exocrine glands, which have ducts for releasing the substances that they produce. Exocrine glands (not part of the endocrine system) secrete products that are passed outside the body. Sweat glands and salivary glands are examples of exocrine glands.

There are three general groups of hormones. These are classified as follows – according to their chemical structure:

- **Steroid hormones** including *prostaglandins* which function especially in a variety of female functions and the *sex hormones* all of which are lipids made from cholesterol.
- **Amino acid derivatives** (like epinephrine) which are derived from amino acids, especially tyrosine.
- **Peptide hormones** (like insulin) which are the most numerous/diverse group of hormones.

## Mechanisms of Hormone Action

Hormones trigger actions in specific target cells, after binding to an appropriate receptor. Receptors are membrane proteins that bind to hormones. A certain hormone receptor located on a specific target cell can only bind to one type of hormone. More than fifty human hormones have been identified; all act by binding to receptor molecules. The binding hormone causes a change in the shape of the receptor. This alteration of the receptor's molecule causes the cell to respond to the hormone.

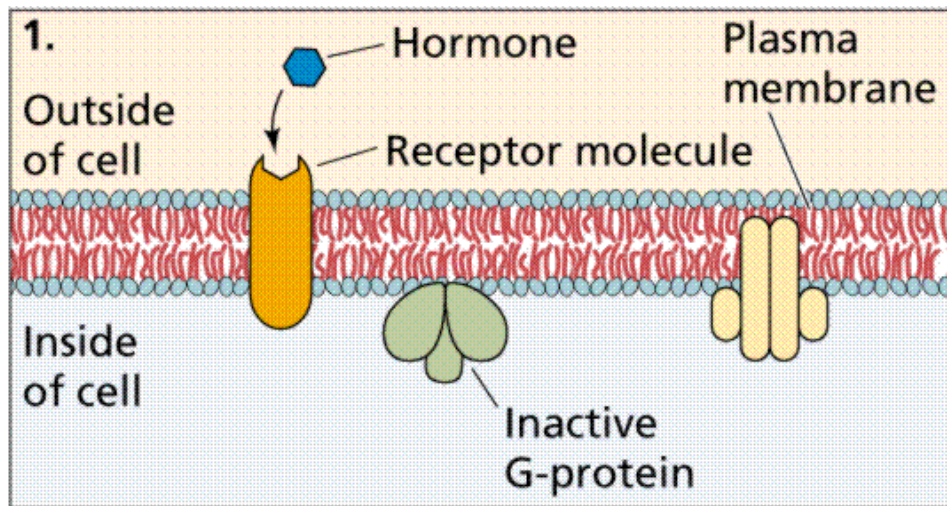
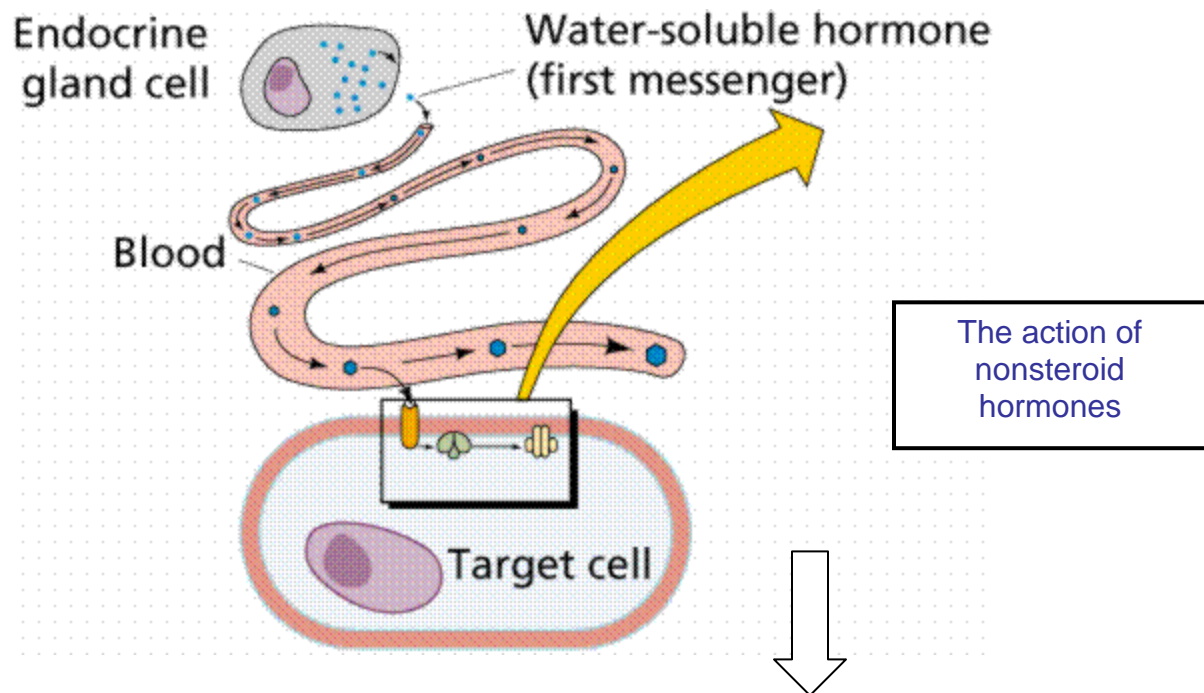


There are two different mechanisms of hormone action on all target cells:

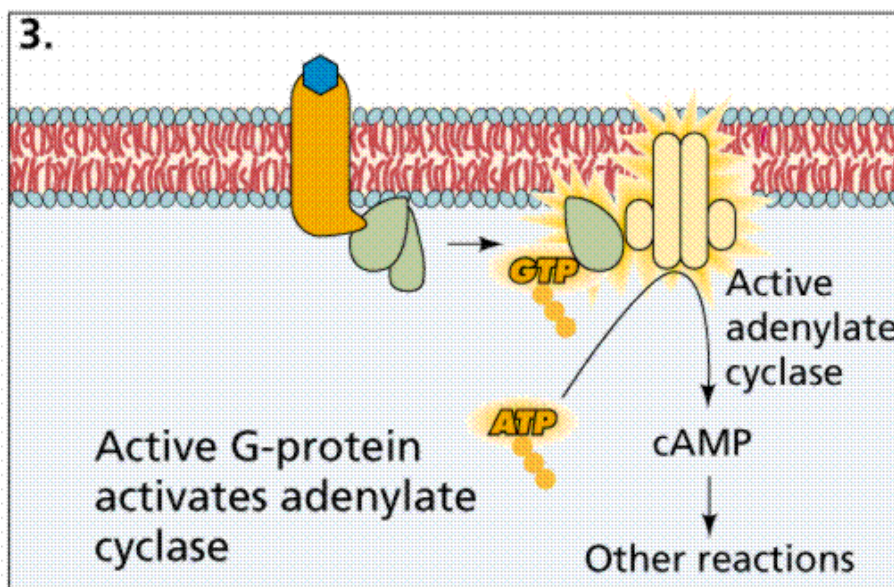
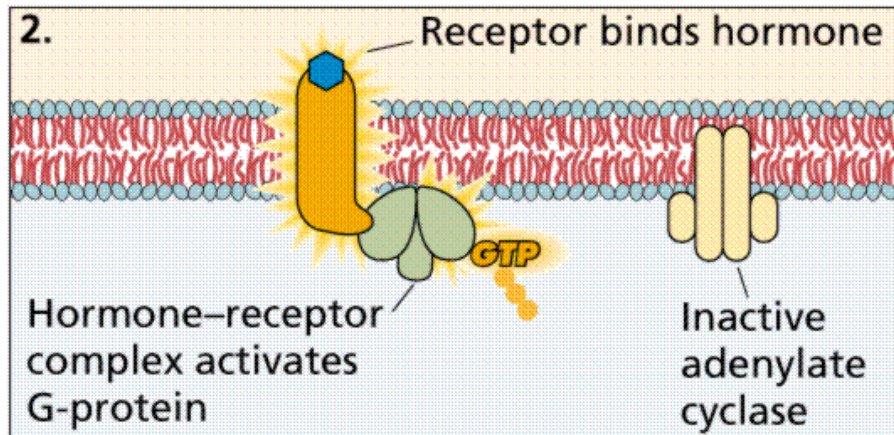
**Steroid** and **non – steroid** hormones

- **Nonsteroid Hormones**

Nonsteroid hormones (water soluble) do not enter the cell but bind to plasma membrane receptors, generating a chemical signal (second messenger) inside the target cell. Five different second messenger chemicals, including cyclic AMP have been identified. Second messengers activate other intracellular chemicals to produce the target cell response.

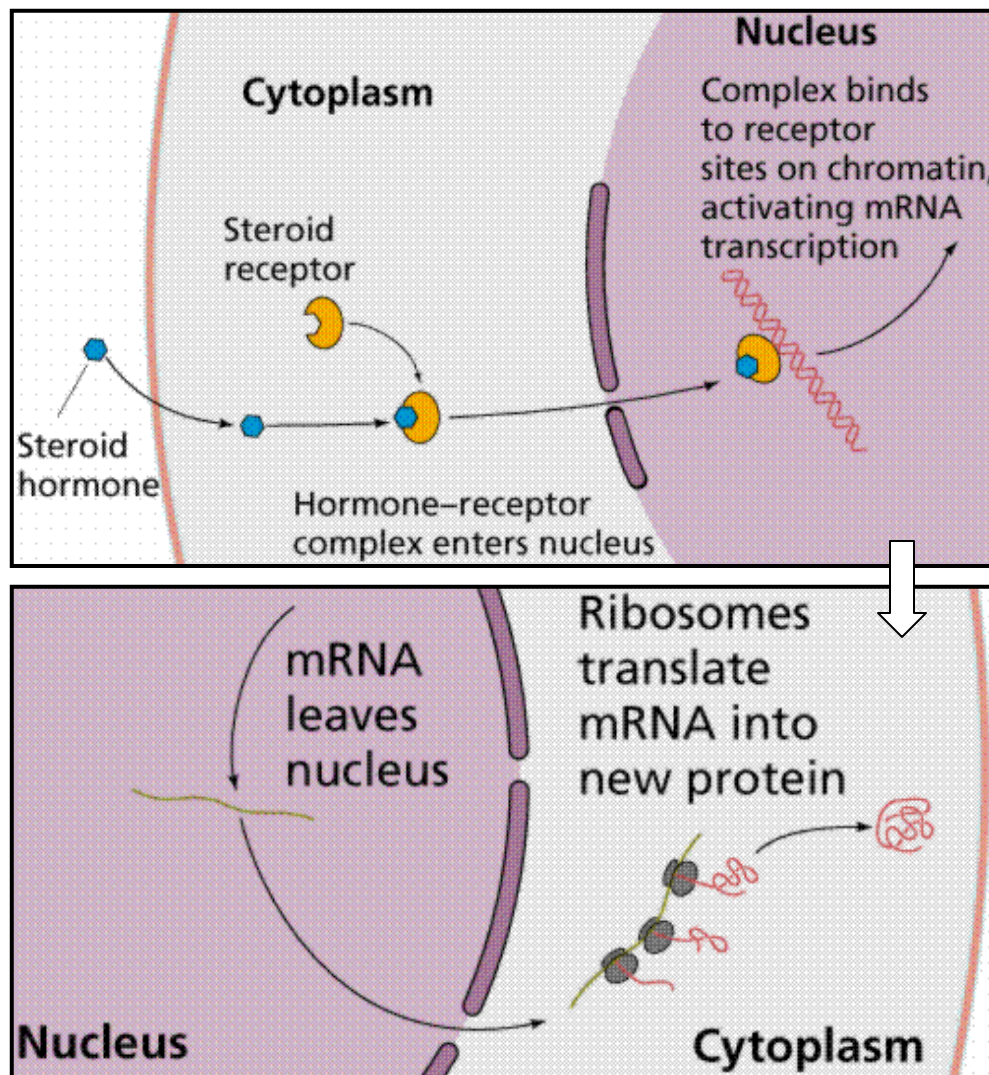






- **Steroid Hormones**

The second mechanism involves steroid hormones, which pass through the plasma membrane and act in a two step process. Steroid hormones bind, once inside the cell, to the nuclear membrane receptors, producing an activated hormone-receptor complex. The activated hormone-receptor complex binds to DNA and activates specific genes, increasing production of proteins.



The action of  
nonsteroid  
hormones




## 1. HYPOTHALAMUS – PITUITARY GLAND

The pituitary gland (often called the master gland) is located in a bony cavity at the base of the brain. A stalk links the pituitary to the hypothalamus, which controls release of pituitary hormones. The pituitary gland has two lobes: the **anterior** and **posterior lobes**. The anterior pituitary is glandular.

The hypothalamus contains neurons that control the releases from the anterior pituitary, through seven hypothalamic hormones which are released into a portal system connecting the hypothalamus and pituitary. These hormones cause targets in the pituitary to release various hormones.

### Anterior Pituitary

*Hormones produced and released:*

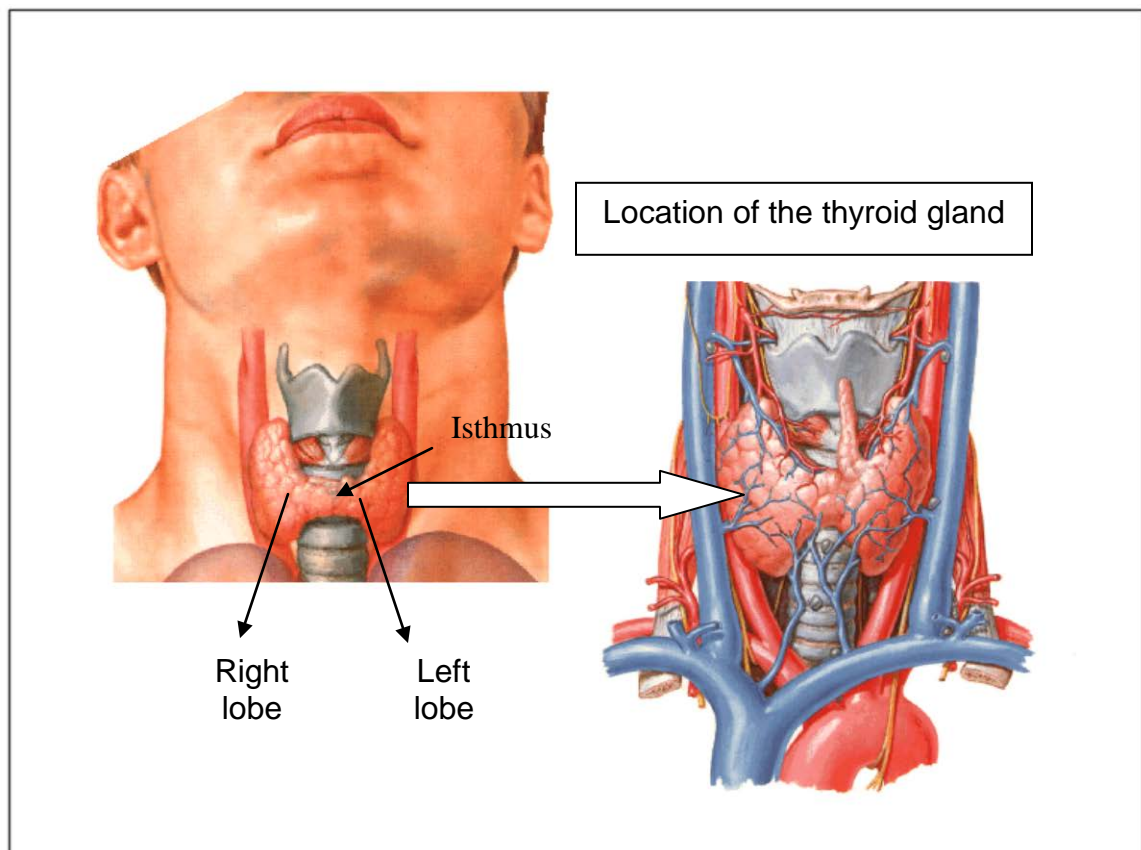
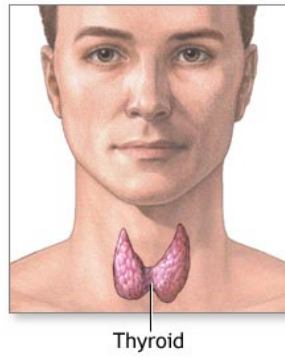
- Growth hormone
  - Thyrotropin
  - Adrenocorticotropin
  - Leutinizing hormone LH
  - Follicle stimulating hormone FSH
  - Prolactin
  - Endorphins
- 
- GONADOTROPINS

### Posterior Pituitary

*Hormones released:*

- Oxytocin
- Vasopressin
- Anti – diuretic hormone (ADH)

# 1. THYROID GLAND



The thyroid gland is located in the front of the neck, below the larynx. The small, two-inch gland consists of two lobes, one on each side of the windpipe, connected by tissue called the isthmus.

thyroid epithelial cells, the thyroid gland houses one other important endocrine cell. Nestled in spaces between thyroid follicles are *parafollicular or C cells*, which secrete the hormone **calcitonin**.

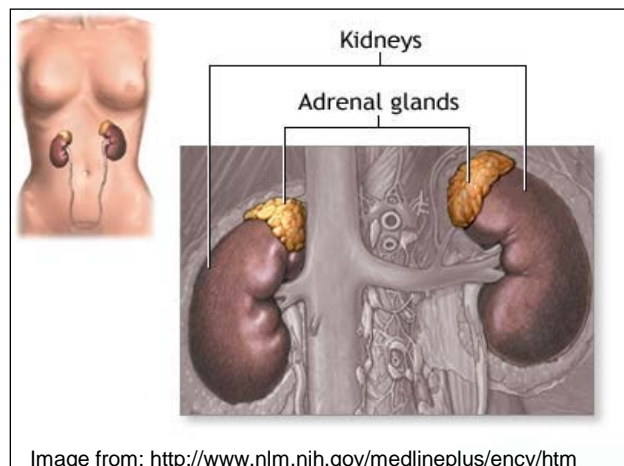
Most of the thyroid tissue consists of the follicular cells, which secrete iodine-containing hormones called **thyroxine (T4)** and **triiodothyronine (T3)**. The parafollicular cells secrete the hormone calcitonin. Iodine is essential in order for the thyroid to produce the hormones.

Thyroid hormones are poorly soluble in water, and more than 99% of the T3 and T4 circulating in blood is bound to carrier proteins. The principle carrier of thyroid hormones is thyroxine-binding globulin, a glycoprotein synthesized in the liver. Two other carriers of import are transthyreïn and albumin. Carrier proteins allow maintenance of a stable pool of thyroid hormones from which the active, free hormones are released for uptake by target cells.

The thyroid hormones play an important role in regulating the body's metabolism and calcium balance. The T4 and T3 hormones stimulate every tissue in the body to produce proteins and increase the amount of oxygen used by cells. The calcitonin hormone works together with the parathyroid hormone to regulate calcium levels in the body. Levels of hormones secreted by the thyroid are controlled by the pituitary gland's thyroid-stimulating hormone, which in turn is controlled by the hypothalamus.

### 3- ADRENAL GLANDS

The adrenal glands are situated on top of the kidneys. They consist of the outer **cortex** and the inner **medulla**. The medulla secretes **epinephrine** (also known as **adrenaline**) and other similar hormones in response to



stressors such as fright, anger, caffeine, or low blood sugar. The cortex secretes several classes of steroid hormones (glucocorticoids and mineralocorticoids). Despite their organization into a single gland, the medulla and cortex are functionally different endocrine organs, and have different embryological origins.

Cells in the adrenal medulla synthesize and secrete norepinephrine and epinephrine. Following release into blood, these hormones bind adrenergic receptors on target cells, where they induce essentially the same effects as direct sympathetic nervous stimulation.

The adrenal cortex is a factory for steroid hormones. In total, at least two to three dozen different steroids are synthesized and secreted from this tissue, but two classes are of particular importance:

Class of Steroid	Major Representative	Physiologic Effects
Mineralocorticoids	Aldosterone	Na <sup>+</sup> , K <sup>+</sup> and water homeostasis
Glucocorticoids	Cortisol	Glucose homeostasis and many others

Additionally, the adrenal cortex produces some sex steroids, particularly androgens.

Like all steroids, adrenal "corticosteroids" are synthesized from cholesterol.

(30) weeks

### Reproductive system

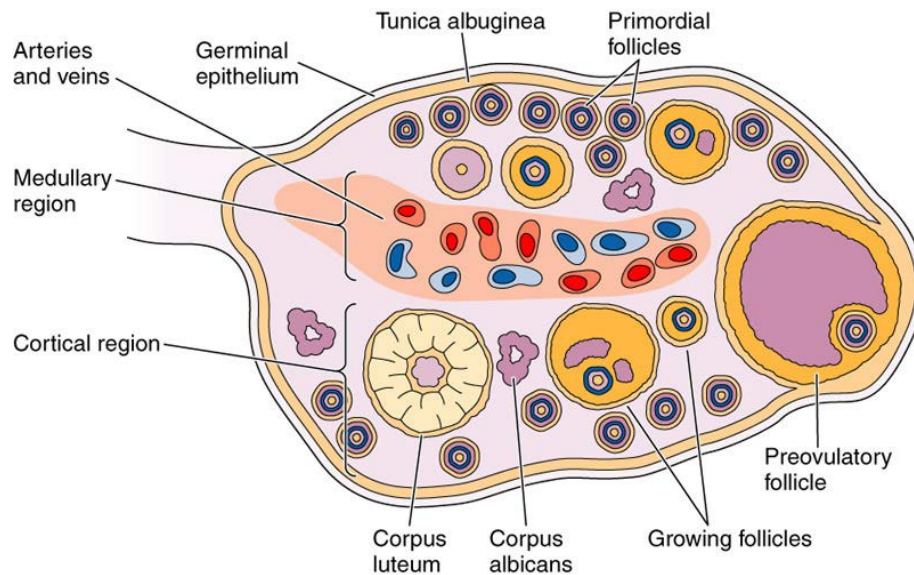
#### ***Female Reproductive System***

This system consists of the ovaries, uterine tubes, external genitalia, mammary glands, and placenta. As in the male, the infantile, childhood, and pubertal developmental stages of the female have distinctive histological characteristics associated with the degree of maturity of the system. In addition, the histology of the ovary and of the uterus is related to the regular cyclic changes in these organs, which occur during reproductive life, and to pregnancy if it occurs.

#### **OVARY**

The two ovaries, like the testes, serve exocrine and endocrine functions. They perform their exocrine or cytogenic function by producing living cells, the **ova**, and their endocrine function by producing two steroid hormones, **estrogen** and **progesterone**. Estrogen, produced by the ovarian follicles, stimulates development of the secondary sexual characteristics. Progesterone, secreted by the corpus luteum, stimulates development of the uterus for reception of the fertilized ovum. Oocytes are found within the cortex. The medulla is composed of connective tissue in which course the major **blood vessels** and **nerves** to the ovary. The stroma of the medulla is looser than that of the cortex. Typical fibroblasts (lacking the potential to produce hormones), strands of smooth muscle (which accompany the blood vessels), and many elastic fibers are present. The ovary is covered by a

thick tough capsule made up of the outer **germinal epithelium** (a misnomer since it does not give rise to ova) and an inner connective tissue layer the **tunica albuginea** the simple cuboidal germinal epithelium, which is a continuation of the peritoneum. The underlying tunica albuginea is thinner than the comparable layer of the testis. Abnormal thickening of this layer may prevent follicle rupture and ovulation.



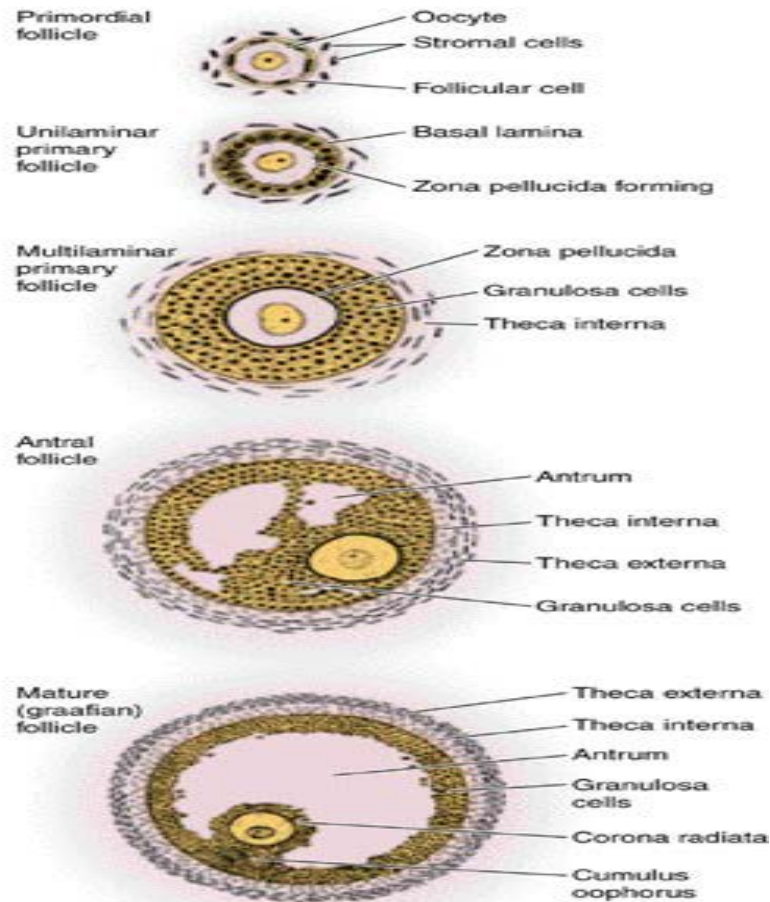
**Figure 1:** Schematic diagram of a human ovary showing its main components.

the section of ovary showed the **primordial follicles** that are usually located near the tunica albuginea. These follicles will be surrounded by flattened **follicular cells**. See Figure 2 below. The **primary oocyte** (about 20 mm in diameter) within the follicle has pale, granular cytoplasm, a pale, round nucleus, and a dark nucleolus. Identify the other types of follicles that are present. **Primary follicles** result from growth of primordial follicles. They can be subdivided into **unilaminar primary follicles** and **multilaminar**

**primary follicles.** The **unilaminar primary follicle** has entered the initial stage of growth due to stimulation by FSH. It resembles a primordial follicle except that it is surrounded by a layer of cuboidal to columnar **granulosa cells**. The **multilaminar primary follicle** is surrounded by two or more layers of granulosa cells, which lack an antrum. The primary oocyte is growing and may reach a diameter of 100  $\mu\text{m}$  or more in the multilaminar primary follicle. A distinct **zona pellucida** can be seen in multilaminar follicles. It is a gel-like membrane, rich in glycoprotein, interposed between the oocyte and the granulosa cell

Further growth of a multilaminar follicle leads to the formation of a **secondary follicle**, which is characterized by an **antrum**. The antrum is a space among the follicular cells, which appears when follicles reach about 0.2 mm in diameter. The antrum is filled in life with a fluid, the **liquor folliculi**, and gradually increases in size by the accumulation of fluid.





**Figure:2** Schematic diagram of the types of ovarian follicles from primordial to mature.

All types of follicles may undergo **atresia** or degeneration. Many primordial follicles undergo atresia before birth. Of those which remain, many degenerate before puberty and others degenerate throughout the reproductive years without entering the growth period. In humans, of the several follicles that begin growth each month, only one, as a rule, is destined for maturity and ovulation. The others undergo atresia. When follicles become atretic, the oocyte is the first structure of the follicle to show signs of dying. Its nucleus becomes **pyknotic** and its cytoplasm



shrinks and then breaks. The zona pellucida of multilaminar follicles thickens and becomes folded. Following death of the oocyte, similar destructive changes occur in the follicular cells. These will be most obvious in secondary follicles, which have more follicular cells. The glassy membrane thickens; the granulosa cells separate and degenerate; the thecal cells accumulate lipid and degenerate. The zona pellucida and thecal cells are the most persistent parts. The final product of an atretic secondary follicle, like that of a degenerating corpus luteum, is a corpus albicans.

The most notable feature of this human ovary is the large **corpus luteum**. This is an endocrine structure formed from a ruptured follicle. Under low power, identify the corpus luteum with its well-vascularized, folded wall and its central lumen, which contains loose connective tissue. **Granulosa lutein cells** (about 25 mm in diameter) constitute the bulk of the wall. These large cells secrete **progesterone** and represent cells of the granulosa membrane, which have undergone hypertrophy. The small **theca lutein cells** (about 12 mm in diameter) can be seen at the periphery of the corpus and in the connective tissue of the folds. They are the estrogen secreting cells derived from the theca interna of the follicles. In addition, there is a large, probably cystic, follicular cavity in the cortex.

### **OVIDUCT** (fallopian tube: uterine tube)

Each oviduct is about 10 cm long. One end opens into the uterine cavity, the other into the peritoneal cavity adjacent to the ovary. The uterine tube is divided into **four regions**. Each tube begins with the fimbriated, funnel-like opening, the **infundibulum**. The next segment is the dilated **ampulla** with its alternating, branching folds and grooves; thereafter, first in

the **isthmus** and then to a larger extent in the **intrauterine segment**, the tube becomes reduced in diameter and its luminal mucosa far less folded.

The oviduct, infundibulum, human, section is from the infundibular portion of a human oviduct. The wall of the oviduct consists of a **mucosa**, **muscularis**, and external **serosa**. These features can be readily seen in this slide at low magnification. The mucosa has deep thin folds in the infundibular region. The **epithelium** is **simple columnar**. The height of the epithelium is highest in the ampulla and is influenced by hormones, being somewhat higher just before ovulation. There are two types of columnar epithelial cells found in the oviduct, **ciliated** and **nonciliated (aka: peg) cells**. The latter are recognized because their nuclei are near the lumen and their cytoplasm (and sometimes nuclei) bulge into the oviduct lumen. Peg cells are probably secretory cells. The **lamina propria** consists of loose connective tissue and is rich in blood vessels. The lamina propria lacks glands.

The smooth muscle in the **muscularis** is loosely arranged into inner circular and outer longitudinal layers, which are separated by a connective tissue layer. The outer longitudinal layer is best defined in the isthmus becoming less distinct as you approach the fimbriae. It may be unrecognizable in the infundibulum. See if you can discern two distinct muscle layers in your slide.

The **serosa** or outermost layer of loose connective tissue contains blood vessels, lymphatics, and nerves. The serosa is lined by **simple squamous layer of mesothelial cells**.

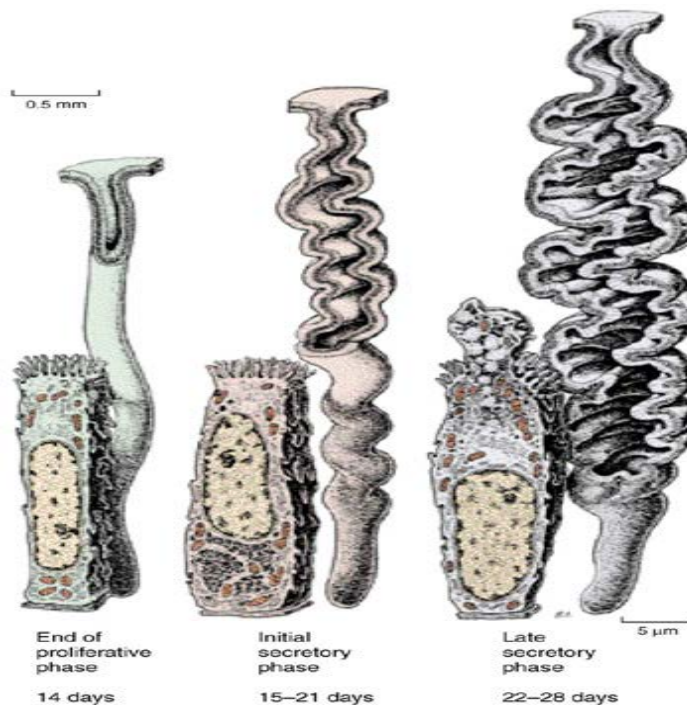
The oviduct in ampulla part showed the Preservation of the epithelium is excellent allowing you to clearly differentiate **ciliated** and **peg** cells. This is

particularly. Although the two muscle layers of the muscularis are incomplete in the.

The oviduct in isthmus shows the overall reduction in folding of the **mucosa** and somewhat thicker appearance of the lamina propria. Also the **muscularis** is thicker and well differentiated into **longitudinal** and **circular layers**.

### **UTERUS, VAGINA, EXTERNAL GENITALIA**

The human uterus can be subdivided into the **fundus**, **corpus** (body), and **cervix**. Functionally, as well as structurally, the fundus and corpus are similar; the cervix differs both structurally and functionally. The layers of the uterus are given special names: the mucosa is called **endometrium**; the muscularis is the **myometrium**; the serosa is the **perimetrium**. During the reproductive years the endometrium in the corpus and fundus undergoes cyclical changes about every 28 days. This **menstrual cycle** can be divided into four phases: **menstrual**, **proliferative**, **secretory**, and **premenstrual**. These stages can be recognized by the histological changes in the endometrium. Figure 3 .



**Figure 3:** Schematic diagram showing the changes in the uterine glands and in the gland cells during the menstrual cycle.

#### In the **proliferative phase**

This is just 2-3 days after the cessation of menstruation. the **endometrium** is divided into two layers. Near the lumen, the stroma of the endometrium appears lighter, this is the **functional layer** (stratum functionalis). The deeper layer is darker in color because the hematoxylin stained nuclei of the stroma are closer together. This is the **basal layer** (stratum basalis). the **glands** are relative straight and project through the length of the endometrium with some even penetrating into the myometrium. The surface **epithelium** contains mostly **ciliated cells** but some non-ciliated **secretory cells** are also present. In contrast, the **glands** are lined primarily by **secretory cells**. The epithelium is a **simple columnar** but may appear

stratified (i.e. is a pseudostratified epithelium) in places, particularly in the glands. This is due to the accumulation of glycogen in the base of the cells, which pushes the nuclei of these cells to a more apical position. endometrium. between the glands the **spiral arteries are present**. and the extreme thickness of the myometrium.

### **early secretory phase.**

The **glands** are more tortuous and the **spiral arteries** extend almost to the epithelial layer. Look closely at the glandular epithelial cells. Many cells will have basally located clear areas. These are areas that were rich in **glycogen** but were extracted during tissue processing. You will also see fewer mitotic figures in the glandular epithelium The stroma and bases of the glands in this region undergo little change during the menstrual cycle. They are maintained during menstruation and regenerate another **stratum functionalis** after menstruation.

### **Later secretory phase**

. The appearance is similar except that the endometrium is thicker and the glandular lumen is larger and sometimes contains **secretory material**.

, , Menstrual phase, The uterus undergoing menstruation. Compare the **stratum basalis**, which is relatively unaffected, with the **stratum functionalis** that is being sloughed off the absence of an epithelial lining

### **uterine cervix**

The human **uterine cervix** has a strikingly different appearance to that of the corpus and fundus. The cervical stroma to that of the endometrium in the

body of the uterus. the cervical epithelium showed abrupt transition from **simple columnar epithelium** (the lining of the cervical canal) to a **stratified squamous epithelium**, like that found in the vagina. This marks the region of the. The branched tubular glands secrete mucous. The mouths of the glands sometimes become plugged and the glands expand into cyst-like formations called **Nabothian follicles**.

The vagina extends from the cervix to the vestibule. It has three layers, **mucosa**, **muscularis**, and **adventitia**. The mucosa is lined by **non-cornified stratified squamous epithelium**. Pale vacuoles in the epithelial cells indicate areas where **glycogen** was stored. Complex **papillae** extend to the epithelium from the lamina propria but glands are not present. The lamina propria is rich in elastic connective tissue. The mucosa is highly vascular,. There is also no muscularis mucosa.

The labia majorum. This gradual blends into a **keratinized stratified squamous epidermis without hair follicles** over the labia minora. The **stratum corneum** is absent on the inner aspect of the labia minora near the **vestibule**. The lining of the vestibule is continuous with that of the vagina.

## **MALE REPRODUCTION**

Proper understanding of male reproductive physiology and related pathology requires appreciation of the anatomy and development of the male genital and ductal system, physiology of the testis, hormonal control of the testis, as well as the processes involved in deposition of the seminal fluid within the female genital tract.

### **Anatomy**

The male genital tract is depicted below, and has several main components. In essence, the testis produces sperm, which pass through a series of ducts and are finally expelled via the urethra together with seminal plasma produced by the accessory sexual organs.

### **The testis**

The testis descends from a retroperitoneal position through the inguinal canal to take its place in the scrotum during the eighth fetal month. Reasons for its unusually vulnerable position are uncertain, but may well be due to the lower temperature required for spermatogenesis. A countercurrent vascular heat exchange system is present to promote cooler temperatures. Seminiferous tubules comprise 95% of testicular volume, and are devoted to the production of spermatozoa. Each tubule is 30-70 cm long and 200-300  $\mu\text{m}$  in diameter. There are approximately 500 tubules per testis. The tubules are divided by fibrous septae, and surrounded by the tough tunica albuginea. Interstitial tissue located between the seminiferous tubules is comprised of connective tissue, blood vessels, lymphatics, and Leydig cells which produce testosterone. Sperm produced by the seminiferous tubules pass out of the testis into the ductal system, beginning with the rete testis and on into the epididymis. The epididymis is a single convoluted duct approximately 20m long, and is divided into caput (head), corpus (body), and cauda (tail), which then continues as the vas deferens. Sperm in the vas deferens is joined by seminal vesicle secretions as they pass through the prostate via the ejaculatory ducts into the urethra.

**DEVELOPMENT** The gonad at eight weeks is undifferentiated, but under the influence of the Y chromosome a complex series of events occur which result in development of the male reproductive system. Testosterone production causes maturation of the Wolffian ducts into the male genital ductsystem (epididymis, vas, seminal vesicles). At the same time, testicular production of Mullerian Inhibiting Substance (MIS) causes degeneration of the Mullerian ducts, which in the female form the uterus and Fallopian tubes. Conversion of testosterone into dihydrotestosterone by the enzyme 5 alpha reductase causes masculinization of the external genital system such as the scrotum and penis.

## Testicular Function

The testes have two main functions in the adult, and an additional one in the developing fetus. In the adult, the testis acts as an exocrine organ, with the production and secretion of sperm. It also acts as an endocrine organ by its production and secretion of testosterone into the blood. The additional fetal function has already been noted, namely the secretion of MIS to cause regression of female structures.

Sperm production occurs within the seminiferous tubules, and is the result of complex local events as well as distant regulatory signals. Under the control of local testosterone production by the Leydig cells, the Sertoli cells within the seminiferous tubules provide an appropriate environment for the development of immature germ cells into mature spermatozoa.

### Sertoli cells

The seminiferous tubules are comprised entirely of Sertoli cells and germ cells. Sertoli cells are tall columnar cells with numerous branches which envelop all the differentiating germ cells from basement membrane to the tubule lumen. Tight junctions between Sertoli cells create a blood-testis barrier, and separate the germinal epithelium into basal and adluminal compartments. Only the most immature germ cells are present in the basal compartment, with more advanced germ cells enjoying a specialized micro-environment within the adluminal compartment. A single Sertoli cell may envelop 10-20 developing germ cells.

Sertoli cell functions include: support and nutrition of germ cells; release of mature germ cells into the lumen; translocation of developing germ cells in an adluminal direction; secretion of androgen binding protein, transferrin, inhibin; cell-cell communication via gap junctions to coordinate spermatogenesis; blood-testis barrier.

## Germ Cells



Germ cells begin as spermatogonia, which are the stem cells lining the basement layer of the seminiferous tubule. They are small, rounded, mitotically active cells which are sensitive to chemotherapy or radiation. Type A spermatogonia develop into Type B spermatogonia, which subsequently become primary spermatocytes during the first meiotic prophase.

Primary spermatocytes go through a series of stages (preleptotene, leptotene, zygotene, pachytene, diplotene) which are identified on the basis of cellular size and increasing nuclear condensation.

Secondary spermatocytes result from the first reduction division. They are diploid, in contrast to the primary spermatocytes which are tetraploid. The second meiotic prophase is very short (1 day) so secondary spermatocytes are not readily visible in tissue sections.

Spermatids result from the second reduction division and are therefore haploid. They are numerous, and are found near the tubule lumen. Spermatids may be in many stages of differentiation, but cells in any one cluster are always synchronized.

### Spermatozoa

The morphologically mature spermatozoon is released into the tubule lumen. It is a highly polarized cell, approximately 60µm long in the human. The head consists of the condensed nucleus, the acrosome, and associated membrane structures. The tail consists of a neck, middle piece containing a sheath of mitochondria, the principal piece, and an end piece. A "9+2" axoneme extends from the neck to the end piece. The entire tail is covered by the plasma membrane.

See Infertility in the Male. p. 108, Lipshultz, L. I. & Howards, S. S. (eds). Churchill Livingstone, Edinburgh.

### Leydig Cells

Leydig cells lie in the testicular interstitium between the seminiferous tubules, and seem primarily involved in the production of testosterone for local and distant purposes. Distant effects of testosterone include masculinization of external and internal

reproductive tissues (alone or via its metabolite DHT), pubertal changes of deepening voice, facial hair pattern, etc., and CNS actions affecting libido and sexual behavior. Local effects appear directed to stimulate and support Sertoli cell function in providing the proper environment for developing germ cells. Testosterone is bound to androgen-binding protein secreted by the Sertoli cell in the testis, and in the circulation is bound to a high affinity plasma globulin (testosterone binding globulin).

### **Sperm Physiology and Male Infertility Evaluation**

Sperm must have certain properties in order to fertilize an ovum.

1. Adequate motility to traverse the female genital tract.
2. Ability to recognize and bind to the ovum and its investments.
3. Ability to penetrate the zona pellucida.
4. Ability to fuse with the plasma membrane of the ovum.

The processes by which many of these events occur are incompletely understood, and this lack of knowledge impacts on the ability to assess and treat certain problems of reproduction.

Freshly ejaculated semen is a gel which liquefies after 5-20 minutes. The seminal vesicles appear responsible for the agent causing the gel state, while the prostate produces the protease responsible for liquefaction. Significance of gel state is unknown.

Among other functions, the seminal vesicles introduce fructose into the seminal plasma, which serves as the energy substrate for sperm.

Sperm removed immediately from seminal plasma are able to fertilize ova, but with relatively minor success. Normal fertilizing ability -follows a process called capacitation, in which sperm develop the capability to fertilize. One step in this process is called the acrosome reaction. During the acrosome reaction, the lysosomal enzymes contained within the acrosome are released, causing alteration of the sperm head plasma membrane. There may be changes resulting from this that affect sperm "stickiness" to ova.

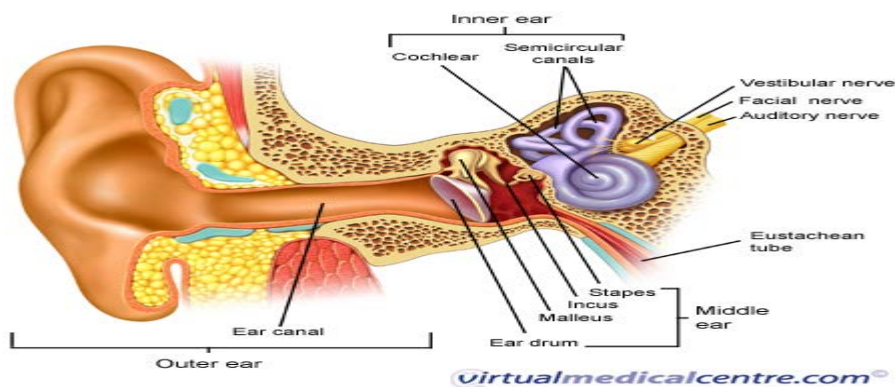
Changes in sperm motility occur with capacitation as well, primarily a change in beat frequency and amplitude which is described as hypermotility.

Evaluation of the possibly sub fertile man always begins with the history and physical examination. Key historical points are a previous history of fertility, normal timing of puberty, congenital or acquired genital abnormalities such as cryptorchidism, post pubertal mumps, or trauma. Medications, chronic illnesses, and prior surgery must be determined.

Physical examination is focused on evidence for endocrine abnormalities, such as body hair pattern or gynecomastia. Examination of the phallus is important mainly for determining that the urethral meatus is situated normally. The best correlate with fertility is normal size and consistency of the testes, which are generally more than 4.5 cm in greatest diameter. The presence of an intact vas deferens should be determined, as well as the presence or absence of varicocele.

#### Ear function

##### **Ear**



The **ear** is the **organ** that detects **sound**. It not only receives sound, but also aids in **balance** and body position. The ear is part of the **auditory system**. Often the entire organ is considered the ear, though it may also be considered just the visible portion. In most mammals, the visible ear is a flap of tissue that is also called the **pinna** (or *auricle* in humans) and is the first

of many steps in [hearing](#). [Vertebrates](#) have a pair of ears placed somewhat symmetrically on opposite sides of the head. This arrangement aids in the ability to localize sound sources.

## human Eye

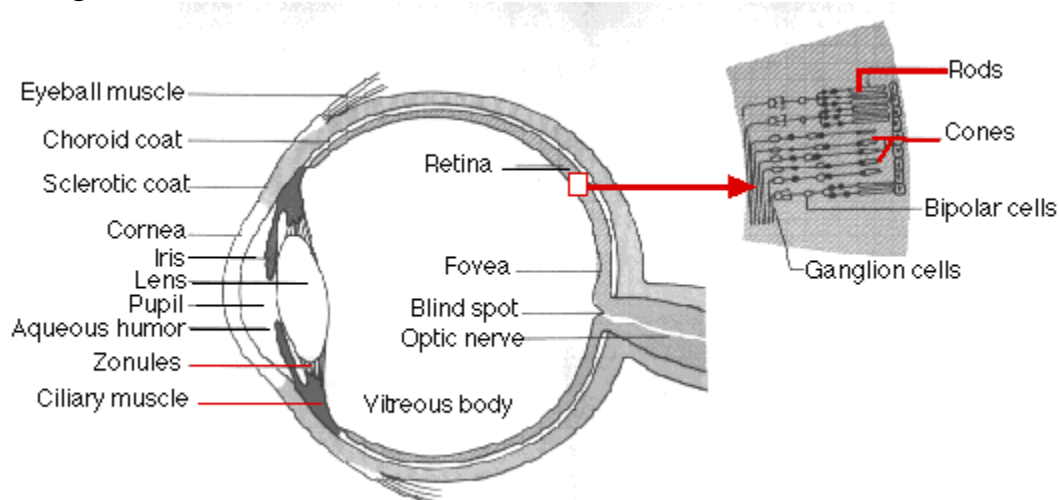
The human eye is wrapped in three layers of tissue:

- the **sclerotic coat**

This tough layer creates the "white" of the eye except in the front where it forms the transparent **cornea**. The cornea

- admits light to the interior of the eye and
- bends the light rays so that they can be brought to a focus.

The surface of the cornea is kept moist and dust-free by secretions from the tear glands.



- the **choroid coat**

This middle layer is deeply pigmented with **melanin**. It reduces reflection of stray light within the eye. The choroid coat forms the **iris** in the front of the eye. This, too, is pigmented and is responsible for eye "color". The size of its opening, the **pupil**, is variable and under the control of the [autonomic nervous system](#). In dim light (or when danger threatens), the pupil opens wider letting more light into the eye. In bright light the pupil closes down. This not only reduces the amount of light entering the eye but also improves its image-forming ability (as does "stopping down" the iris diaphragm of a camera).

- the **retina** The retina is the inner layer of the eye. It contains the light receptors, the **rods** and **cones** (and thus serves as the "film" of the eye). The retina also has many interneurons that process the signals arising in the rods and cones before passing them back to the brain.

(**Note:** the rods and cones are **not at the surface** of the retina but lie underneath the layer of interneurons.)

### **The blind spot**

All the nerve impulses generated in the retina travel back to the brain by way of the axons in the optic nerve (above). At the point on the retina where the approximately 1 million axons converge on the optic nerve, there are no rods or cones. This spot, called the blind spot, is thus insensitive to light.

You can demonstrate the presence of the blind spot. Cover your right eye with your hand and stare at the red circle as you move closer to the screen (the square will disappear). Or cover your left eye and stare at the red square as you move.

### **The lens**

The lens is located just behind the iris. It is held in position by **zonules** extending from an encircling ring of muscle. When this **ciliary muscle** is

- **relaxed**, its diameter increases, the zonules are put under tension, and the lens is flattened;
- **contracted**, its diameter is reduced, the zonules relax, and the lens becomes more spherical.

These changes enable the eye to adjust its focus between far objects and near objects.

**Farsightedness.** If the eyeball is too short or the lens too flat or inflexible, the light rays entering the eye — particularly those from nearby objects — will not be brought to a focus by the time they strike the retina. Eyeglasses with convex lenses can correct the problem. Farsightedness is called **hypermetropia**.

**Nearsightedness.** If the eyeball is too long or the lens too spherical, the image of distant objects is brought to a focus in front of the retina and is out of focus again before the light strikes the retina. Nearby objects can be seen more easily. Eyeglasses with concave lenses correct this problem by diverging the light rays before they enter the eye. Nearsightedness is called **myopia**.

**Cataracts** One or both lenses often become cloudy as one ages. When a cataract seriously interferes with seeing, the cloudy lens is easily removed and a plastic one substituted. The entire process can be done in a few minutes as an outpatient under local anesthesia.

The iris and lens divide the eye into two main chambers:

- the front chamber is filled with a watery liquid, the **aqueous humor**.
- the rear chamber is filled with a jellylike material, the **vitreous body**.

## The Retina

Four kinds of light-sensitive receptors are found in the retina:

- **rods**
- three kinds of **cones**, each "tuned" to respond best to light from a portion of the **spectrum of visible light**
  - cones that absorb long-wavelength light (red)
  - cones that absorb middle-wavelength light (green)
  - cones that absorb short-wavelength light (blue)

This scanning electron micrograph (courtesy of Scott Mittman and David R. Copenhagen) shows rods and cones in the retina of the tiger salamander. Each type of receptor has its own special pigment for absorbing light. Each consists of:

- a **transmembrane protein** called **opsin** coupled to
- the **prosthetic group retinal**. Retinal is a derivative of **vitamin A** (which explains why night blindness is one sign of vitamin A deficiency) and is used by all four types of receptors.

The amino acid sequence of each of the four types of opsin are similar, but the differences account for their differences in **absorption spectrum**. The retina also contains a complex array of interneurons:

- **bipolar cells** and **ganglion cells** that together form a path from the rods and cones to the brain
- a complex array of other interneurons that form **synapses** with the bipolar and ganglion cells and modify their activity.

Ganglion cells are always active. Even in the dark they generate trains of **action potentials** and conduct them back to the brain along the **optic nerve**. Vision is based on the modulation of these nerve impulses. There is not the direct relationship between visual stimulus and an action potential that is found in the senses of **hearing**, **taste**, and **smell**. In fact, action potentials are not even generated in the rods and cones.

## Rod Vision

Rhodopsin is the light-absorbing pigment of the rods. This **G-protein-coupled receptor** (GPCR) is incorporated in the membranes of disks that are neatly stacked (some 1000 or more of them) in the outer portion of the rod. (This arrangement is reminiscent of the organization of **thylakoids**, another light-absorbing device.)

The electron micrograph (courtesy of Keith Porter) shows the rod cells of the kangaroo rat. The outer segments of the rods contain the orderly stacks of membranes which incorporate rhodopsin. The inner portion contain many mitochondria. The two parts of the rod are connected by a stalk (arrow) that has the same structure as a **primary cilium**.

Although the disks are initially formed from the plasma membrane, they become separated from it. Thus signals generated in the disks must be transmitted by a chemical mediator (a "**second messenger**" called **cyclic GMP** (cGMP) to alter the potential of the plasma membrane of the rod. Rhodopsin consists of an opsin of 348 amino acids coupled to **retinal**. Like all G-protein-coupled receptors, opsin has 7 segments of **alpha helix** that pass back and forth through the lipid bilayer of the disk membrane. Retinal consists of a system of alternating single and double bonds. In the dark, the hydrogen atoms attached to the #11 and #12 carbon atoms of retinal (red arrows) point in the same direction producing a kink in the molecule. This configuration is designated *cis*. When light is absorbed by retinal, the molecule straightens out forming the all-*trans* isomer.

This physical change in retinal triggers the following chain of events culminating in a change in the pattern of impulses sent back along the optic nerve.

1. Formation of all-*trans* retinal activates its **opsin**.
2. Activated rhodopsin, in turn, activates many molecules of a **G protein** called **transducin**.
3. Transducin activates an enzyme that breaks down **cyclic GMP**.
4. The drop in cGMP **closes** **Na<sup>+</sup> channels** in the plasma membrane of the rod. Because these positive ions can no longer enter, the interior of the cell becomes more negative (hyperpolarized) increasing its membrane potential from about -30 to some -70 mV.
5. This **slows** the release of the neurotransmitter **glutamate** at synapses between the rod and interneurons (e.g., bipolar cells).
6. This reduction in glutamate release activates some interneuron pathways, inhibits others.
7. The interplay of excited and inhibited interneurons modulates the spontaneous firing of the ganglion cells to which they are connected and gives rise to the ability of the retina to discriminate shapes.

So the retina is not simply a sheet of photoreceptors, but a tiny brain center that carries out complex information processing before sending signals back along the optic nerve. In fact, the retina really **is** part of the brain and grows out from it during embryonic development

### **Rod vision is acute but coarse.**

Rods do not provide a sharp image for several reasons.

- Adjacent rods are connected by **gap junctions** and so share their changes in membrane potential.



- Several nearby rods often share a single circuit to one ganglion cell.
- A single rod can send signals to several different ganglion cells.

So if only a single rod is stimulated, the brain has no way of determining exactly where on the retina it was.

However, rods are extremely sensitive to light. A single photon (the minimum unit of light) absorbed by a small cluster of adjacent rods is sufficient to send a signal to the brain. So although rods provide us with a relatively grainy, colorless image, they permit us to detect light that is over a billion times dimmer than what we see on a bright sunny day.

### **Cone Vision**

Although cones operate only in relatively bright light, they provide us with our sharpest images and enable us to see colors. Most of the 3 million cones in each retina are confined to a small region just opposite the lens called the **fovea**. So our sharpest and colorful images are limited to a small area of view. Because we can quickly direct our eyes to anything in view that interests us, we tend not to be aware of just how poor our peripheral vision is.

The three types of cones provide us the basis of color vision. Cones are "tuned" to different portions of the visible spectrum.

- red absorbing cones; those that absorb best at the relatively long wavelengths peaking at 565 nm
- green absorbing cones with a peak absorption at 535 nm
- blue absorbing cones with a peak absorption at 440 nm.

Retinal is the prosthetic group for each pigment. Differences in the amino acid sequence of their opsins accounts for the differences in absorption. The response of cones is not all-or-none. Light of a given wavelength (color), say 500 nm (green), stimulates all three types of cones, but the green-absorbing cones will be stimulated most strongly. Like rods, the absorption of light does not trigger action potentials but modulates the membrane potential of the cones.

### **Color Blindness**

The term color blindness is something of a misnomer. Very few ( $\sim 1$  in  $10^5$ ) people cannot distinguish colors at all. Most "color-blind" people actually have abnormal color vision such as confusing the red and green of traffic lights. As high as 8% of the males in some populations have an inherited defect in their ability to discriminate reds and greens. These defects are found almost exclusively in males because the genes that encode the red-absorbing and green-absorbing opsins are on the X chromosome.

[Discussion of [X-linkage](#)]



The X chromosome normally carries a cluster of from 2 to 9 opsin genes. The minimum basis for normal red-green vision is one gene whose opsin absorbs efficiently in the red and one that absorbs well in the green (chromosome **1** in the figure). Multiple copies of these genes are also fine (**2** and **3**). Males with either a "green gene" or "red gene" missing are severely color blind (**4** and **5**). However, if all the red genes carry mutations (this seldom seems to be the case for the green genes — nobody knows why), then they may have red-green color blindness that ranges from mild to severe depending on the particular mutations involved (**6**). The rule seems to be that the more the mutations shift the pigment towards green, the more serious the defect. However, a large number of mutations don't always produce serious defects. Multiple mutations in a single gene may offset each other producing only mild defects. And as long as one normal copy of each gene is present, the presence of additional mutated genes seldom produce a serious problem

