Digestive System

Small Intestine

The small intestine consists of three parts: the duodenum, the jejunum, and the ileum. The entire small intestine is about 6 m long (range: 4.6 - 9m). The duodenum is about 25 cm long (the term duodenum means 12, suggesting that it is 12 inches long). The jejunum, constituting about two-fifths of the total length of the small intestine, is about 2.5m long; and the ileum, constituting three-fifths of the small intestine, is about 3.5m long. Two major accessory glands, the liver and the pancreas, are associated with the duodenum.

The small intestine is the site at which the greatest amount of digestion and absorption occur. Each day, about 9L of water enters the digestive system. It comes from water that is ingested and from fluid secretions produced by glands along the length of the digestive tract. Most of the water, 8 - 8.5L, moves by osmosis, with the absorbed solutes, out of the small intestine. A small part, 0.5 - 1L, enters the colon.The mucous membrane of small intestine is covered by minute projections called villi.

The villi are lined by columnar cells, which are called enterocytes. Each enterocyte gives rise to hair like projections called microvilli. Within each villus, there is a central channel called lacteal. The lacteal opens into lymphatic vessels. It contains blood vessels also.

FUNCTIONS OF SMALL INTESTINE

1. MECHANICAL FUNCTION

The mixing movements of small intestine help in the thorough mixing of chyme with the digestive juices like succus entericus, pancreatic juice and bile.

2. SECRETORY FUNCTION

Small intestine secretes succus enteric us , enterokinase and the GI hormones.

3. HORMONAL FUNCTION

Small intestine secretes many GI hormones such as secretin, cholecystokinin, etc. These hormones regulate the movement of GI tract and secretory activities of small intestine and pancreas .

4. ABSORPTIVE FUNCTIONS

The presence of villi and microvilli in small intestinal mucosa increases the surface area of the mucosa. This facilitates the absorptive function of intestine. The digested products of foodstuffs, proteins, carbohydrates, fats and other nutritive substances such as vitamins, minerals and water are absorbed mostly in small intestine. From the lumen of intestine, these substances pass through lacteal of villi, cross the mucosa and enter the blood directly or through lymphatics

Secretions of the Small Intestine

The mucosa of the small intestine produces secretions that primarily contain mucus, electrolytes, and water. Intestinal secretions lubricate and protect the intestinal wall from the acidic chyme and the action of digestive enzymes. They also keep the chyme in the small intestine in a liquid form to facilitate the digestive process.

The intestinal mucosa produces most of the secretions that enter the small intestine, but the secretions of the liver andthe pancreas also enter the small intestine and play essential roles in the process of digestion.

Most of the digestive enzymes entering the small intestine are secreted by the pancreas.

The intestinal mucosa also produces enzymes, but these remain associated with the intestinal epithelial surface. The duodenal glands, intestinal glands, and goblet cells secrete large amounts of mucus. This mucus provides the wall of the intestine with protection against the irritating effects of acidic chyme and against the digestive enzymes that enter the duodenum from the pancreas.

Secretin and cholecystokinin are released from the intestinal mucosa and stimulate hepatic and pancreatic secretions.

The vagus nerve, secretin, and chemical or tactile irritation of the duodenal mucosa stimulate secretion from the duodenal glands.

Goblet cells produce mucus in response to the tactile and chemical stimulation of the mucosa.

Enzymes of the intestinal mucosa are bound to the membranes of the absorptive cell microvilli. These surfac-bound enzymes include disaccharidases, which break disaccharides down to monosaccharides; peptidases, which hydrolyze the peptide bonds between small amino acid chains; and nudeases, which break down nucleic acids. Although these enzymes are not secreted into the intestine, they influence the digestive process significantly, and the large surface area of the intestinal epithelium brings these enzymes into contact with the intestinal contents. Small molecules, which are breakdown products of digestion, are absorbed through the microvilli and enter the circulatory or lymphatic systems.

Movement in the Small Intestine

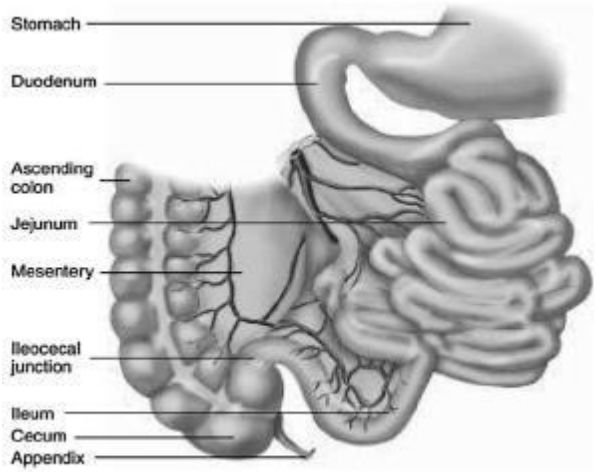
Mixing and propulsion of chyme are the primary mechanical events that occur in the small intestine. These functions are the result of segmental or peristalic contractions, which are accomplished by the smooth muscle in the wall of the small intestine and which are only propagated for short distances. Segmental contractions mix the intestinal contents, and peristaltic contractions propel the intestinal contents along the digestive tract. A few peristaltic contractions may precede the entire length of the intestine. Frequently, intestinal peristaltic contractions are continuations of peristaltic contractions that begin in the stomach. These contractions both mix and propel substances through the small intestine as the wave of contraction proceeds. The contractions move at a rate of about 1 cm/min. The movements are slightly faster at the proximal end of the small intestine and slightly slower at the distal end. It usually takes 3-5 hours for chyme to move from the pyloric region to the ileocecal junction.

Local mechanical and chemical stimuli are especially important in regulating the motility of the small intestine. Smooth muscle contraction increases in response to distention of the intestinal wall.

Solutions that are either hypertonic or hypotonic, solutions with a low pH, and certain products of digestion like amino acids and peptides also stimulate contractions of the small intestine. Local reflexes, which are integrated within the enteric plexus of the small intestine, mediate the response of the small intestine to these mechanical and chemical stimuli.

Stimulation through parasympathetic nerve fibers may also increase the motility of the small intestine, but the parasympathetic influences in the small intestine are not as important as those in the stomach.

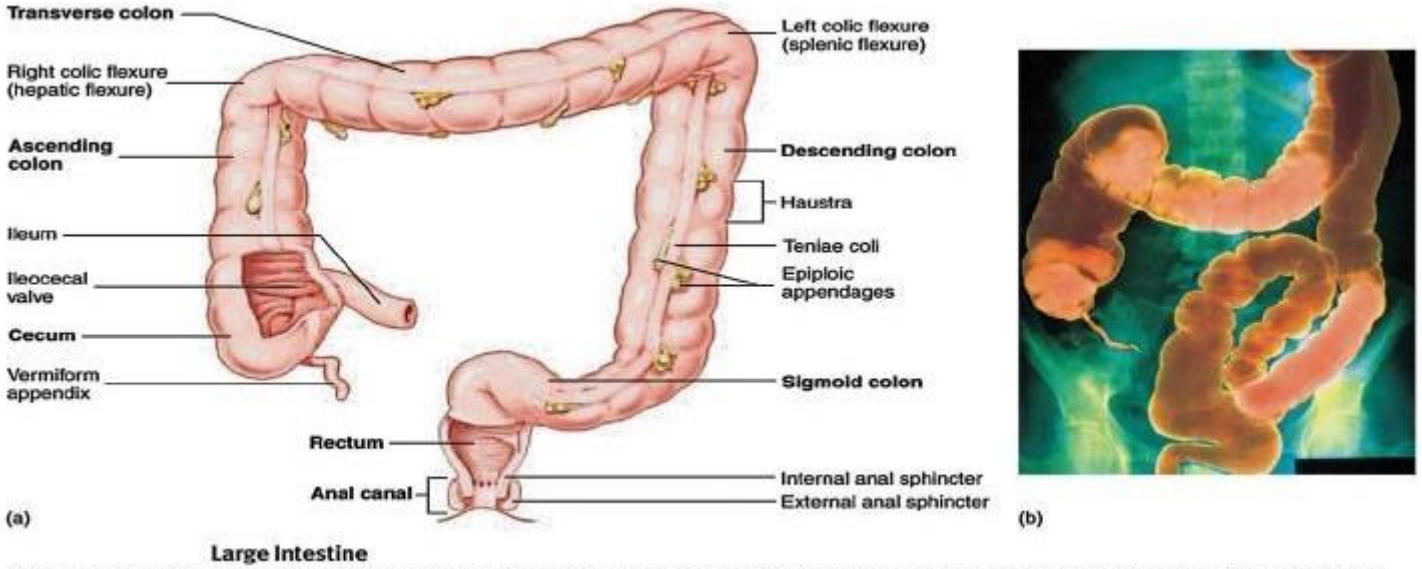
The ileocecal sphincter at the juncture between the ileum and the large intestine remains mildly contracted most of the time, but peristaltic waves reaching it from the small intestine cause it to relax and allow movement of chyme from the small intestine into the cecum. Cecal distention, however, initiates a local reflex that causes more intense constriction of the ileocecal sphincter. Closure of the sphincter facilitates digestion and absorption in the small intestine by slowing the rate of chyme movement from the small intestine into the large intestine and prevents material from returning to the ileum from the cecum.



The Small Intestine

Large Intestine

The large intestine is the portion of the digestive tract extending from the ileocecal junction to the anus. It consists of the cecum, colon, rectum, and anal canal. Normally 18-24 hours are required for material to pass through the large intestine, in contrast to the 3-5 hours required for movement of chyme through the small intestine. Thus, the movements of the colon are more sluggish than those of the small intestine. While in the colon, chyme is converted to feces . Absorption of water and salts, the secretion of mucus, and extensive action of microorganisms are involved in the formation of feces, which the colon stores until the feces are eliminated by the process of defecation. About 1500mL of chyme enters the cecum each day, but more than 90% of the volume is reabsorbed so that only 80-150 mL of feces is normally eliminated by defecation.



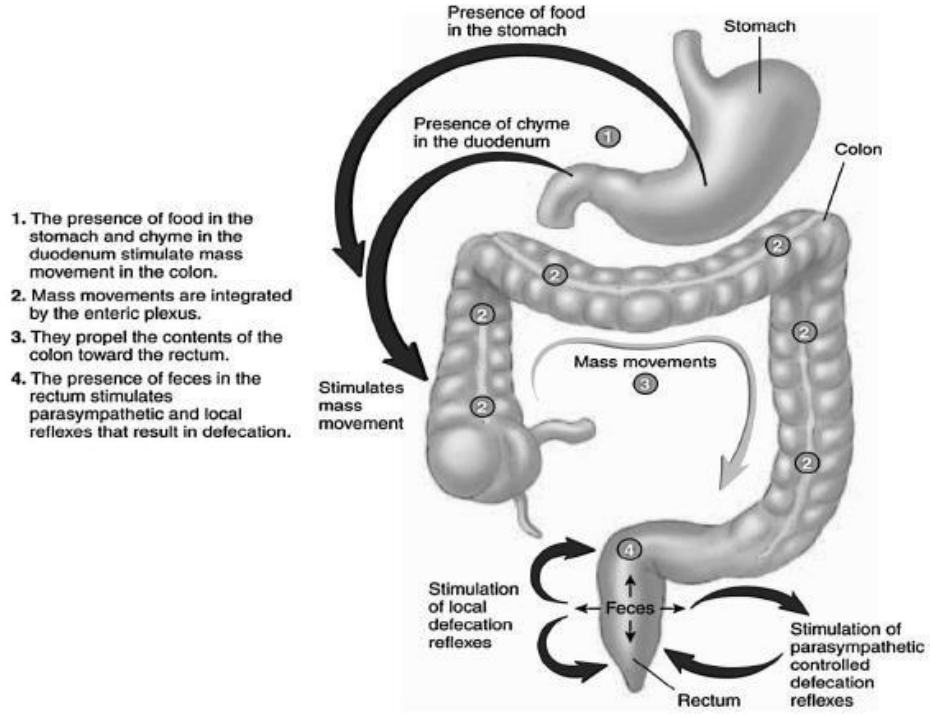
Large Intestine

(a) Large intestine (i.e., cecum, colon, and rectum) and anal canal. The teniae coli and epiploic appendages are along the length of the colon. (b) A radiograph of the large intestine following a barium enema.

Movement in the Large Intestine

Segmental mixing movements occur in the colon much less often than in the small intestine. Peristaltic waves are largely responsible for moving chyme along the ascending colon. At widely spaced intervals (normally three or four times each day), large parts of the transverse and descending colon undergo several strong peristaltic contractions, called mass movements. Each mass movement contraction extends over a much longer part of the digestive tract (≥ 20 cm) than does a Peristaltic contraction and propels the colon contents a considerable distance toward the anus. Mass movements are very common after meals because the presence of food in the stomach or duodenum initiates them. Mass movements are most common about 15 minutes after breakfast. They usually persist for 10-30 minutes and then stop for perhaps half a day. Local reflexes in the enteric plexus, which are called gastrocolic reftexes if initiated by the stomach or duodenocolic reftexes if initiated by the duodenum, integrate mass movements.

Distention of the rectal wall by feces acts as a stimulus that initiates the defecation reftex. Local reflexes cause weak contractions of the rectum and relaxation of the internal anal sphincter. Parasympathetic reflexes cause strong contractions of the rectum and are normally responsible for most of the defecation reflex. Action potentials produced in response to the distention travel along afferent nerve fibers to the sacral region of the spinal cord, where efferent action potentials are initiated that reinforce peristaltic contractions in the lower colon and rectum. The defecation reflex reduces action potentials to the internal anal sphincter, causing it to relax. The external anal sphincter, which is composed of skeletal muscle and is under conscious cerebral control, prevents the movement of feces out of the rectum and through the anal opening. If this sphincter is relaxed voluntarily, feces are expelled.
The defecation reflex persists for only a few minutes and quickly declines. Generally, the reflex is reinitiated after a period that may be as long as several hours. Mass movements in the colon are usually the reason for the reinitiation of the defecation reflex.
Defecation is usually accompanied by voluntary movements that support the expulsion of feces. These voluntary movements include large inspiration of air followed by closure of the larynx and forceful contraction of the abdominal muscles. As a consequence, the pressure in the abdominal cavity increases, thereby helping force the contents of the colon through the anal canal and out of the anus.



Reflexes in the Colon and Rectum

Liver

Digestive System

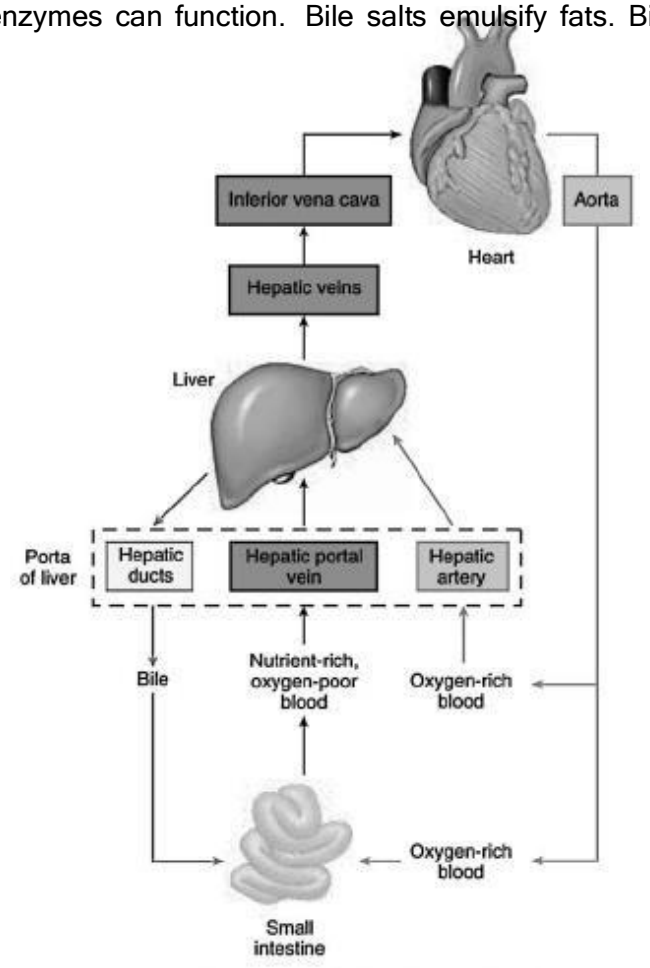
Functions of the Liver

The liver performs important digestive and excretory functions, stores and processes nutrients, synthesizes new molecules, and detoxifies harmful chemicals.

1- Bile Production

The liver produces and secretes about 600-1000 mL of bile each day. Bile contains no digestive enzymes, but it plays a role indigestion because it neutralizes and dilutes stomach acid and emulsifies fats. The pH of chyme as it leaves the stomach is too low for the normal function of pancreatic enzymes. Bile helps to neutralize the acidic chyme and to bring the pH up to a level at which pancreatic enzymes can function. Bile salts emulsify fats. Bile also contains excretory products like bile pigments. Bilirubin is a bile pigment that results from the breakdown of hemoglobin. Bile also contains cholesterol, fats, fat-soluble hormones, and lecithin.

Secretin stimulates bile secretion, primarily by increasing the water and bicarbonate ion content of bile. Bile salts also increase bile secretion through a positive-feedback system. Most bile salts are reabsorbed in the ileum and carried in the blood back to the liver, where they contribute to further bile secretion. The loss of bile salts in the feces is reduced by this recycling process. Bile secretion into the duodenum continues until the duodenum empties.



Blood and Bile Flow Through the Liver

2- Storage

Hepatocytes can remove sugar from the blood and store it in the form of glycogen. They can also store fat, vitamins (A, B_{12}, D, E, and K), copper, and iron. This storage function is usually short term, and the amount of stored material in the hepatocytes and, thus, the cell size fluctuate during a given day.

Hepatocytes help control blood sugar levels within very narrow limits. If a large amount of sugar enters the general circulation after a meal, it will increase the osmolality of the blood and produce hyperglycemia. This is prevented because the blood from the intestine passes through the hepatic portal vein to the liver, where glucose and other substances are removed from the blood by hepatocytes, stored, and secreted back into the circulation when needed.

3- Nutrient Interconversion

Interconversion of nutrients is another important function of the liver. Ingested nutrients are not always in the proportion needed by the tissues. If this is the case, the liver can convert some nutrients into others. If, for example, a person is on a diet that is excessively high in protein, an oversupply of amino acids and an undersupply of lipids and carbohydrates may be delivered to the liver. The hepatocytes break down the amino acids and cycle many of them through metabolic pathways so they can be used to produce adenosine triphosphate, lipids, and glucose.

Hepatocytes also transform substances that cannot be used by most cells into more readily usable substances. For example, ingested fats are combined with choline and phosphorus in the liver to produce phospholipids, which are essential components of plasma membranes. Vitamin D is hydroxylated in the liver. The hydroxylated form of vitamin D is the major circulating form of vitamin D, which is transported through the circulation to the kidney, where it's again hydroxylated. The double-hydroxylated vitamin D is the active form of the vitamin, which functions in calcium maintenance.

4- Detoxification

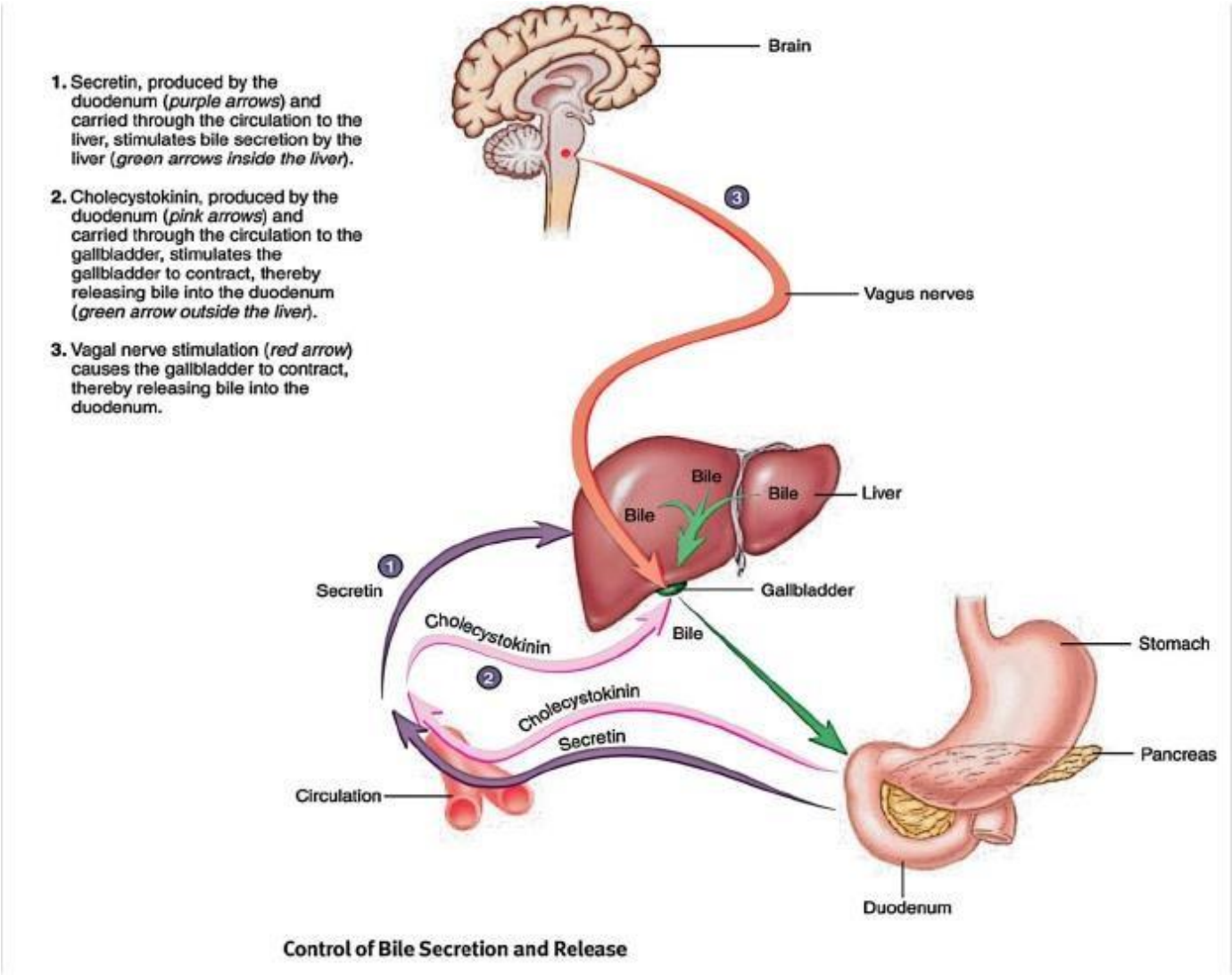
Many ingested substances are harmful to the cells of the body. In addition, the body itself produces many by-products of metabolism that, if accumulated, are toxic. The liver forms a major line of defense against many of these harmful substances. It detoxifies many substances by altering their structure to make them less toxic or make their elimination easier. Ammonia, for example, a by-product of amino acid metabolism, is toxic and is not readily removed from the circulation by the kidneys. Hepatocytes remove ammonia from the circulation and convert it to urea, which is less toxic than ammonia and is secreted into the circulation and then eliminated by the kidneys in the urine. Other substances are removed from the circulation and excreted by the hepatocytes into the bile.

5- Phagocytosis

Hepatic phagocytic cells (Kupffer cells), which lie along the sinusoid walls of the liver, phagocytize "worn-out" and dying red and white blood cells, some bacteria, and other debris that enters the liver through the circulation.

6- Synthesis

The liver can also produce its own unique new compounds. It produces many blood proteins, such as albumins, fibrinogen, globulins, heparin, and clotting factors, which are released into the circulation.



Control of Bile Secretion and Release

Pancreatic Secretions

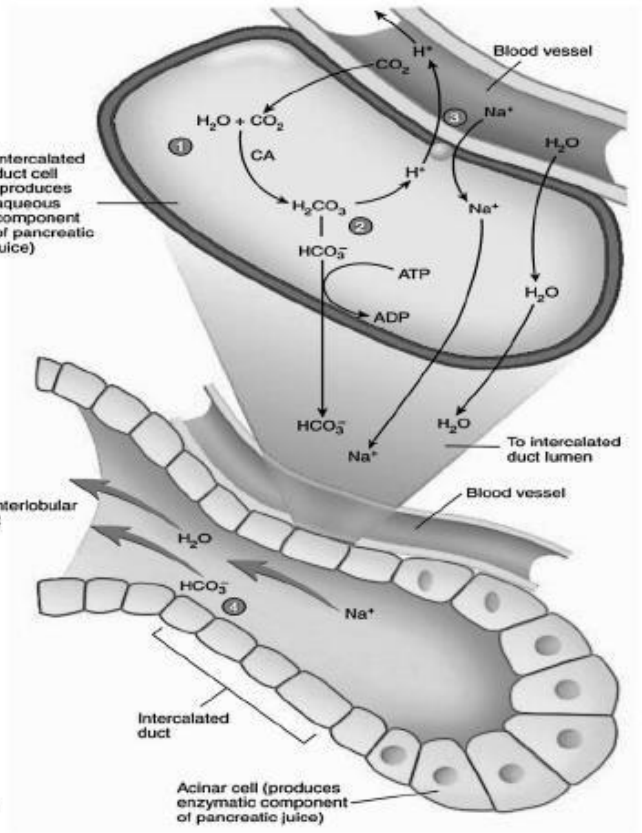
The exocrine secretions of the pancreas are called pancreatic juice and have two major components: an aqueous component and an enzymatic component. Pancreatic juice is produced in the pancreas and is then delivered through the pancreatic ducts to the small intestine, where it functions in digestion. The aqueous component is produced principally by columnar epithelial cells that line the smaller ducts of the pancreas. It contains Na^+ and K^+ ions in about the same concentration found in extracellular fluid. Bicarbonate ions are a major part of the aqueous component, and they neutralize the acidic chyme that enters the small intestine from the stomach. The increased pH caused by pancreatic secretions in the duodenum stops pepsin digestion but provides the proper environment for the function of pancreatic enzymes. Bicarbonate ions are actively secreted by the duct epithelium, and water follows passively to make the pancreatic juice isotonic.

The enzymes of the pancreatic juice are produced by the acinar cells of the pancreas and are important for the digestion of all major classes of food. Without the enzymes produced by the pancreas, lipids, proteins, and carbohydrates are not adequately digested.

The proteolytic pancreatic enzymes, which digest proteins, are secreted in inactive forms, whereas many of the other enzymes are secreted in active form. The major proteolytic enzymes are trypsin, chymotrypsin, and carboxypeptidase. They are secreted in their inactive forms as trypsinogen, chymotrypsinogen, and procarboxypeptidase and are activated by the removal of certain peptides from the larger precursor proteins. If these were produced in their active forms, they would digest the tissues producing them. The proteolytic enzyme enterokinase (intestinal enzyme), which is an enzyme attached to the brush border of the small intestine, activates trypsinogen. Trypsin then activates more trypsinogen, as well as chymotrypsinogen and procarboxypeptidase.

Pancreatic juice also contains pancreatic amylase, which continues the polysaccharide digestion that was initiated in the oral cavity. In addition, pancreatic juice contains a group of lipid-digesting enzymes called pancreatic lipases, which break down lipids into free fatty acids, glycerides, cholesterol, and other components.

Enzymes that reduce DNA and ribonucleic acid to their component nucleotides, deoxyribonucleases and ribonucleases, respectively, are also present in pancreatic juice.



1. Water (H_2O) and carbon dioxide (CO_2) combine under the influence of carbon anhydrase (CA) to form carbonic acid.
2. Carbonic acid (H_2CO_3) dissociates to form hydrogen ions (H^+) and bicarbonate ions (HCO_3^-).
3. The H^+ are exchanged for sodium ions (Na^+) and are removed in the bloodstream.
4. The HCO_3^- are actively transported into the intercalated ducts. Na^+ and water follow the HCO_3^- ions into the ducts.

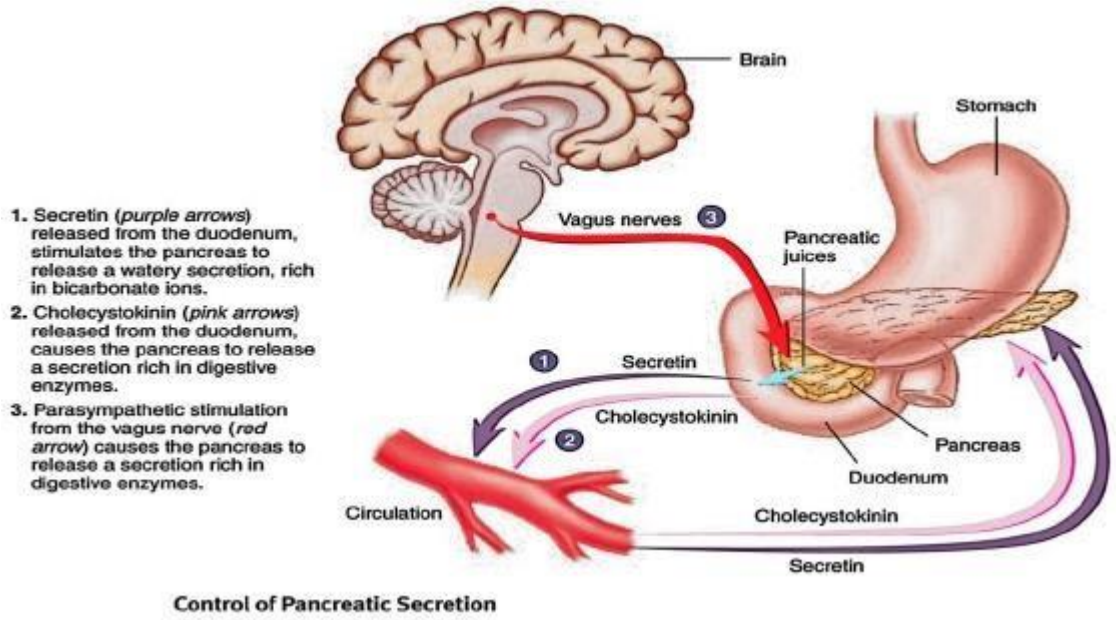
Bicarbonate Ion Production in the Pancreas

Regulation of Pancreatic Secretion

Both hormonal and neural mechanisms control the exocrine secretions of the pancreas. Secretin stimulates the secretion of a watery solution that contains a large amount of bicarbonate ions from the pancreas. The primary stimulus for secretin release is the presence of acidic chyme in the duodenum.

Cholecystokinin stimulates the release of bile from the gallbladder and the secretion of pancreatic juice rich in digestive enzymes. The major stimulus for the release of cholecystokinin is the presence of fatty acids and other lipids in the duodenum.

Parasympathetic stimulation through the vagus (X) nerves also stimulates the secretion of pancreatic juices rich in pancreatic enzymes, and sympathetic impulses inhibit secretion. The effect of vagal stimulation on pancreatic juice secretion is greatest during the cephalic and gastric phases of stomach secretion.



Control of Pancreatic Secretion

Digestion, Absorption, and Transport

Digestion is the breakdown of food to molecules that are small enough to be absorbed into the circulation. Mechanical digestion breaks large food particles down into smaller ones. Chemical digestion involves the breaking of covalent chemical bonds in organic molecules by digestive enzymes. Carbohydrates are broken down into monosaccharides, proteins are broken down into amino acids, and fats are broken down into fatty acids and glycerol. Absorption and transport are the means by which molecules are moved out of the digestive tract and into the circulation for distribution throughout the body. Not all molecules (e.g., vitamins, minerals, and water) are broken down before being absorbed. Digestion begins in the oral cavity and continues in the stomach, but most digestion occurs in the proximal end of the small intestine, especially in the duodenum.
Absorption of certain molecules can occur all along the digestive tract. A few chemicals, such as nitroglycerin, can be absorbed through the thin mucosa of the oral cavity below the tongue. Some small molecules (e.g., alcohol and aspirin) can diffuse through the stomach epithelium into the circulation. Most absorption, however, occurs in the duodenum and jejunum, although some absorption occurs in the ileum.

Once the digestive products have been absorbed, they are transported to other parts of the body by two different routes. Water, ions, and water-soluble digestion products, such as glucose and amino acids, enter the hepatic portal system and are transported to the liver. The products of lipid metabolism are coated with proteins and transported into lymphatic capillaries called lacteals. The lacteals are connected by lymphatic vessels to the thoracic duct, which empties into the left subclavian vein. The protein-coated lipid products then travel in the circulation to adipose tissue or to the liver.

Carbohydrates

Ingested carbohydrates consist primarily of polysaccharides, such as starches and glycogen; disaccharides, such as sucrose (table sugar) and lactose (milk sugar); and monosaccharides, such as glucose and fructose (found in many fruits). During the digestion process, polysaccharides are broken down into smaller chains and finally into disaccharides and monosaccharides. Disaccharides are broken down into monosaccharides. Carbohydrate digestion begins in the oral cavity with the partial digestion of starches by salivary amylase. A minor amount of digestion occurs in the stomach through the action of gastric amylase and gelatinase. Carbohydrate digestion is continued in the intestine by pancreatic amylase. A series of disaccharidases that are bound to the microvilli of the intestinal epithelium digest disaccharides into monosaccharides

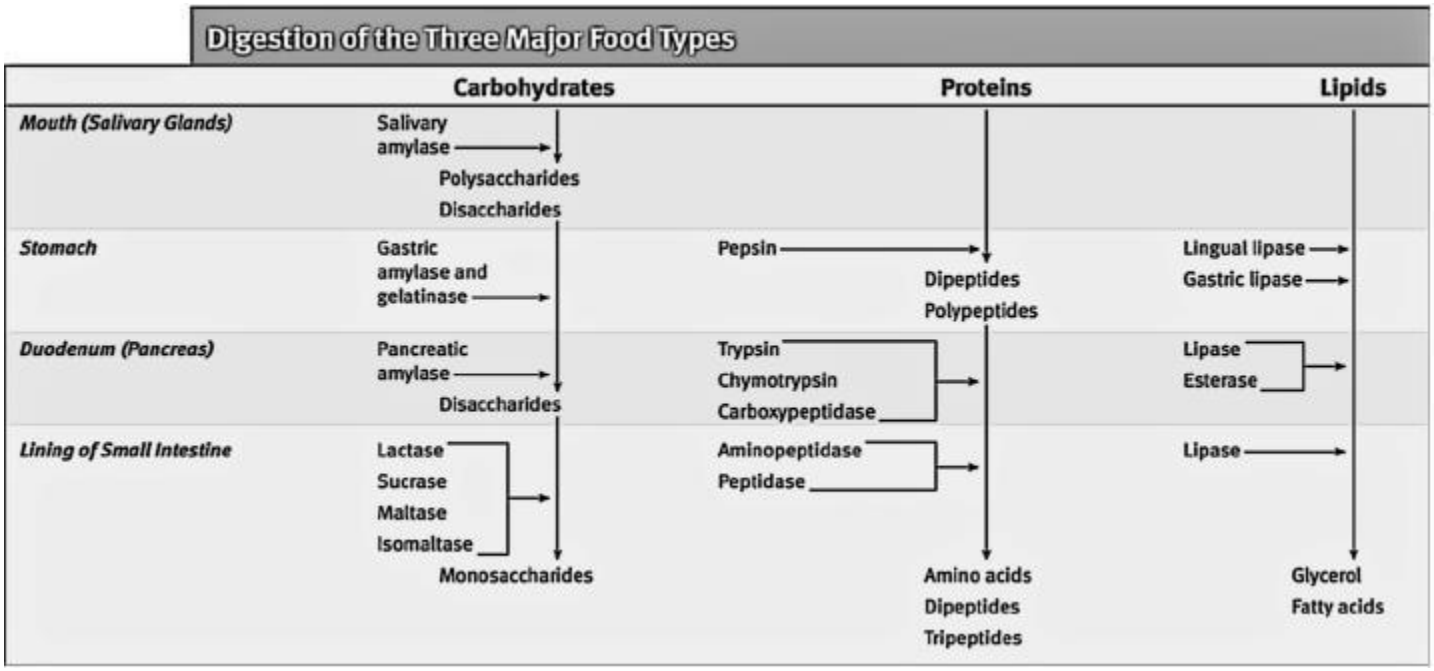
Monosaccharides such as glucose and galactose are taken up into intestinal epithelial cells by cotransport, powered by a sodium ion gradient. Monosaccharides such as fructose are taken up by facilitated diffusion. The monosaccharides are transferred by facilitated diffusion to the capillaries of the intestinal villi and are carried by the hepatic portal system to the liver, where the nonglucose sugars are converted to glucose. Glucose enters the cells through facilitated diffusion. The rate of glucose transport into most types of cells is greatly influenced by insulin and may increase 10-fold in its presence.

Lipids

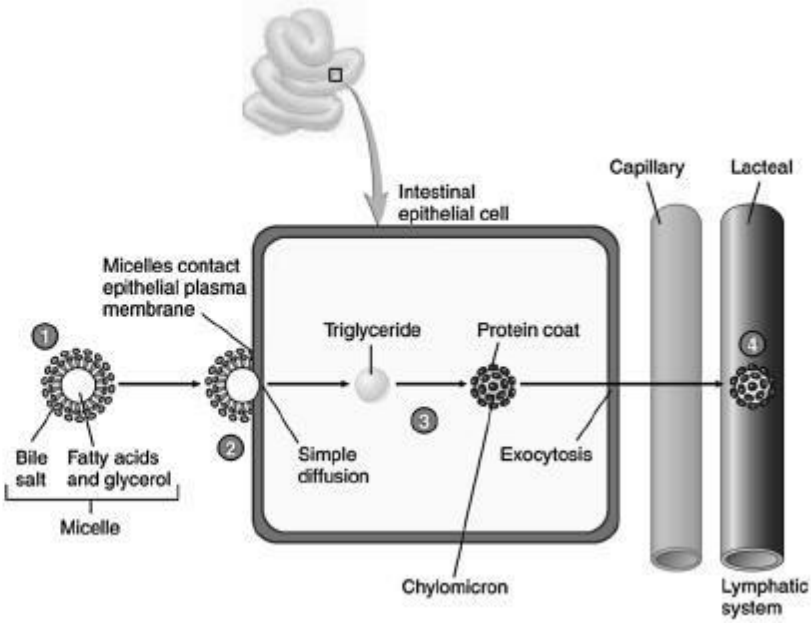
Lipids are molecules that are insoluble or only slightly soluble in water. They include triglycerides, phospholipids, cholesterol, steroids, and fat-soluble vitamins. Triglycerides, also called triacylglycerol, consist of three fatty acids and one glycerol molecule covalently bound together. The first step in lipid digestion is emulsification, which is the transformation of large lipid droplets into much smaller droplets. The enzymes that digest lipids are water-soluble and can digest the lipids only by acting at the surface of the droplets. The emulsification process increases the surface area of the lipid exposed to the digestive enzymes by decreasing the droplet size. Emulsification is accomplished by bile salts secreted by the liver and stored in the gallbladder.
Lipase digests lipid molecules. The vast majority of lipase is secreted by the pancreas. A minor amount of lingual lipase is secreted in the oral cavity, is swallowed with the food, and digests a small amount (< 10%) of lipid in the stomach.

The stomach also produces very small amounts of gastric lipase. The primary products of lipase digestion are free fatty acids and glycerol. Cholesterol and phospholipids also constitute part of the lipid digestion products.

Once lipids are digested in the intestine, bile salts aggregate around the small droplets to form micelles (small morsel). The hydrophobic ends of the bile salts are directed toward the free fatty acids, cholesterol, and glycerides at the center of the micelle; and the hydrophilic ends are directed outward toward the water environment. When a micelle comes into contact with the epithelial cells of the small intestine, the contents of the micelle pass by means of simple diffusion through the plasma membrane of the epithelial cells.

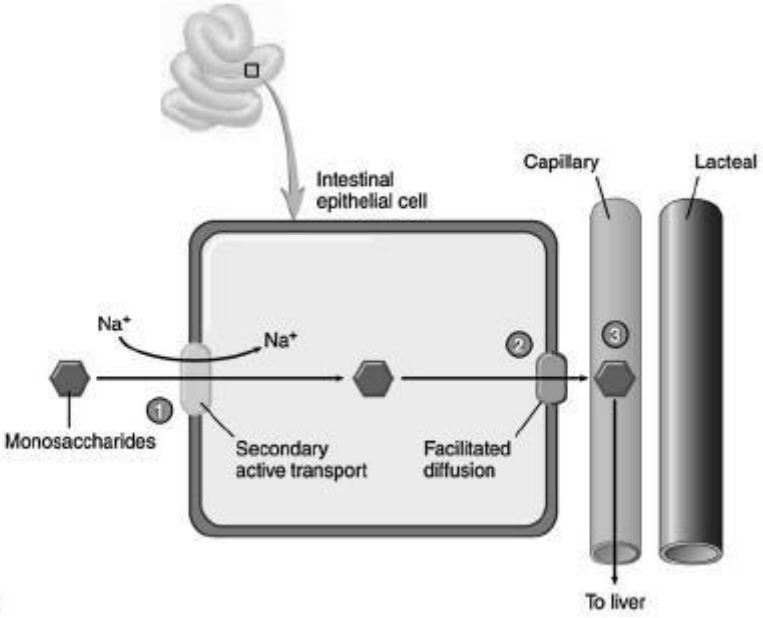


1. Bile salts surround fatty acids and glycerol to form micelles.
2. Micelles attach to the plasma membranes of intestinal epithelial cells, and the fatty acids and glycerol pass by simple diffusion into the intestinal epithelial cells.
3. Within the intestinal epithelial cell, the fatty acids and glycerol are converted to triglyceride; proteins coat the triglyceride to form chylomicrons, which move out of the intestinal epithelial cells by exocytosis.
4. The chylomicrons enter the lacteals of the intestinal villi and are carried through the lymphatic system to the general circulation.



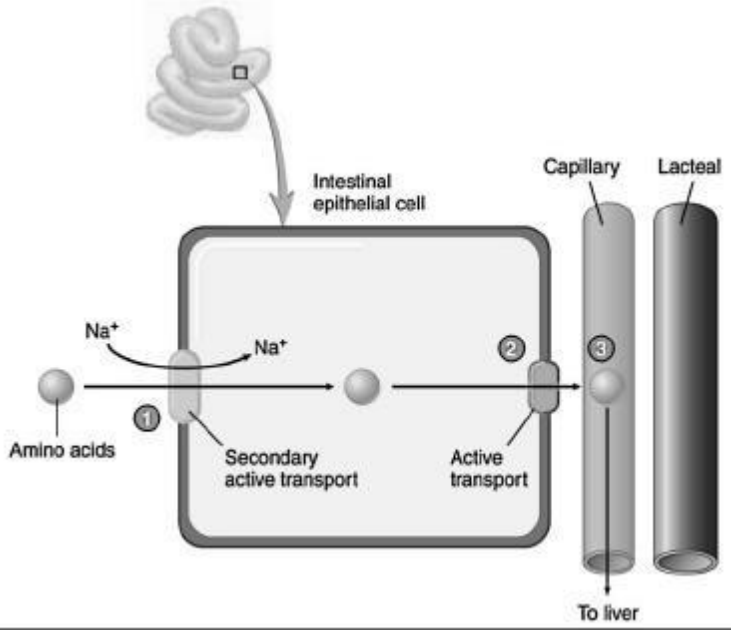
Lipid Transport

1. Monosaccharides are absorbed by secondary active transport into intestinal epithelial cells.
2. Monosaccharides move out of intestinal epithelial cells by facilitated diffusion.
3. They enter the capillaries of the intestinal villi and are carried through the hepatic portal vein to the liver.



Monosaccharide Transport

1. Amino acids are absorbed by secondary active transport into intestinal epithelial cells.
2. Amino acids move out of intestinal epithelial cells by active transport.
3. They enter the capillaries of the intestinal villi and are carried through the hepatic portal vein to the liver.



Amino Acid Transport

SPECIAL SENSES
Sensation of vision

SPECIAL SENSES

1. Sensation of vision

The eyes are complex sense organs-is optically equivalent to the usual photographic camera. It has a lens system, a variable aperture system (the pupil), and a retina that corresponds to the film. The lens system of the eye is composed of four refractive interfaces:

The light rays are refracted by the lens and cornea.

The refractory power is measured in diopter (D). A diopter is the reciprocal of focal length expressed in meters.

The focal length of cornea is 24 mm and refractory power is 42D. The focal length of lens is 44 mm and refractory power is 23D.

Consideration of All Refractive Surfaces of the Eye as a Single Lens—The "Reduced" Eye. If all the refractive surfaces of the eye are algebraically added together and then considered to be one single lens,

Human eyeball (bulbus oculi)

The center of anterior curvature of eyeball is called= anterior pole, & the center of posterior curvature is called= posterior pole.

The line joining 2 poles is called= optic axis.

The line joining a point in cornea little medial to anterior pole & the fovea centralis situated lateral to posterior pole is = visual axis.

ORBITAL CAVITY

Except the anterior 1/6, the eyeball is situated in bony orbital cavity or eye socket. It serves as a cushion to protect the eyeball from external force. Eyeballs are attached to orbital cavity by ocular muscles.

EYELIDS

protect eyeball from foreign particles coming in contact with its surface & cutoff the light during sleep. opened & closed voluntarily(reflexly). The margins of eyelids have sensitive hairs (cilia), arises from a follicles, which is surrounded by a sensory nerve plexus. When dust particle comes in contact with cilia, these sensory nerves are activated resulting inrapid blinking of eyelids- prevents dust particles from reaching the eyeball. The opening between the 2 eyelids is called palpebral fissure.

Formation of an Image on the Retina.

The lens system of eye can focus an image on retina. The image is inverted & reversed with respect to the object. However, the mind perceives objects in the upright position despite the upside-down orientation on the retina because the brain is trained to consider an inverted image as normal.

"ACCOMMODATION"

In children, the refractive power of lens of eye can be increased voluntarily from 20 diopters to about 34 diopters, which is an "accommodation" of 14 diopters.

To make this accommodation, the shape of the lens is changed from a moderately convex to a very convex lens. Controlled by Parasympathetic Nerves. The ciliary muscle is controlled by parasympathetic nerve signals transmitted to the eye through the third cranial nerve from the third nerve nucleus in the brain stem.

. (Sympathetic stimulation has an additional effect in relaxing the ciliary muscle, but this effect is so weak that it plays almost no role in the normal accommodation mechanism;

Presbyopia—Loss of Accommodation by the Lens.

As a person grows older, the lens grows larger and thicker and becomes far less elastic, partly because of progressive denaturation of the lens proteins. The ability of the lens

to change shape decreases with age.

The power of accommodation decreases from about 14 diopters in a child to less than 2 diopters by the time a person reaches 45 to 50 years and to essentially 0 diopters at age 70 years.

Thereafter, the lens remains almost totally nona ccommodating, a condition known as presbyopia.

Once a person has reached the state of presbyopia, each eye remains focused permanently at an almost constant distance; this distance depends on the physical characteristics of each person’s eyes. The eyes can no longer accommodate for both near and far vision.

characterized by progressive decrease in the ability of eyes to focus on near objects with age. It is due to the gradual reduction in the amplitude of accommodation.

PRESBYOPIA

„CAUSES

1. Decreased elasticity of lens is because of the physical changes in lens and its capsule during old age. So, the anteriorcurvature is not increased during near vision.

2. Decreased convergence of eyeballs due to the concomitant weakness of ocular muscles in old age.

„CORRECTION OF PRESBYOPIA

Presbyopia is corrected by using biconvex lens.

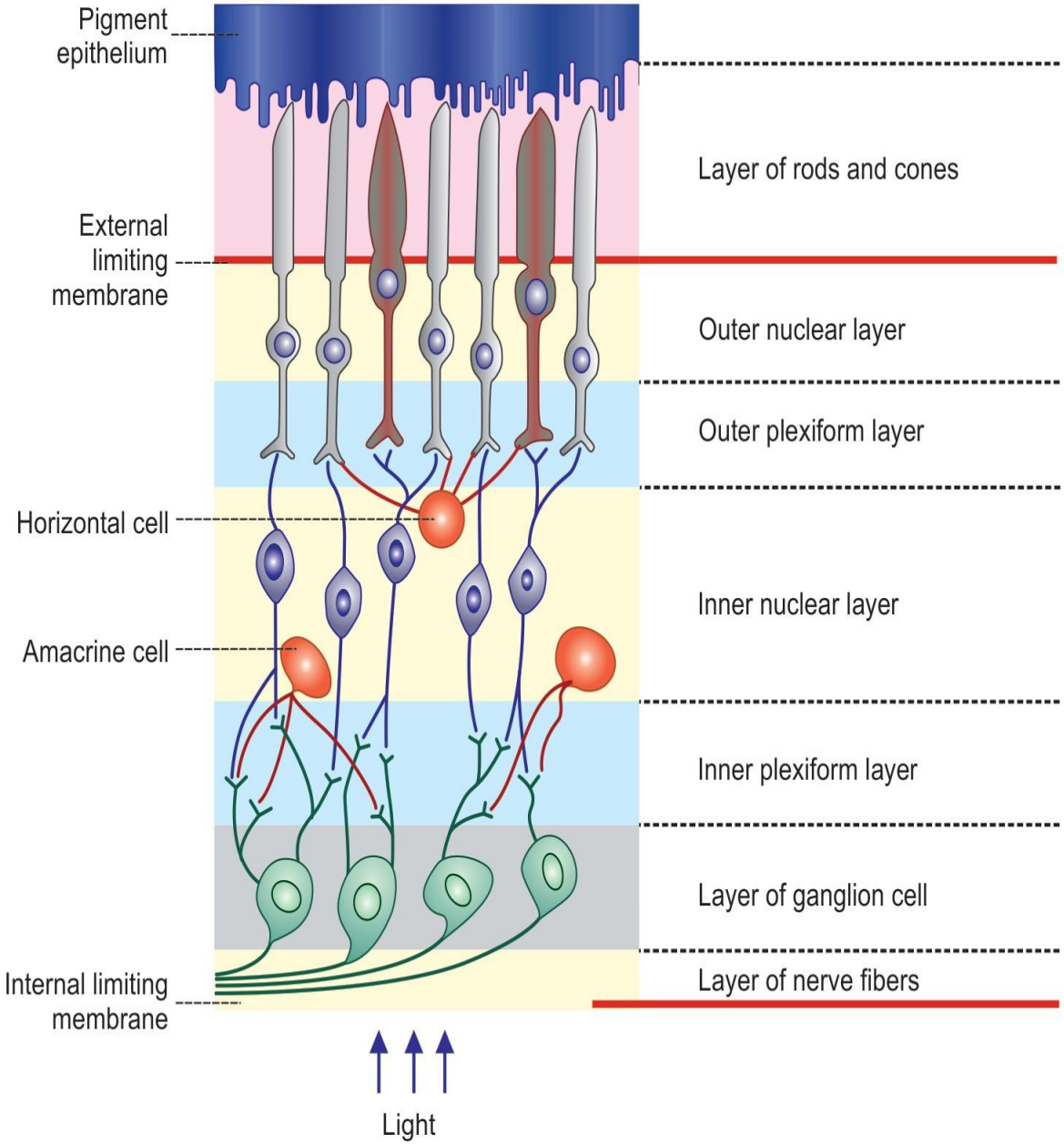
To see clearly both in the distance and nearby, an older person must wear bifocal glasses, with the upper segment focused for far-seeing and the lower segment focused for near-seeing (e.g., for reading).

INNER LAYER OR TUNICA INTERNA OR TUNICA NERVOSA OR **RETINA**

Retina is the light-sensitive membrane that forms the innermost layer of eyeball. has the receptors of vision. Structurally, is made up of 10 layers:

1. Layer of pigment epithelium.
2. Layer of rods and cones.
3. External limiting membrane.
4. Outer nuclear layer.
5. Outer plexiform layer.
6. Inner nuclear layer.
7. Inner plexiform layer.
8. Ganglion cell layer.
9. Layer of nerve fibers.
10. Internal limiting membrane.

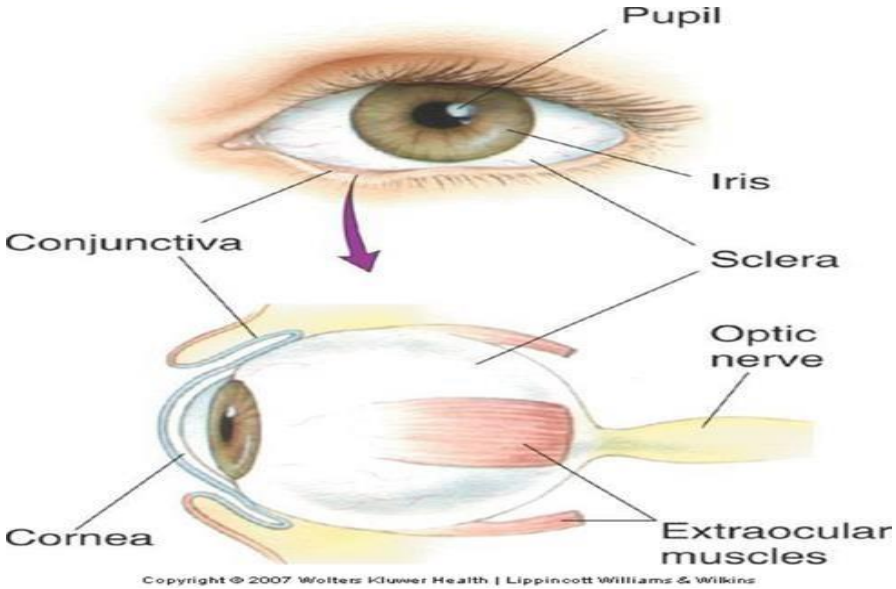
contains the
Rods and cones,
which are the visual receptors,
plus four types of neurons:
bipolar cells, ganglion
cells, horizontal cells,
and
amacrine cells

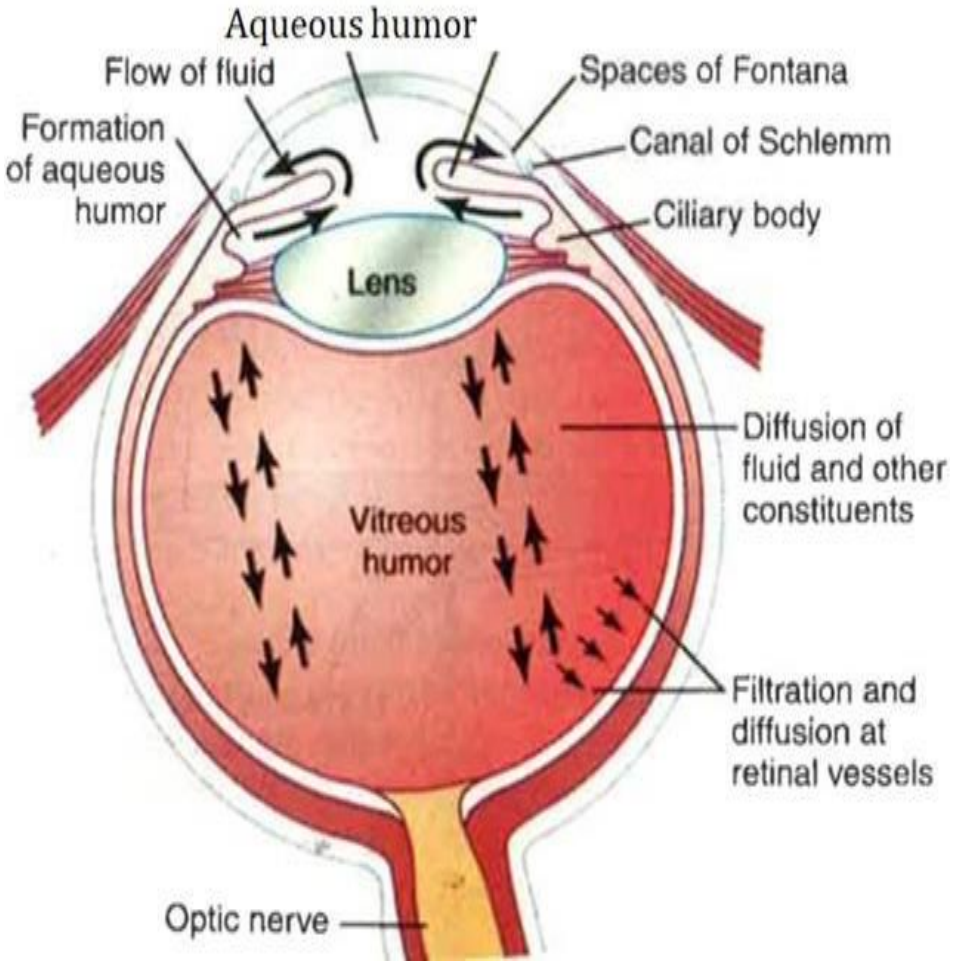


CONJUNCTIVA-

It is a thin mucous membrane, which covers the exposed part of the eye.

The part of conjunctiva covering the eyeball is called the bulbar portion. The part covering the eyelid is called the palpebral portion. lacrimal gland is situated in the shelter of bone, forming the upper & outer border of wall of the eye socket. Tear is a hypertonic fluid. Due to its continuous washing & lubrication, the conjunctiva is kept moist & is protected from infection. Tear also contains lysozyme that kills bacteria.





Fluid System of the Eye—Intraocular Fluid

The eye is filled with intraocular fluid, which maintains sufficient pressure in the eyeball to keep it distended.

INTRAOCULAR FLUIDS

Two types of fluids are present in the eye:

1. **Vitreous humor-is** a viscous fluid present behind the lens in the space between the lens and retina. helps maintain the shape of the eyeball.

2. AQUEOUS HUMOR

a thin fluid present in front of retina. It fills the space between the lens & cornea. This space is divided into anterior and posterior chambers by iris. Both the chambers communicate with each other through pupil.

Aqueous humor is formed by ciliary processes. passes through the angle between cornea & iris, meshwork of trabeculae and canal of Schlemm and reaches the venous system via anterior ciliary vein.

Functions of Aqueous humor:

1. Maintains shape of the eyeball
2. Maintains the intraocular pressure
3. Provides nutrients, oxygen and electrolytes to the avascular structures like lens and cornea
4. Removes metabolic end products from lens and cornea.

INTRAOCULAR PRESSURE

Intraocular pressure is the measure of fluid pressure in the eye exerted by aqueous humor. The normal intraocular pressure varies between 12and 20 mm Hg. It is measured by tonometer.

When intraocular pressure increases to about60 to 70 mm Hg, glaucoma occurs.

"Glaucoma"—a Principal Cause of Blindness, is one of the most common causes of blindness, a disease of the eye in which the intraocular pressure becomes pathologically high, sometimes rising acutely to 60 to 70 mm Hg.

Pressures above 25 to 30 mm Hg can cause loss of vision when maintained for long periods. Extremely high pressures can cause blindness within days or even hours. As the pressure rises, the axons of the optic nerve are compressed where they leave the eyeball at the optic disc. This compression is believed to block axonal flow of cytoplasm from the retinal neuronal cell bodies into the optic nerve fibers leading to the brain. The result is lack of appropriate nutrition of the fibers.

which eventually causes death of the involved fibers. It is possible that compression of the retinal artery, which enters the eyeball at the optic disc, also adds to the neuronal damage by reducing nutrition to the retina. A degenerative disease in which there is loss of retinal ganglia cells.

CATARACT

Cataract is the opacity or cloudiness in the natural lens of the eye. It is the major cause of blindness worldwide. When the lens becomes cloudy, light rays cannot pass through it easily, and vision is blurred.

Cataract develops in old age after 55 to 60 years. The lens is situated within the sealed capsule. The old cells die and accumulate within the capsule. Over years, the accumulation of cells is associated with accumulation of fluid and denaturation of the proteins in the lens fibers causing cloudiness of lens and blurred image.

NEURAL BASIS OF VISUAL PROCESS

retina has visual receptors- called photoreceptors, are rods & cones. The distribution of photoreceptors varies in different areas of retina. Fovea has only cones & no rods.

While proceeding from fovea towards the periphery of retina, the rods increase & cones decrease in number. At the periphery of retina, only rods are present & cones are absent.

Functions of Rods

Rods are very sensitive to light, have a low threshold, are responsible for dim light vision or night vision or scotopic vision. But, rods do not take part in resolving the details & boundaries of objects (visual acuity) or the color vision. The vision by rod is black, white or in the combination of black & white namely, gray. Therefore, the colored objects appear faded or grayish in twilight.

Functions of Cones

Cones have high threshold for light stimulus, are sensitive only to bright light- are called receptors of bright light vision or photopic vision or day light vision. also responsible for acuity of vision and the color vision.

Photosensitive pigments present in rods & cones are concerned with chemical basis of visual process. The chemical reactions involved in these pigments lead to development of electrical activity in retina & generation of impulses (action potentials)which are transmitted through optic nerve. The photochemical changes in the visual receptors are called Wald’s visual cycle.

Dark Adaptation

is the process by which the person is able to see the objects in dim light. If a person enters a dim lighted room (darkroom) from a bright lighted area, he is blind for some time, i.e. he cannot see any object. After sometime his eyes get adapted and he starts seeing the objects slowly. The maximum duration for dark adaptation is about 20 minutes.

Causes for dark adaptation

1. Resynthesis of rhodopsin: The time required for dark adaptation is partly determined by the time to resynthesize rhodopsin. In bright light, much of the pigment is being bleached (broken down). But in dim light, it requires sometime for the regeneration of certain amount of rhodopsin, which is necessary for optimal rod function.

2. Dilatation of pupil: The dilatation of pupil during dark adaptation allows more and more light to enter the eye.

Light Adaptation

Light adaptation is the process in which eyes get adapted to bright light. When a person enters a bright lighted area from a dim lighted area, he feels discomfort due to the dazzling effect of bright light. After some time, when the eyes become adapted to light, he sees the objects around him without any discomfort. It is the mere disappearance of dark adaptation. The maximum period for light adaptation is about 5 minutes.

Causes for light adaptation

1. Reduced sensitivity of rods during light adaptation due to the breakdown of rhodopsin.

2. Constriction of pupil which reduces quantity of light rays entering the eye.

Night Blindness

is defined as the loss of vision in dim light, is otherwise called nyctalopia or defective dim light (scotopic) vision.

Causes

is due to the deficiency of vitamin A, which is essential for the function of rods.

The deficiency of vitamin A which occurs because of:

1. The diet containing less amount of vitamin A.
2. Decreased absorption of vitamin A from the intestine.

Initially, vitamin A deficiency causes defective rod function. Prolonged deficiency leads to anatomical changes in rods and cones, and finally the degeneration of other retinal layers occurs. So, retinal function can be restored, only if treatment is given with vitamin A before the visual receptors start degenerating.

Visual acuity

is the degree to which the details & contours of objects are perceived, it is usually defined in terms of the shortest distance by which two lines can be separated & still be perceived as two lines. Clinically, is often determined by the use of the familiar Snellen letter charts viewed at a distance of 20 ft (6 m). The individual being tested reads aloud the smallest line distinguishable. The results are expressed as a fraction.

The numerator of the fraction is 20, the distance at which the subject reads the chart. The denominator is the greatest distance from the chart at which a normal individual can read the smallest line. Normal visual acuity is 20/20; a subject with 20/15 visual acuity has better than normal vision (not farsightedness); and one with 20/100 visual acuity has subnormal vision. Test for Acuity of Vision

Acuity of vision is tested for distant vision as well as near vision. If there is any difficulty in seeing the distant object or the near object, the defect is known as error of refraction.

FIELD OF VISION

The part of the external world seen by one eye when it is fixed in one direction is called field of vision or visual field of that eye.

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Binocular Vision

is the vision in which both the eyes are used together, so that a portion of external world is seen by the eyes together.

Monocular Vision

It is the vision in which each eye is used separately. In some animals like dog, rabbit and horse, the eyeballs are present at the sides of head. So, the visual fields of both eyes overlap to a very small extent. Because of this, different portion of the external world is seen by each eye.

DIVISIONS OF VISUAL FIELD

The visual field of human eye has an angle of 160° in horizontal meridian & 135° in vertical meridian. The visual field is divided into four parts:

1. Temporal field.
2. Nasal field.
3. Upper field.
4. Lower field.

Diplopia

means double vision. Normal single sensation is because of the ocular muscles, which direct the axes of the eyes in such a way, that the light rays from the object fall upon

the corresponding points of both retinas. If the light rays do not fall on the corresponding retinal points, diplopia occurs.

‚BLIND SPOT

is the small area of retina where visual receptors are absent. The optic disk in the retina does not have any visual receptors and, if the image of any object falls on the optic disk, the object can notbe seen. So this part of the retina is blind hence the name blind spot.

Normally, the darkness in the visual field due to the blind spot does not cause any inconvenience because, the fixation of each eye is at different angles. Even when one eye is closed or blind, the person is not aware of blind spot. However, one can recognize blind spot by some experimental procedures.

SPECIAL SENSES
Sensation of vision

Visual Pathway

Visual pathway or optic pathway is the nervous pathway that carries the retinal impulses to cerebral cortex.

VISUAL RECEPTORS

Rods & cones, which are present in retina of eye, form the visual receptors. Fibers from the visual receptors synapse with dendrites of bipolar cells of inner nuclear layer of retina.

First order neurons (primary neurons)

are bipolar cells in the retina. Axons from the bipolar cells synapse with dendrites of

ganglionic cells.

Second order neurons (secondary neurons)

are the ganglionic cells in ganglionic cell layer of retina--he axons of ganglionic cells form optic nerve-- optic nerve leaves the eye & terminates in lateral geniculate body.

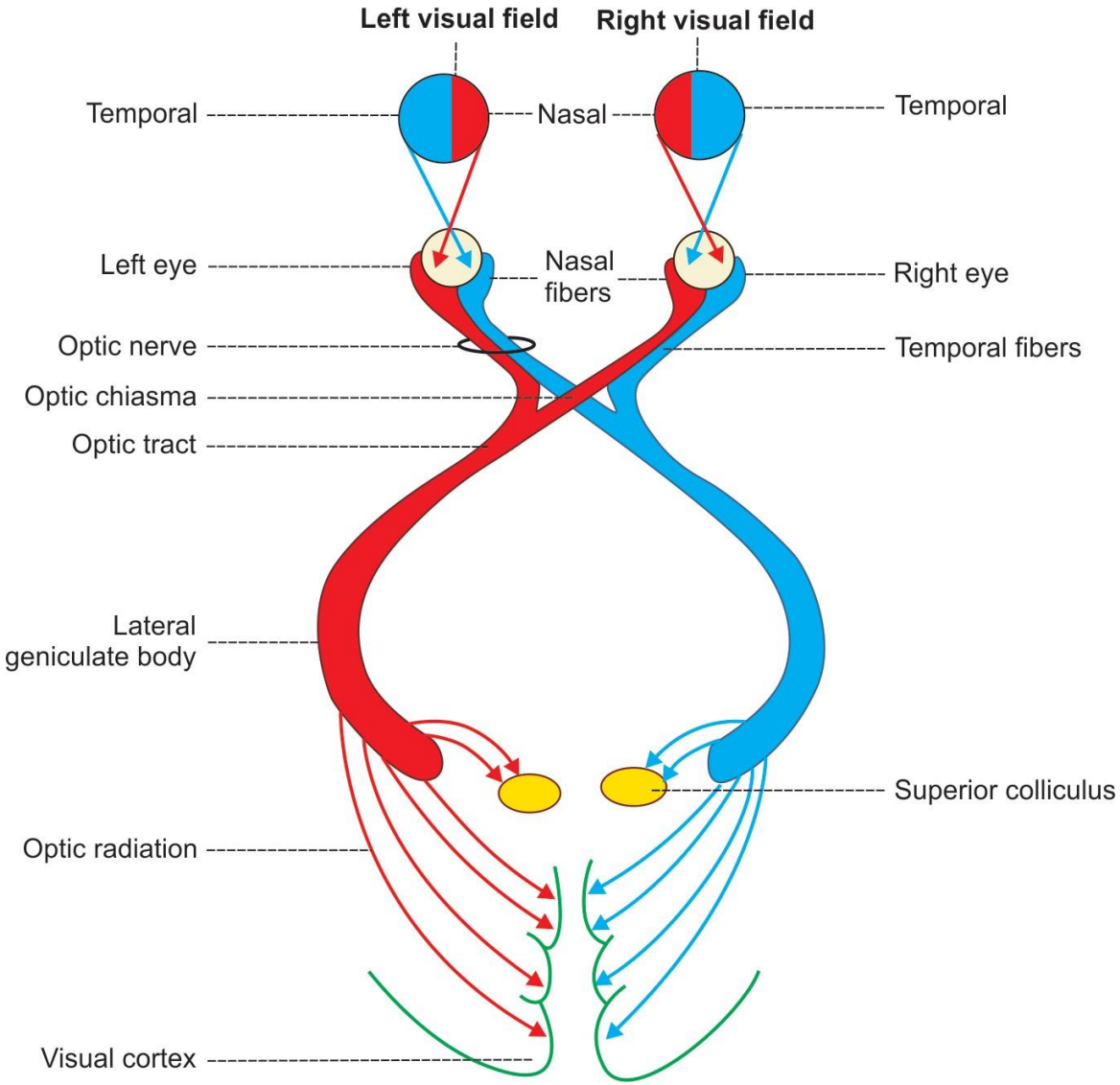
”

The third order neurons

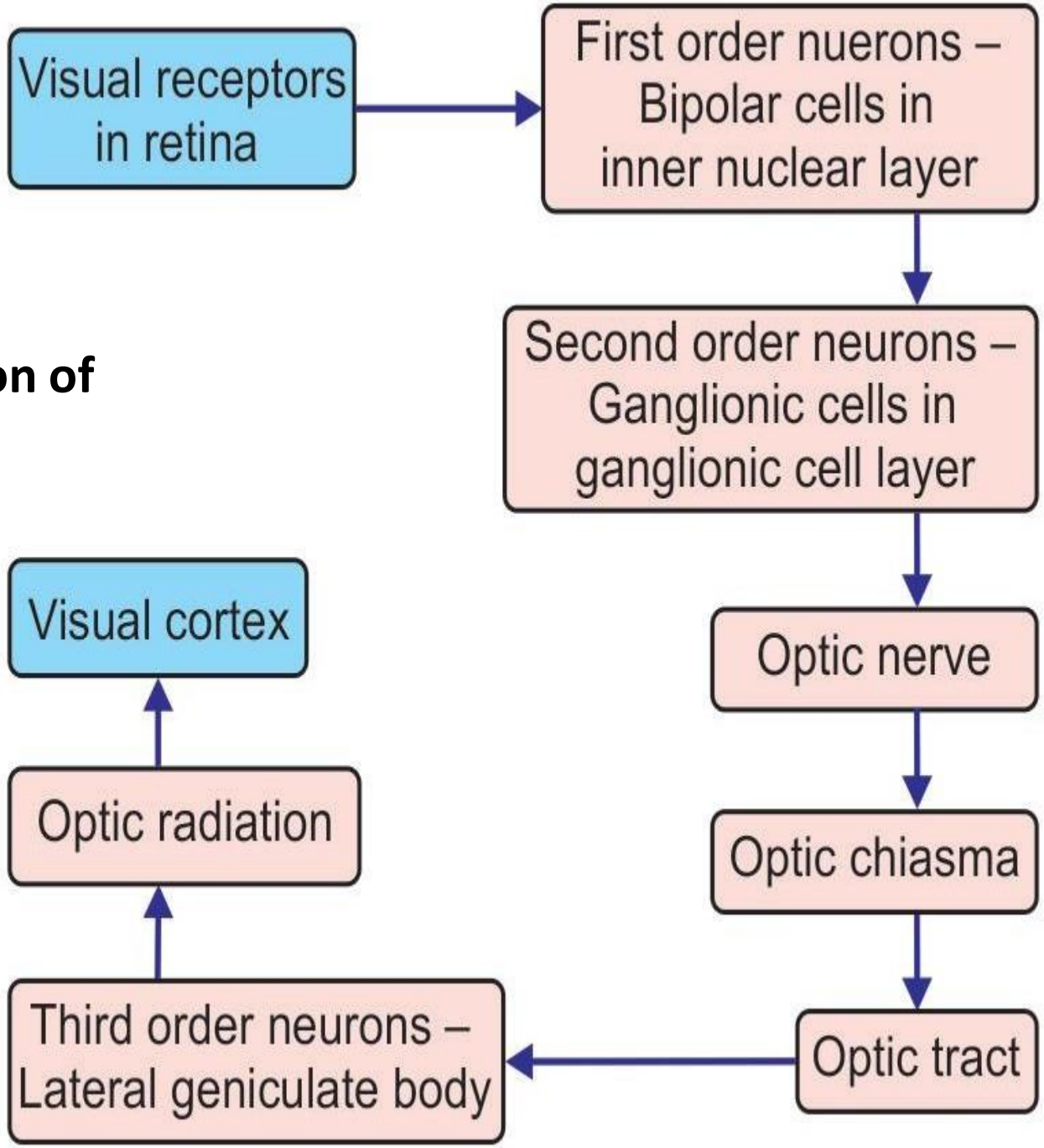
are in the lateral geniculate body. Fibers arising from here reach the visual cortex.

The visual pathway consists of six components:

1. Optic nerve.
2. Optic chiasma.
3. Optic tract.
4. Lateral geniculate body.
5. Optic radiation.
6. Visual cortex.



Schematic representation of visual pathway



APPLIED PHYSIOLOGY

The injury to any part of optic pathway causes visual defect & the nature of defect depends upon the location and extent of injury.

The loss of vision in one visual field is known as anopia.

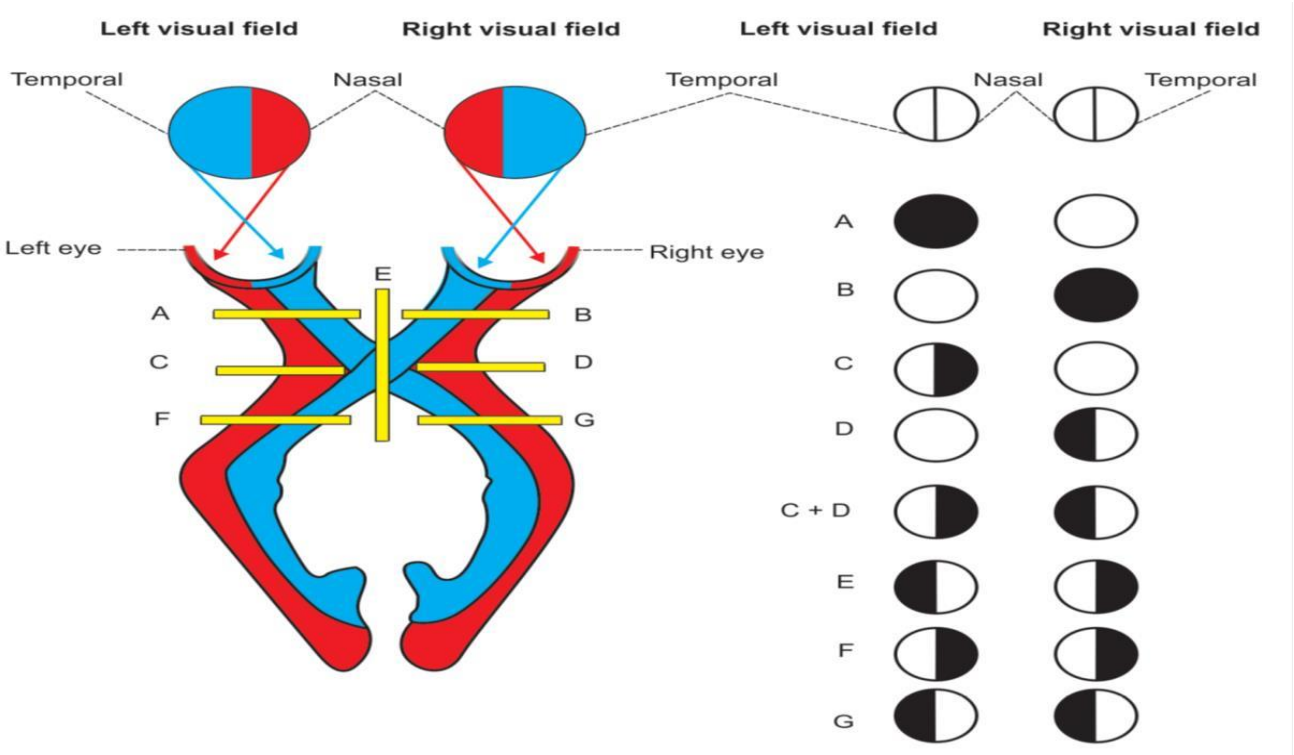
Loss of vision in one half of visual field is called hemianopia.

Hemianopia is classified into two types:

1. Homonymous hemianopia: Loss of vision in the same halves of both visual fields.
2. Heteronymous hemianopia: Loss of vision in opposite halves of visual field.

EFFECTS OF LESION AT DIFFERENT LEVELS OF VISUAL PATHWAY

1. Lesion of left optic nerve: Total blindness (anopia) of left eye (Fig: A).
2. Lesion of right optic nerve: Total blindness (anopia) of right eye (Fig. : B).
3. Lesion of lateral fibers in left side of optic chiasma: Left nasal hemianopia
4. Lesion of lateral fibers in right side of optic chiasma: Right nasal hemianopia(Fig.D).
5. Lesion of lateral fibers in both sides of optic chiasma: Binasal hemianopia (Fig.C ,D).
6. Lesion of medial fibers in optic chiasma: Bitemporal hemianopia (Fig.: E).
7. Lesion of left optic radiation: Right homonymous hemianopia (Fig.: F).
8. Lesion of right optic radiation: Left homonymous hemianopia (Fig.: G).



Color Vision

The human eye can recognize about 150 different colors in the visible spectrum. The discrimination & appreciation of colors depend upon the ability of cones in retina.

„

VISIBLE SPECTRUM AND SPECTRAL COLORS

„When the sunlight or white light is passed through a glass prism, is separated into different colors. The series of colored light produced by the prism is called the visible spectrum & the colors that form the spectrum are called the spectral colors.

The spectral colors are red, orange, yellow, green, blue, indigo & violet (ROYGBIV or VIBGYOR).

In the spectrum, the colors occupy the position according to their wavelengths.

red has got the maximum wavelength & the violet has got the minimum wavelength

The light rays longer than the red are called infrared rays or the heat waves, &the rays shorter than violet are called the ultraviolet rays. But, these two extraordinary types of rays do not evoke the sensation of vision.

EXTRASPECTRAL COLORS

are the colors other than those present in visible spectrum. These are formed by the combination of two or more spectral colors. For example, purple is the combination of violet and red. Pink is the combination of red and white.

”

PRIMARY COLORS

are those, which when combined together produce the white,, are red, green and blue. These three colors in equal proportion give white.

COMPLEMENTARY COLORS

are the pair of two colors which produce white when mixed or combined in proper proportion. Examples- are red and greenish blue; orange and cyan blue; yellow and indigo blue; violet and greenish yellow; and purple and green.

COLOR BLINDNESS

is the failure to appreciate one or more colors. It is common in 8% of males and only in 0.4% of females, as mostly- is an inherited sex-linked recessive character. In addition to hereditary conditions, color blindness occurs due to acquired conditions also, such as ocular diseases or injury, or disease of retina. TESTS FOR COLOR BLINDNESS

Color blindness is determined by using:

1. Ishihara's color charts.
2. Colored wool.
3. Edridge-Green lantern.

CLASSIFICATION OF COLOR BLINDNESS

Based on Young-Helmholtz trichromatic theory, is classified into 3 types:

1. Monochromatism.

is the condition characterized by total inability to perceive color, also called total color blindness or achromatopsia. is very rare.

The persons with monochromatism called monochromats. The retina of monochromats is totally insensitive to color and they see the whole spectrum in only black, white and different shades of gray. So, their vision is similar to black and white photography.

.

2. Dichromatism

is the color blindness in which the subject can appreciate only two colors. Persons with this defect are called dichromats.

They can match the entire spectrum of colors by only two primary colors because the receptors for third color are defective.The defects are classified into three groups.

i. Protanopia

caused by defect in the receptor of first primary color-red.(red color not be appreciated). They use blue and green to match the colors. Thus, they confuse red with green.

ii. Deuteranopia

caused due to the defect in the receptor of the second primary color, i.e. green. use blue and red colors and they cannot appreciate green color.

iii. Tritanopia

caused due to the defect in the receptor of third primary color, i.e. blue, use red and green colors and they cannot appreciate blue color.

3. Trichromatism

is the color blindness in which the intensity of one of the primary colors cannot be appreciated correctly though the affected persons are able to perceive all the 3colors. Even the dark shades of one particular color look dull for them, is classified into 3types.

”

Errors of Refraction

Emmetropia

is the vision with lens having normal refractive power & eye is called emmetropic eye. Any deviation in the refractive power from normal condition resulting in inadequate focusing on retina is called ametropia & the eye is called ametropic eye. The defect is due to the change in shape of the eyeball.

MYOPIA

is the eye defect characterized by inability to focus on distant object, called short sightedness, because the person can see near objects clearly, but not the distant objects.

In myopia, the near vision is normal, but the far point is not infinite, the refractive power of the lens is usually normal. But, the anteroposterior diameter of the eyeball is abnormally long.

Therefore, the image is brought to a focus a little in front of retina (the refractory power of lens is too strong for the length of eyeball). The light rays, after coming to a focus, disperse again, so a blurred image is formed upon retina.

Correction

in order to form a clear image on the retina, the light rays entering the eye must be divergent & not parallel. Thus, is corrected by using biconcave lens. The light rays are diverged by the concave lens before entering the eye.

HYPERMETROPIA OR LONG SIGHTEDNESS

is the eye defect characterized by the inability to focus on near object= known as long sightedness because the person can see the distant objects clearly, but not the near objects. also called hyperopia. In this defect, the distant vision is normal, but the near vision is affected.

Causes

is due to decreased anteroposterior diameter of the eyeball. So, even though the refractive power of the lens is normal, light rays are not converged enough to form a clear image on retina, i.e. the light rays are brought to a focus behind retina. It causes a blurred image of near objects.

occurs in childhood, if the eyeballs fail to develop to the correct size. It is common in old age also.

Correction

corrected by using biconvex lens. The light rays are converged by convex lens before entering the eye.

Anisometropia

the condition in which the two eyes have unequal refractive power, corrected by using different appropriate lens for each eye.

„ASTIGMATISM

is the condition in which the light rays are not brought to a sharp point upon retina. It is the common optical defect present in all eyes.

When it is moderate, known as physiological astigmatism. When it is well marked, it is considered abnormal.

For example, the stars appear as small dots of light to a person with normal eye. But in astigmatism, the stars appear as radiating short lines of light.

CAUSE

The light rays pass through all meridians of lens. In normal eye, lens has approximately same curvature in all meridians. So, the light rays are refracted almost equally in all meridians and brought to a focus.

If the curvature is different in different meridians – vertical, horizontal and oblique, the refractive power is also different in different meridians. The meridian with greater curvature refracts the light rays more strongly than other meridians. So, these light rays are brought to a focus in front of the light rays, which pass through other meridians. Such irregularity of curvature of lens causes astigmatism.

Astigmatism is of two types:

1. Regular Astigmatism

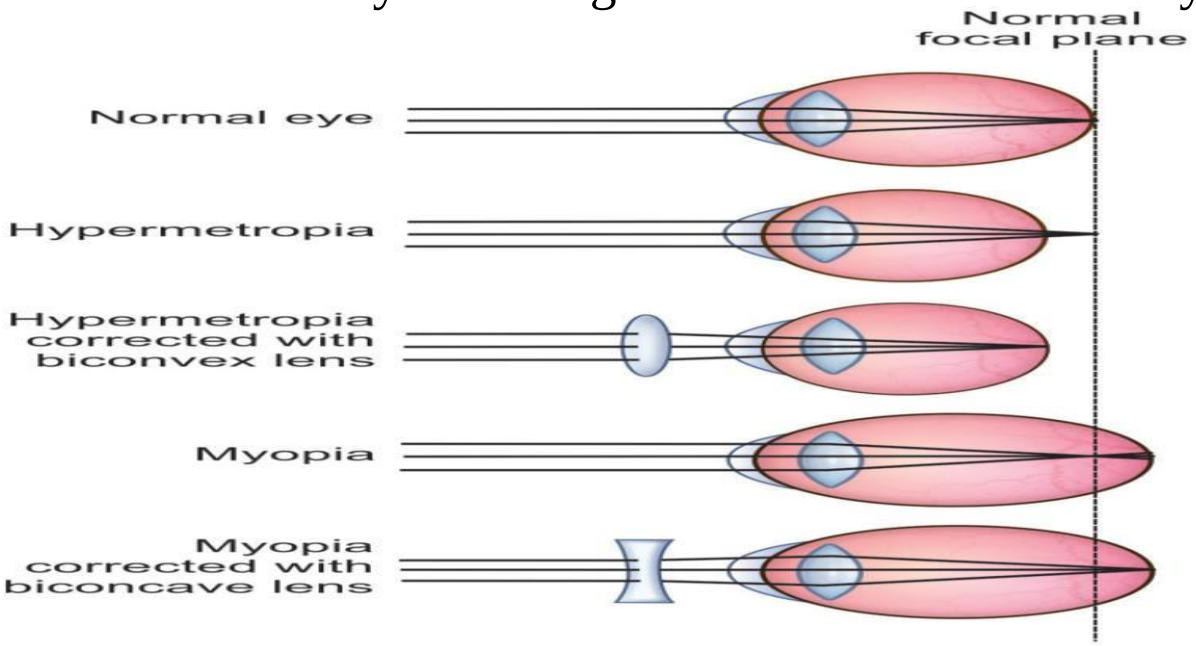
the refractive power is unequal in different meridians because of alteration of curvature in one meridian. But, it is uniform in all points throughout the affected meridian.

2. Irregular Astigmatism

Here, the refractive power is unequal not only in different meridians but it is also unequal in different points of same meridian.

„CORRECTION OF ASTIGMATISM

is corrected by using cylindrical glass lens having the convexity in the meridians corresponding to that of lens of eye having a lesser curvature, i.e. if the Horizontal curvature of lens is less, the person should use cylindrical glass lens with the convexity in horizontal meridian.



Cardiovascular physiology

HEART RATE

Normal heart rate is 72/minute. It ranges = 60 & 80 per minute.

TACHYCARDIA

is the increase in the heart rate above 100/minute.

Physiological conditions when tachycardia occurs are:

1. Childhood
2. Exercise
3. Pregnancy
4. Emotional conditions such as anxiety.

Pathological conditions when tachycardia occurs are:

1. Fever
2. Anemia
3. Hypoxia4. Hyperthyroidism
5. Hypersecretion of catecholamines
6. Cardiomyopathy
7. Valvular heart diseases.

BRADYCARDIA

is the decrease in the heart rate below 60/minute.

Physiological conditions when bradycardia occurs are:

1. Sleep
2. Athletic heart.

Pathological conditions when bradycardia occurs are:

1. Hypothermia
2. Hypothyroidism
3. Heart attack
4. Congenital heart disease
5. Degenerative process of aging
6. Obstructive jaundice
7. Increased intracranial pressure.

REGULATION OF HEART RATE

Heart rate is maintained within normal range constantly. It is subjected for variation during normal physiological conditions such as exercise, emotion, etc. However, under physiological conditions, the altered heart rate is quickly brought back to normal. Heart rate is regulated by the nervous mechanism which consists of three components:

I. Vasomotor center

II. Motor (efferent) nerve fibers to the heart

III. Sensory (afferent) nerve fibers from the heart.

Nerve supply to heart

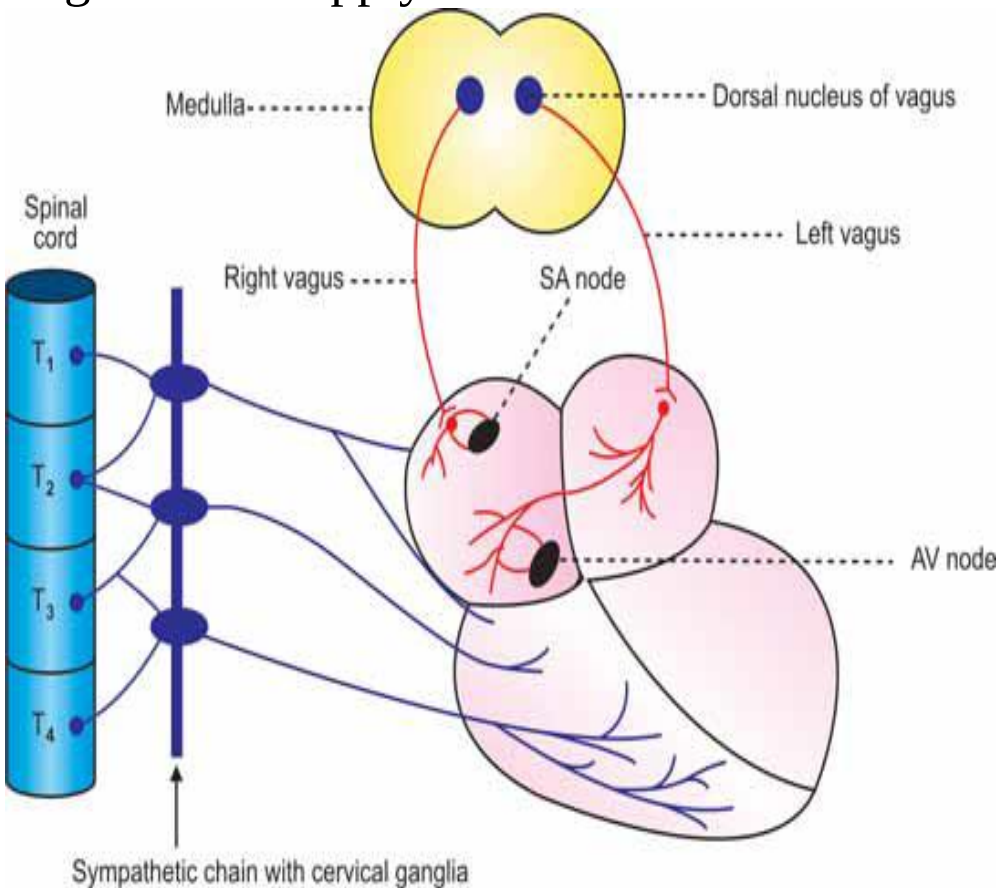
The parasympathetic nerve fibers supplying heart arise from the dorsal nucleus of vagus

The preganglionic parasympathetic nerve fibers from dorsal nucleus of vagus reach the heart and terminate on postganglionic neurons. The postganglionic fibers from these neurons innervate heart muscle. Most of the fibers from right vagus terminate in SA node. Remaining supply the atrial muscles and AV node.

Most of the fibers from left vagus supply AV node and some supply the atrial muscle and SA node. Ventricles do not receive the vagus nerve supply.

SYMPATHETIC NERVE FIBERS

The preganglionic fibers of the Sympathetic nerves to heart arise from lateral grey horns of the first 4 thoracic (T1 to T4) segments of thespinal cord. The sympathetic nerves are cardioaccelerator in function and carry cardioaccelerator impulsesfrom vasoconstrictor area to the heart.



FACTORS AFFECTING VASOMOTOR CENTER –

The vasomotor center regulates the cardiac activity by receiving impulses from different sources in the body. After receiving the impulses from different sources, the vasodilator area alters the vagal tone and modulates the activities of the heart. The various sources from which the impulses reach the vasomotor center are:

1. IMPULSES FROM HIGHER CENTERS(Cerebral Cortex, Hypothalamus)
2. IMPULSES FROM RESPIRATORY CENTERS
3. IMPULSES FROM BARORECEPTORS – MAREY'S REFLEX

The baroreceptors or pressoreceptors are the receptors, which give response to change in blood pressure. two types, carotid baroreceptors and aortic baroreceptors

The baroreceptors regulate the heart rate through a reflex called Marey's reflex. The stimulus for this reflex is increase in blood pressure.

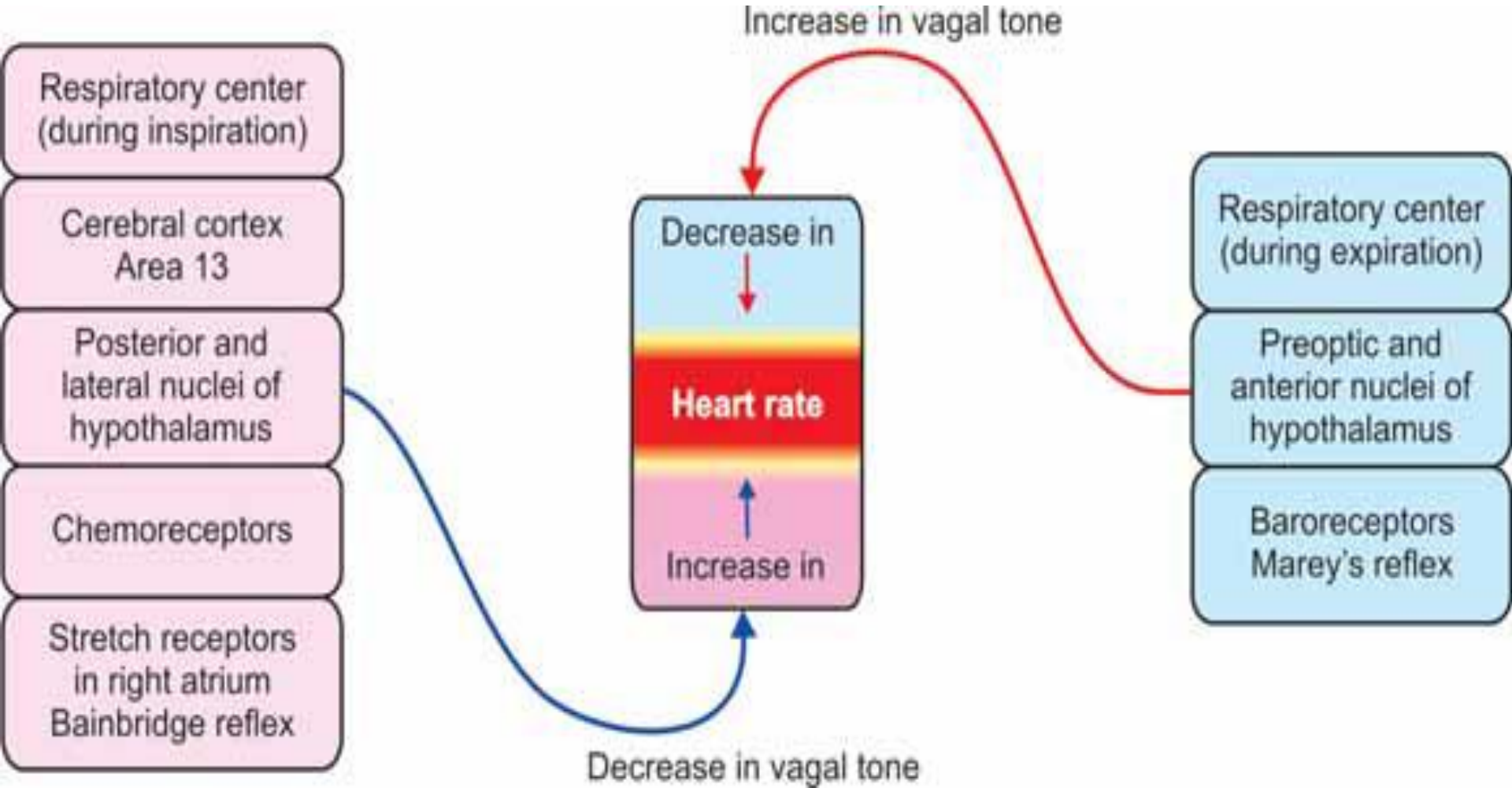
4. IMPULSES FROM CHEMORECEPTORS

Chemoreceptors are receptors giving response to change in chemical constituents of blood, particularly oxygen, carbon dioxide and hydrogen ion concentration.

Peripheral chemoreceptors are situated in thecarotid body and aortic body adjacent to baroreceptors.

5. IMPULSES FROM RIGHT ATRIUM – BAINBRIDGE REFLEX
6. IMPULSES FROM OTHER AFFERENT NERVES

Factors regulating vagal tone and heart rate



Arterial blood pressure

is the lateral pressure exerted by the column of blood on the wall of arteries. is expressed in four different terms:

1. Systolic blood pressure
2. Diastolic blood pressure
3. Pulse pressure
4. Mean arterial blood pressure.

Systolic blood pressure (systolic pressure) is the maximum pressure exerted in the arteries during systole of the heart. The normal systolic pressure is 120 mm Hg. It ranges = 110 & 140 mm Hg.

Diastolic blood pressure (diastolic pressure) is the minimum pressure in the arteries during diastole of the heart. The normal diastolic pressure is 80 mm Hg. It varies between 60 and 80 mm Hg.

Pulse pressure is the difference between systolic pressure and diastolic pressure. Normally, it is 40 mm Hg (120 to 80).

PHYSIOLOGICAL VARIATIONS

1. Age2. Sex

In females, up to the period of menopause, the arterial pressure is about 5 mm Hg less than in males of same age. After menopause, the pressure in females becomes equal to that in males of same age.

3. Body Built

The pressure is more in obese persons than in lean persons.

4. Diurnal Variation

In early morning, the pressure is slightly low. It gradually increases and reaches the maximum at noon. It becomes low in evening.

5. After Meals

The arterial blood pressure is increased for few hours after meals due to increase in cardiac output.

6. During Sleep

Usually, the pressure is reduced up to 15 to 20 mm Hg during deep sleep. However, it increases slightly during sleep associated with dreams.

7. Emotional Conditions

During excitement or anxiety, the blood pressure is increased due to release of adrenaline.

8. After Exercise

After moderate exercise, systolic pressure increases by 20 to 30 mm Hg above the basal level due to increase in force of contraction and stroke volume. Normally, diastolic pressure is not affected by moderate exercise. It is because the diastolic pressure depends upon peripheral resistance, which is not altered by moderate exercise.

After severe muscular exercise, the systolic pressure rises by 40 to 50 mm Hg above the basal level. But, the diastolic pressure reduces because the peripheral resistance decreases in severe muscular exercise.

DETERMINANTS OF ARTERIAL BLOOD PRESSURE – FACTORS MAINTAINING ARTERIAL BLOOD PRESSURE

Some factors are necessary for maintenance of normal blood pressure, which are called local factors, mechanical factors or determinants of blood pressure. These factors are divided into 2 types:

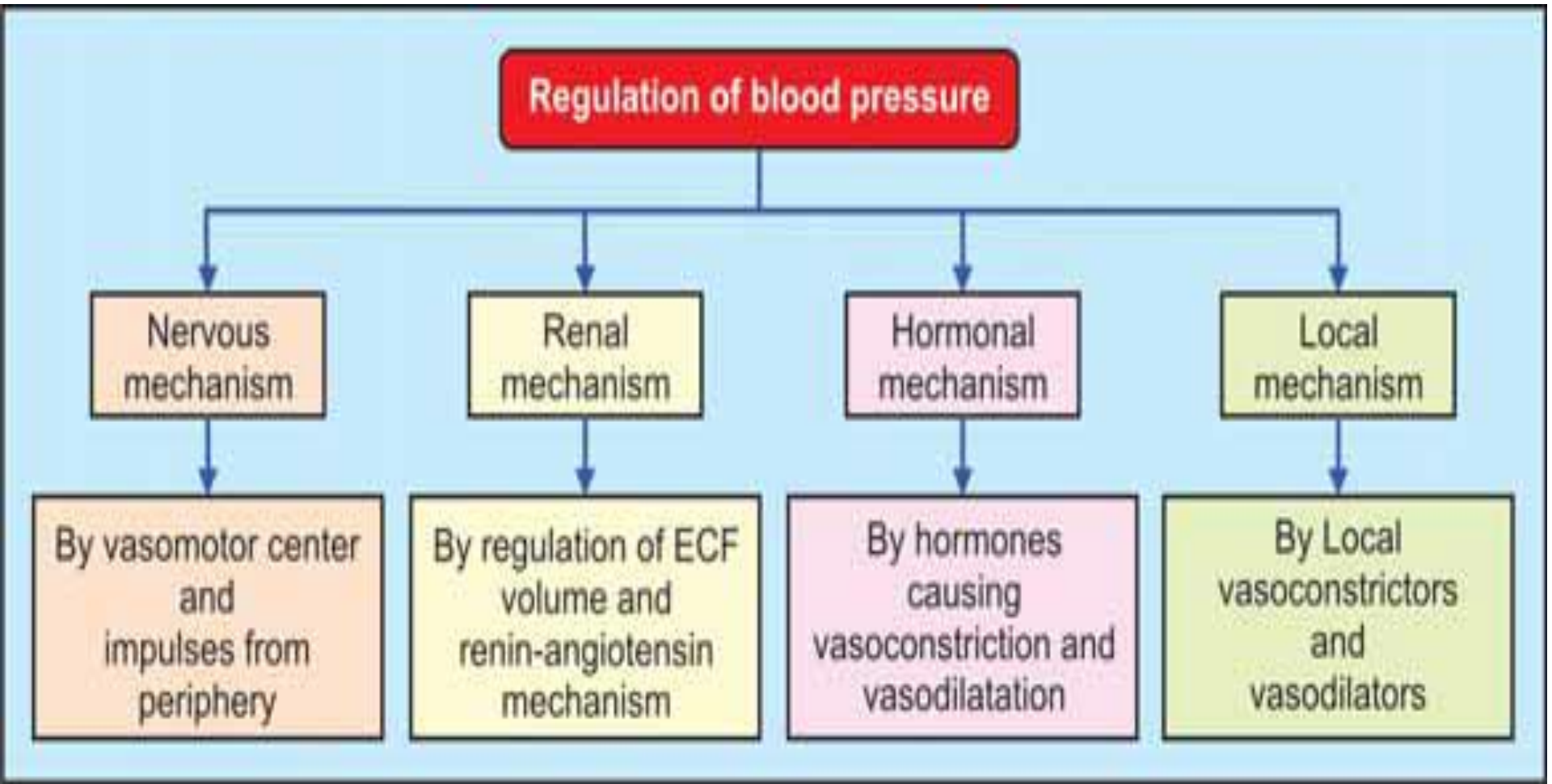
I. Central factors -pertaining to the heart:(Cardiac output& Heart rate).

II. Peripheral factors-- pertaining to blood and blood vessels:

1. Peripheral resistance
2. Blood volume
3. Venous return
4. Elasticity of blood vessels
5. Velocity of blood flow
6. Diameter of blood vessels
7. Viscosity of blood.

REGULATION OF ARTERIAL BLOOD PRESSURE

Arterial blood pressure varies even under physiological conditions. immediately it is brought back to normal level because of the presence of well organized regulatory mechanisms in the body. Body has four such regulatory mechanisms.



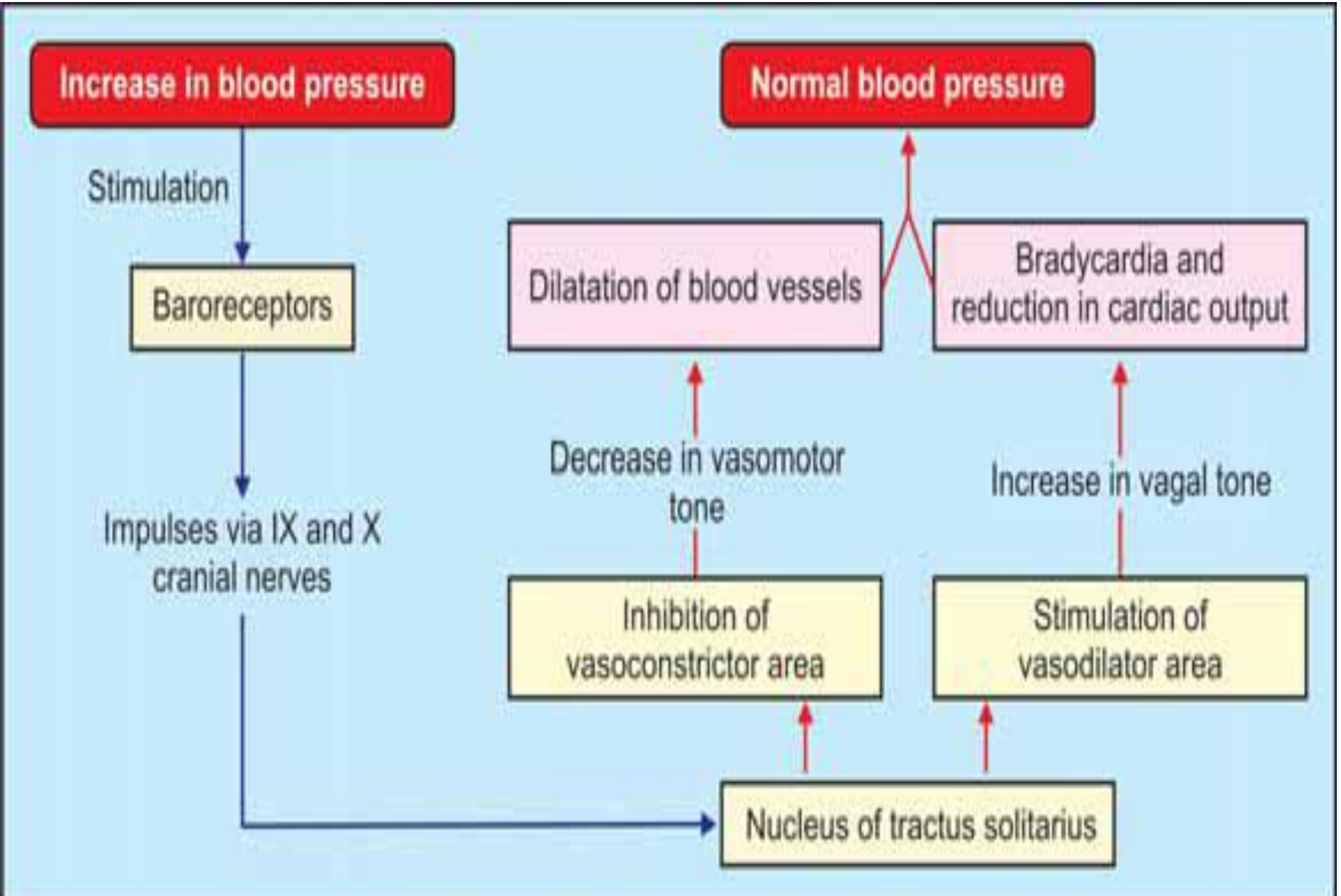
The nervous regulation is rapid among all the mechanisms involved in regulation of ABP. When BP alters, nervous system brings the pressure back to normal within few minutes. Although nervous mechanism is quick in action, it operates only for a short period & then it adapts to the new pressure= called short-term regulation.

The nervous mechanism regulating ABP operates through the vasomotor system. The vasomotor system includes three components:

1. Vasomotor center
2. Vasoconstrictor fibers
3. Vasodilator fibers.

The vasomotor center regulates ABP by causing vasoconstriction or vasodilatation, its actions depend upon the impulses it receives from other structures such as baroreceptors, chemoreceptors, higher centers and respiratory centers. --baroreceptors and chemoreceptors play a major role in the short-term regulation of blood pressure.

Regulation of blood pressure by baroreceptor mechanism



2. Chemoreceptor Mechanism

Chemoreceptors are receptors giving response to change in chemical constituents of blood. Peripheral chemoreceptors influence the vasomotor center.

Peripheral chemoreceptors are sensitive to lack of oxygen, excess of carbon dioxide and hydrogen ion concentration in blood. Whenever

blood pressure decreases, the blood flow decreases resulting in decreased oxygen content and excess of carbon dioxide and hydrogen ion.

These factors stimulate the chemoreceptors, which send impulses to stimulate the vasoconstrictor center. The blood pressure rises and blood flow increases.

Chemoreceptors play a major role in maintaining respiration rather than blood pressure.

Sinoaortic mechanism

Mechanism of action of baroreceptors and chemoreceptors in carotid and aortic region. The nerves from the baroreceptors and chemoreceptors are called buffer nerves because these nerves regulate the heart rate, blood pressure and respiration.

RENAL MECHANISM FOR REGULATION OF B P – LONG-TERM REGULATION

kidneys play an important role in the long term regulation of ABP. by 2 ways:

1. By regulation of ECF volume
2. Through renin-angiotensin mechanism.

BY REGULATION OF EXTRACELLULAR FLUID VOLUME

When the BP increases, kidneys excrete large amounts of water & salt, particularly sodium by means of pressure diuresis & pressure natriuresis. Pressure diuresis is the excretion of large quantity of water in urine because of increased BP

Even a slight increase in BP doubles the water excretion.

Pressure natriuresis is the excretion of large quantity of sodium in urine.

Because of diuresis & natriuresis, there is decrease in the ECF volume &blood volume, which in turn brings the ABP back to normal level.

When blood pressure decreases, the reabsorption of water from renal tubules is increased. This in turn, increases ECF volume, blood volume & cardiac output resulting in restoration of BP.

Actions of Angiotensin II

When BP & ECF volume decrease, renin secretion from kidneys is increased. It converts angiotensinogen into angiotensin I. This is converted into angiotensin II by ACE (angiotensin converting enzyme). Angiotensin II acts in 2 ways to restore the BP:

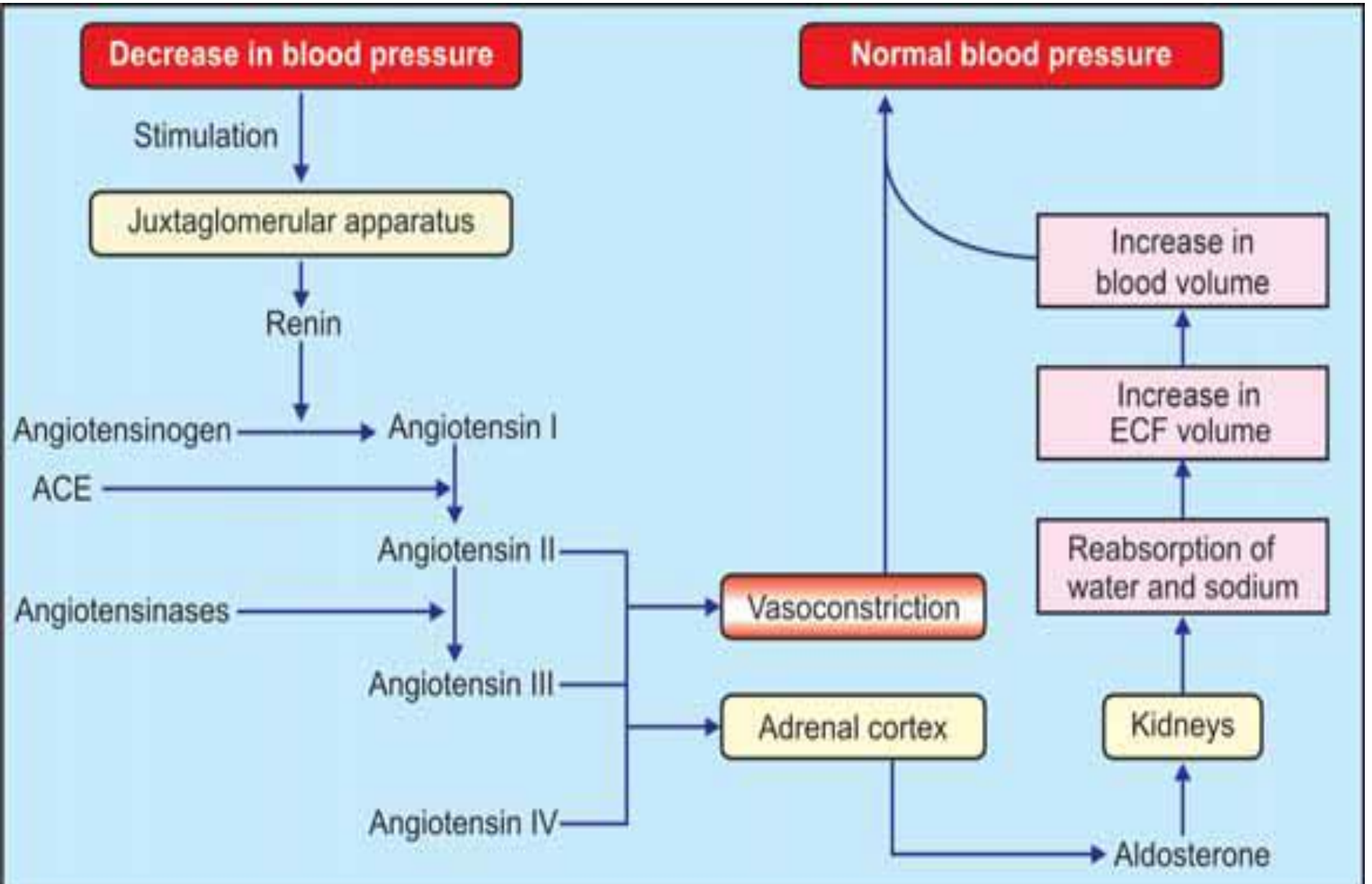
i. It causes constriction of arterioles in body so that the peripheral resistance is increased, & BP rises. In addition, angiotensin II causes constriction of afferent arterioles in kidneys so that the glomerular filtration reduces.

This results in retention of water & salts. This increases ECF volume to normal level. This in turn increases the BP to normal level.

ii. Simultaneously, angiotensin II stimulates the adrenal cortex to secrete aldosterone.

This hormone increases reabsorption of sodium from renal tubules. Sodium reabsorption is followed by water reabsorption resulting in increased ECF volume & blood volume. It increases the BP to normal level.

Regulation of blood pressure by renin-angiotensin mechanism.
ACE = Angiotensin converting enzyme



HORMONAL MECHANISM FOR REGULATION Of BP

Hormones which **Increase** the Blood Pressure

1. Adrenaline
2. Noradrenaline
3. Thyroxine
4. Aldosterone
5. Vasopressin
6. Angiotensin
7. Serotonin.

Hormones which **Decrease** the Blood Pressure

1. Vasoactive intestinal polypeptide (VIP)
2. Bradykinin
3. Prostaglandin
4. Histamine
5. Acetylcholine
6. Atrial natriuretic peptide
7. Brain natriuretic peptide
8. C-type natriuretic peptide.

LOCAL MECHANISM FOR REGULATION OF BP

some local substances also regulate the BP.-- by vasoconstriction or vasodilatation.

LOCAL VASOCONSTRICTORS

The local vasoconstrictor substances are of vascular endothelial origin= known as endothelins (ET). Endothelins are produced by stretching of blood vessels. These peptides act by activating phospholipase, which activates the prostacyclin & thromboxane A2. These two substances cause constriction of blood vessels & increase in blood pressure.

LOCAL VASODILATORS

The local vasodilators are of two types:

1. Vasodilators of metabolic origin such as carbon dioxide, lactate, hydrogen ions & adenosine
2. Vasodilators of endothelial origin such as nitric oxide (NO).

HYPERTENSION

the persistent high blood pressure. Clinically, systolic pressure remains elevated above 150 mm Hg & diastolic pressure remains elevated above 90 mm Hg, it is considered as hypertension. If there is increase only in systolic pressure, it is called systolic hypertension.

Types of Hypertension

1. **Primary hypertension or essential hypertension**

Primary hypertension is the elevated blood pressure in the absence of any underlying disease- called essential hypertension.

The arterial blood pressure is increased because of increased peripheral resistance, which occurs due to some unknown cause.

2**. Secondary hypertension**

is the high blood pressure due to some underlying disorders. The different forms of secondary hypertension are:

- i. Cardiovascular hypertension that is produced due to the cardiovascular

disorders such as atherosclerosis(hardening of blood vessels by fat deposition) and coarctation (narrowing) of aorta

- ii. Endocrine hypertension which is due to hyperactivity of some endocrine glands such as pheochromocytoma, hyperaldosteronism and Cushing's syndrome
- iii. Renal hypertension that is caused by renal diseases like glomerulonephritis and stenosis of renal arteries
- iv. Neurogenic hypertension which is developed by nervous disorders such as increased intracranial pressure and lesion in tractus solitarius
- v. Hypertension during pregnancy which is due to toxemia of pregnancy.

HYPOTENSION

is the low BP. When the systolic pressure is less than 90 mm Hg, considered as hypotension. Types

1. Primary hypotension

is the low BP that develops in the absence of any underlying disease & develops due to some unknown cause. It is also called essential hypotension. Frequent fatigue and weakness are the common symptoms of this condition. However, the persons with primary hypotension are not easily susceptible to heart or renal disorders.

2. Secondary hypotension

occurs due to some underlying diseases. The diseases which cause hypotension are:

- i. Myocardial infarction
- ii. Hypoactivity of pituitary gland
- iii. Hypoactivity of adrenal glands
- iv. Tuberculosis
- v. Nervous disorders.

Oral cavity

General physiology

Oral cavity

Functional anatomy of mouth

The mouth is known as oral cavity or buccal cavity. It is formed by cheeks, lips and palate. It encloses the teeth, tongue and salivary glands. It opens anteriorly to the exterior through lips and posteriorly into the pharynx. Digestive juice present in the mouth is saliva which is secreted by the salivary glands.

Functions of mouth

The primary function of mouth is **eating**. It has few other important functions also. The functions of the mouth are:

1. Ingestion of food materials.
2. Chewing the food and mixing it with saliva.
3. Appreciation of the taste.
4. Transfer of food (bolus) to the esophagus by swallowing.
5. Role in speech.
6. Social functions such as smiling and other expressions.

Salivary Glands

In humans, the saliva is secreted by three pairs of major (larger) salivary glands and some minor (small) salivary glands in the oral and pharyngeal mucous membrane. The major glands are:

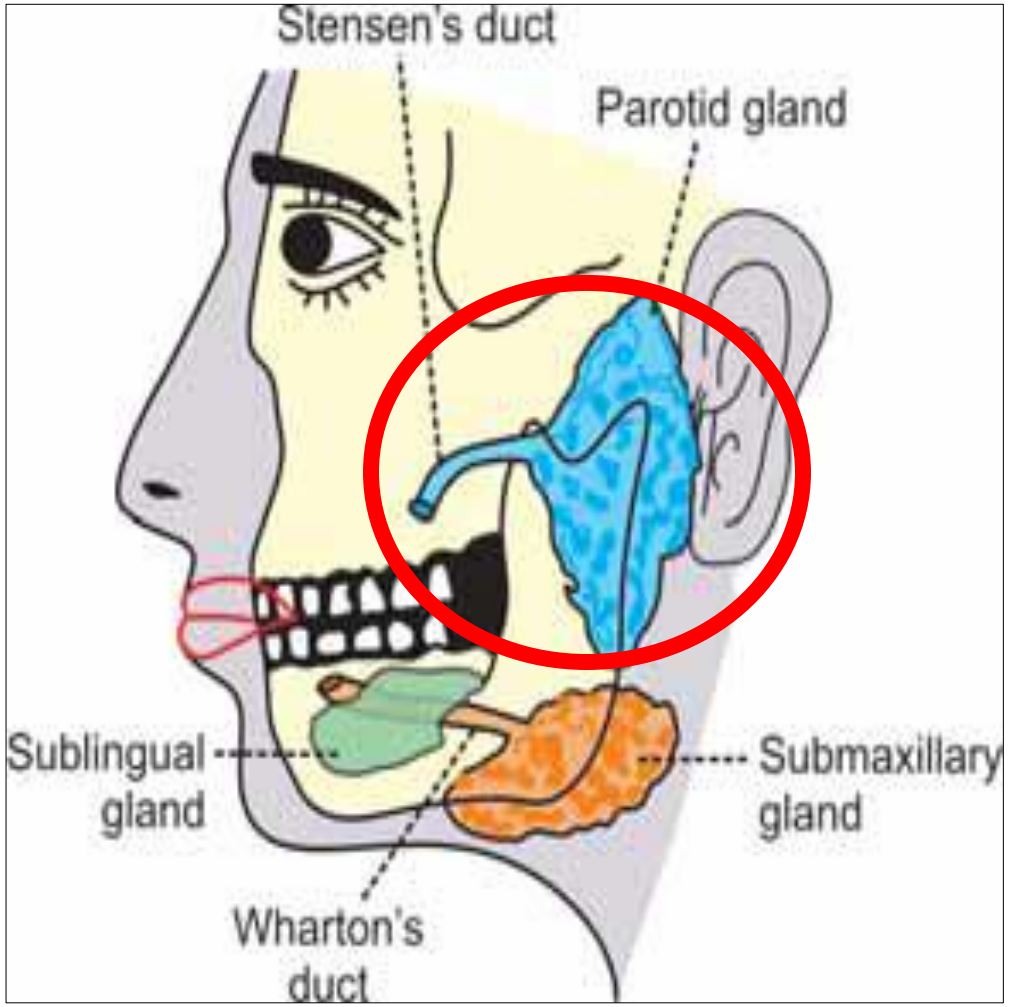
1. Parotid glands.

2. Submaxillary or submandibular glands.

3. Sublingual glands.

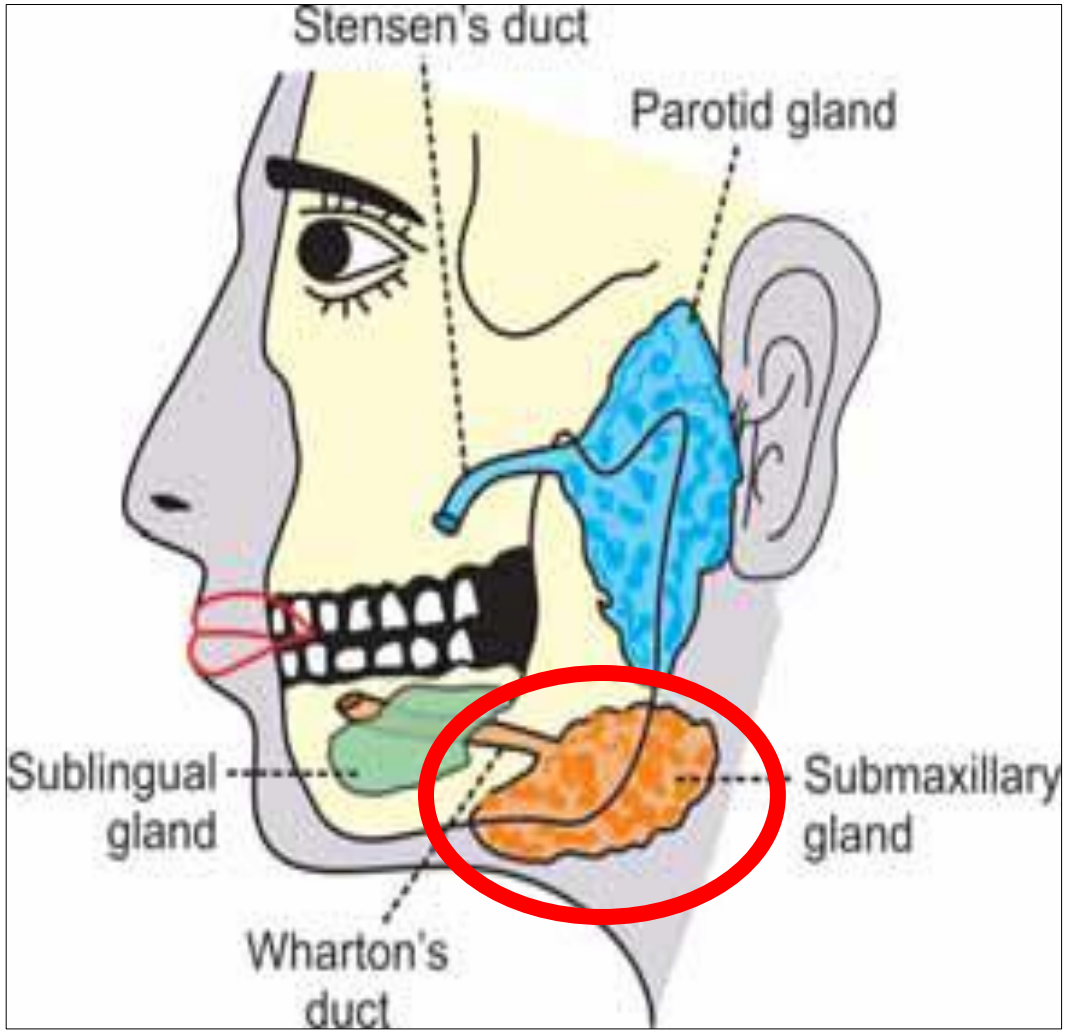
Parotid glands

Parotid glands are the largest of all salivary glands situated at the side of the face just below and in front of the ear. Secretions from these glands are emptied into the oral cavity by Stensen's duct that opens inside the cheek against the upper second molar tooth.



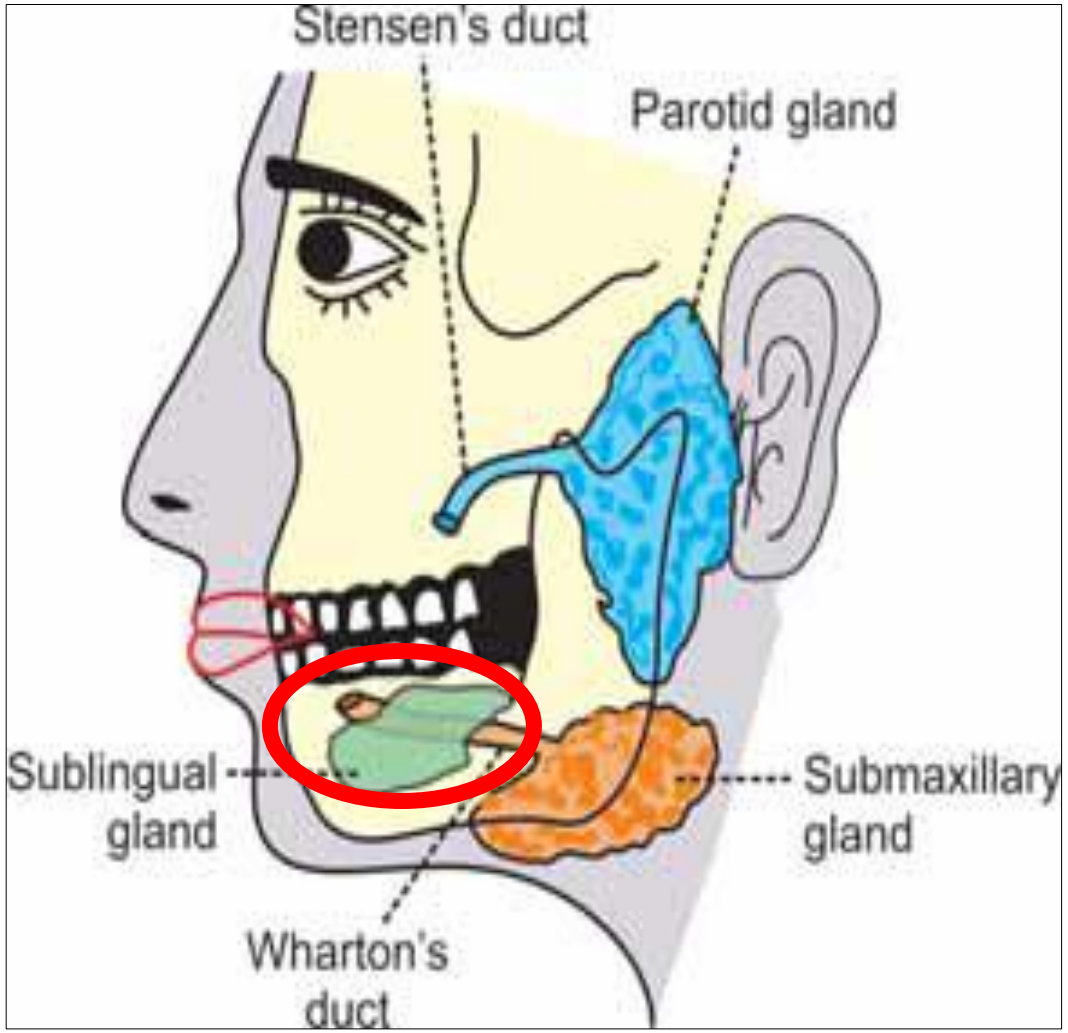
Submaxillary glands

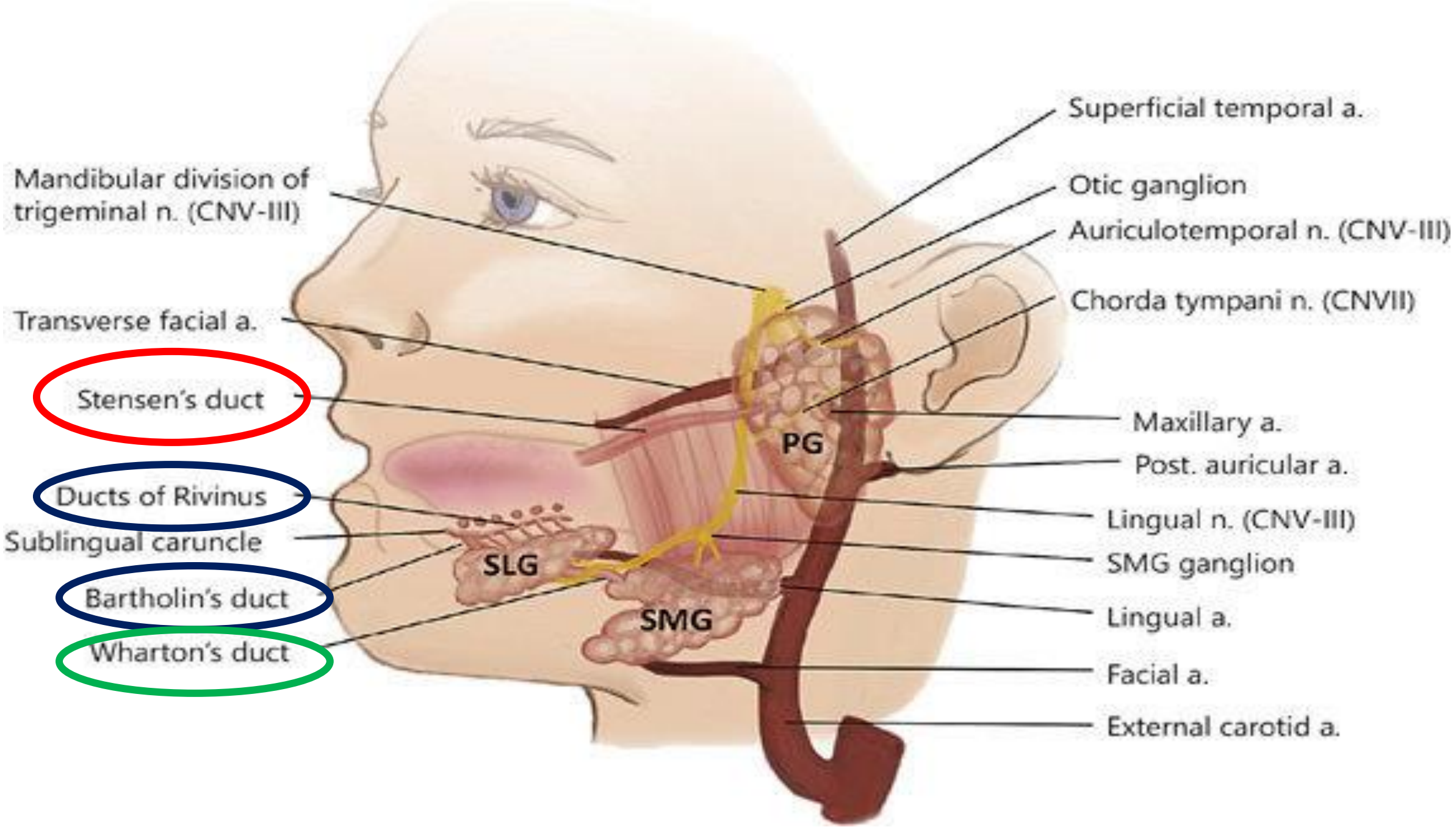
Submaxillary glands or submandibular glands are located in submaxillary triangle medial to mandible. Saliva from these glands is emptied into the oral cavity by Wharton's duct. The duct opens at the side of frenulum of tongue.



Sublingual glands

Sublingual glands are the smallest salivary glands situated in the mucosa at floor of mouth. Saliva from these glands is poured into 5-15 small ducts called ducts of Ravinus. These ducts open on small papillae beneath the tongue. One of the ducts is larger and it is called Bartholin's duct. It drains the anterior part of the gland and opens near the opening of submaxillary duct.




Mandibular division of trigeminal n. (CNV-III)
Transverse facial a.
Stensen's duct
Ducts of Rivinus
Sublingual caruncle
Bartholin's duct
Wharton's duct
Superficial temporal a.
Otic ganglion
Auriculotemporal n. (CNV-III)
Chorda tympani n. (CNVII)
Maxillary a.
Post. auricular a.
Lingual n. (CNV-III)
SMG ganglion
Lingual a.
Facial a.
External carotid a.
PG
SLG
SMG

Minor salivary glands

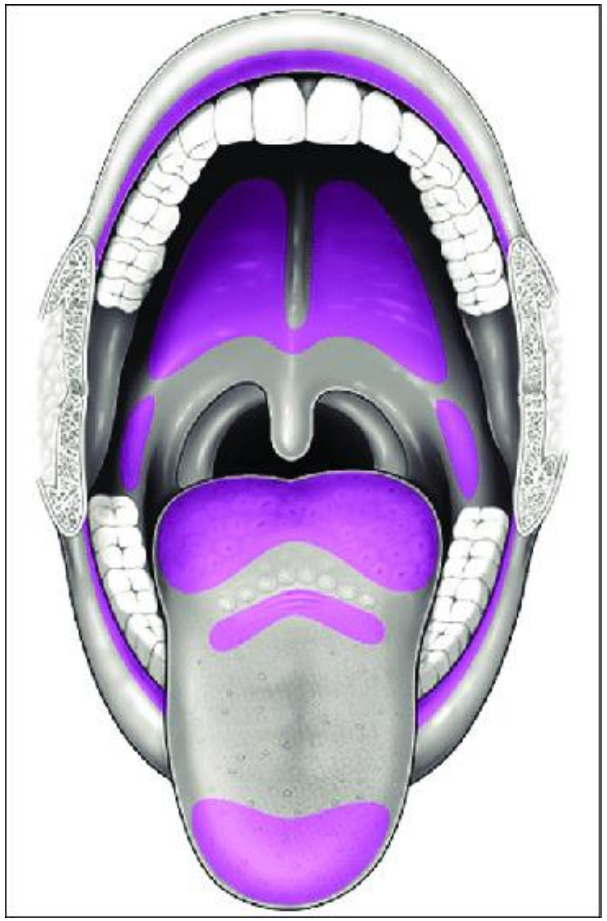
1. Lingual mucus glands.

2. Lingual serous glands

3. Buccal glands.

4. Labial glands.

5. Palatal glands.



Classification of salivary glands

Salivary glands are classified into three types based on the type of secretion.

1. Serous Glands

This type of gland is made up of serous cells. These glands secrete thin and watery saliva. Contain alfa amylase (ptyalin) for starch digestion. Parotid glands (25% of saliva) and lingual serous glands are serous glands.

2. Mucus Glands

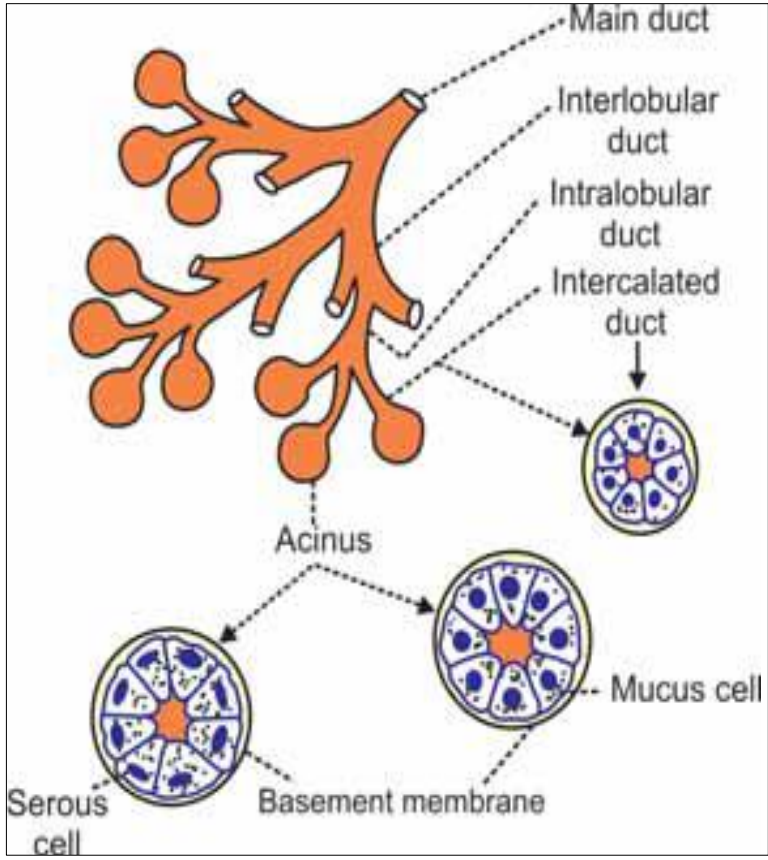
This type of glands is made up of the mucus cells. These glands secrete thick, viscus mucus with high mucin content. Sublingual gland (5% of saliva) , lingual mucus glands, buccal glands and palatal glands belong to this type.

3. Mixed Glands

Mixed glands are made up of both serous and mucus cells. Submandibular (70% of saliva) and labial glands are the mixed glands.

Structure and duct system of salivary glands

Salivary glands are made up of acini or alveoli. Each acinus is formed by a small group of cells which surround a central globular cavity. The central cavity of each acinus is continuous with the lumen of the duct. The fine duct draining each acinus is called intercalated duct. Many intercalated ducts join together to form intralobular duct. Few intralobular ducts join to form interlobular ducts, which unite to form the main duct of the gland.



Mastication

Mastication is the act of chewing food, and it consists of the coordinated function of various parts of the oral cavity to prepare the food for swallowing and digestion.

The pattern of the individual cycle varies depending on the state of breakdown of the food. The masticatory sequence can be divided into three consecutive periods:

1. **Preparatory**: Initial period where food is transported back to the posterior teeth.
2. **Reduction:** Intermediate period where food is ground up.
3. **Pre-swallowing:** Final period where bolus is formed for swallowing.

Structures involved in mastication

Teeth are the most important structures involved in mastication, but other structures such as lips, cheeks, tongue, palate, gingiva and periodontium, muscles of mastication and the temporomandibular joint, along with the lubricating and enzymatic action of saliva, are important for mastication.

Mechanism of mastication:

Muscles of mastication all supplied by trigeminal nerve V mastication partially voluntary and partially involuntary

Bolus in mouth = reflex inhibition of muscles of mastication = Drop of lower jaw = stretch of muscles of mastication = reflex contraction of muscles of mastication =elevation of jaw =compress bollus in mouth = reflex inhibition in muscles and so on

Composition of Saliva

Mixed saliva contains 99.5% water and 0.5% solids.

Properties of Saliva

1. Volume: 1000 to 1500 mL of saliva is secreted per day and, it is approximately about 1 mL/ minute. Contribution by each major salivary gland is:

i. Parotid glands: 25%

ii. Submandibular glands: 70%

iii. Sublingual glands: 5%.

2. pH: neutral during rest pH=7. during activity Alkalin pH=8

3. Contents: ptyalin , mucin, electrolytes, IgA antibodies, lysozyme (antibacterial enzyme)

4. Tonicity: Saliva is hypotonic to plasma less Nacl and more K& Hco3

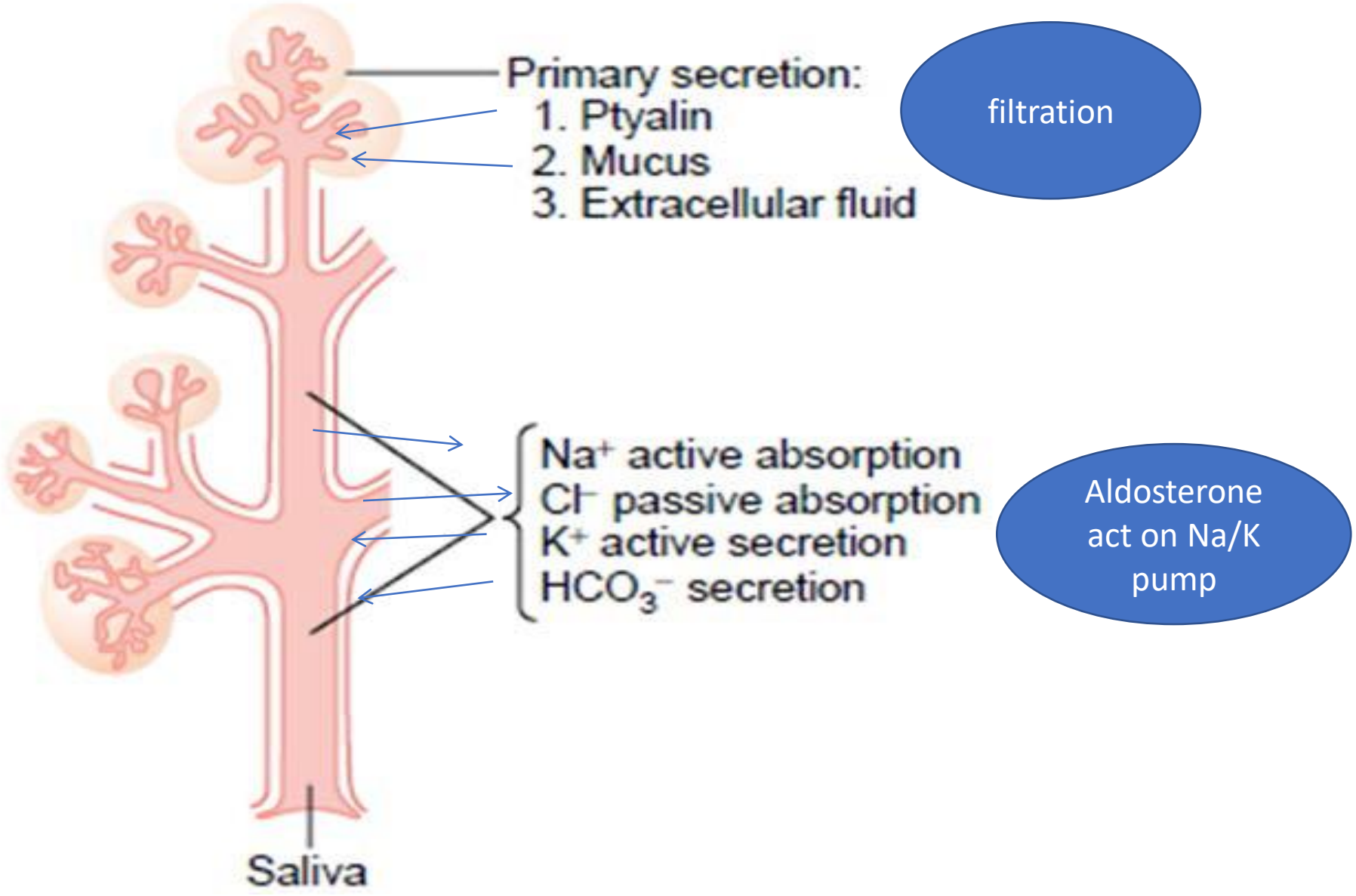
Stages of secretion of saliva

Its an active process begin with vasodilatation of blood vessels

1. Primary secretion: in acini the saliva is isotonic (the same concentration to plasma), from blood ions filtered to acini if the gland is serous ptyalin filtered to acini and if the gland mucous the mucin filtered from plasma to acini .
2. Secondary secretion : in duct the saliva is hypotonic ,

As the primary secretion flows through the ducts, two major active transport processes take place that modify the ionic composition of the fluid in the saliva.

1. First: sodium ions are actively reabsorbed from the salivary ducts and potassium ions are actively secreted in exchange for the sodium (3Na/2K pump). Therefore, the sodium ion concentration of the saliva reduced, whereas the potassium ion concentration becomes increased, and this creates electrical negativity in the salivary ducts; this causes chloride ions to be reabsorbed passively.
2. Second: bicarbonate ions are secreted into the lumen of the duct by active secretory process.


Primary secretion:
1. Ptyalin
2. Mucus
3. Extracellular fluid
filtration
Na^+ active absorption
Cl^- passive absorption
K^+ active secretion
HCO_3^- secretion
Aldosterone act on Na/K pump
Saliva

Function of saliva

1. Preparation of food for swallowing.
2. Stimulated taste buds.
3. Digestive function.
4. Cleansing and protective functions.
5. Role in speech.
6. Excretory function
7. Regulation of body temperature.
8. Regulation of water balance

Function of saliva for oral Hygiene

Due to the constant secretion of saliva, the mouth and teeth are rinsed and kept free off food debris, shed epithelial cells and foreign particles. In this way,

1. saliva prevents bacterial growth by removing materials, which may serve as culture media for the bacterial growth.
2. The enzyme lysozyme of saliva kills some bacteria such as staphylococcus, streptococcus, and Brucella.
3. The proline-rich proteins and lactoferrin present in saliva possess antimicrobial property. These proteins also protect the teeth by stimulating enamel formation.
4. Saliva also contains secretory immunoglobulin IgA which has antibacterial and antiviral actions.
5. Mucin present in the saliva protects the mouth by lubricating the mucous membrane of the mouth.

Regulation of salivary secretion

Salivary secretion is regulated only by nervous mechanism.

Autonomic nervous system is involved in the regulatory function. **Nerve supply to salivary glands**

Salivary glands are supplied by parasympathetic and sympathetic divisions of autonomic nervous system.

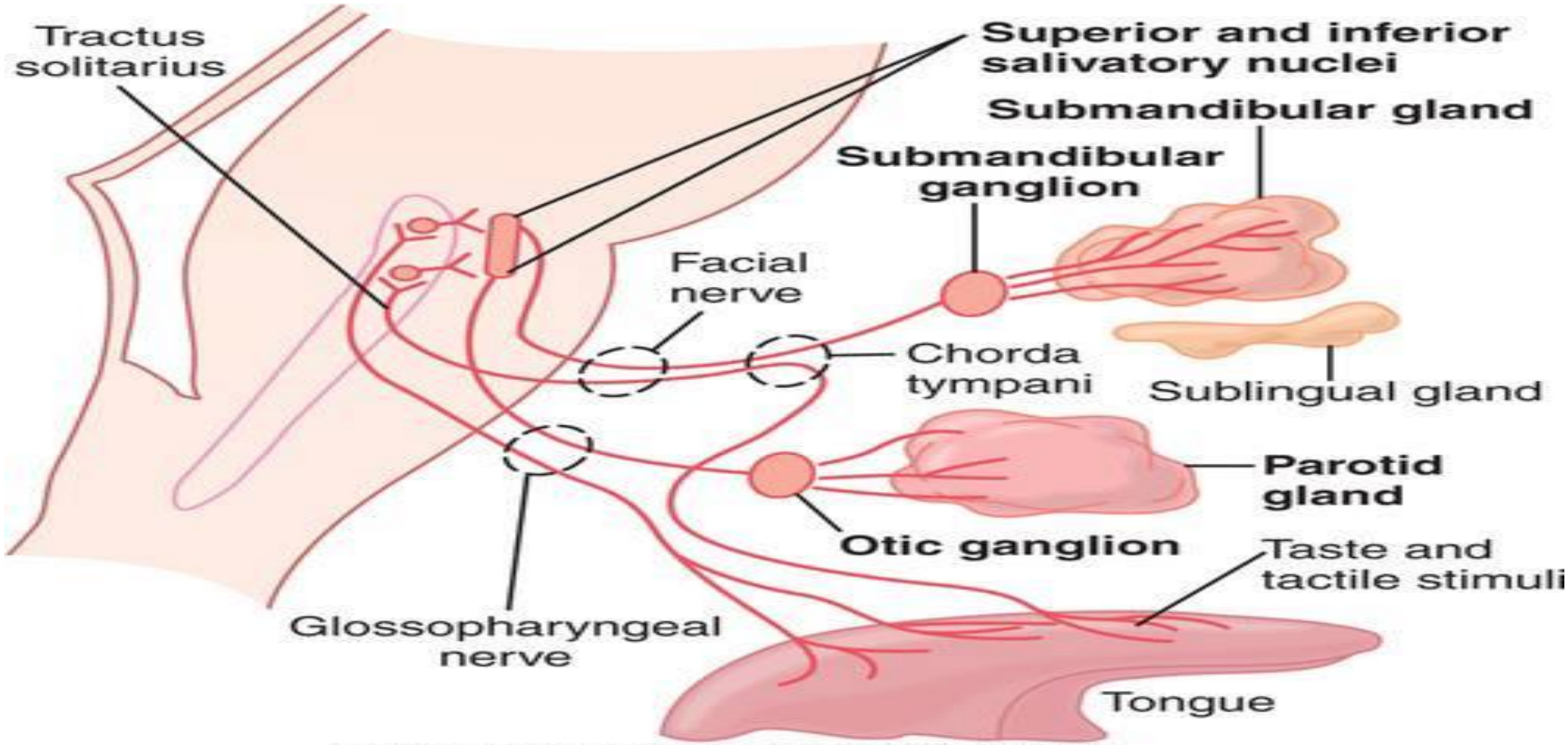
Parasympathetic fibers

Parasympathetic Fibers to Submandibular and Sublingual Glands

The parasympathetic preganglionic fibers to submandibular and sublingual glands arise from the superior salivatory nucleus situated in pons. After taking origin from this nucleus, the preganglionic fibers run through nervous intermedius of the motor fibers of facial nerve, chorda tympani branch of facial nerve and lingual branch of trigeminal nerve and finally reach the submandibular ganglion. The postganglionic fibers arise from this ganglion and supply the submandibular and sublingual glands

- **Parasympathetic Fibers to Parotid Gland**
- The parasympathetic preganglionic fibers to parotid gland arise from inferior salivatory nucleus situated in the upper part of medulla oblongata. From here, the fibers pass through the tympanic branch of glossopharyngeal nerve and end in otic ganglion . The postganglionic fibers arise from otic ganglion and reach the parotid gland.
- **Function of Parasympathetic Fibers**

When the parasympathetic fibers of salivary glands are stimulated, a large quantity of watery saliva is secreted with less amount of organic constituents. It is because the parasympathetic fibers activate the acinar cells and dilate the blood vessels of salivary glands. The neurotransmitter is acetylcholine

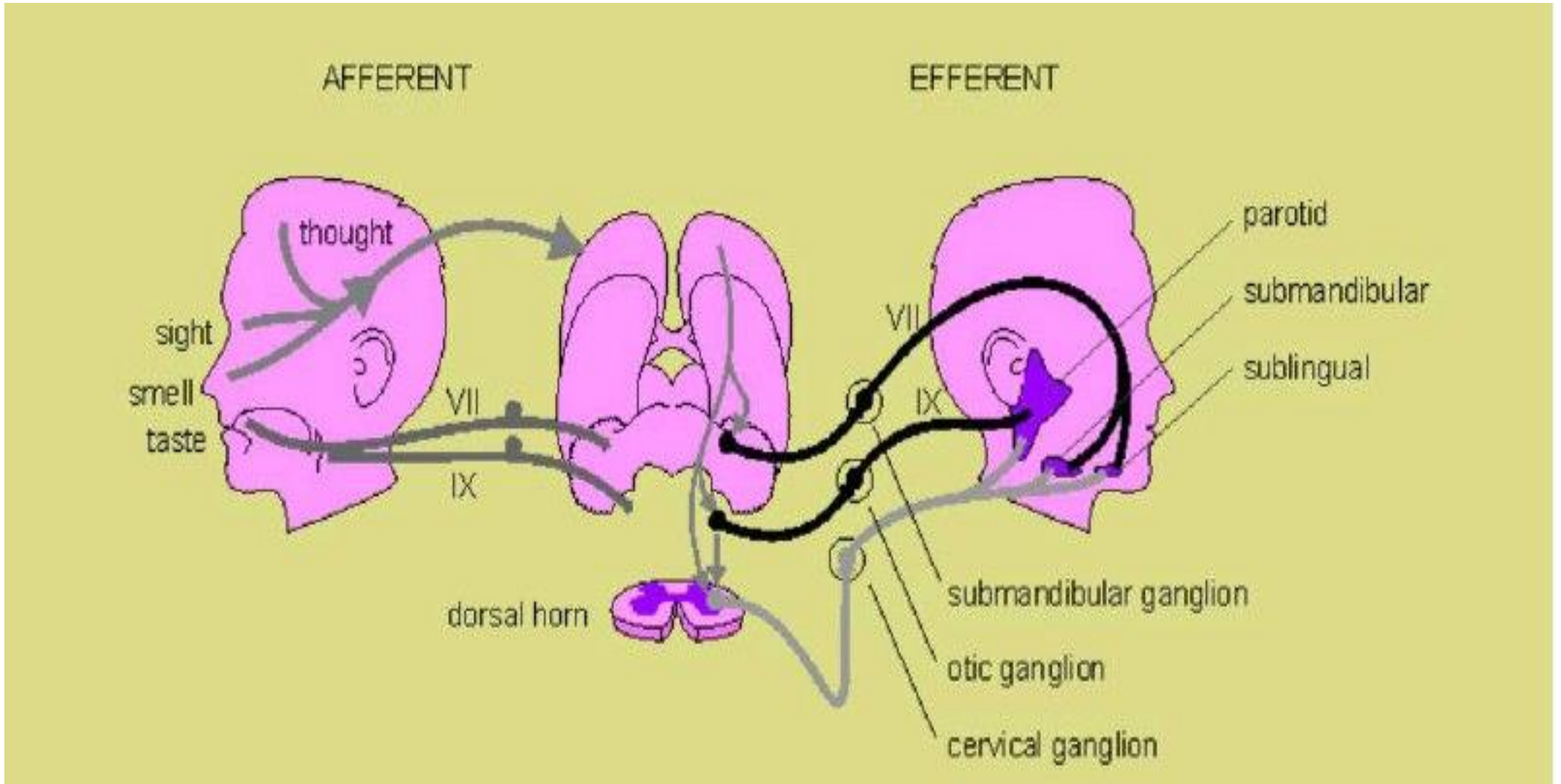


Sympathetic fibers

The sympathetic preganglionic fibers to salivary glands arise from the lateral horns of first and second thoracic segments of spinal cord. The fibers leave the cord through the anterior nerve roots and end in superior cervical ganglion of the sympathetic chain. The postganglionic fibers from this ganglion are distributed to the salivary glands along the nerve plexus around the arteries supplying the glands.

Function of Sympathetic Fibers

The stimulation of sympathetic fibers causes less secretion of saliva, which is thick and rich in mucus. It is because these fibers activate the acinar cells and cause vasoconstriction by secreting noradrenaline


AFFERENT
EFFERENT
thought
sight
smell
taste
VII
IX
VII
IX
parotid
submandibular
sublingual
dorsal horn
submandibular ganglion
otic ganglion
cervical ganglion

- **Reflex regulation of salivary secretion**

Salivary secretion is regulated by nervous mechanism through reflex action. Salivary reflexes are of two types:

1. Unconditioned reflex
2. Conditioned reflex.

1. Unconditioned Reflex is the inborn reflex that is present since birth. It does not need any previous experience. This reflex induces salivary secretion when any substance is placed in the mouth. It is due to the stimulation of nerve endings in the mucous membrane of the oral cavity.

Examples: i. When food is taken ii. When any unpleasant or unpalatable substance enters the mouth iii. When the oral cavity is handled with instruments by dentists.

2. Conditioned Reflex is the one that is acquired by experience and it needs previous experience. Presence of food in the mouth is not necessary to elicit this reflex. The stimulus for this reflex is the sight, smell, hearing or thought of food. It is due to the impulses arising from eyes, nose, ear, etc

Deglutition (swallowing)

Deglutition (swallowing) is the process by which food is passed into the stomach from the oral cavity. Swallowing is a reflex activity consisting of muscle contractions and relaxations that help push the ingested food and saliva from the mouth to the stomach. Although swallowing can be initiated voluntarily, much of the swallowing occurs without any conscious effort.

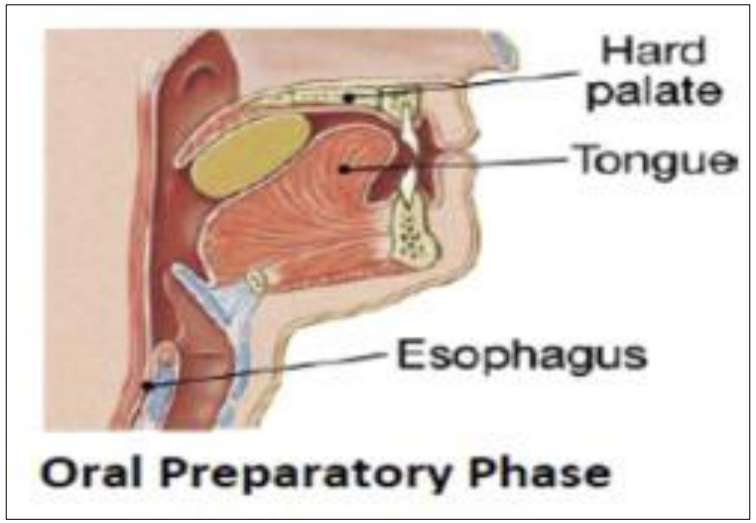
Center Medulla &lower pons

Phases of Swallowing

Swallowing can be divided into preparatory, oral, pharyngeal and esophageal phases.

1- Preparatory Phase:

Formation of food bolus occurs during this phase. Food bolus is a round or oval-shaped mass of food formed in the mouth after thorough chewing. The food bolus is formed as a preparatory event for swallowing.

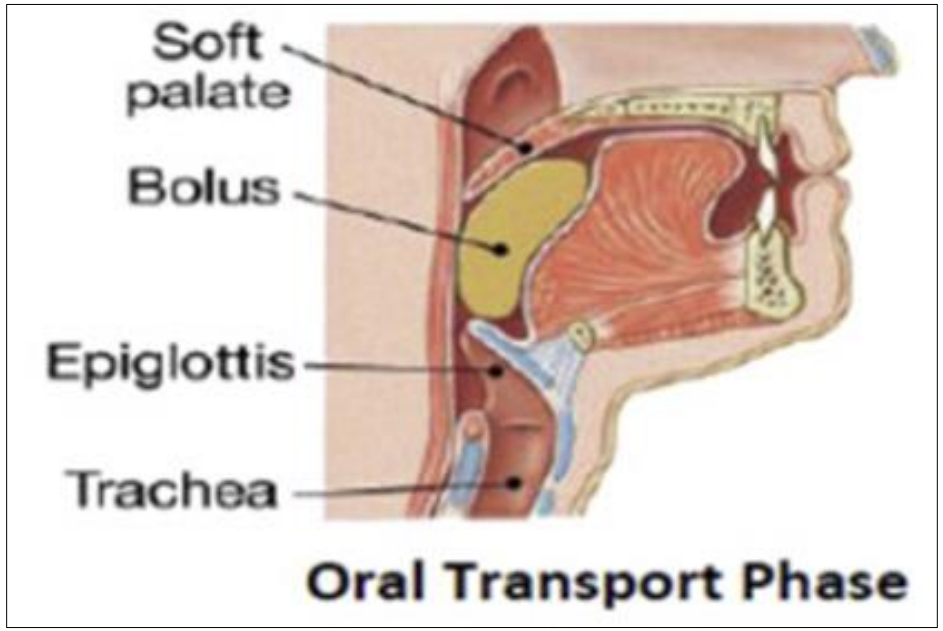


2- (Buccal Phase) voluntary

1. Once the bolus is positioned on the tongue, the oral phase begins. The lips close and the maxillary and mandible incisors come closer together.

2. The tongue upward and backward against palate.

3. Bolus is squeezed post in pharynx by contraction of myeloid muscle.

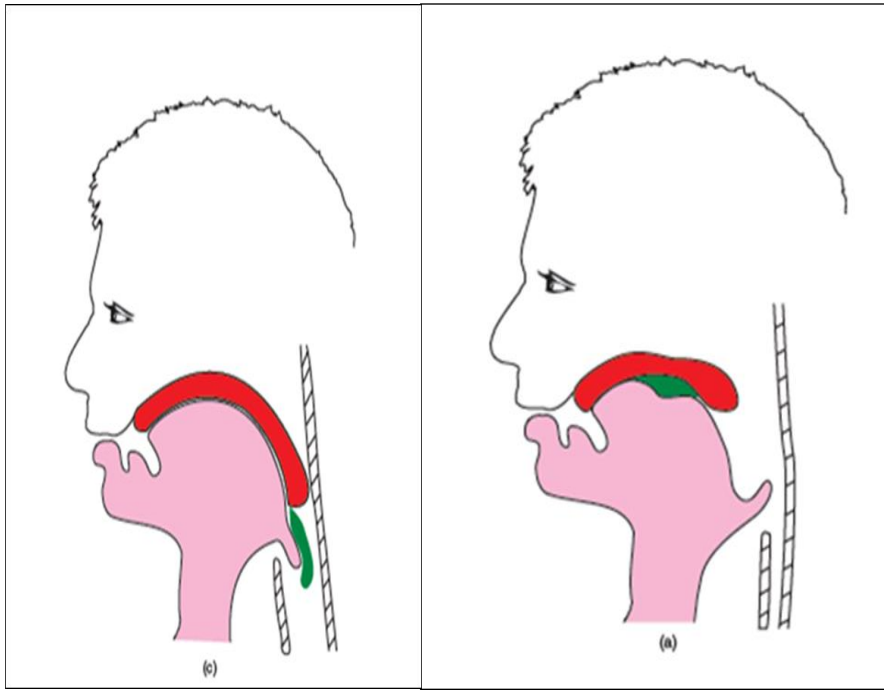


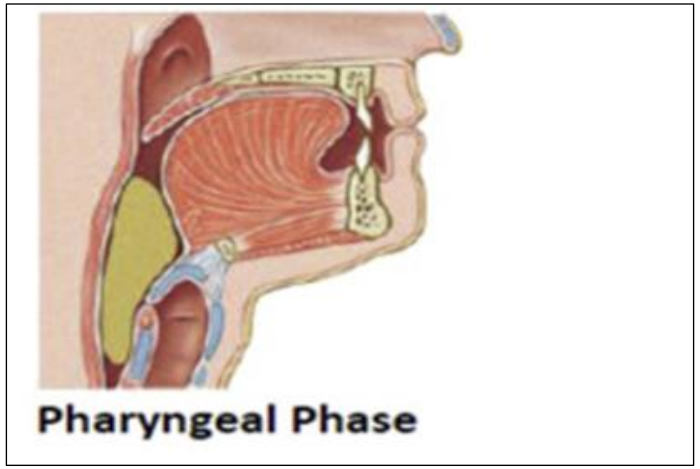
3- Pharyngeal Phase involuntary (1-2 second)

Bolus of food has one out of 4ways:

1. Nose closed by elevation of soft palate
2. Mouth closed by elevation of tongue and contraction of myeloid muscles
3. Larynx closed by elevation of larynx to be covered by epiglottis, closure the glottis and apnea.
4. Pharynx successive contraction of pharyngeal sphincters (superior middle and inferior) , relaxation pharyngo-esophageal sphincters (upper esophageal sphincter opens, and the bolus enters the esophagus.

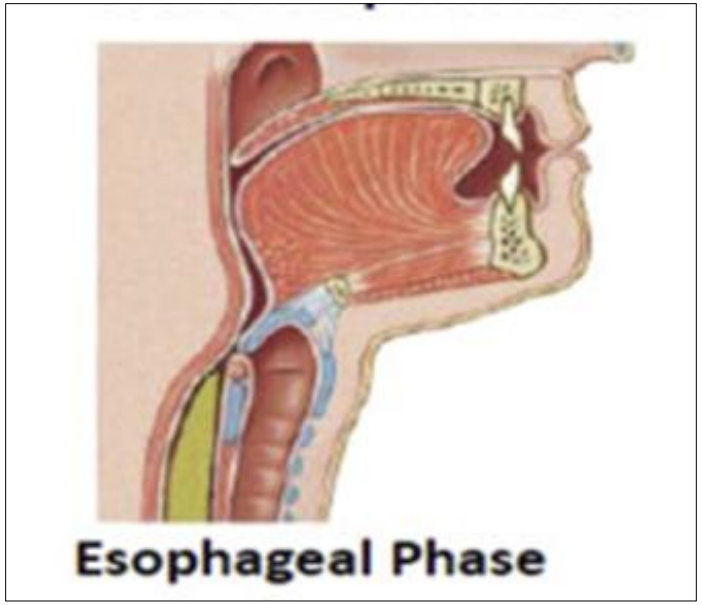
(Forcing food and liquids into the nasal cavity is known as nasal regurgitation. It can occur in patients with palatal clefts or paralysis of soft palate where the nasal cavity cannot be sealed off from the oropharynx.)





4- Esophageal Phase

After the food is placed in the upper end of esophagus, the upper esophageal sphincter contracts, causing peristaltic contractions (wave-like movements) that can send the bolus to the stomach with the help of gravity. The lower esophageal sphincter opens to allow the bolus into the stomach.



Effect of drugs and chemicals on salivary secretion

Substances which Increase the Salivary Secretion

1. Sympathomimetic drugs like adrenaline and ephedrine
2. Parasympathomimetic drugs like acetylcholine and pilocarpine
3. Histamine.

Substances which Decrease the Salivary Secretion

1. Sympathetic depressants like ergotamine and dibenamine
2. Parasympathetic depressants like atropine, and scopolamine.

- Applied physiology
- Hyposalivation The reduction in the secretion of saliva is called hyposalivation. It is of two types, namely, the temporary hyposalivation and the permanent hyposalivation.

1. Temporary hyposalivation occurs in:

i. Emotional conditions like fear

ii. Fever

iii. Dehydration.

2. Permanent hyposalivation occurs in:

i. Obstruction of salivary duct (sialolithiasis)

ii. Congenital absence or hypoplasia of salivary glands

iii. Paralysis of facial nerve (Bell's palsy).

- **Hypersalivation**

The excess secretion of saliva is known as hypersalivation.

The physiological condition when hypersalivation occurs is pregnancy.

Hypersalivation occurs in the following conditions:

1. Decay of tooth or neoplasm (abnormal new growth or tumor) in mouth or tongue.
2. Disease of esophagus, stomach and intestine.
3. Neurological disorders such as mental retardation.
4. Some psychological conditions.
5. Nausea and vomiting

- **Other disorders**
- In addition to hyposalivation and hypersalivation, salivary secretion is affected by other disorders also which include:
- 1. **Xerostomia** Xerostomia means dry mouth. It is also called cotton mouth. It is due to hyposalivation or absence of salivary secretion (aptyalism).

Xerostomia causes difficulties in mastication, swallowing and speech.

It also causes halitosis (bad breath).

The causes of this disease are:

i. **Dehydration or renal failure**

ii. Sjögren's syndrome

iii. Radiotherapy

iv. Trauma to salivary gland or their ducts

v. Side effect of drugs like antihistamines, antidepressants drugs

vi. Shock

vii. After smoking marijuana (psychoactive compound from the plant cannabis).

- **2. Drooling**

Uncontrolled flow of saliva outside the mouth is called drooling.

It is often called ptyalism. Drooling occurs because of excess production of saliva in association with inability to retain saliva within the mouth. Drooling occurs in the following conditions:

i. During teeth eruption in children

ii. Upper respiratory tract infection or nasal allergies in children

iii. Difficulty in swallowing

iv. Tonsillitis

- **Chorda Tympani Syndrome**

Chorda tympani syndrome is the condition characterized by sweating while eating. During trauma or surgical procedure some of the parasympathetic nerve fibers to salivary glands may be severed. And, during the regeneration some of these nerve fibers, which run along with chorda tympani branch of facial nerve may deviate and join with the nerve fibers supplying sweat glands.

When the food is placed in the mouth, salivary secretion is associated with sweat secretion

- **4. Mumps**
- Mumps is the acute viral infection affecting the parotid glands.

The virus causing this disease is paramyxovirus.

It is common in children who are not immunized.

It occurs in adults also.

5. Sjögren's Syndrome

It is an autoimmune disorder in which the immune cells destroy exocrine glands such as lacrimal glands and salivary glands. Common symptoms of this syndrome are dryness of the mouth due to lack of saliva (xerostomia), persistent cough and dryness of eyes. In severe conditions the organs like kidneys, lungs, liver, pancreas, thyroid, blood vessels and brain are affected.

Endocrine system

The endocrine system is a system of ductless glands that secrete hormones directly into the circulatory system to be carried long distances to other target organs that regulate vital body and organ functions.

All the physiological activities are regulated by two major systems in the body:

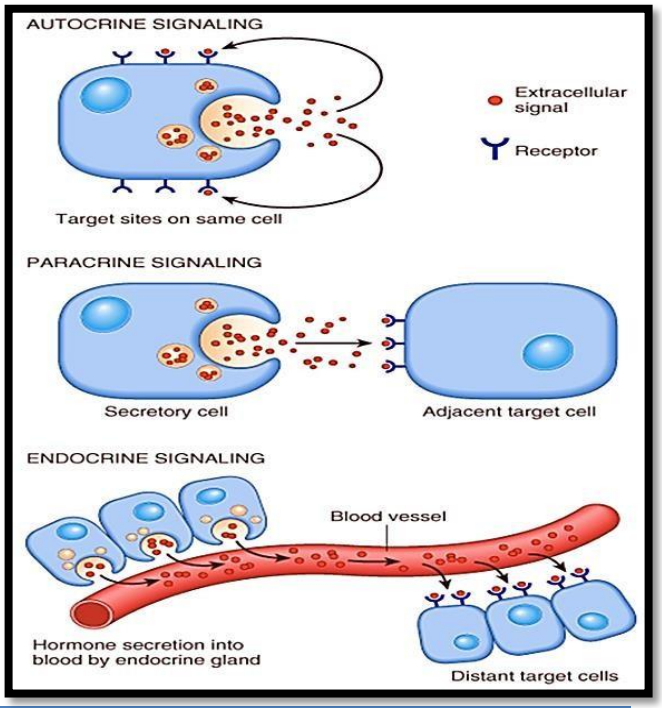
1- Nervous system.

2- Endocrine system.

These two systems interact with one another and regulate the body's functions.

The multiple activities of the cells, tissues, and organs of the body are coordinated by the interplay of several types of chemical messenger systems:

1. Neurotransmitters are released by axon terminals of neurons into the synaptic junctions and act locally to control nerve cell functions.
2. Endocrine hormones are released by glands or specialized cells into the circulating blood and influence the function of target cells at another location in the body.
3. Neuroendocrine hormones are secreted by neurons into the circulating blood and influence the function of target cells at another location in the body.
4. Paracrine is secreted by cells into the extracellular fluid and affects neighboring target cells of a different type.
5. Autocrines are secreted by cells into the extracellular fluid and affect the function of the same cells that produced them.
6. Cytokines are peptides secreted by cells into the extracellular fluid and can function as autocrines, paracrines, or endocrine hormones.



Endocrine glands

Endocrine glands are the glands which synthesize and release the classical hormones directly into the blood without any duct, so they called ductless glands.

Hormones secreted by major endocrine glands

Hypothalamus	1. Thyrotropin-releasing hormone (TRH) 2. Growth hormone -releasing hormone (GRH) 3. Growth hormone inhibitory hormone (somatostatin) (GHRH) 4. Corticotropin-releasing hormone (CRH) 5. Gonadotropin-releasing hormone (GnRH) 6. Dopamine or prolactin- inhibiting factor
Anterior pituitary	1. Growth hormone (GH) 2. Thyroid stimulating hormone (TSH) 3. Endorphins 4. Adrenocorticotropichormone (ACTH) 5. Follicle stimulating hormone (FSH) 6. Luteinizing hormone (LH) 7. Prolactin
Posterior pituitary	1. Antidiuretic hormone (ADH) 2. Oxytocin
Thyroid gland	1. Thyroxin (T_4) 2. Tri-iodothyronine (T_3) 3. Calcitonin
Parathyroid gland	Parathormone
Pancreas - islets of Langerhans	1. Insulin 2. Glucagon 3. Somatostatin 4. Pancreatic polypeptide
Adrenal cortex *(adrenocortical hormones or corticosteroids)*	
Mineralocorticoids	1. Aldosterone 2. 11 deoxycorticosterone
Glucocorticoids	1. Cortisol 2. Corticosterone
Sex hormones	1. Androgens 2. Estrogen 3. Progesterone
Adrenal medulla	
Catecholamine	1. Adrenaline (Epinephrine) 2. Noradrenaline (Norepinephrine) 3. Dopamine

Hormones

Hormones are type of chemical signal molecules, released by a cell or special endocrine gland in one part of the body that sends out messages affecting cells in other parts of the body, transported by the circulatory system to target distant organs to regulate physiology of the body, maintaining homeostasis and regulating reproduction and development.

Nature of Hormones

1- Hormones are secreted from their source directly into the blood.
2- Blood carries the hormone to the target cells which respond to it.
3- Hormones regulate the physiological processes.
4- They are produced in very small quantities and are biologically very active; usually measured in micrograms or milligrams per day.
5- Their excess and deficiency, both, cause serious disorders.

Classification of hormones

Based on chemical nature the hormones are classified into three types:

1. ***Proteins and polypeptides,*** including hormones secreted by the anterior and posterior pituitary gland, the pancreas (insulin and glucagon), the parathyroid gland (parathyroid hormone), and many others.
2. ***Steroids*** secreted by the adrenal cortex (cortisol and aldosterone), the ovaries (estrogen and progesterone), the testes (testosterone), and the placenta (estrogen and progesterone).
3. ***Derivatives of the amino acid tyrosine***, secreted by the thyroid (thyroxine and triiodothyronine) and the adrenal medullae (epinephrine and norepinephrine).

Hormone Secretors

In humans there are many tissues and organs that produce hormones. These can be listed under two categories:

(a) Exclusively endocrine: Pituitary, thyroid, parathyroid, thymus and the adrenal glands

(b) Partially endocrine: The pancreas, gastric and duodenal epithelium, the gonads (testis in males and ovary in females) and placenta in females.

Differences between endocrine and exocrine glands

	Endocrine glands	Exocrine glands
1.	Secrete hormones	Produce enzyme
2.	These are ductless gland released hormones into interstitial space surround cell and nearest capillary then to blood.	Glands may have ducts (tubes) to carry substances outside the body (sweat to skin) or into body cavity (pancreatic juice to intestine).
3.	They pour secretion directly into the blood.	The secretion is poured directly at the site of action or reaches the target.
4.	They control long term of target organ.	They control short term activity.
5.	Thyroid, pituitary and adrenal glands	Salivary, sweat and gastric gland

Hormonal action

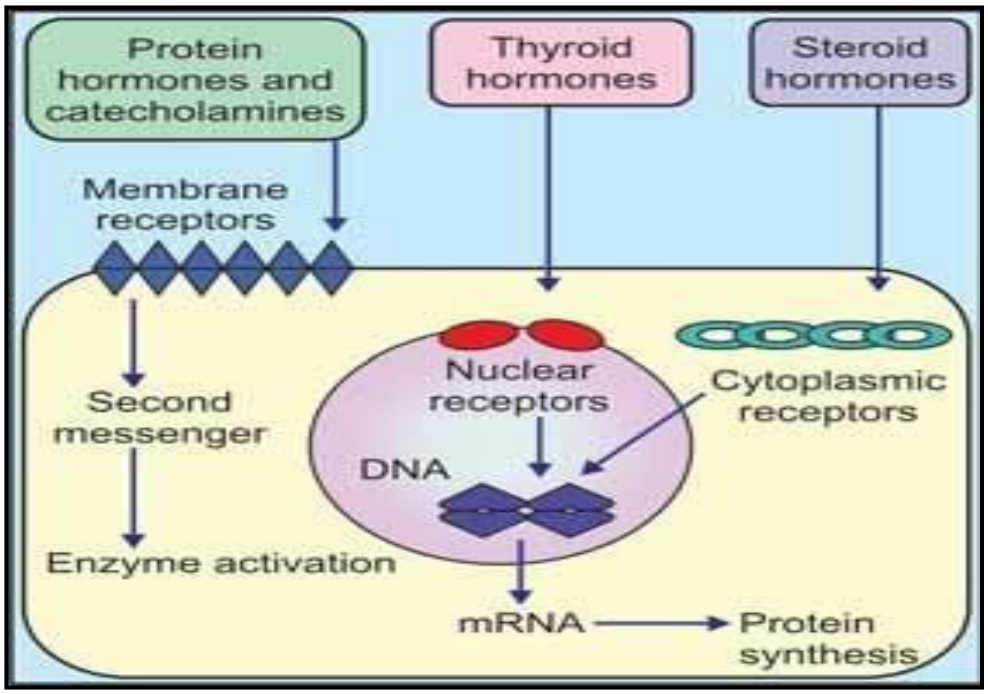
Hormone does not act directly on the cellular structures. First it combines with receptors present on the target cells and forms a hormone- receptor complex. This hormone-receptor complex induces various changes or reactions in the target cells.

Hormone receptors

The hormone receptors are the large proteins present in the target cells. Each receptor is specific for one single hormone, (each receptor can combine with only one hormone).

Hormone receptors are situated either in cell membrane or cytoplasm or nucleus of the cells as follows:

1. ***In or on the cell membrane***: The membrane receptors are specific mostly for the protein, peptide, and catecholamine hormones.
2. ***Cytoplasm***: Receptors of steroid hormones are situated in cytoplasm of the cells.



3. ***Nucleus***: Receptors of thyroid hormones are in the nucleus of the target cell.

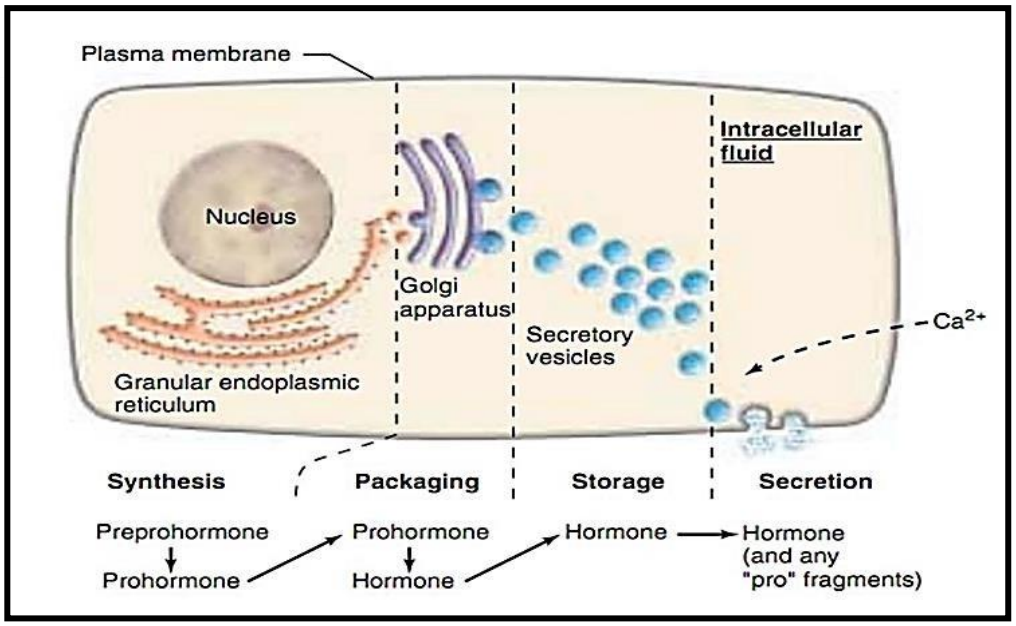
Synthesis and storage of hormones

Most of the hormones in the body are polypeptides and proteins. These hormones range in size from small peptides with as few as three amino acids {Thyrotropin-releasing hormone (TRH)} to proteins with almost 200 amino acids {growth hormone and prolactin}. In general, polypeptides with 100 or more amino acids are called proteins, and those with fewer than 100 amino acids are referred to as peptides.

Protein and peptide hormones are synthesized on the rough endoplasmic reticulum of the different endocrine cells. They are usually synthesized first as larger proteins that are not biologically active called ***preprohormones*** and are cleaved to form smaller ***prohormones*** in the endoplasmic reticulum.

These prohormones are then transferred to the Golgi apparatus for packaging into secretory vesicles. Enzymes in the vesicles cleave the prohormones to produce smaller, biologically active hormones. The vesicles are stored within the cytoplasm and serve as reservoir to hormones. ***Polypeptide and protein hormones are stored in secretory vesicles until needed.***

Secretion of the hormones occurs when the secretory vesicles fuse with the cell membrane and the granular contents are extruded into the interstitial fluid or directly into the blood stream by exocytosis. The peptide hormones are water soluble, allowing them to enter the circulatory system easily, where they are carried to their target tissues.



Mechanism of hormonal function

On the target cell, the hormone–receptor complex acts by any one of the following mechanisms:

1. By altering the permeability of the cell membrane

The neurotransmitter substances in a synapse or neuromuscular junction act by changing the permeability of postsynaptic membrane.

2. By Activating the Intracellular Enzyme

The protein and catecholamines hormones act by activating intracellular enzymes. The hormone, which acts on a target cell, is called ***first messenger***. These hormones, in combination with receptor forms hormone-receptor complex; which activates the enzymes of the cell and causes the formation of the ***second messenger***; which produces the effects of the hormone inside the cells; like adenosine mono- phosphate (cyclic AMP or cAMP).

3. By Acting on Genes

Thyroid and steroid hormones act by activating the genes of the target cells.

Some hormones, such as norepinephrine and epinephrine, are secreted within seconds after the gland is stimulated and may develop full action within few seconds to minutes. The actions of other hormones, such as thyroxin or growth hormone, may require months for full effect. Thus, each of the different hormones has its own characteristic onset and duration of action to perform its specific control function.

Measurement of Hormone Concentrations in the Blood

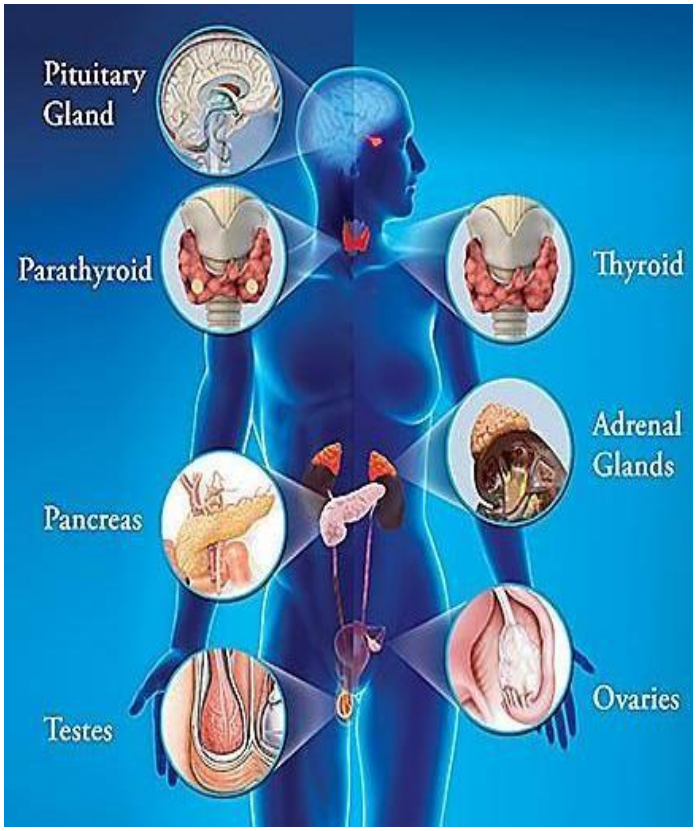
Most hormones are present in the blood in extremely minute quantities. Therefore, it was difficult to measure these concentrations by the usual chemical means. Therefore, the method used is called ***radioimmunoassay***. More recently, additional methods, such as ***enzyme-linked immunosorbent assays (ELIZA),*** have been developed for accurate measurements of hormones.

Major Endocrine Glands

Many different glands make up the endocrine system. The hypothalamus, pituitary gland, and pineal gland are in the brain. The thyroid and parathyroid glands are in neck. The thymus is between lungs, the adrenals are on top of kidneys, and the pancreas is behind stomach. Ovaries (in woman) or testes (in man) are in pelvic region.

Oral manifestations of endocrine dysfunction

The effects of over and under-secretion of each endocrine gland is showing an influence on the development and maintenance of the health of the teeth and supporting structures.



Control Systems Involving Hypothalamus and Pituitary glands

Hypothalamus gland is a small but important gland located at the base of the forebrain, between the pituitary gland and thalamus, has a vital role in controlling many bodily functions including the release of hormones from the pituitary gland and helps to stimulate many important processes in the body. Major functions of the hypothalamus are to maintain homeostasis, to keep the human body in a stable, constant condition. When the hypothalamus is not working properly, it can cause problems in the body that lead to a wide range of rare disorders.

The main job of hypothalamus is to order pituitary gland to start or stop making hormones. Also, most important functions of the hypothalamus are to link the nervous system to the endocrine system via the pituitary gland. It synthesizes and secretes certain neurohormones, called hypothalamic hormones, and these in turn control the secretion of pituitary hormones.

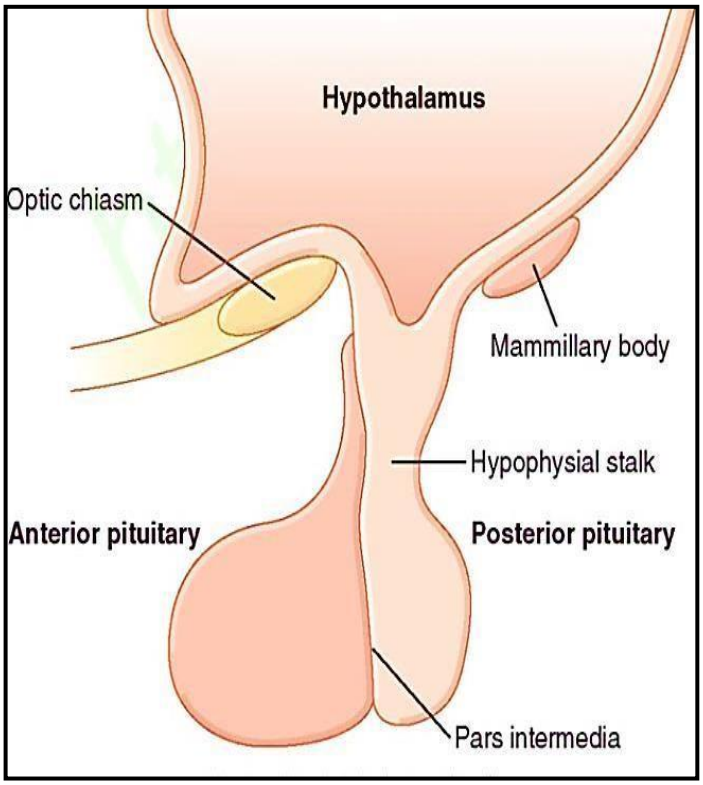
The pituitary gland

The pituitary gland also called the ***hypophysis***, is a small gland that lies at the base of the brain, and is connected to the hypothalamus by the pituitary stalk. Whilst the pituitary gland is known as the ***master endocrine gland***, consist of two lobes, both of lobes are under the control of the hypothalamus.

Physiologically, the pituitary gland is divided into two distinct portions:

1- The anterior pituitary gland, (adenohypophysis).

2- The posterior pituitary gland, (neurohypophysis).



hormones are secreted by the posterior pituitary gland. Secretion of anterior pituitary hormones is regulated by hypothalamus. Hypothalamus secretes some releasing and inhibitory hormones which are transported from hypothalamus to anterior pituitary. Many of the hormones produced by the anterior pituitary stimulate other endocrine glands to secrete their hormones. The hormones of the anterior pituitary play major roles in the control of metabolic functions throughout the body.

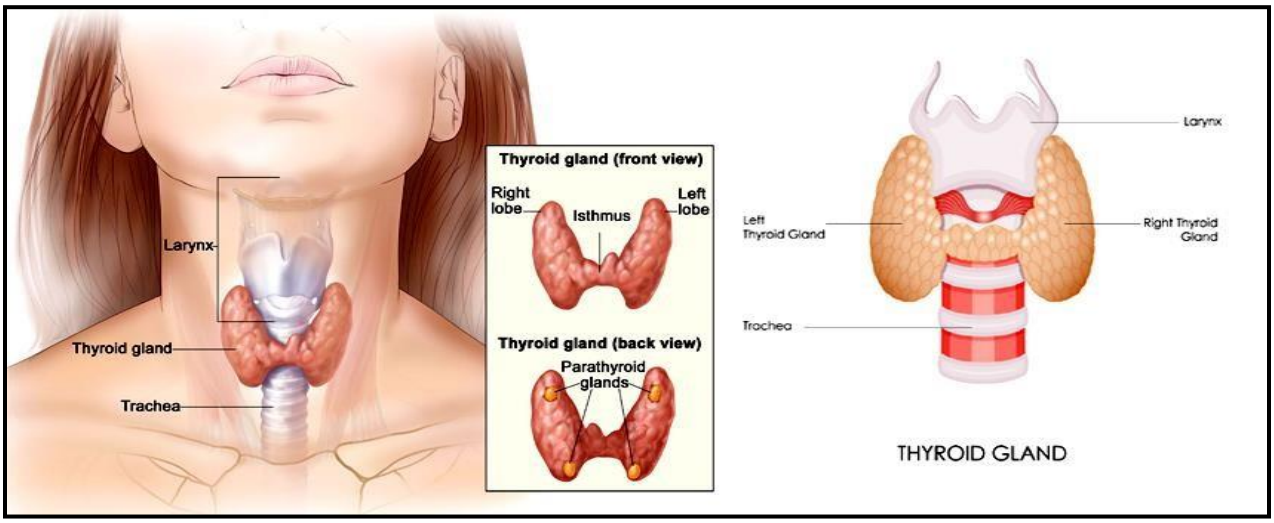
The posterior pituitary gland secretes tow hormones. Actually, the posterior pituitary does not secrete any hormone; rather, it stores and secretes two hormones made in the hypothalamus. Antidiuretic hormone (ADH) and oxytocin are synthesized in the hypothalamus. Hence, these two hormones are called ***neurohormones***.

The control of release hormones from the pituitary is via negative feedback mechanism from the target gland. For example homeostasis of thyroid hormones is achieved by the following mechanism; TRH from the hypothalamus stimulates the release of TSH from the anterior pituitary. The TSH, in turn, stimulates the release of thyroid hormones form the thyroid gland. The thyroid hormones then cause negative feedback, suppressing the release of TRH and TSH.

Thyroid gland

Thyroid gland is largest classic endocrine organ consist of two lobes , shaped like a butterfly, synthesizes and secretes Thyroxin (T_4) and Triiodothyronin (T_3) that influences most and every cell of the body's organ which helps regulate growth and the metabolic rate of the body. Also, help the body to control body temperature, make energy and helps control organ function. The amount of T_4 being secreted is controlled by thyroid stimulating hormone (TSH) made in the pituitary gland through a negative feedback mechanism.

Thyroid hormones provide negative feedback to the hypothalamus and anterior pituitary gland. When thyroid levels in the blood are elevated TSH and TRH production is reduced. Excessive TSH can also inhibit the production of further TRH.



The thyroid also produces and releases calcitonin hormone (thyrocalcitonin) that contributes to the regulation of blood calcium levels. It is involved, with parathyroid hormone and vitamin D, in regulating serum calcium and phosphorus levels. Thyroid dysfunction can affect any system of the body; the oral cavity can be adversely affected by either an excess (hyperthyroidism) or deficiency of these hormones (hypothyroidism).

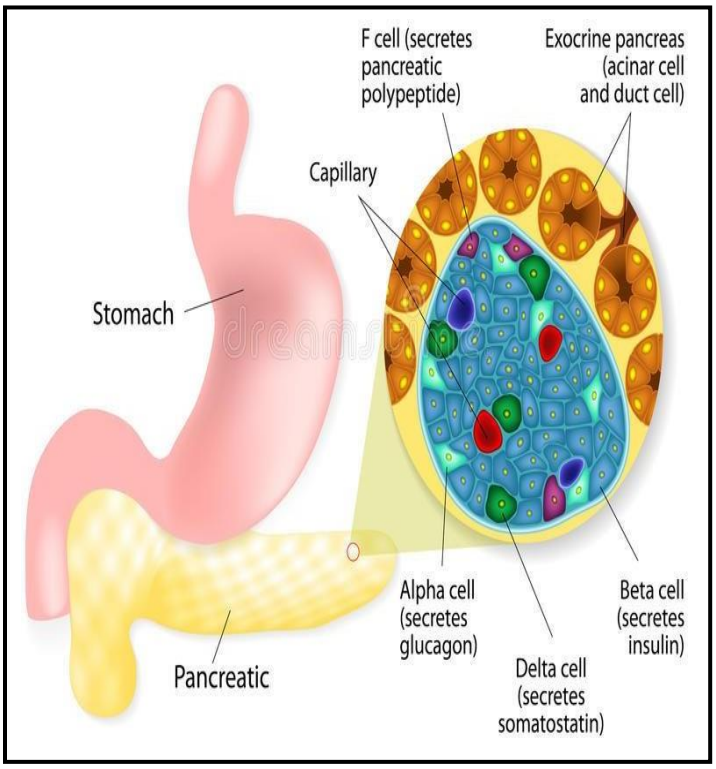
Oral manifestation of thyroid gland disorder	
Hyperthyroidism	**Hypothyroidism**
1. Accelerated dental eruption 2. Increased susceptibility to caries 3. Increased susceptibility to Periodontal disease 4. Burning mouth syndrome 5. Development of connective-tissue diseases like Sjögren's syndrom 6. Maxillary or mandibular osteoporosis 7. Enlargement of mainly in lateral posterior tongue	1. Delayed dental eruption 2. Salivary gland enlargement 3. Compromised Periodontal health 4. Macroglossia 5. Micrognathia 6. Thick lips 7. Mouth breathing 8. Enamel hypoplasia

Pancreas gland

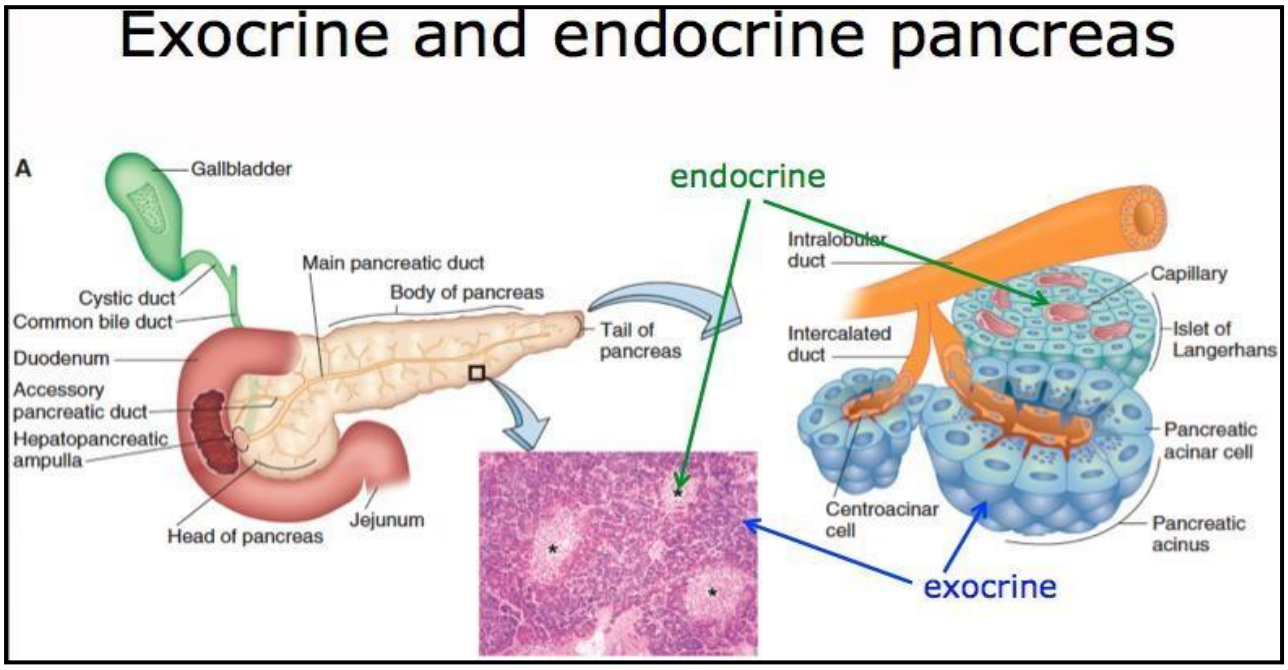
The pancreas, in addition to its digestive functions, secretes two important hormones, *insulin and glucagon, that are essential for normal regulation of glucose, lipid, and protein metabolism*. Pancreas contains about 1 to 2 million islets of Langerhans. It has both endocrine and exocrine functions, secrete several digestive enzyme.

The endocrine function of pancreas is performed by the islets of Langerhans which consist of four types of cells:

1) A cells or α cell secrete glucagon
2) B cells or β cells secrete insulin
3) D cells or δ cells secrete somatostatin
4) F cells or PP cells which secrete pancreatic polypeptide.



Insulin is secreted by β cells in the islets of Langerhans of pancreas. It is the important hormone that is concerned with regulation of carbohydrate metabolism and blood sugar level. It is also concerned with metabolism of proteins and fats.

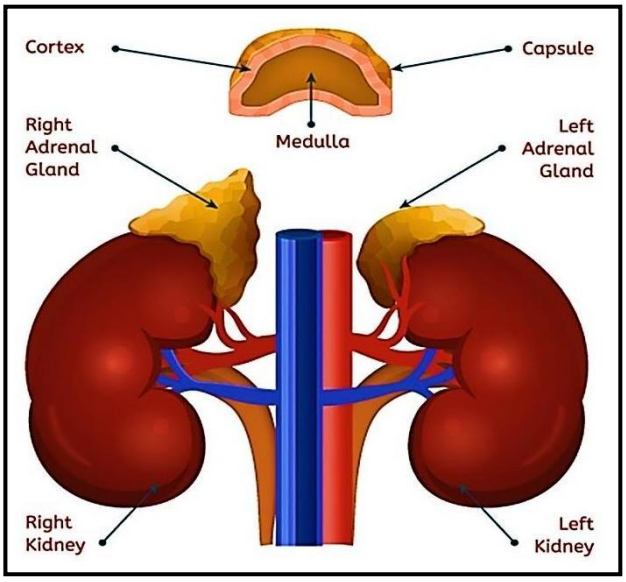


Diabetes mellitus (DM) represents a group of metabolic diseases that are characterized by hyperglycaemia due to a total or relative lack of insulin secretion or insulin resistance or both. The metabolic abnormalities involve carbohydrate, protein and fat metabolism. DM affects all age groups, but is more common in adults with an incidence of 3%. Diabetic patients have a risk of periodontitis 3 times greater than in general population.

Oral signs and symptoms of diabetes can include:

1- Neurosensory disorder (burning mouth syndrome), and abnormal wound healing
2- Dental carries and tooth loss.
3- Can lead to complications include periodontal diseases (periodontitis and gingivitis)
4- Salivary dysfunction leading to a reduction in salivary flow and changes in saliva composition, and taste dysfunction.
5- Oral fungal and bacterial infections have been reported in patients with diabetes.

Adrenal glands



There are two adrenal glands. Each gland is situated on the upper pole of each kidney. Because of the situation, adrenal glands are otherwise called *suprarenal glands*. Each gland is made of two parts, the adrenal cortex and adrenal medulla. Adrenal cortex is the outer portion constituting 80% of the gland. Adrenal medulla is the central portion of gland constituting 20%.

Adrenal glands produce hormones that help regulate body metabolism, immune system, blood pressure, response to stress and other essential functions. Adrenal medullary hormones are called ***catecholamines***. The adrenal medulla produces:

1- Epinephrine (adrenaline)
2- Norepinephrine (noradrenaline)
3- Dopamine.

While the cortex, responsible for the production of steroid hormones, collectively known as ***adrenocortical hormones*** or ***corticosteroids***.

Based on their functions the corticosteroids are classified into three groups:

1- Mineralocorticoids (Aldosterone and 11-deoxycorticosterone)
2- Glucocorticoids (Cortisol and Corticosterone)
3- Sex hormones (Androgens, Estrogen and Progesterone)

Addison's disease or primary adrenal insufficiency: This disease is with a deficiency in the secretion of glucocorticoid and mineralocorticoid hormones by the adrenal cortex. The oral mucosa can develop black-bluish plaques, mainly affecting buccal mucosa but it can also be seen on the gums, palate, tongue and lips.

Gland/Tissue	Hormones	Major Functions	Chemical Structure
Hypothalamus	**Thyrotropin-releasing hormone (TRH)**	Stimulates secretion of thyroid-stimulating hormone and prolactin	Peptide
	Growth hormone - releasing hormone (GRH)	Causes release of growth hormone	Peptide
	Growth hormone inhibitory hormone (somatostatin) (GHRH)	Inhibits release of growth hormone	Peptide
	Corticotropin-releasing hormone (CRH)	Causes release of adrenocorticotropic hormone	Peptide
	Gonadotropin-releasing hormone (GnRH)	Causes release of luteinizing hormone and follicle-stimulating hormone	Peptide
	Dopamine or prolactin-inhibiting factor	Inhibits release of prolactin	Amine
Anterior pituitary	**Growth hormone (GH)**	Stimulates protein synthesis and overall growth of most cells and tissues	Peptide
	Thyroid-stimulating hormone (TSH)	Stimulates synthesis and secretion of thyroid hormones (thyroxine and triiodothyronine)	Peptide
	Endorphin	reduces the pain by stopping the pain signals and gives a good mood and happy	Peptide
	Adrenocorticotropic hormone (ACTH)	Stimulates synthesis and secretion of adrenocortical hormones (cortisol, androgens)	Peptide
	Follicle stimulating hormone (FSH)	Causes growth of follicles in the ovaries and sperm maturation in Sertoli cells of testes	Peptide
	Luteinizing hormone (LH)	Stimulates testosterone synthesis in Leydig cells of testes; stimulates ovulation, formation of corpus luteum, and estrogen and progesterone synthesis in ovaries	Peptide
	Prolactin	Promotes development of the female breasts and secretion of milk	Peptide
Posterior pituitary	**Antidiuretic hormone (called *vasopressin*)**	Increases water reabsorption by the kidneys and causes vasoconstriction and increased blood pressure	Peptide
	Oxytocin	Stimulates milk ejection from breasts and uterine contractions	Peptide
Thyroid	**Thyroxine (T4)and Triiodothyronine (T3)**	Increases rates of chemical reactions in most cells, thus increasing body metabolic rate.	Amine
	Calcitonin	Promotes deposition of Ca^{+2} in bones and decreases extracellular fluid Ca^{+2} concentration	Peptide
Adrenal cortex	**Cortisol**	Control metabolism of proteins, carbohydrates, and fats; also has anti-inflammatory effects	Steroid

	Aldosterone	Increases renal sodium reabsorption, potassium secretion, and hydrogen secretion	Steroid
Adrenal medulla	**Norepinephrine, epinephrine**	Same effects as sympathetic stimulation	Amine
Pancreas	**Insulin (β cells)**	Promotes glucose entry in many cells, and in this way controls carbohydrate metabolism	Peptide
	Glucagon (α cells)	Increases synthesis and release of glucose from the liver into the body fluids	Peptide
Parathyroid	**Parathyroid hormone**	Controls serum Ca^{+2} ion concentration by increasing Ca^{+2} absorption by the gut and kidneys and releasing Ca^{+2} from bones	Peptide
Testes	Testosterone	Promotes development of male reproductive system and male secondary sexual characteristics	Steroid
Ovaries	Estrogens	Promotes growth and development of female reproductive system, female breasts, and female secondary sexual characteristics	Steroid
	Progesterone	Stimulates secretion of "uterine milk" by the uterine endometrial glands and promotes development of secretory apparatus of breasts	Steroid
Placenta	Human chorionic gonadotropin	Promotes growth of corpus luteum and secretion of estrogens and progesterone by corpus luteum	Peptide
	Human somatomammotropin	Probably helps promote development of some fetal tissues, as well as the mother's breasts	Peptide
	Estrogens	See actions of estrogens from ovaries	Steroid
	Progesterone	See actions of progesterone from ovaries	Steroid
Kidney	Renin	Catalyzes conversion of angiotensinogen to angiotensin I (acts as an enzyme)	Peptide
	1,25-Dihydroxycholecalciferol	Increases intestinal absorption of calcium and bone mineralization	Steroid
	Erythropoietin	Increases erythrocyte production	Peptide
Heart	Atrial natriuretic peptide	Increases sodium excretion by kidneys, reduces blood pressure	Peptide
Stomach	Gastrin	Stimulates hydrogen chloride secretion by parietal cells	Peptide
Small intestine	Secretin	Stimulates pancreatic acinar cells to release bicarbonate and water	Peptide
	Cholecystokinin	Stimulates gallbladder contraction and release of pancreatic enzymes	Peptide
Adipocytes	Leptin	Inhibits appetite, stimulates thermogenesis	Peptide

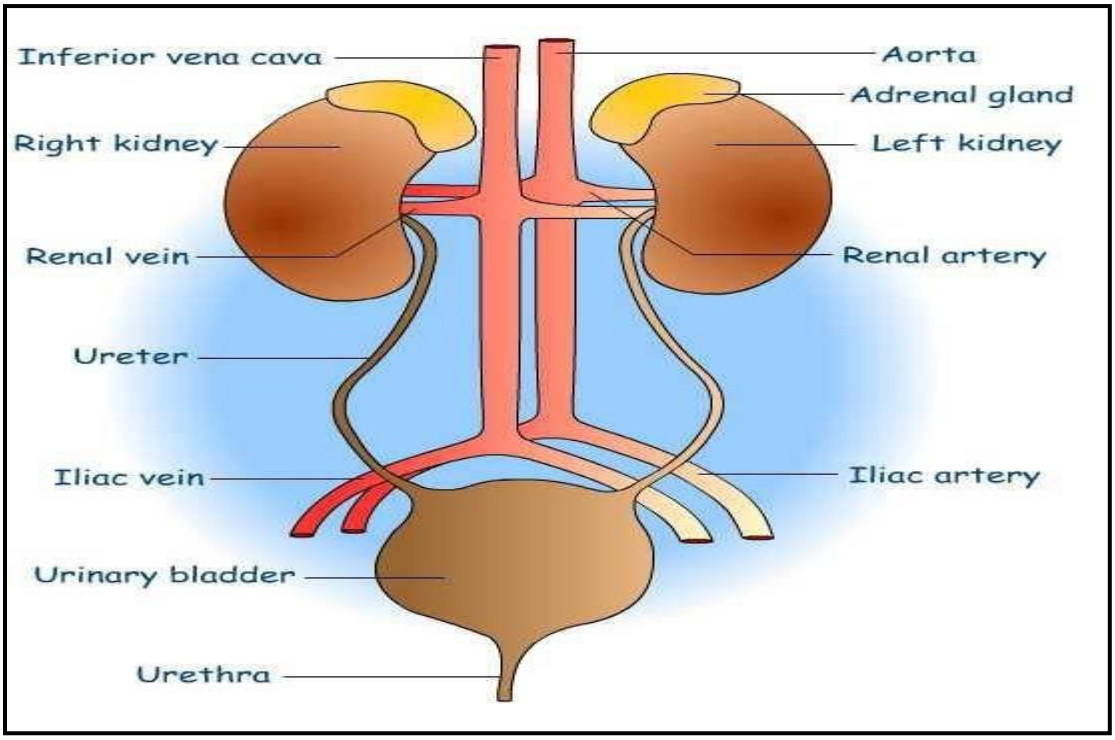
Urinary system

Excretion is the process by which the unwanted substances and metabolic wastes are eliminated from the body. Although various organs such as gastro intestinal (GI) tract, liver, skin and lungs are involved in removal of wastes from the body, their excretory capacity is limited. But, the renal system or urinary system has maximum capacity of excretory function.

Parts of Renal system include:

1. A pair of kidneys
2. Ureters
3. Urinary bladder
4. Urethra.

Kidneys produce the urine. Ureters transport the urine to urinary bladder. Urinary bladder stores urine until it is voided (emptied). Urine is voided from bladder through urethra.



Urinary system

The Kidney

Kidney is a compound tubular gland covered by a connective tissue capsule. There is a depression on the medial border of kidney called ***hilum***, through which renal artery, renal veins, nerves and ureter pass.

Kidneys perform several vital functions besides formation of urine. By excreting urine, kidneys play the principal role in homeostasis. Thus, ***the functions of kidneys*** are:

1. Role of homeostasis

The primary function of kidneys is homeostasis. It is accomplished by the formation of urine. During the formation of urine, kidneys regulate various activities in the body, which are concerned with homeostasis such as:

i. Excretion of Waste Products.

Kidneys excrete the unwanted waste products which are formed during metabolic activities:

a. Urea – end product of amino acid metabolism.

b. Uric acid – end product of nucleic acid metabolism.

c. Creatinine – end product of metabolism in muscles.

d. Bilirubin – end product of hemoglobin degradation.

e. Products of metabolism of other substances

f. Harmful foreign chemical substances like toxins, drugs, heavy metals, pesticides, etc.

ii. Maintenance of Water Balance

Kidneys maintain the water balance in the body by conserving water when it is decreased and excreting water when it is excess in the body.

iii. Maintenance of Electrolyte Balance

Maintenance of electrolyte balance, especially sodium is in relation to water balance. Kidneys retain sodium if the osmolarity of body water decreases and eliminate sodium when osmolarity increases.

iv. Maintenance of Acid–Base Balance

The kidneys contribute to acid-base regulation, along with the lungs and body fluid buffers, by excreting acids and by regulating the body fluid buffer stores. The kidneys are the only means of eliminating from the body certain types of acids.

2. Hemopoietic function

Kidneys stimulate the production of erythrocytes by secreting erythropoietin, which stimulates the production of red blood cells by *hematopoietic stem cells* in the bone marrow. Erythropoietin is the important stimulating factor for erythropoiesis. Kidney also secretes another factor called thrombopoietin, which stimulates the production of thrombocytes.

3. Endocrine function

Kidneys secrete many hormonal substances in addition to erythropoietin and thrombopoietin. And there are other hormones

4. Regulation of blood pressure

Kidneys play an important role in long-term regulation of arterial blood pressure by excreting variable amounts of sodium and water. The kidneys also contribute to short-term arterial pressure regulation by secreting hormones and vasoactive factors.

5. Regulation of blood calcium level

Kidneys play a role in the regulation of blood calcium level by producing the active form of vitamin D,1,25-dihydroxyvitamin D3 (calcitriol), by hydroxylating this vitamin. Calcitriol is essential for normal calcium deposition in bone and for calcium reabsorption by the gastrointestinal tract.

6. Glucose Synthesis (gluconeogenesis)

The kidneys synthesize glucose from amino acids and other precursors during prolonged fasting, a process referred to as gluconeogenesis. The kidneys' capacity to add glucose to the blood during prolonged periods of fasting rivals that of the liver.

The components of kidney are arranged in three layers:

1. Outer Cortex

Cortex is dark and granular in appearance. It contains renal corpuscles and convoluted tubules. At intervals, cortical tissue penetrates medulla in the form of columns, which are called renal columns or columns of Bertini.

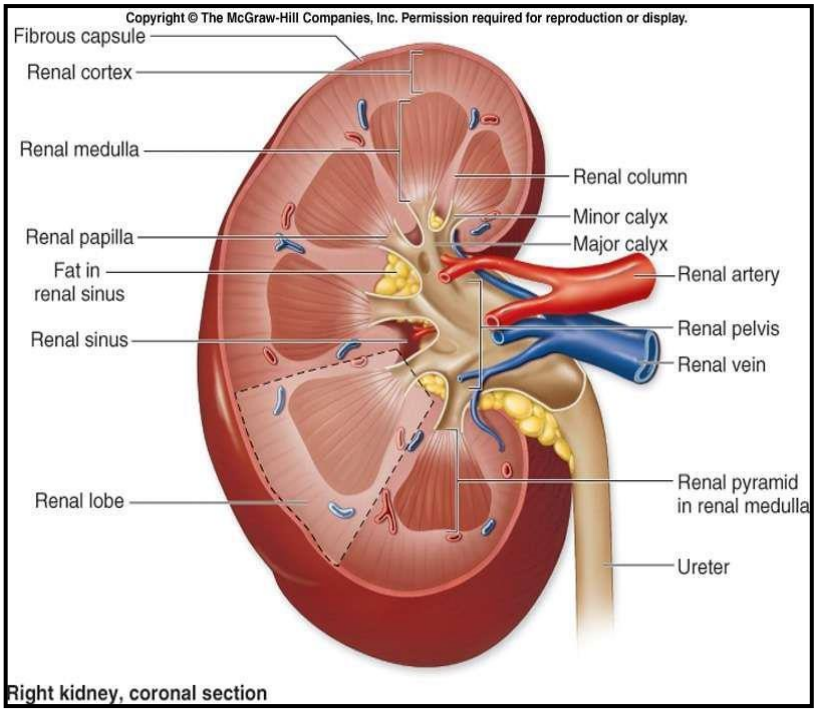
2. Inner Medulla

Medulla contains tubular and vascular structures arranged in parallel radial lines. It is divided into 8 to 18 medullary or ***Malpighian pyramids***.

3. Renal Sinus

Renal sinus consists of the following structures:

a. Renal pelvis: Upper expanded part of ureter.
b. Subdivisions of pelvis –major calyces and minor calyces.
c. Branches of nerves, arteries and veins.
d. Loose connective tissues and fat.



Parenchyma of kidney

It is made up of tubular structures called ***uriniferous tubules***, which are of two types:

1. **Terminal or secretary tubules called nephrons**, which are concerned with formation of urine

2. **Collecting ducts or tubules** which are concerned with transport of urine from nephrons to pelvis of ureter. The collecting ducts unite to form ducts of Belini, which open into minor calyces through papilla.

Nephron and Juxtaglomerular Apparatus

Nephron is defined as the structural and functional unit of kidney. Each kidney consists of 1 to 1.3 million of nephrons. The kidney cannot regenerate new nephrons. Therefore, with renal injury, disease, or normal aging, the number of nephrons gradually decreases. After age 40 years, the number of functioning nephrons usually decreases about 10 percent every 10 years.

Each nephron is formed by two parts:

1. A blind end called renal corpuscle or ***Malpighian corpuscle***

2. A tubular portion called ***renal tubule.***

Renal corpuscle

The renal corpuscle is also known as Malpighian corpuscle. It is a spheroidal and slightly flattened structure with a diameter of about 200 μ. The function of the renal corpuscle is the filtration of blood which forms the first phase of urine formation.

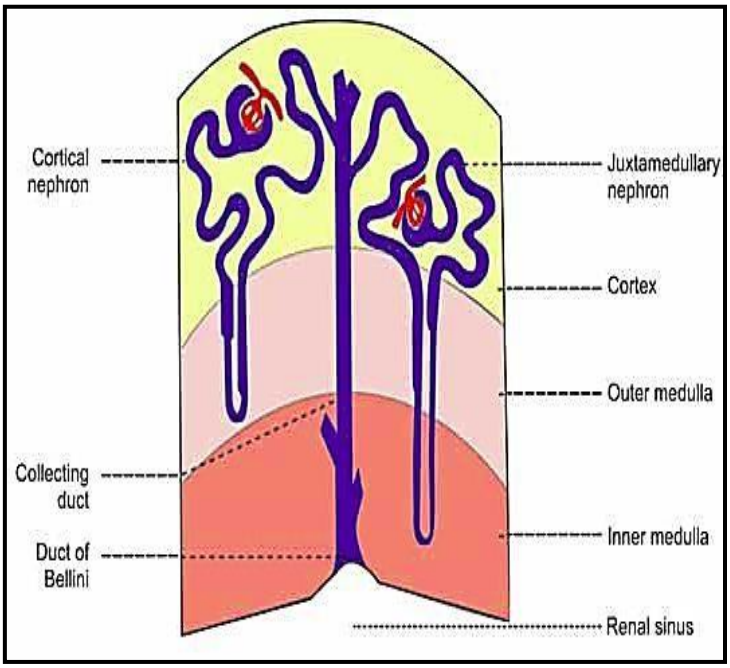
Renal corpuscle is situated in the cortex of the kidney either near the periphery or near the medulla. Based on the situation of renal corpuscle, the nephrons are classified into two types:

1. Cortical Nephrons or superficial nephrons

Cortical nephrons are the nephrons, which have their corpuscles in the outer cortex of the kidney near the periphery. In human kidneys 85% nephrons are cortical nephrons.

2. Juxtamedullary Nephrons

Juxtamedullary nephrons are the nephrons which have their corpuscles in the inner cortex near medulla or corticomedullary junction.



Structure of renal corpuscle

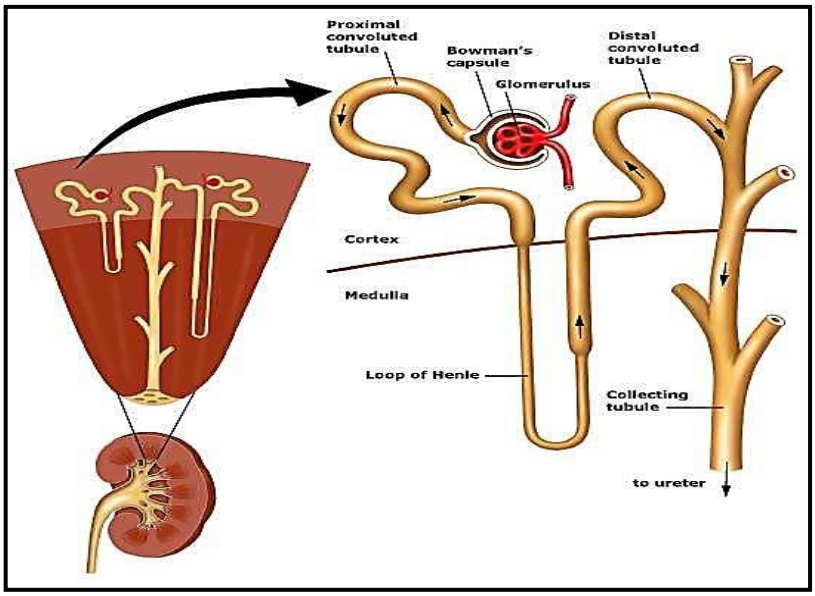
The renal corpuscle is formed by two portions:

1. ***Glomerulus***: It is a cluster of branching capillaries enclosed by Bowman's capsule.
2. ***Bowman's capsule:*** The structure of Bowman's capsule is like a funnel with filter paper, encloses the glomerulus.

Tubular portion of nephron

This portion is the continuation of Bowman's capsule. It is made up of three parts:

1. The proximal convoluted tubule
2. The distal convoluted tubule.
3. Loop of Henle.



- **Proximal convoluted tubule**

  It is the coiled portion arising from Bowman's capsule. It is situated in the cortex. It is continued as descending limb of loop of Henle.

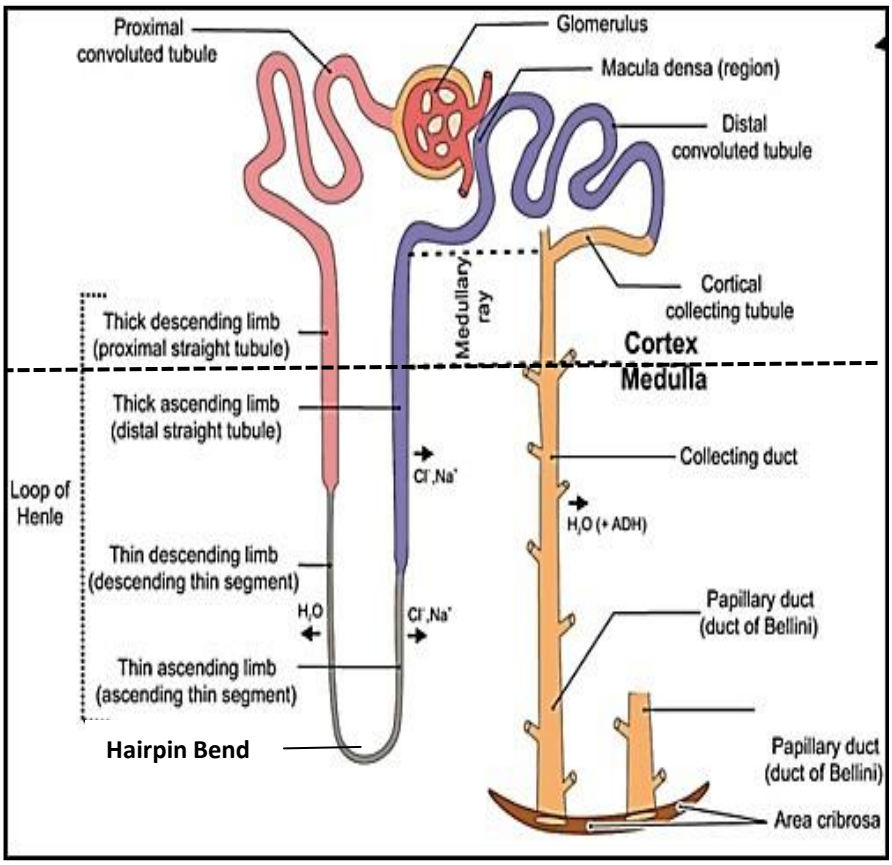
- **Loop of Henle**

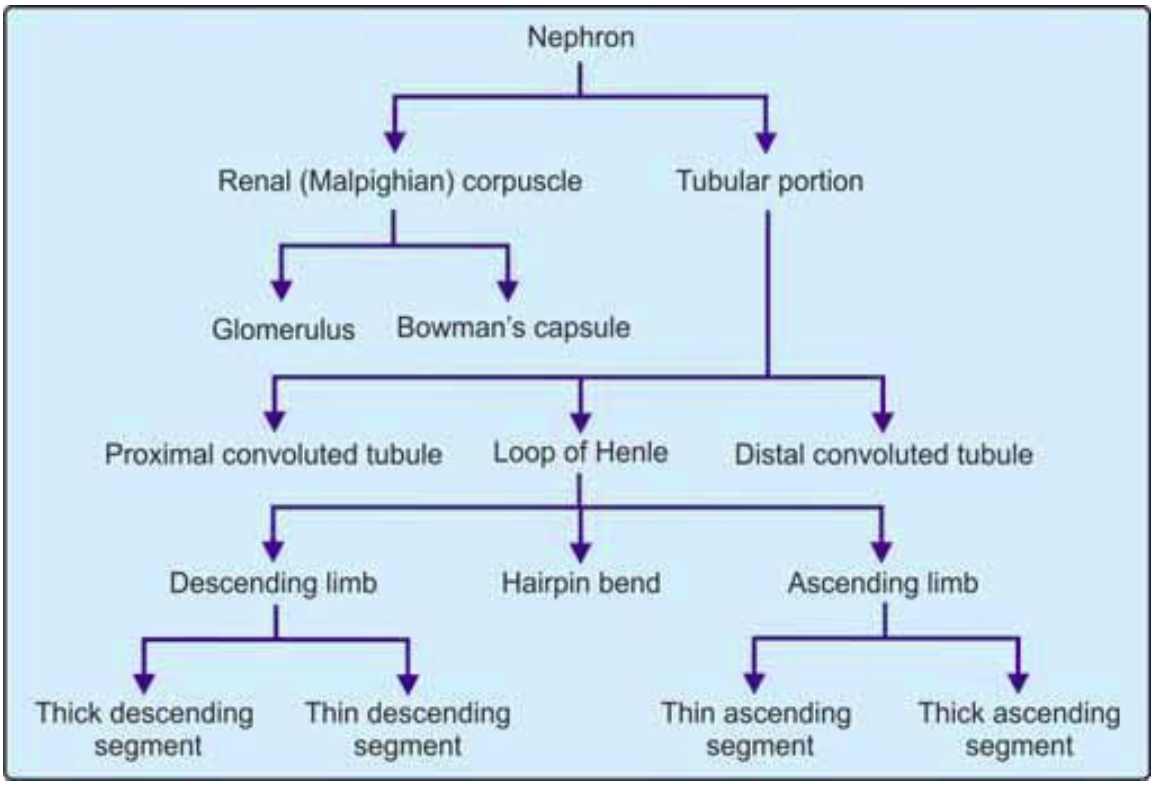
  Loop of Henle consists of:

  a. ***Descending Limb:*** It is made up of thick descending segment and thin descending segment. The thick descending segment is the direct continuation of the proximal convoluted tubule. It descends down into medulla. The thick descending segment is continued as thin descending segment.

  b. ***Hairpin Bend:*** It is continued as hairpin bend of the loop. The hairpin bend is continued as the ascending segment of loop of Henle.

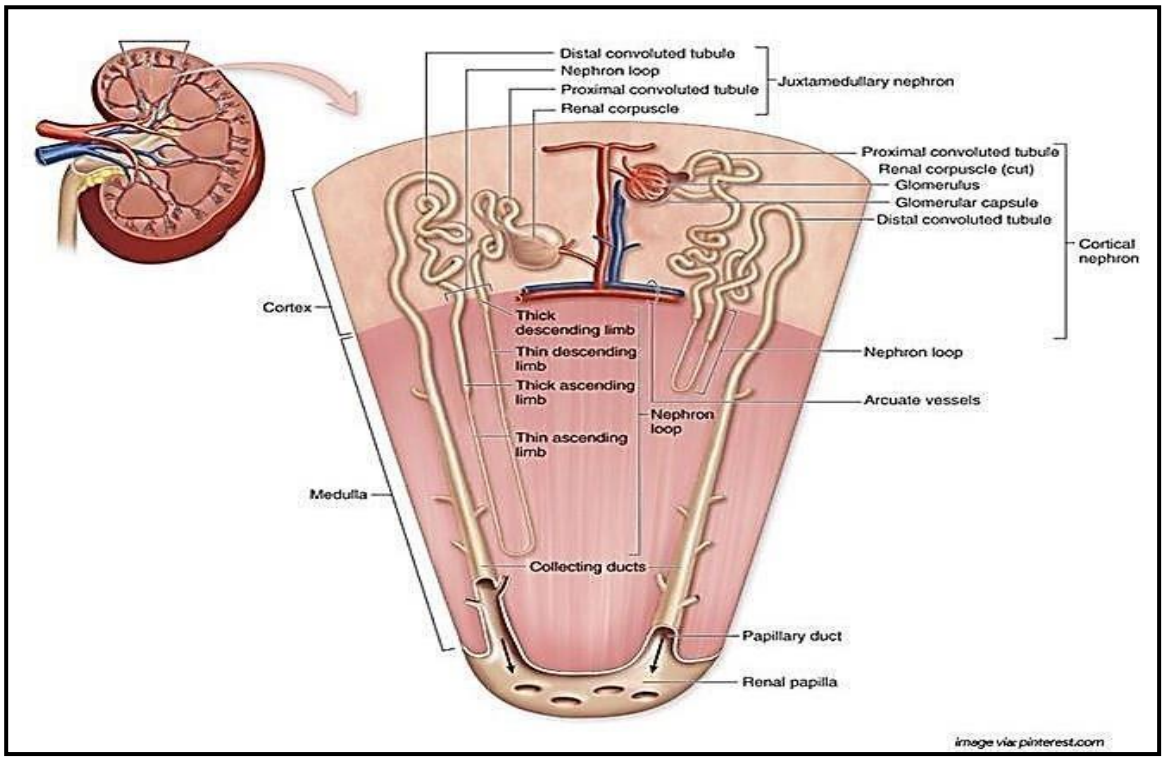
  c. ***Ascending Limb:*** Ascending limb of Henle's loop has two parts, thin and thick ascending segment. Thin segment is the continuation of hairpin bend. The thin ascending segment is continued as thick ascending segment. Thick ascending segment ascends to the cortex and continues as distal convoluted tubule.


Proximal convoluted tubule
Glomerulus
Macula densa (region)
Distal convoluted tubule
Cortical collecting tubule
Medullary ray
Cortex
Medulla
Thick descending limb (proximal straight tubule)
Thick ascending limb (distal straight tubule)
Loop of Henle
Cl⁻,Na⁺
Collecting duct
H₂O (+ ADH)
Thin descending limb (descending thin segment)
H₂O
Cl⁻,Na⁺
Papillary duct (duct of Bellini)
Thin ascending limb (ascending thin segment)
Hairpin Bend
Papillary duct (duct of Bellini)
Area cribrosa


Nephron
Renal (Malpighian) corpuscle
Tubular portion
Glomerulus
Bowman's capsule
Proximal convoluted tubule
Loop of Henle
Distal convoluted tubule
Descending limb
Hairpin bend
Ascending limb
Thick descending segment
Thin descending segment
Thin ascending segment
Thick ascending segment

Features of two types of nephron

Features	Cortical nephron	Juxtamedullary nephrons
Situation of renal corpuscle	Outer cortex near the periphery	Inner cortex near medulla
Loop of Henle	Short	Long
	Hairpin bend penetrates only up to outer zone of medulla	Hairpin bend penetrates up to the inner zone of medulla
Function	Formation of urine	Mainly the concentration of urine and formation of urine



Collecting duct

The distal convoluted tubule continues as the initial or arched collecting duct, which is in cortex. The lower part of the collecting duct lies in medulla. Seven to ten initial collecting ducts unite to form the straight collecting duct, which passes through medulla.

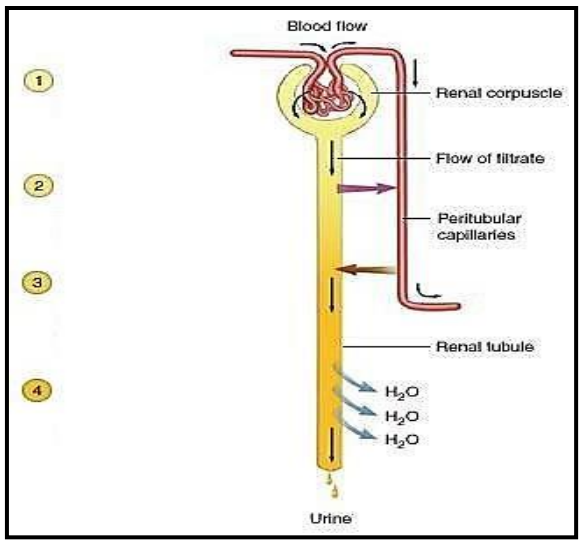
Urine formation

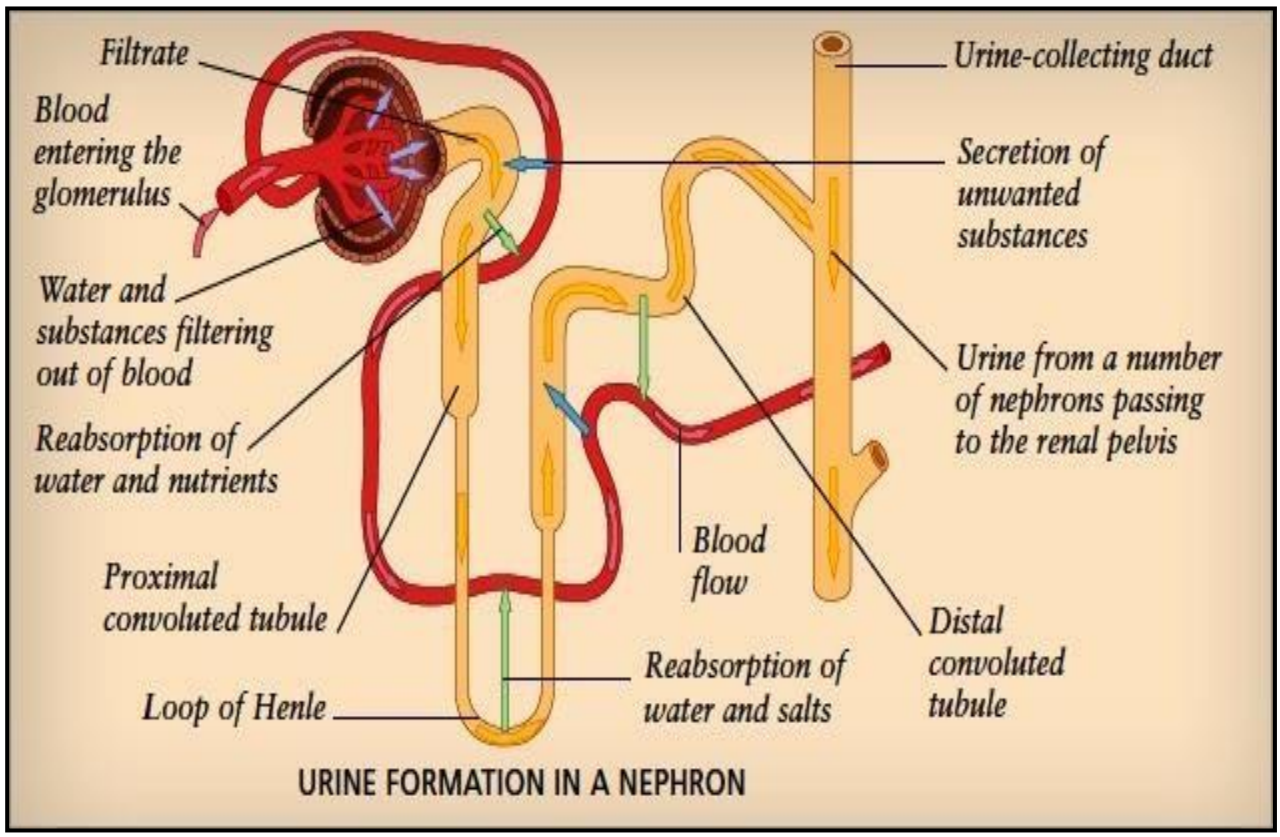
Urine formation is a blood cleansing function. Normally, about 26% of cardiac output enters the kidneys to get rid of unwanted substances. Kidneys excrete the unwanted substances in urine. Normally, about 1 to 1.5 L of urine is formed every day.

The mechanism of urine formation includes the following processes:

1. Glomerulus filtration.
2. Tubular reabsorption.
3. Tubular secretion.

Then **water conservation** and finally **Excretion**.





Glomerular Filtration

A process by which the blood passes through the glomerular capillaries, much of its fluid, containing both useful chemicals and dissolve waste materials, filtered through the filtration membrane where it is filtered and then flows into Bowman's capsule.

Glomerular Filtration Rate: It is the amount of fluid filtered from the blood into the capsule each minute.

Factors governing the filtration rate at the capillary beds are:

1. Total surface area available for filtration.
2. Filtration membrane permeability.
3. Net filtration pressure.

Pressure determining filtration

The pressures, which determine the glomerular filtration rate (GFR), are:

1. Glomerular Capillary Pressure

It is the pressure exerted by the blood in glomerular capillaries. It is about 60 mm Hg and, varies between 45 and 70 mm Hg. Glomerular capillary pressure is the highest capillary pressure in the body.

2. Colloidal Osmotic Pressure in the glomeruli

It is exerted by plasma proteins in the glomeruli. The plasma proteins are not filtered through the glomerular capillaries and remain in the glomerular capillaries. These proteins develop the colloidal osmotic pressure which is about 25 mm Hg. It opposes glomerular filtration.

3. *Hydrostatic Pressure in Bowman's capsule*

It is the pressure exerted by the filtrate in Bowman's capsule. It is also called capsular pressure. It is about 15 mm Hg. It also opposes glomerular filtration.

Net Filtration Pressure

Net filtration pressure is the balance between pressure favoring filtration and pressures opposing filtration. It is otherwise known as effective filtration pressure or essential filtration pressure.

The net filtration pressure **=** 60 – (25 + 15) = 20 mm Hg.
=Glomerular capillary pressure – {Colloidal osmotic pressure + Hydrostatic pressure in Bowman's capsule}

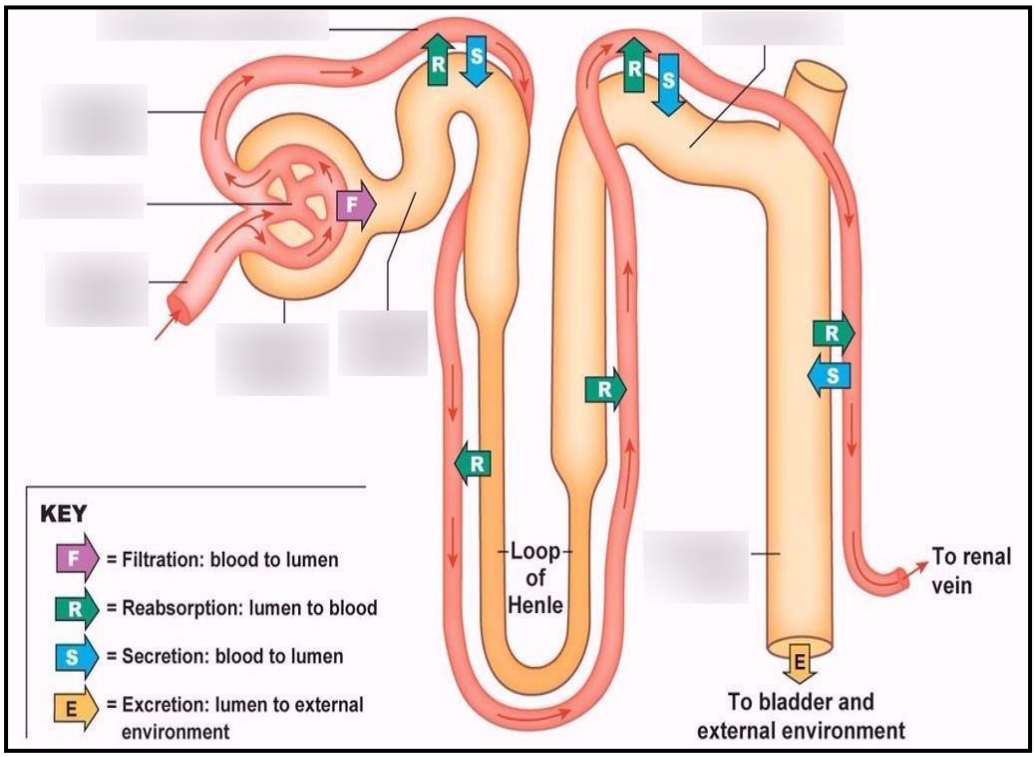
*** Normal net filtration pressure is about 20 mm Hg, and, it varies between 15 and 20 mm Hg.

Tubular Reabsorption

It is the process by which water and other substances are transported from renal tubules back to the blood. Large quantity of water (more than 99%), electrolytes and other substances are reabsorbed by the tubular epithelial cells. The reabsorbed substances move into the interstitial fluid of renal medulla, then move into the blood in peritubular capillaries. Tubular reabsorbtion mainly occurs in the proximal tubule and the Loop of Henele.

Selective reabsorption

Tubular reabsorption is known as selective reabsorption because the tubular cells reabsorb only the substances necessary for the body. Essential substances such as glucose, amino acids and vitamins are completely reabsorbed from renal tubule. Whereas the unwanted substances like metabolic waste products are excreted through urine.



Tubular secretion

Tubular secretion is the process by which the substances are transported from blood into renal tubules. It is also called tubular excretion.

Micturition

Micturition is a process by which urine is voided from the urinary bladder. It is a reflex process. However, in grown up children and adults, it can be controlled voluntarily to some extent. The functional anatomy and nerve supply of urinary bladder are essential for the process of micturition.

Nerve supply to urinary bladder and sphincters

Urinary bladder and the internal sphincter are supplied by sympathetic and parasympathetic divisions of autonomic nervous system whereas; the external sphincter is supplied by the somatic nerve fibers.

Sympathetic nerve supply

Fibers of sympathetic nerve arise from spinal cord. The stimulation of sympathetic nerve causes relaxation of detrusor muscle and constriction of the internal sphincter, which supplies the detrusor muscle and internal sphincter. It results in filling of urinary bladder and so, the sympathetic nerve is called the **nerve of filling**.

Parasympathetic nerve supply

Fibers of pelvic nerve (parasympathetic nerve fiber) situated in close relation to urinary bladder and internal sphincter. The stimulation of pelvic (parasympathetic) nerve causes contraction of detrusor muscle and relaxation of the internal sphincter leading to emptying of urinary bladder. So, the parasympathetic nerve is called the **nerve of emptying or nerve of micturition**.

Somatic nerve supply

The external sphincter is innervated by the somatic nerve called the pudendal nerve. It maintains the tonic contraction of the skeletal muscle fibers of the external sphincter and keeps the external sphincter constricted always. During micturition, this nerve is inhibited. It causes relaxation of external sphincter leading to voiding of urine. Thus, the pudendal nerve is responsible for voluntary control of micturition.

Table: Functions of nerves supplying urinary bladder and sphincters

Nerve	On detrusor Muscle	On internal sphincter	On external sphincter	Function
Sympathetic nerve	Relaxation	Constriction	Not supplied	Filling of urinary bladder
Parasympathetic nerve	Contraction	Relaxation	Not supplied	Emptying of urinary bladder
Somatic nerve	Not supplied	Not supplied	Constriction	Voluntary control of micturition

Renal Function Tests

Renal function tests: are the groups of tests that are performed to assess the functions of kidney.

The renal function tests are of three types:

1) Examination of urine alone.
2) Examination of blood alone.
3) Examination of blood and urine.

Routine Examination of Urine

During the routine examination of urine, the following are determined:

a. **Specific gravity:** Normally it is 1.010 to 1.025. But, in some conditions like chronic nephritis, it is decreased.

b. **Presence of normal constituents of urine in abnormal quantity**:
Normally, substances like water, salt, amino acids and creatinine are excreted in urine either in greater or lesser amount. But, if abnormally large amount is excreted, it suggests some abnormal functional status of kidney.

c. **Microscopic examination:** This reveals the presence of red blood cells, pus cells, epithelial cells and crystals which suggests the renal pathology.

Examination of blood

The level of plasma proteins, urea, uric acid and creatinine are determined in blood. The blood level of these substances is altered in renal failure.

Examination of blood and urine

Plasma Clearance: It is defined as the amount of plasma that is cleared off a substance in a given unit of time. It is also known as renal clearance.

The determination of clearance value for certain substances helps in assessing the following renal functions:

1. Glomerular filtration rate
2. Renal plasma flow
3. Renal blood flow.

To determine the plasma clearance of a particular substance, measurement of the following factors is required:

1. Volume of urine excreted.
2. Concentration of the substance in urine.
3. The concentration of the substance in blood.

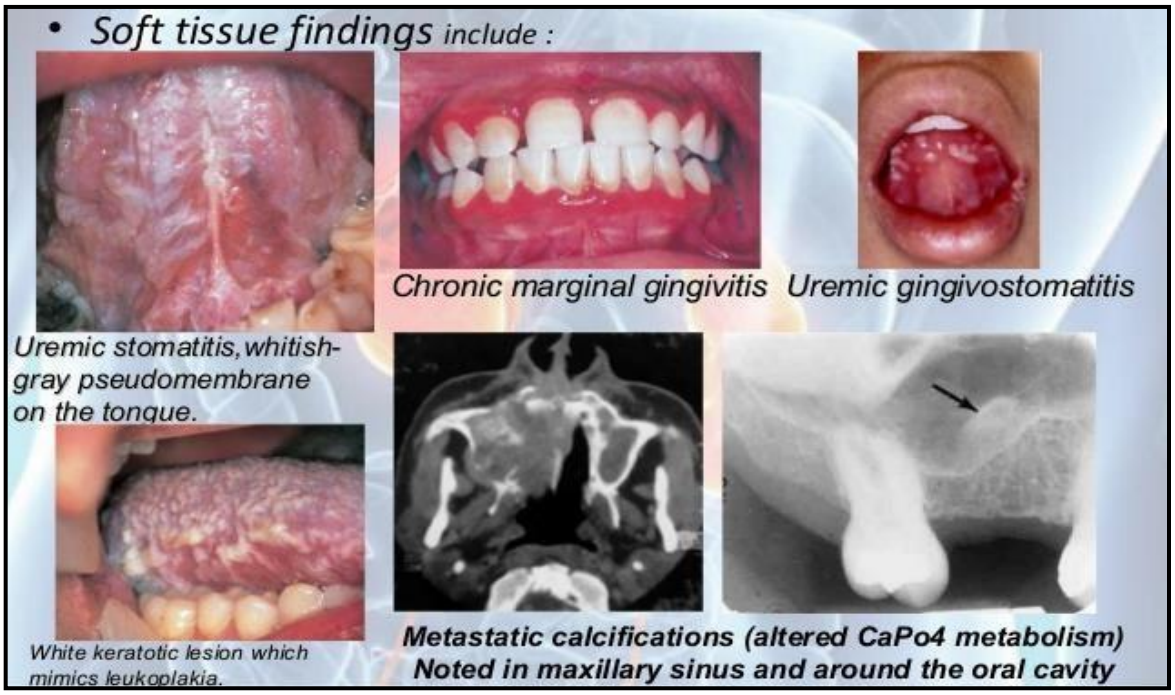
Relation between renal disease & oral health

- Chronic kidney disease, the gradual and usually permanent reduction of the glomerular filtration rate of the kidneys, leads to increases in serum creatinine and blood urea nitrogen levels, resulting in uraemia or azotaemia. Uraemia develops and adversely affects every system of the body. An oral manifestation of chronic renal disease is common during the progression of uraemia.

- **Oral manifestations in uraemia:**
  - ♦ Enlarged (asymptomatic) salivary glands
  - ♦ Decreased salivary flow
  - ♦ Dry mouth
  - ♦ Odor of urea on breath
  - ♦ Metallic taste
  - ♦ Increased calculus formation
  - ♦ Low caries rate
  - ♦ Enamel hypoplasia
  - ♦ Dark brown stains on crowns
  - ♦ Prolonged bleeding from gingiva
  - ♦ Candidal infections.

Dental problems with renal disease

- Uraemic patients have more dental problems than healthy controls in oral mucosa, teeth, salivary glands and jaw bones, problems that seem to develop before dialysis.
- Xerostomia, uraemic stomatitis, periodontal disease and maxillary and mandibular radiographic alterations can be observed in patients with chronic renal failure.
- Periodontal diseases are highly prevalent among patients with chronic renal failure, specifically gingivitis, excessive plaque formation and poor oral hygiene in uraemic patients; however, there are previous reports that periodontal diseases and other dental problems, such as loss of teeth, periapical lesions and mucosal lesions, are contradictory findings.
- Other studies have confirmed that periodontal health is poor in haemodialysis patients and that it correlates with markers of malnutrition and inflammation.



Electrocardiogram (ECG)

Electrocardiography

is the technique by which the electrical activities of the heart are studied.

Electrocardiograph

is the instrument (ECG machine) by which the electrical activities of the heart are recorded.

USES OF ECG- is useful in determining and diagnosing the following:

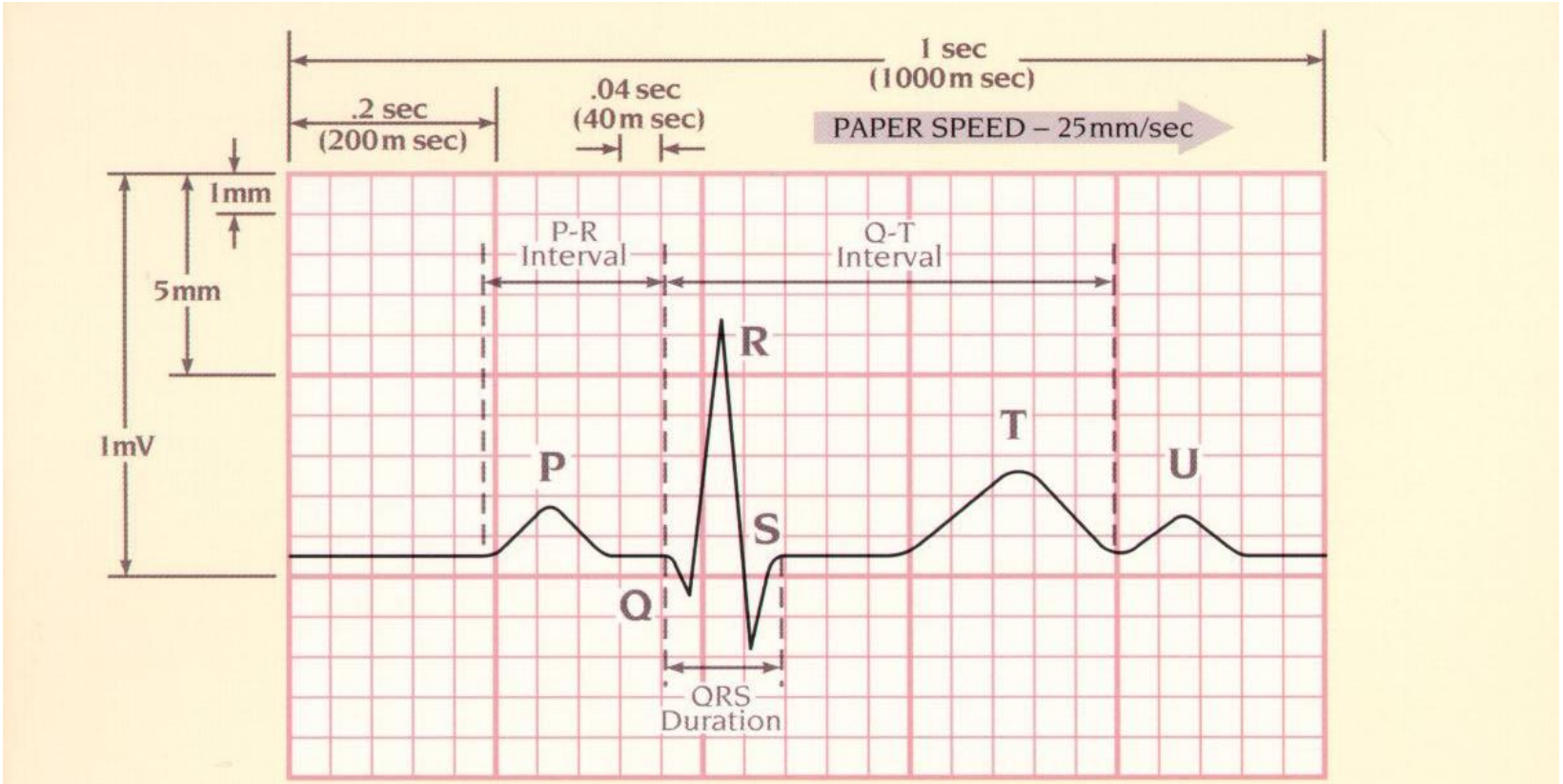
1. Heart rate
2. Heart rhythm 3. Abnormal electrical conduction
4. Ischemia
5. Heart attack
6. Coronary artery disease
7. Hypertrophy of heart chambers.

ELECTROCARDIOGRAPHIC

The paper that is used for recording ECG is called ECG paper.

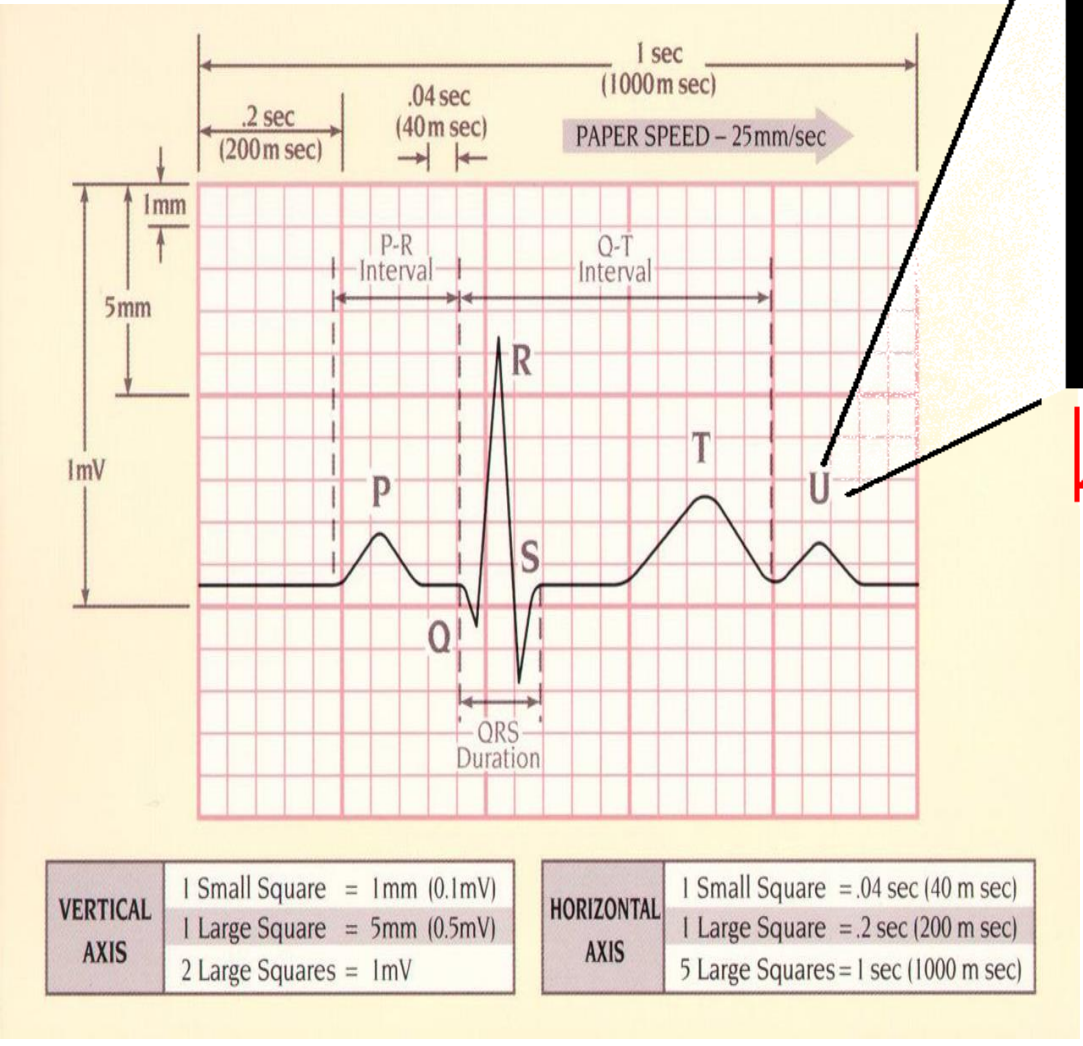
ECG grid refers to the markings (lines)on ECG paper, has horizontal & vertical lines at regular intervals of 1 mm.

Large square (5 mm) = 0.2 second small square (1 mm) = 0.04 second.



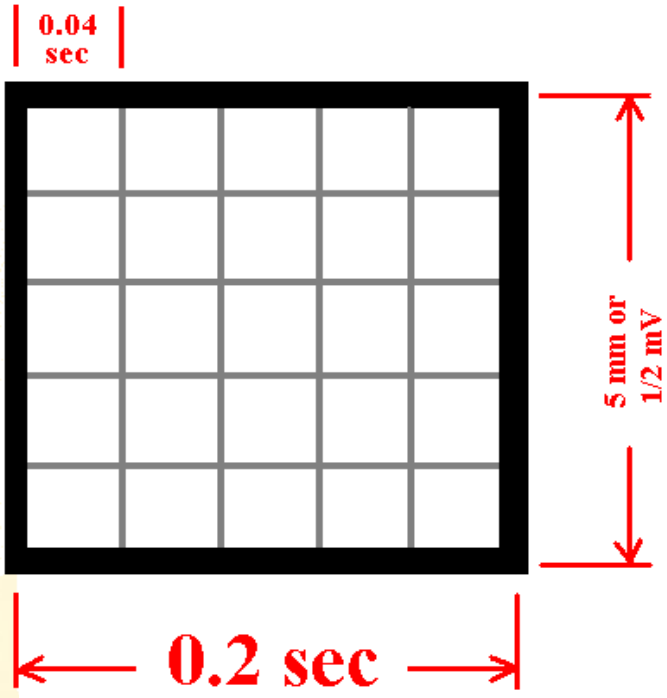
VERTICAL AXIS	1 Small Square	= 1mm	(0.1mV)
	1 Large Square	= 5mm	(0.5mV)
	2 Large Squares	= 1mV	

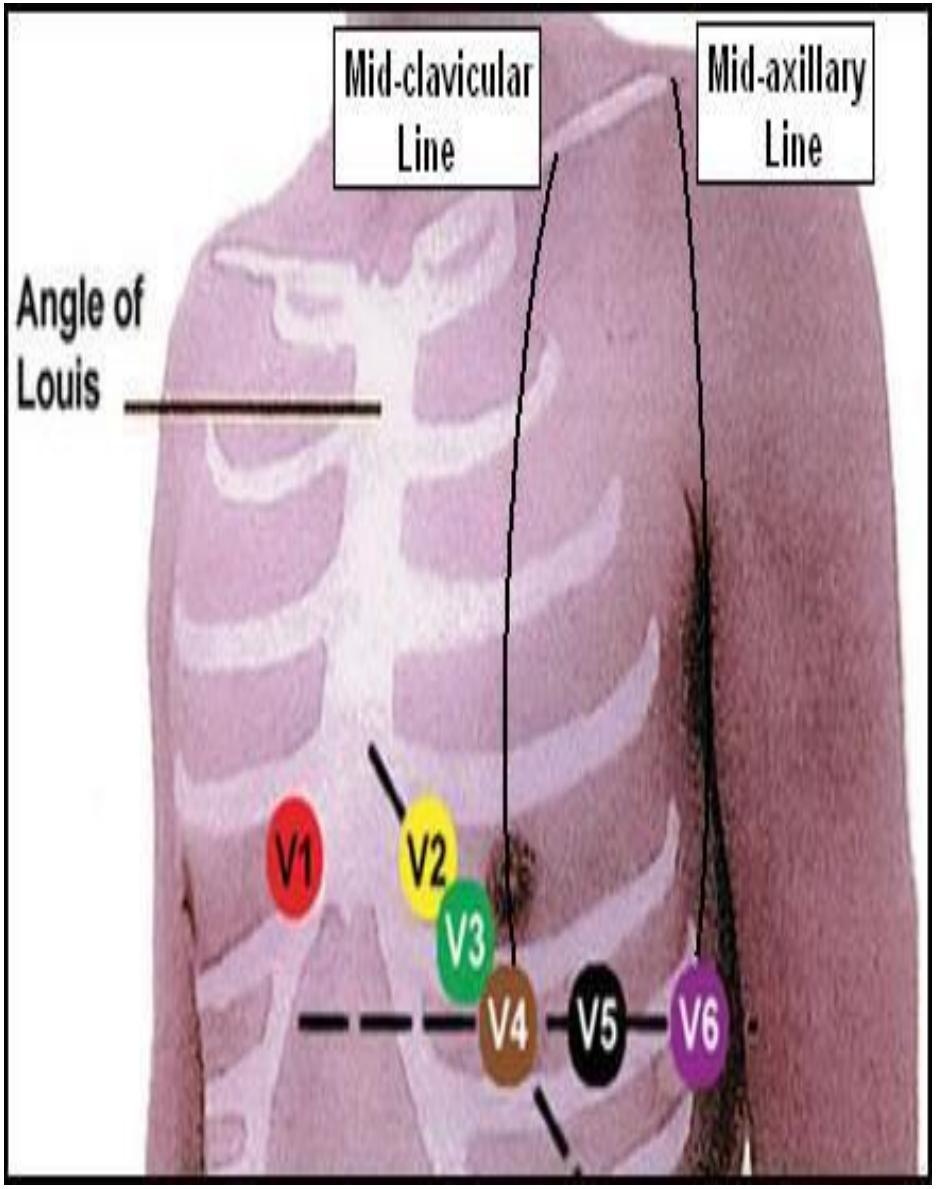
HORIZONTAL AXIS	1 Small Square	= .04 sec (40 m sec)
	1 Large Square	= .2 sec (200 m sec)
	5 Large Squares	= 1 sec (1000 m sec)

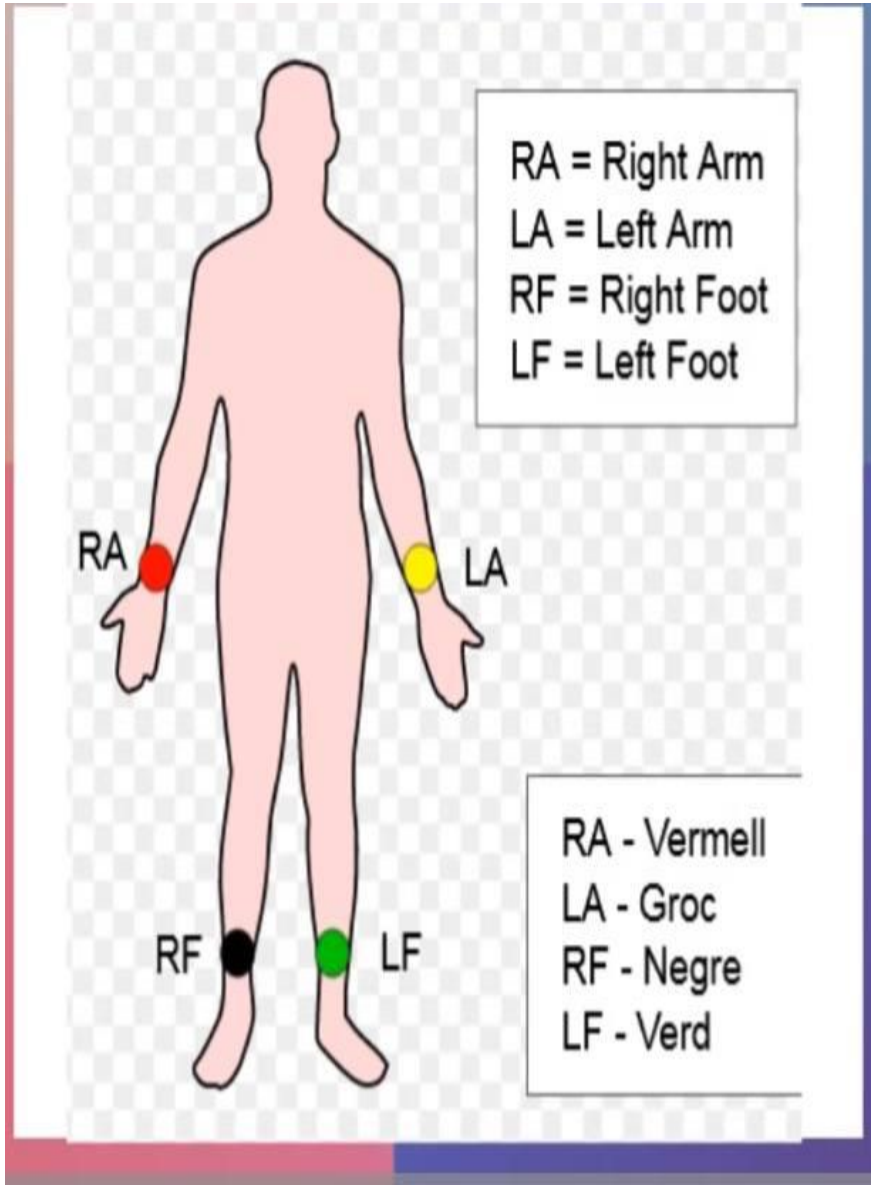


VERTICAL AXIS	
	1 Small Square = 1mm (0.1mV)
	1 Large Square = 5mm (0.5mV)
	2 Large Squares = 1mV

HORIZONTAL AXIS	
	1 Small Square = .04 sec (40 m sec)
	1 Large Square = .2 sec (200 m sec)
	5 Large Squares = 1 sec (1000 m sec)




Mid-clavicular Line
Mid-axillary Line
Angle of Louis
V1
V2
V3
V4
V5
V6


RA = Right Arm
LA = Left Arm
RF = Right Foot
LF = Left Foot
RA
LA
RF
LF
RA - Vermell
LA - Groc
RF - Negre
LF - Verd

ECG LEADS

ECG is recorded by placing series of electrodes on the surface of body. These electrodes
are= ECG leads & are connected to the ECG machine.

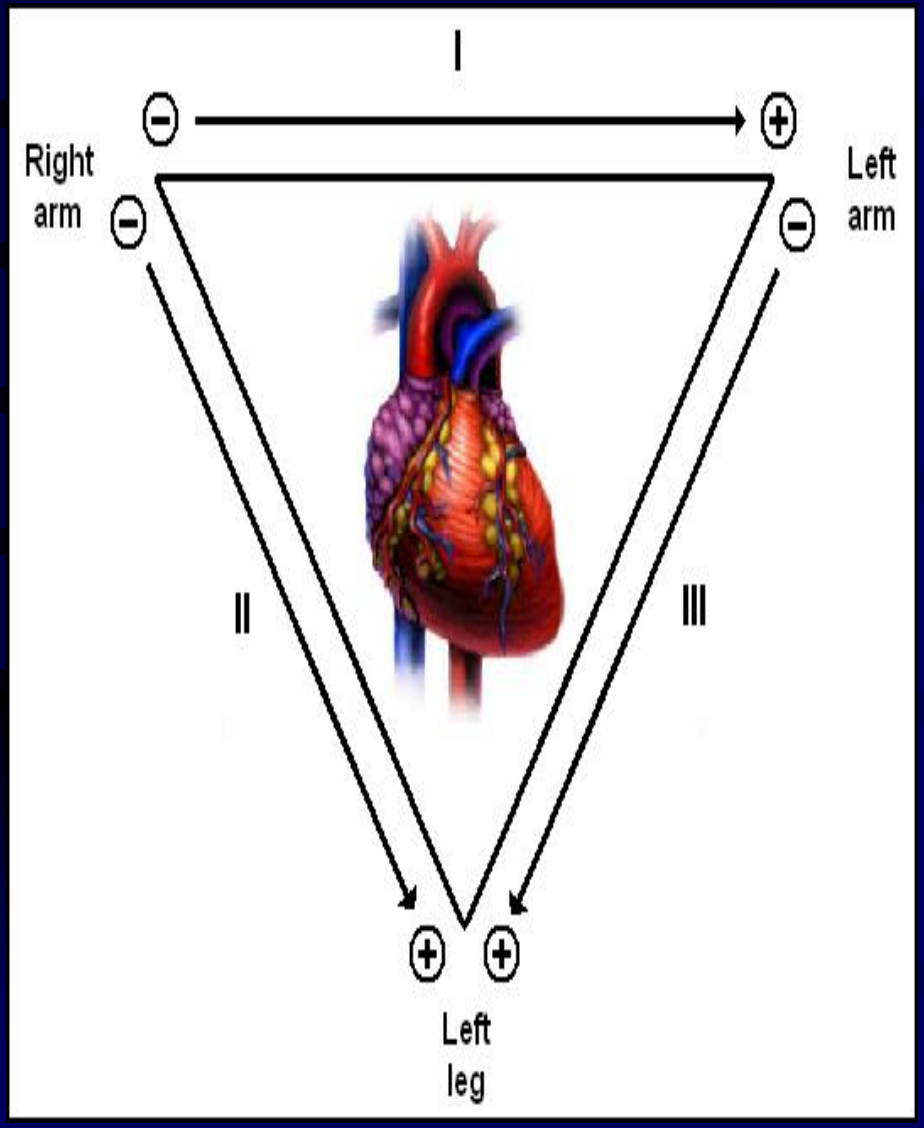
The electrodes are fixed on the limbs. The heart is said to be in the center of an imaginary equilateral triangle drawn by connecting the roots of these three limbs. This triangle is = Einthoven's triangle. The electrical potential generated from the heart appears simultaneously on the roots of these three limbs.

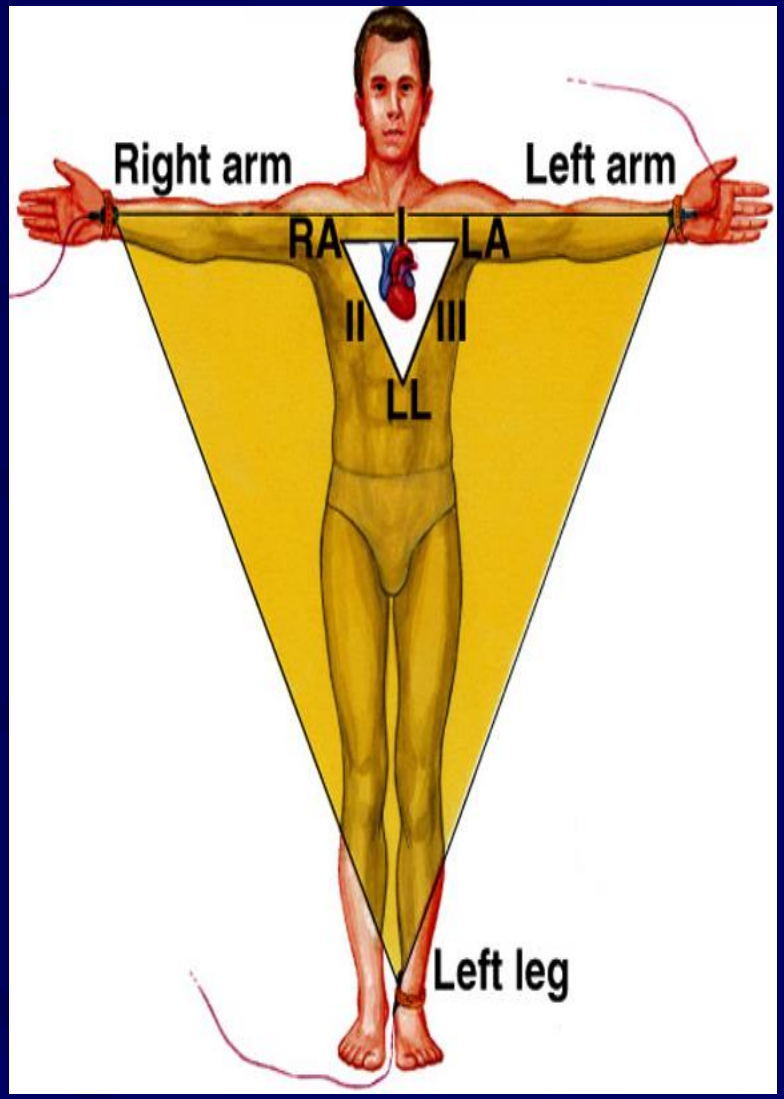
ECG is recorded in 12 leads which are generally classified into two categories.

A. Bipolar leads I , II , III

B. Unipolar leads AVR, AVL, AVF

STANDARD LIMB LEADS





Lead I

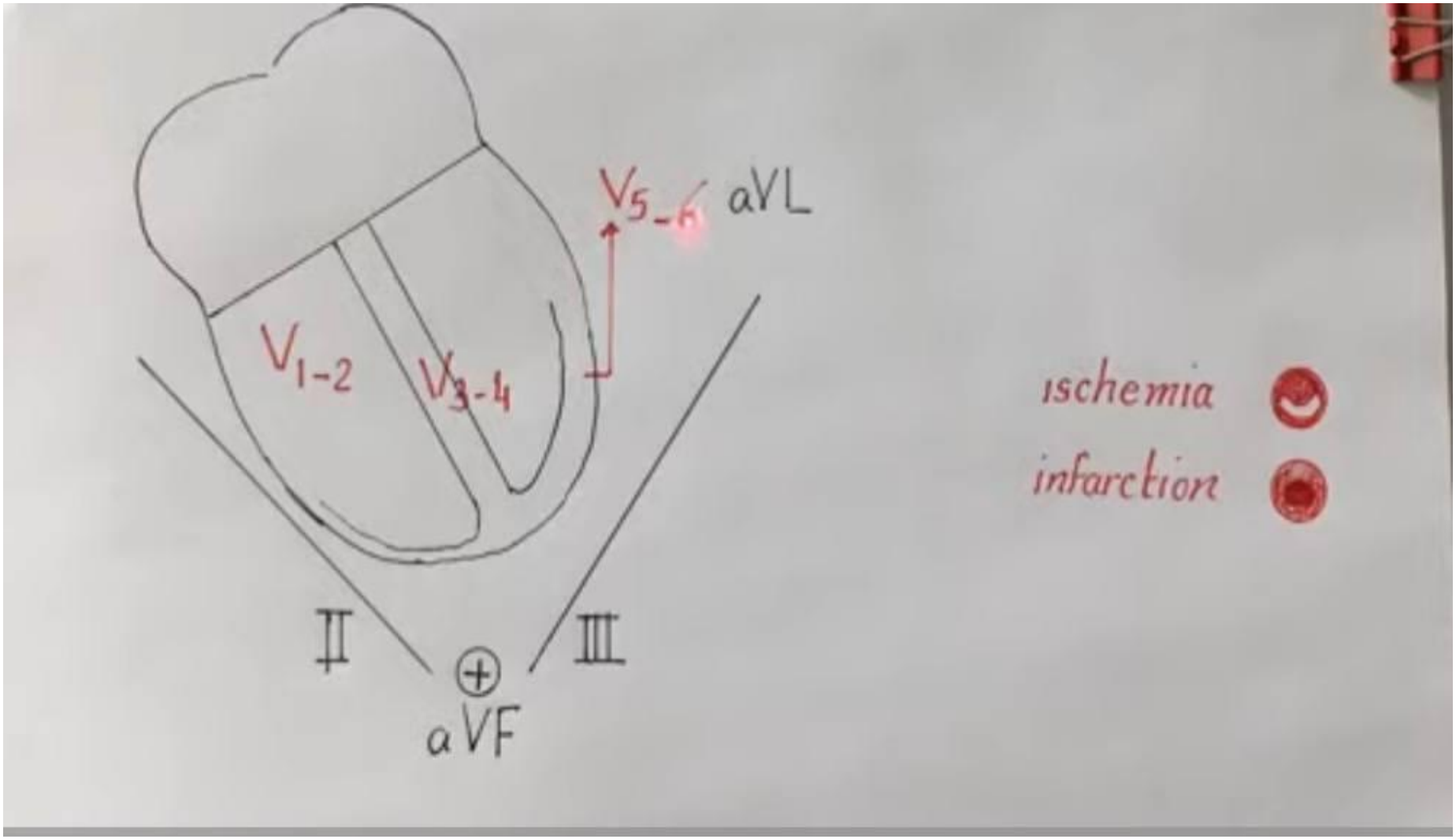
Lead I is obtained by connecting right arm and left arm. The right arm is connected to the negative terminal of the instrument and the left arm is connected to the positive terminal.

Lead II

Lead II is obtained by connecting right arm and left leg. The right arm is connected to the negative terminal of the instrument and the left leg is connected to the positive termina-l.

Lead III

Lead III is obtained by connecting left arm and left leg. The left arm is connected to the negative terminal of the instrument and the left leg is connected to the positive terminal.


V5-6
aVL
V1-2
V3-4
II
III
aVF
ischemia
infarction

UNIPOLAR LEADS

Here, one electrode is active electrode is positive and the other one is an indifferent electrode-is serving as a composite negative electrode. The unipolar leads are 2 types:

.1Unipolar limb leads

also called augmented limb leads..

Unipolar limb leads are of 3 types:

i. aVR lead in which the active

electrode is from right arm

ii.aVL lead in which the active

electrode is from left arm

iii.aVF lead in which the active

electrode is from left leg (foot)

2. Unipolar chest leads . V1, V2,V3, V4,V5,V6

Limb Leads

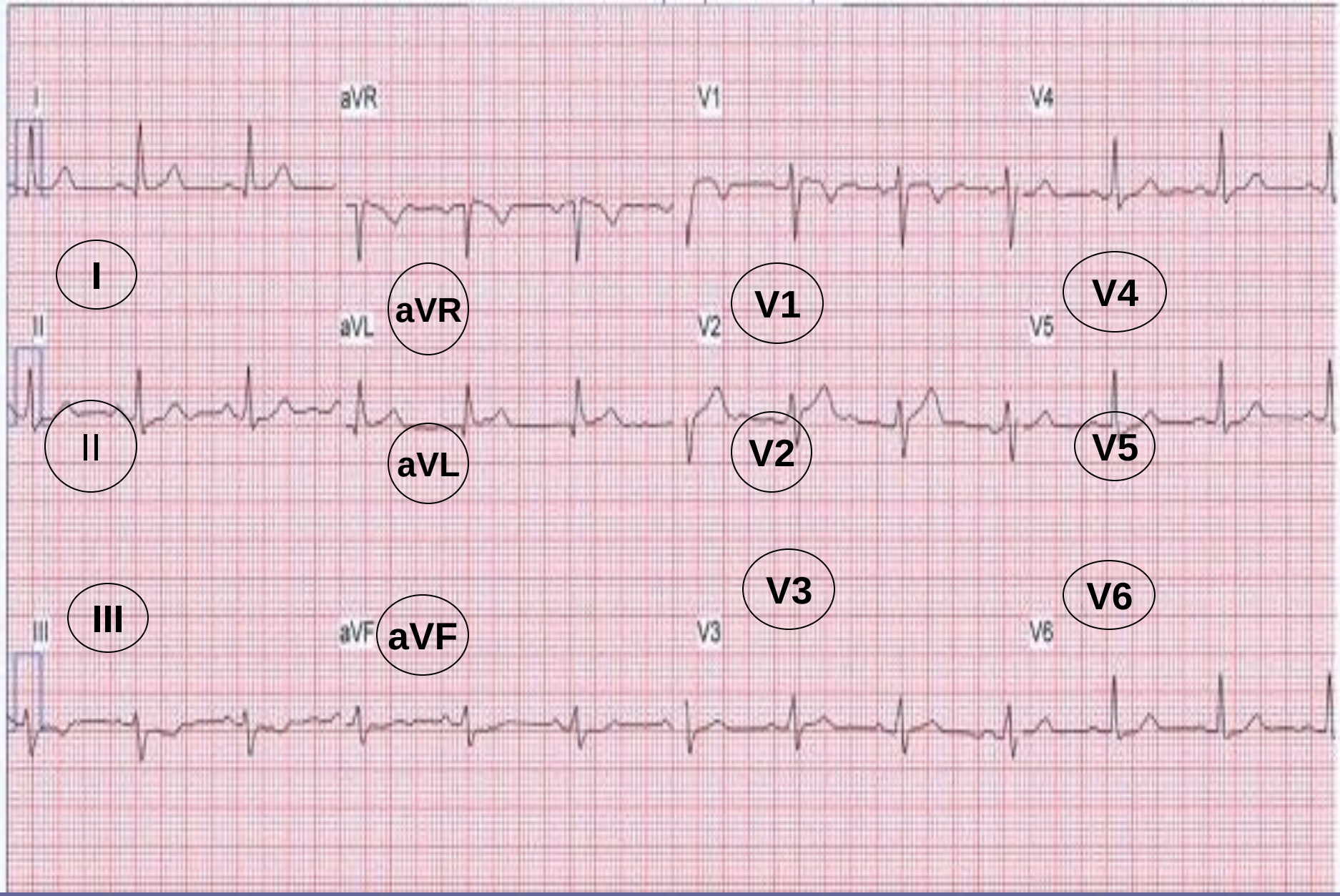
Bipolar I, II, III

Unipolar aVR, aVL, aVF

chest Leads (unipolar) V_1, V_2, V_3, V_4, V_5, V_6

ARRANGEMENT OF LEADS ON THE ECG

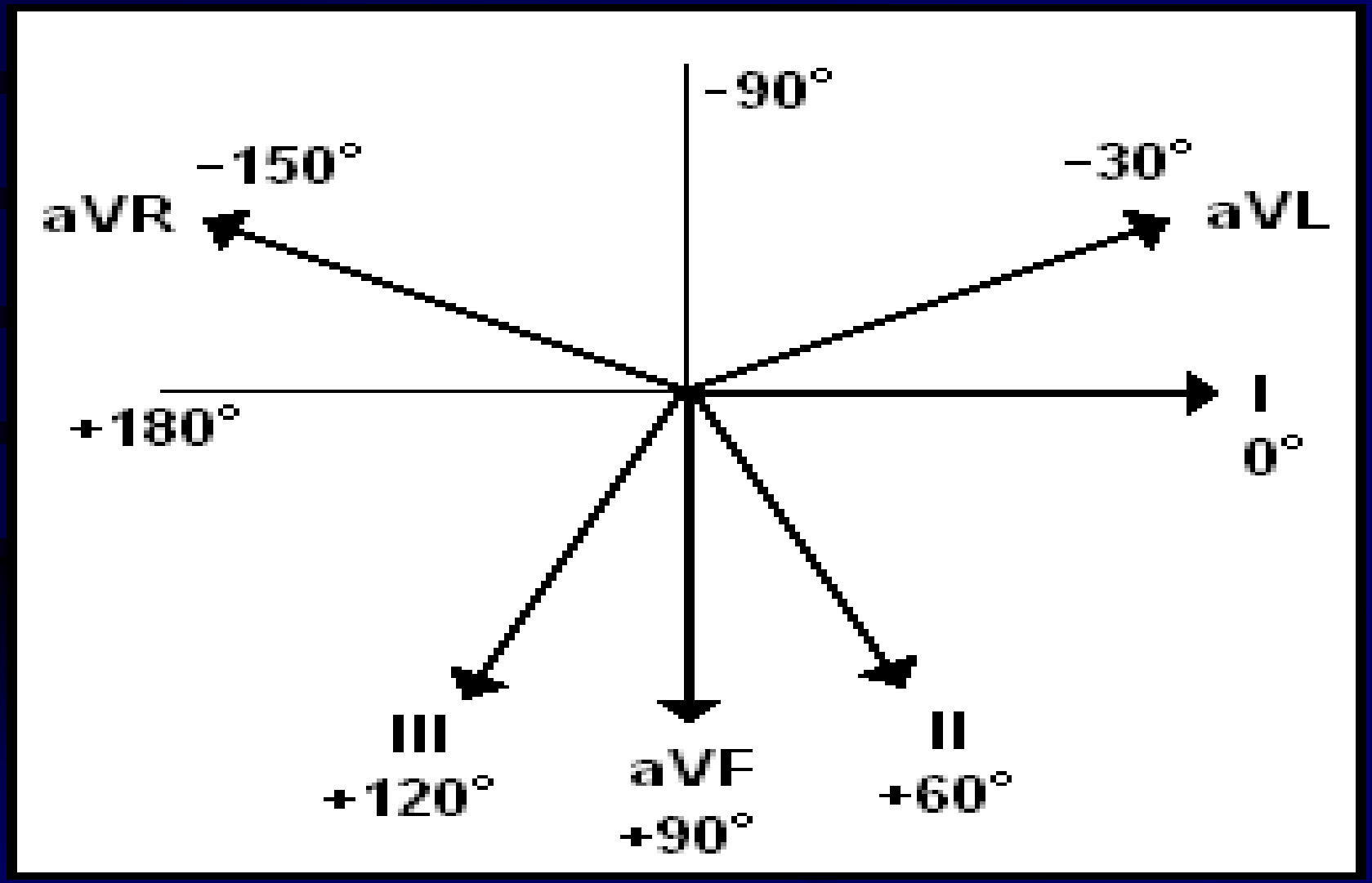
I	aVR	V_1	V_4
II	aVL	V_2	V_5
III	aVF	V_3	V_6


I
aVR
V1
V4
II
aVL
V2
V5
III
aVF
V3
V6

ANATOMICAL PRESENTATION
(SUMMARY)

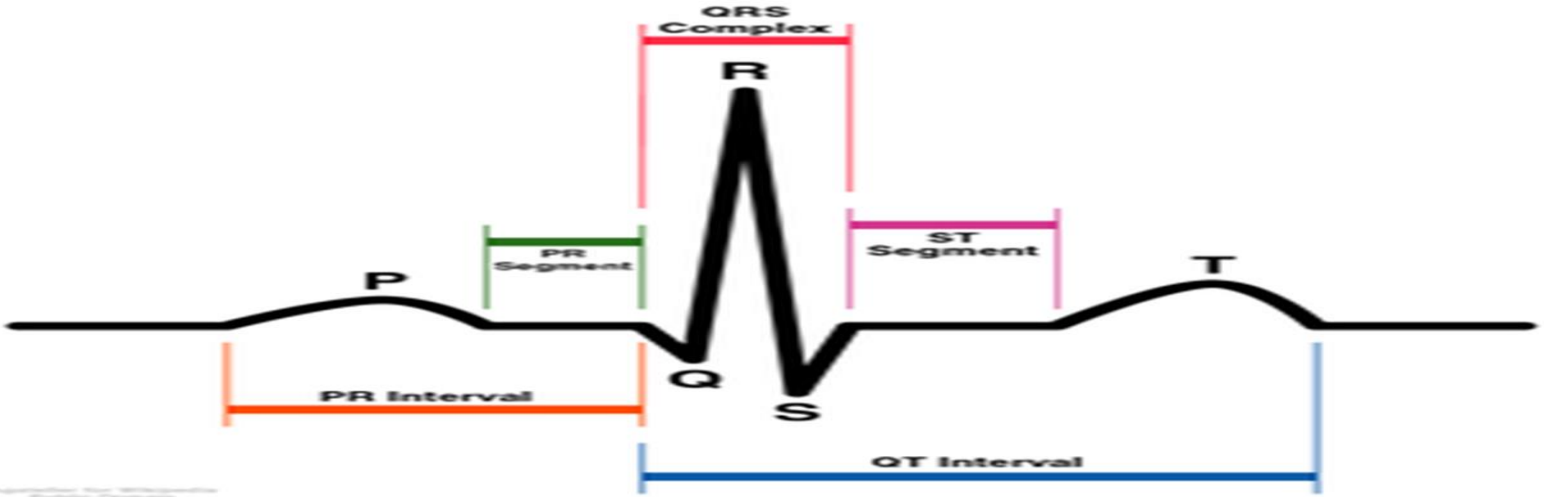
I Lateral	aVR None	V_1 Septal	V_4 Anterior
II Inferior	aVL Lateral	V_2 Septal	V_5 Lateral
III Inferior	aVF Inferior	V_3 Anterior	V_6 Lateral

ALL LIMB LEADS



WAVES OF NORMAL ELECTROCARDIOGRAM

A normal ECG consists of waves, complexes, intervals and segments, has the waves namely P, Q, R, S & T.)



The major complexes in ECG are:

1. 'P' wave, the atrial wave produced due to the depolarization of atrial musculature.

Atrial repolarization is not recorded as a separate wave in ECG because it merges with QRS complex.

2. '. 'QRS' complex is due to depolarization of ventricular musculature.

3. 'T' wave : a positive wave, due to the repolarization of ventricular musculature

4. 'U' WAVE: is not always seen. It is supposed to be due to repolarization of papillary muscle.

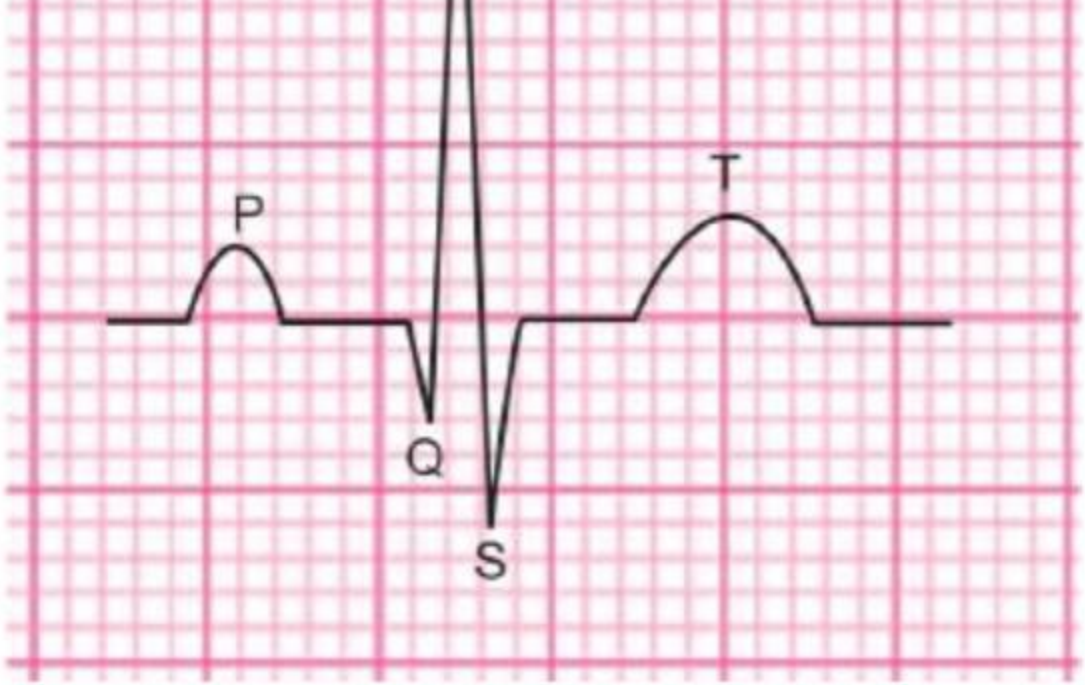


Fig. 6.3: ECG wave morphology

e-atrial depolarization

omplex-ventricular depolarization

gment, T wave-ventricular repolarization

tter understanding:

mm = 0.04 sec

mm = 0.08 sec

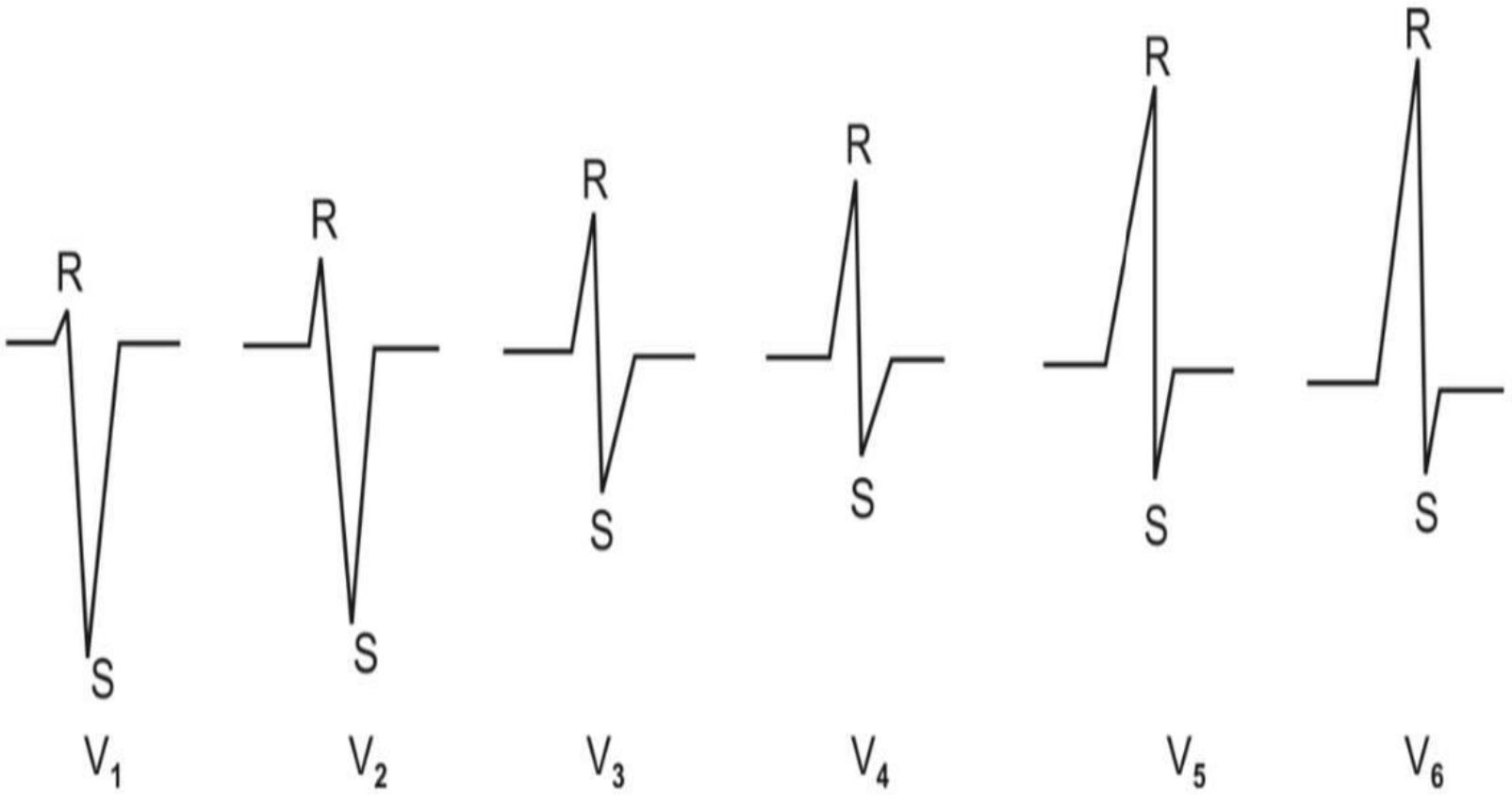


Fig. 6.7: Normal R wave progression in chest leads

What are the steps to read an ECG?

1. Look for Standardization and Lead aVR

At the end of each ECG strip, a standardization box is present which should be 10 mm in height 0.20 second in width (5 mm).

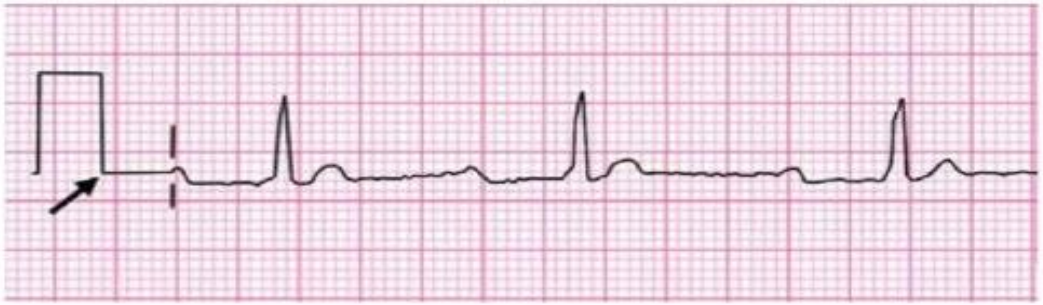


Fig. 7.1: Standardization mark

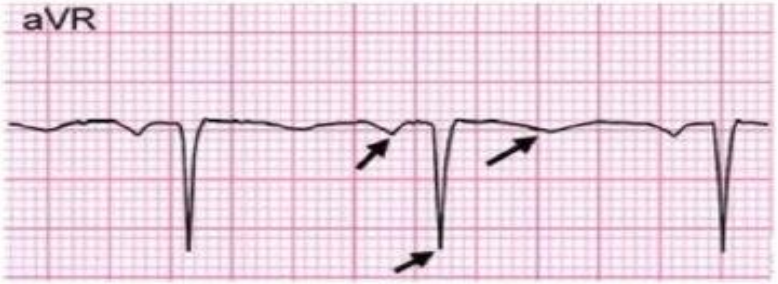


Fig. 7.2: Lead aVR showing inverted P, QRS & T

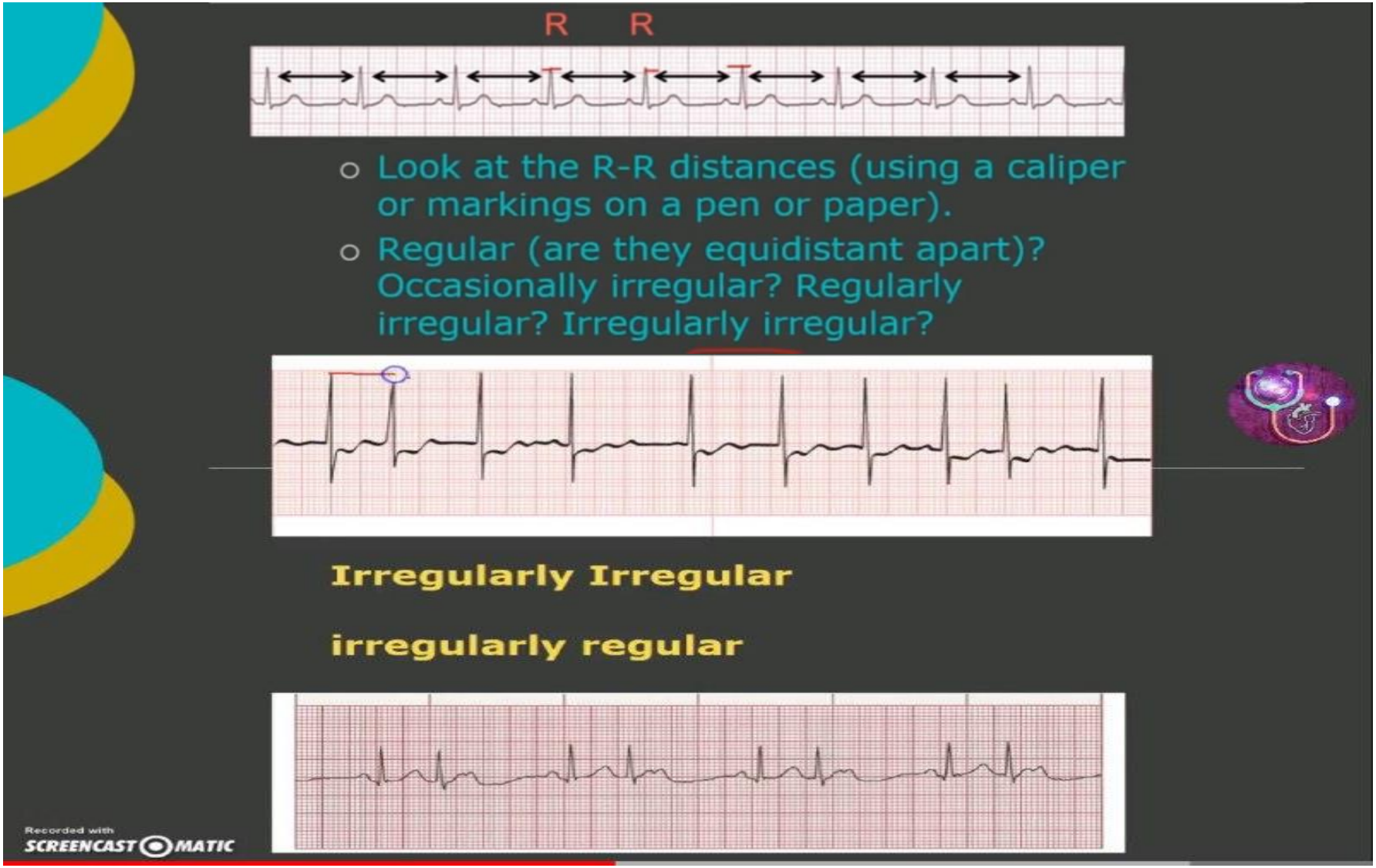
All waves should be inverted in lead aVR unless the limb leads are wrongly connected except in dextrocardia.

2. Determin regularty:

Rhythm

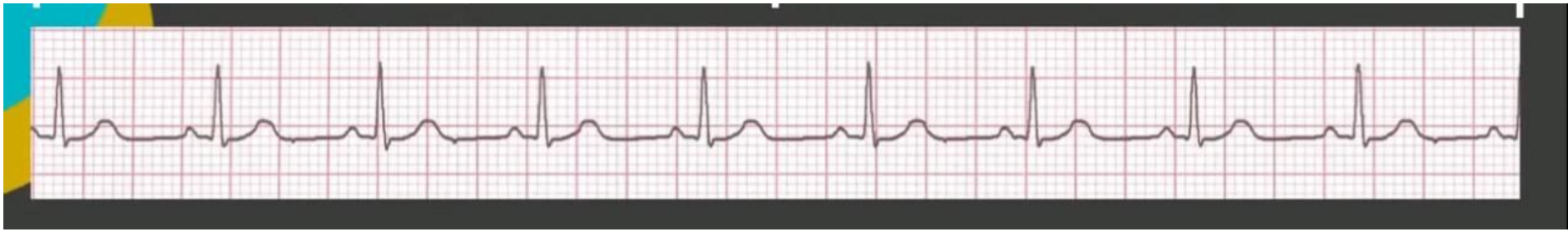
Regular : each R-R interval will be the same distance.

Irregular each R-R interval will be different.



3. Calculate rate

If Rhythm is regular
300/ R_R



300/3= 100

If the rhythm is irregular each R-R interval will be different, in that case the number of R waves in the 30 large squares (6 seconds) should be counted and multiply the number by 10 to get an approximate heart rate per minute.

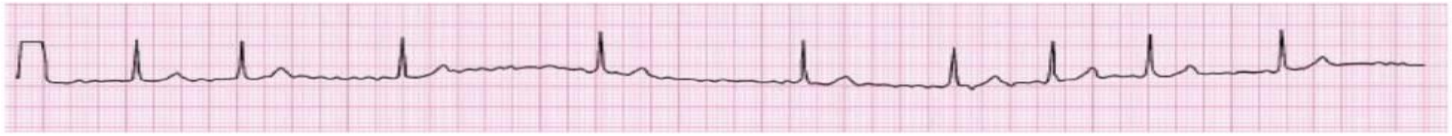


Fig. 7.5: Irregular R-R interval

9*10=90

4. Axis

Look at Lead I and Lead aVF for electrical axis of the heart. In both these leads, normally, QRS complex is upwards.

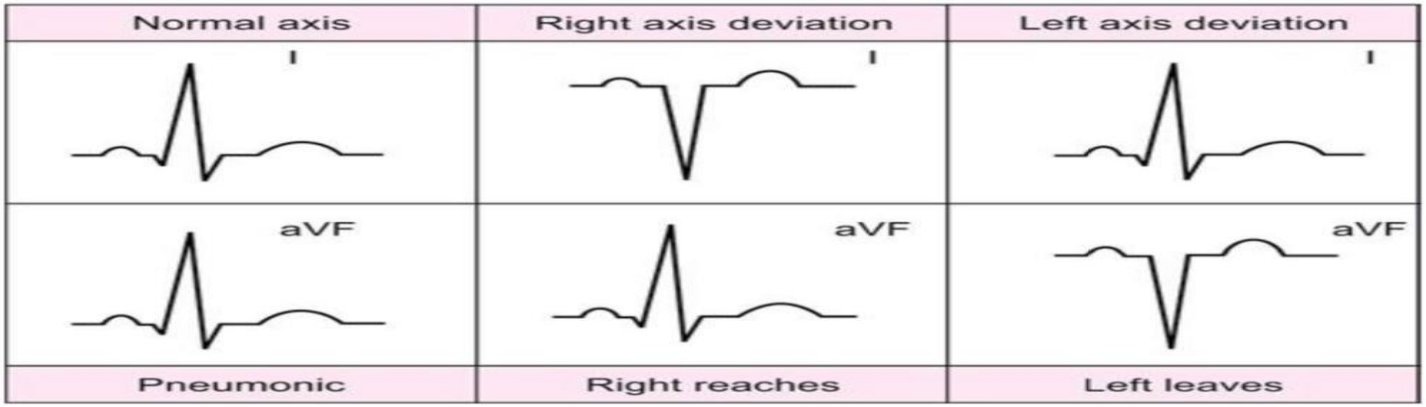


Fig. 7.6: Comparison of lead I with aVF to get the axis

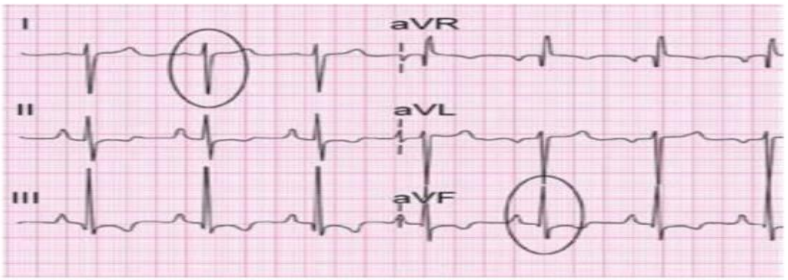


Fig. 7.7: Right axis deviation

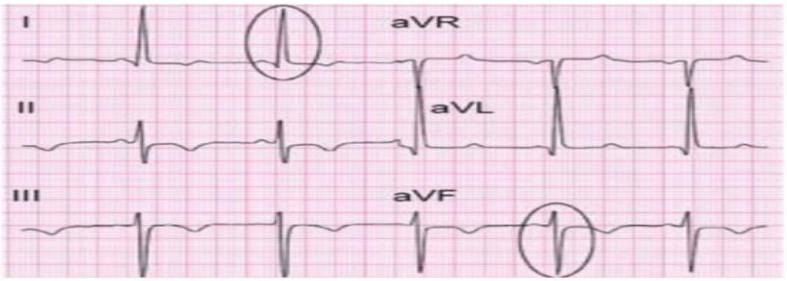


Fig. 7.8: Left axis deviation

Causes

Right axis deviation	*Left axis deviation*
Right ventricular hypertrophy	Left ventricular hypertrophy
Right bundle branch block	Left bundle branch block

5.

P wave : clinical importance

absent replaced by F wave (saw teeth) Atrial fibrillation

Small multiple Atrial flutter

Large Atrial enlagment

Inverted AV nodal pacemaker

PR segment and ST segment

Flat isoelectric

Elevated ischemia

Depressing myocardial infarction (MI)

QRS complex

Very tall ventricular enlargement

Very short pericardial effusion

Bizarre MI or bundle branch block BBB

T wave

Invered in ischemia

Peaked increase K

Flat decrease K

INTERVALS AND SEGMENTS OF ECG

‘P-R’ INTERVAL

It is the interval between the onset of ‘P’ wave & the onset of ‘Q’ wave.

it signifies the atrial depolarization & conduction of impulses through AV node. It shows the duration of conduction of the impulses from the SA node to ventricles through atrial muscle and AV node.

It is represented by the short isoelectric (zero voltage) period after the end of ‘P’ wave & onset of ‘Q’ wave. It denotes the time taken for the passage of depolarization within AV node.

The normal duration is 0.18 second & varies between 0.12 - 0.2 sec. If it is more than 0.2 second, signifies the delay in the conduction of impulse from SA node to the ventricles. Usually, the delay occurs in the AV node. So it is called= the AV nodal delay.

‘Q-T’ INTERVAL

the interval between the onset of ‘Q’ wave and the end of ‘T’ wave.

indicates the ventricular depolarization & ventricular repolarization, i.e. it signifies the electrical activity in ventricles. Duration--Between 0.4 and 0.42 second.

‘S-T’ SEGMENT

The time interval between the end of ‘S’ wave and the onset of ‘T’ wave is called ‘S-T’ segment. It is an isoelectric period.

Duration of ‘S-T’ Segment 0.08 second.

J Point

The point where ‘S-T’ segment starts is called ‘J’ point. It is the junction between the QRS complex and ‘S-T’ segment.

‘R-R’ INTERVAL

‘R-R’ interval is the time interval between two consecutive ‘R’ waves. signifies the duration of one cardiac cycle.

The normal duration of ‘R-R’ interval is 0.8 second.

Cardiovascular Adjustments during Exercise

During exercise, there is an increase in metabolic needs of body tissues, particularly the muscles. Various adjustments, which take place in the body, are aimed at

1.Supply of nutrients& oxygen to muscles &other tissues involved in exercise

2.Prevention of increase in body temperature.

In exercise, the heart rate, force of contraction, cardiac output and systolic blood pressure increase. However, the diastolic blood pressure is unaltered or decreased- because= the peripheral resistance is unaltered or decreased.

EFFECTS OF EXERCISE ON CARDIOVASCULAR SYSTEM

- ON BLOOD

Red blood cell count increases because of release of erythropoietin from juxtaglomerular apparatus due to hypoxia. The pH of blood decreases due to increased carbon dioxide content.

- ON BODY FLUIDS

More heat is produced during exercise and the thermoregulatory system is activated. This in turn, causes secretion of large amount of sweat leading to:

i. Fluid loss

ii. Reduced blood volume

iii. Hemoconcentration

iv. Sometimes, severe exercise leads to dehydration.

- ON HEART RATE

Heart rate increases during exercise. Even the thought of exercise orpreparation for exercise-because of impulses from cerebral cortex to medullary centers, which reduces vagal tone.

In moderate exercise, the heart rate increases to 180 beats/minute.

In severe muscular exercise it reaches 240 to 260 beats/minute. The increased heart rate during exercise is mainly vagal with drawal and increase in sympathetic tone.

7. ON BLOOD PRESSURE

During **moderate isotonic exercise**, systolic pressure is increased-due to increase in heart rate & stroke volume. Diastolic pressure is not altered because peripheral resistance is not affected during moderate exercise.

In **severe exercise involving isotonic muscular contraction**, the systolic pressure increases but the diastolic pressure decreases-- because of the decrease in peripheral resistance-due to vasodilatation caused by metabolites.

During **exercise involving isometric contraction**, the peripheral resistance increases. So, the diastolic pressure also increases along with systolic pressure.

Blood Pressure after Exercise

After exercise, blood pressure falls below the resting level- because of vasodilatation caused by metabolic end products accumulated in muscles during exercise.-- the pressure returns to resting level quickly as soon as the metabolic end products are removed from muscles.

CORONARY ARTERY DISEASE (CAD)

CORONARY ARTERY DISEASE (CAD)

heart disease that caused by inadequate blood supply to cardiac muscle due to occlusion of coronary artery, also called coronary heart disease.

Coronary Occlusion

means the partial or complete obstruction of coronary artery. The occlusion occurs because of atherosclerosis, a condition associated with deposition of cholesterol on the walls of the artery= this part of the arterial wall becomes fibrotic & it is called atherosclerotic plague.

The plague is made up of cholesterol, calcium &other substances from blood. Because of the atherosclerotic plague the lumen of the coronary artery becomes narrow. In severe conditions, the artery is completely occluded.

Smaller blood vessels are occluded by the thrombus or part of atherosclerotic plague detached from coronary artery. This thrombus or part of the plague is called embolus.

Myocardial Ischemia

is the reaction of a part of myocardium in response to hypoxia. Hypoxia develops when blood flow to a part of myocardium decreases severely due to occlusion of a coronary artery.

When the ischemia is mild due to obstruction of smaller blood vessel, the blood flow can be restored by rapid development of coronary collateral arteries.

Necrosis

refers to death of cells or tissues by injury or disease in a localized area. When coronary occlusion is severe involving larger blood vessels, the severe ischemia leads to necrosis of myocardium. Necrosis is irreversible.

Myocardial Infarction – Heart Attack

Myocardial infarction is the necrosis of myocardium caused by insufficient blood flow due to embolus, thrombus or vascular spasm.

It is also called heart attack. In myocardial fibrillation. Common symptoms of myocardial infarction are:

1. Cardiac pain
2. Nausea
3. Vomiting
4. Palpitations
5. Difficulty in breathing
6. Extreme weakness
7. Sweating
8. Anxiety.

Cardiac Pain – Angina Pectoris

Cardiac pain is the chest pain that is caused by myocardial ischemia. It is also called angina pectoris. It is the common manifestation of coronary artery disease. The pain starts beneath the sternum and radiates to the surface of left arm and left shoulder. The cardiac pain is called referred pain since it is felt over the body away from the heart. It is because, heart and left arm develop from the same dermatomal segment inembryo.

CEREBRAL CIRCULATION

Brain tissues need adequate blood supply continuously. Stoppage of blood flow for 5 seconds leads to unconsciousness, and for 5 minutes leads to irreparable damage to the brain cells.

STROKE

Stroke is the sudden death of neurons in localized area of brain due to inadequate blood supply. It is characterized by reversible or irreversible paralysis with other symptoms. Stroke is also called cardiovascular accident (CVA) or brain attack. Causes

1. Heart disease
2. Hypertension
3. High cholesterol in blood
4. High blood sugar – diabetes mellitus
5. Heavy smoking
6. Heavy alcohol consumption. Symptoms of stroke depend upon the area of brain that is damaged. Generally, stroke causes dizziness, loss of consciousness, coma or death.

Other features of stroke are:

1. Weakness
2. Numbness or paralysis particularly on one side of the body
3. Impairment of speech
4. Emotional disturbances
5. Loss of coordination
6. Loss of memory.

HEMORRHAGE

is the excess loss of blood due to the rupture of blood vessels.

TYPES AND CAUSES OF HEMORRHAGE

Hemorrhage occurs due to various reasons. Based on the cause, is classified into five categories:

1. Accidental hemorrhage
2. Capillary hemorrhage
3. Internal hemorrhage
4. Postpartum hemorrhage
5. Hemorrhage due to premature detachment of placenta.

EFFECTS OF HEMORRHAGE

Many effects are observed during and after hemorrhage. The effects are different in acute hemorrhage and chronic hemorrhage.

Acute Hemorrhage

Acute hemorrhage is the sudden loss of large quantity of blood. It occurs in conditions like accidents. Decreased blood volume in acute hemorrhage causes hypovolemic shock.

Chronic Hemorrhage

Chronic hemorrhage is the loss of blood either by internal or by external bleeding over a long period of time. Internal bleeding occurs in conditions like ulcer. External bleeding occurs in conditions like hemophilia and excess vaginal bleeding (menorrhagia). Chronic hemorrhage produces different types of effects such as anemia. produced by any disorder.

Circulatory shock

refers to the shock developed by inadequate blood flow throughout the body. It is a lifethreatening condition and if the affected person is not treated immediately it may result in death.

MANIFESTATIONS OF SHOCK

The characteristic feature of all types of circulatory shock is the insufficient blood flow to the tissues particularly the brain. The blood flow decreases due to the reduction in cardiac output. Following are the manifestations of circulatory shock:

1. When cardiac output reduces, the arterial blood pressure drops down
2. Low blood pressure produces reflex tachycardia and reflex vasoconstriction
3. The pulse also becomes feeble
4. The velocity of the blood flow decreases resulting in stagnant hypoxia
5. Skin becomes pale and cold
6. Cyanosis in many parts of the body, particularly ear lobes and fingertips
8. Decrease in renal blood flow, GFR and urinary output
9. Acceleration of metabolic activities of myocardium resulting in accumulation of excess lactic acid and acidosis
11. Acidosis decreases the efficiency of myocardium leading to further reduction in cardiac output
12. So, the blood flow to vital organs is severely affected
13. The lack of blood flow to the brain tissues produces ischemia resulting in fainting and irreparable damage to the brain.
14. Finally the damage of brain tissues and cardiac arrest kill the victim.

HEART FAILURE

Heart failure or cardiac failure is the condition in which the heart looses the ability to pump sufficient amount of blood to all parts of the body.

Heart failure may involve left ventricle or right ventricle or both. It may be acute or chronic.

Acute Heart Failure

refers to sudden & rapid onset of signs and symptoms of abnormal heart functions. Its symptoms are severe initially. However, the symptoms last for a very short-time and the condition improves rapidly.

Chronic Heart Failure

is the heart failure that is characterized by the symptoms that appear slowly over a period of time and become worst gradually.

Congestive Heart Failure

It is a general term used to describe heart failure resulting in accumulation of fluid in lungs and other tissues. When heart is not able to pump blood through aorta, the blood remains in heart. It results in dilatation of the chambers and accumulation of blood in veins (vascular congestion). This condition is also manifested by fluid retention and pulmonary edema.

CAUSES OF HEART FAILURE

1. Coronary artery disease
2. Defective heart valves
3. Arrhythmia (abnormal heartbeat)
4. Cardiac muscle disease such as cardiomyopathy
5. Hypertension
6. Congenital heart disease
7. Diabetes
8. Hyperthyroidism
9. Anemia
10. Lung disorders
11. Inflammation of cardiac muscle (myocarditis) due to viral infection, drugs, alcohol, etc.

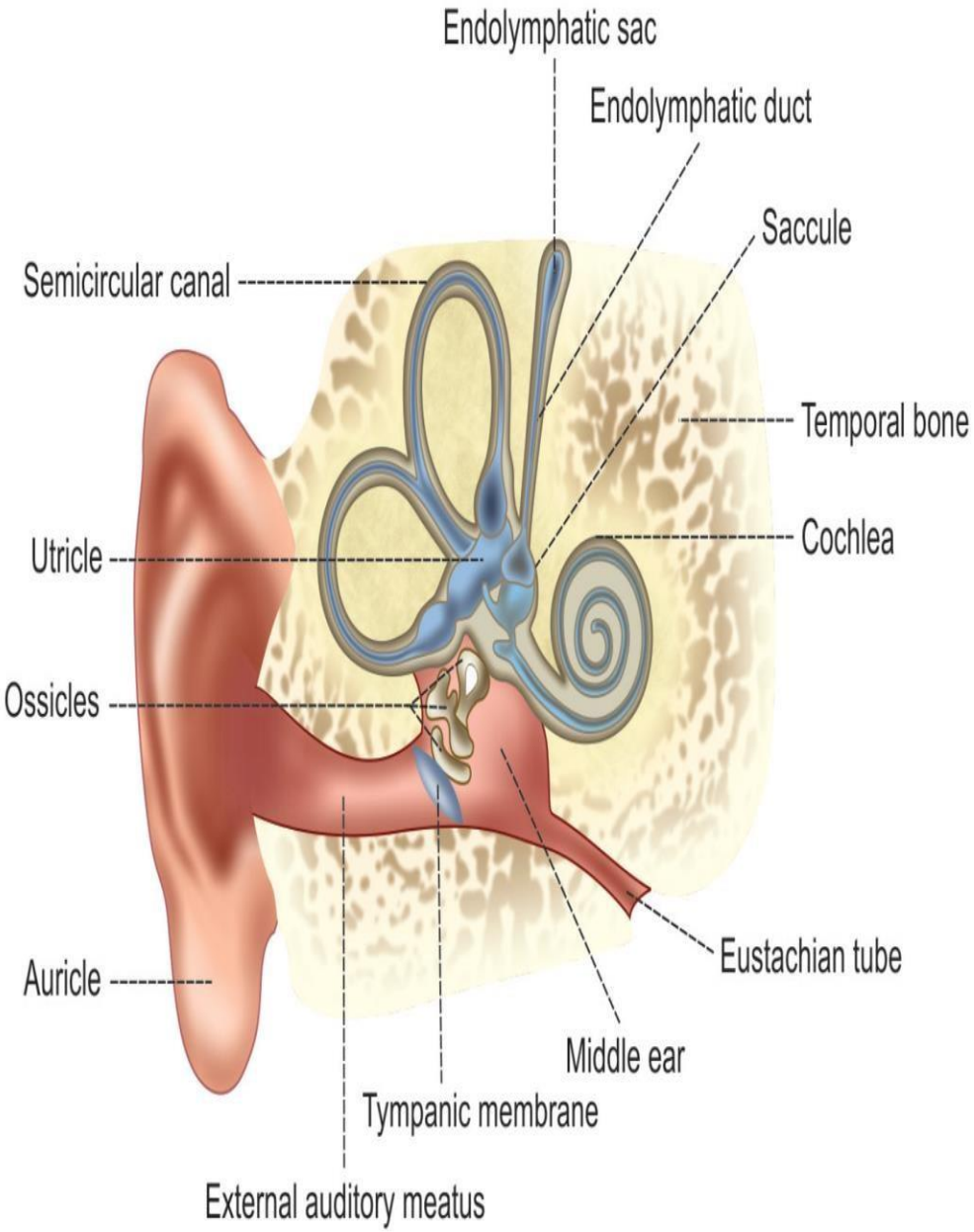
Signs and Symptoms of Chronic Heart Failure

1. Fatigue and weakness
2. Rapid and irregular heartbeat
3. Shortness of breathing
4. Fluid retention and weight gain
5. Loss of appetite, nausea and vomiting
6. Cough
8. Chest pain, if developed by myocardial infarction.

Signs and Symptoms of Acute Heart Failure

The signs and symptoms of acute heart failure may be same as chronic heart failure. But the signs and symptoms appear suddenly and severely. When heart starts to fail suddenly, the fluid accumulates in lungs causing pulmonary edema. It results in sudden and severe shortness of breath, cough with pink, foamy mucus and heart palpitations. It may lead to sudden death, if not attended immediately.

He



The ear consists of 3 parts:

- ✓ External ear,
- ✓ middle ear &
- ✓ internal ear.

external ear is formed by 2 parts:

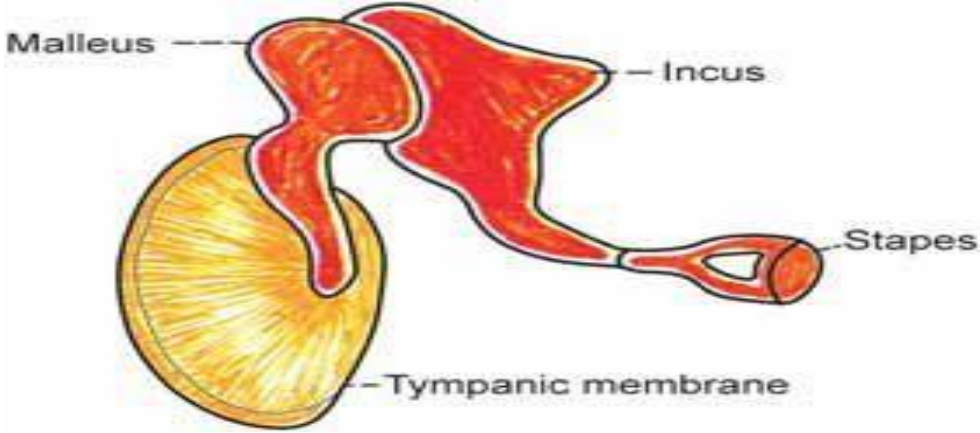
1. Auricle or pinna
2. External auditory meatus.

MIDDLE EAR

or tympanic cavity is situated

within the temporal bone.,separated from external
Auditory meatus by a thin
semitransparent
membrane called tympanic membrane

Middle ear consists of :



1. Auditory ossicles: are 3 miniature bones, arranged in form of a chain extending across the middle ear from tympanic membrane to oval window. auditory ossicles are:

a. Malleus, called hammer. attached to the tympanic membrane.

b. Incus also known as anvil.

c. Stapes. called stirrup smallest bone present in the body.

2. Auditory muscles: 2 skeletal muscles are attached to the ossicles:

a. Tensor tympani

b. Stapedius.

3. Eustachian tube. or auditory tube connects the middle ear with posterior part of nose and forms the passage of air between middle ear and atmosphere. So, the pressure on both sides of tympanic membrane is equalized.

INTERNAL EAR

or labyrinth is a membranous structure, consists of The sense organ for hearing is the cochlea & the sense organ for equilibrium is the vestibular apparatus.

COCHLEA

is a coiled structure like a snail's shell , consists of 2 structures:

1. Central conical axis formed by spongy bone called modiolus
2. Bony spiral canal, which winds around the modiolus.

- ❑ COMPARTMENTS OF COCHLEA

Two membranous partitions called basilar membrane & vestibular membrane divide the spiral canal of cochlea into 3 compartments.

The compartments of spiral canal of cochlea are:

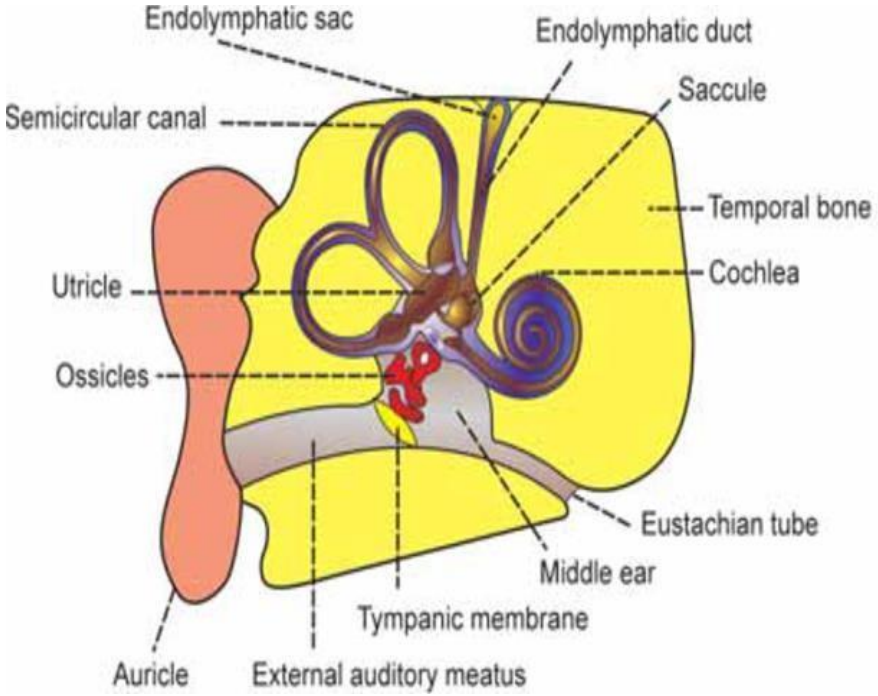
i. Scala vestibuli

ii. Scala tympani

iii. Scala media. cochlear duct.

All the 3 compartments are filled with fluid. Scala vestibuli & scala tympani contain perilymph. The scala media is filled with endolymph.

The sensory part of cochlea called organ of Corti is situated on the upper surface of basilar membrane



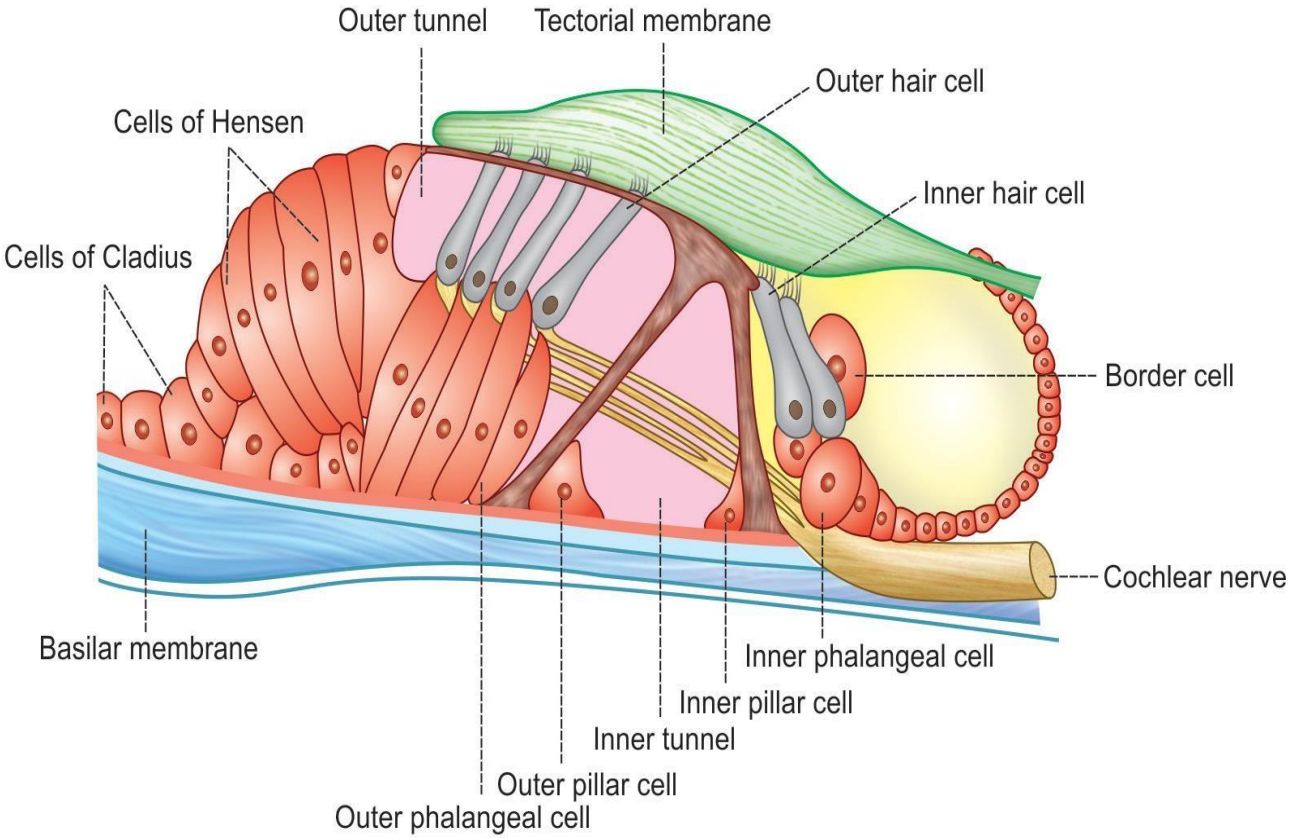
ORGAN OF CORTI

is the receptor organ for hearing. is the neuroepithelial structure in cochlea. extends through out the cochlear duct, except for a short distance on either end. The roof of the organ of Corti is formed by gelatinous tectorial membrane.

Structure

made up of sensory elements, called hair cells &various supporting cells. All the cells of organ of Corti are arranged in order from center towards periphery of the cochlea:

1. Border cells
2. Inner hair cells
3. Inner phalangeal cells
4. Inner pillar cells
5. Outer pillar cells
6. Outer phalangeal cells
7. Outer hair cells
8. Cells of Hensen
9. Cells of Claudius
10. Tectorial membrane & lamina reticularis.



Hair Cells of Organ of Corti

are the receptors of the auditory sensation. The hair cells are of 2 types, outer hair cells and inner hair cells.

The surface of the hair cells bears a cuticular plate and a number of short stiff hairs which are called stereocilia. Each hair cell has about100 stereocilia. One of the stereocilia is larger & it is called kinocilium. The stereocilia are in contact with the tectorial membrane. Sensory nerve fibers are distributed around thehair cells.

The sound waves travel through the external auditory meatus & produce vibrations in the tympanic membrane. The vibrations from tympanic membrane travel through malleus and incus and reach the stapes resulting in the movement of stapes.

The movements of stapes produce vibrations in the fluids of cochlea, which stimulate the hair cells in the organ of Corti. =, causes the generation of action potential (auditory impulses) in the auditory nerve fibers. When the auditory impulses reach the cerebral cortex, the perception of hearing occurs.

Role of External ear

External ear directs the sound waves towards the tympanic membrane. The sound waves produce pressure changes over the surface of tympanic membrane.

”

Role of Middle Ear

„Role of Tympanic membrane

Due to the pressure changes produced by sound waves, the tympanic membrane vibrates, i.e. it moves in and out of middle ear. Thus, the tympanic membrane acts as a resonator that produces the vibration of sound.

ROLE OF AUDITORY OSSICLES

The vibrations set up in tympanic membrane are transmitted through the malleus and incus and reach the stapes, causing to and fro movement of stapes against oval window and against the perilymph present in scala vestibuli of cochlea.

Impedance Matching

is the process, by which the tympanic membrane & auditory ossicles convert the sound energy into the mechanical vibrations in the fluid of internal ear with minimum loss of energy by matching the impedance offered by the fluid.

Significance of impedance matching

Impedance matching is the most important function of middle ear. Because of impedance matching the sound waves (stimuli) are transmitted to cochlea with minimum loss of intensity. Without impedance matching conductive deafness occurs.

ROLE OF EUSTACHIAN TUBE

is not concerned with hearing directly. it is responsible for equalizing the pressure on either side of tympanic membrane.

ROLE OF INNER EAR

- ✓ **„TRAVELING WAVE**

The movement of stapes against oval window causes movement of perilymph in scala vestibuli. The fluid does not move all the way from oval window toward round window through the helicotrema. It immediately hits the vestibular membrane near oval window and displaces the fluid in scala media.

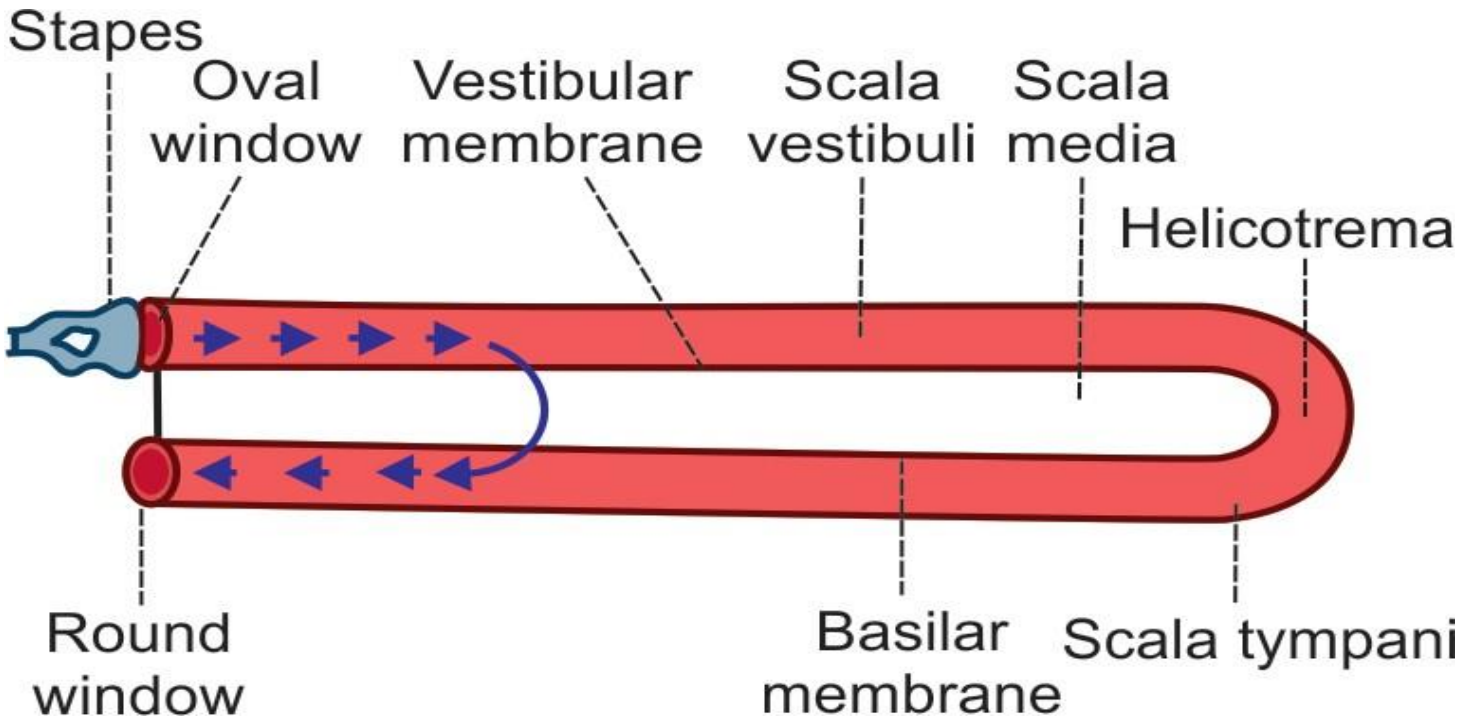
This causes bulging of basal portion of basilar membrane towards scala tympani.

The elastic tension developed in the bulged portion of basilar membrane initiates a travelling wave- travels along basilar membrane towards the helicotrema like that of arterial pulse wave.

EXCITATION OF HAIR CELLS

The stereocilia of hair cells in organ of Corti are embedded in tectorial membrane. When the traveling wave produces vibration of basilar membrane, all the structures move as a single unit. It causes movements of stereocilia leading to excitement of hair cells and generation of receptor potential.

Diagrammatic representation of
cochlea. The arrows show displacement of fluid.



ELECTRICAL EVENTS DURING PROCESS OF HEARING

- ✓ „**SOUND TRANSDUCTION**

Sound transduction is a type of sensory transduction in the hair cell (receptor) by which the energy (movement of cilia in hair cell) caused by sound is converted into action potentials in the auditory nerve fiber.

”

- ✓ **RECEPTOR POTENTIAL OR COCHLEAR MICROPHONIC POTENTIAL**

Receptor potential or cochlear microphonic potential is the mild depolarization that is developed in the hair cells of cochlea when sound waves are transmitted to internal ear. Receptor potential in the hair cells causes generation of action potential in auditory nerve fibers.

The resting membrane potential in hair cells is about – 60 mV.

The sensory transduction mechanism in cochlear receptor cells is different from the mechanism in other sensory receptors.

❑ PROPERTIES OF SOUND

Sound has two basic properties:

1. The pitch which depends upon the frequency of sound waves. Frequency of sound is expressed in hertz.

The frequency of sound audible to human ear lies between 20 and 20,000 Hz or cycles/second. The range of greatest sensitivity lies between 2,000 &3,000 Hz (cycles/second).

2. The loudness or intensity which depends upon the amplitude of sound waves. It is expressed in decibel (dB). The threshold intensity of sound wave is not constant. It varies in accordance to the frequency of the sound.

APPRECIATION OF PITCH OF THE SOUND – THEORIES OF HEARING

to explain the mechanism by which the pitch of the sound is appreciated. The accepted theories are:

1. Place Theory

According to this theory, the nerve fibers from different places of organ of Corti on basilar membrane give response to sounds of different frequency. Accordingly, the corresponding nerve fiber from organ of Corti gives information to the brain regarding the portion of organ of Corti that is stimulated.

2. Traveling Wave Theory

Appreciation of loudness of sound

depends upon the activities of auditory nerve fibers.

When the loudness of sound increases, it produces longer vibrations which spread over longer area of basilar membrane. This activates large number of hair cells and recruits more number of auditory nerve fibers. So, the frequency of action potential is also increased.

„LOCALIZATION OF SOUND

Sound localization is the ability to detect the source from where the sound is produced or the direction through which the sound wave is traveling. It is important for survival and helps to protect us from moving objects such as vehicles. Cerebral cortex and medial geniculate body are responsible for localization of sound.

AUDITORY DEFECTS

The auditory defects may be either partial or complete, are of two types:

„1. CONDUCTION DEAFNESS

occurs due to impairment in the transmission of sound waves in external ear or middle ear. Causes of Conduction Deafness

i. Obstruction of external auditory meatus with dry wax or foreign bodies.

ii. Thickening of tympanic membrane due to infection.

iii. Perforation of tympanic membrane due to inequality of pressure on either side.

iv. Inflammation of middle ear (otitis media).

v. Fixation of footplate of stapes against oval window (otosclerosis).

„2. NERVE DEAFNESS

is caused by damage of any structure in cochlea such as hair cell, organ of Corti, basilar membrane or cochlear duct or the lesion in auditory pathway. Causes of Nerve Deafness

i. Degeneration of hair cells.

ii. Damage of cochlea by prolonged exposure to loud noise.

iii. Tumoraffecting VIII cranial nerve.

AUDITORY PATHWAY

The fibers of auditory pathway pass through cochlear division of vestibulocochlear nerve (VIII cranial nerve). It is also known as auditory nerve.

RECEPTORS

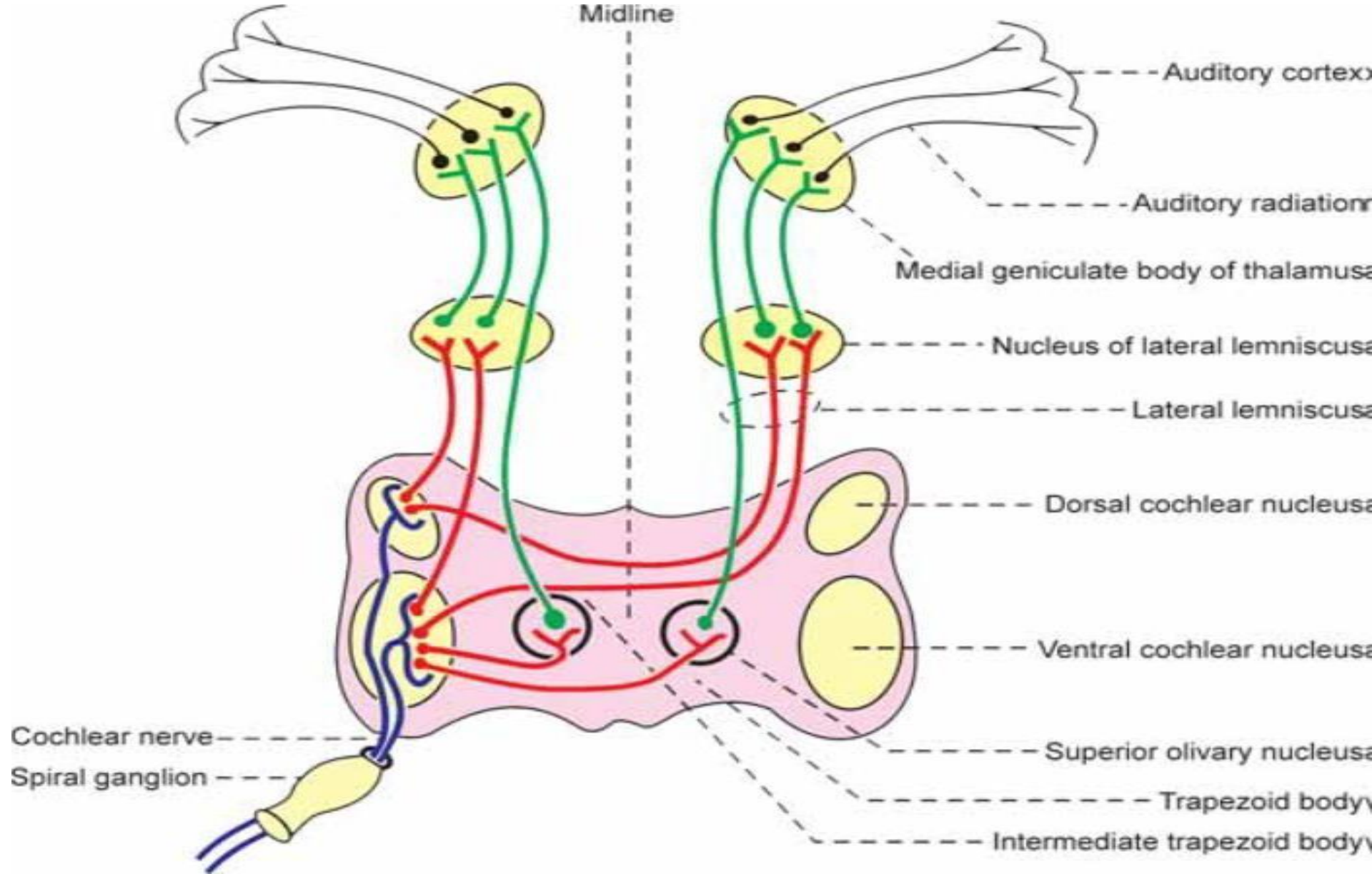
The outer & inner hair cells in organ of Corti are the receptors auditory sensation. The afferent nerve fibers which innervate hair cells form the auditory nerve.

FIRST ORDER NEURONS

The first order neurons of auditory pathway are the bipolar cells of spiral ganglion situated in the modiolus of cochlea.

The dendrites of bipolar cells distributed around the hair cells of organ of Corti. Their axons leave ear as cochlear nerve fibers & enter medulla oblongata. Immediately after entering, the fibers divide into 2 groups which end on ventral & dorsal cochlear nuclei of the same side in medulla oblongata.

AUDITORY PATHWAY



SECOND ORDER NEURONS

The neurons of dorsal and ventral cochlear nuclei in the medulla oblongata form the second order neurons of auditory pathway. The axons of the second order neurons run in four different directions.

THIRD ORDER NEURONS

are in the superior olivary nuclei and nucleus of lateral lemniscus. The fibers from here end in medial geniculate body which forms the subcortical auditory center. Fibers from medial geniculate body go to the temporal cortex, via internal capsule as auditory radiation.

CORTICAL AUDITORY CENTERS

The cortical auditory centers are in the temporal lobe of cerebral cortex. The auditory areas are area 41, area 42 and Wernicke's area.

Areas 41 and 42 are the primary auditory areas which are concerned with the perception of auditory impulses. Wernicke's area is responsible for the analysis and interpretation of sound with the help of auditopsychic area.

APPLIED PHYSIOLOGY – EFFECT OFLESION

1. Lesion of cochlear nerve causes deafness
2. Unilateral lesion of auditory pathway above the level of cochlear nuclei causes diminished hearing
3. Degeneration of hair cells in organ of Corti leads to gradual loss of hearing that is common in old age.
4. Lesion in superior olivary nucleus results in poor localization of sound

.

Lec. 1

Collage of dentistry - 2nd class
Tikrit university
Suggested books and resources:
Medical Physiology 4th edition (Guyton and Hall)
Essential of physiology for dental students (K Sembulingam &prema sembulinam

General Physiology

Physiology: The science that is concerned with the function of the living organism and its component parts, includes all its chemical and physical processes.

The goal of physiology is to explain the physical and chemical factors that are responsible for the origin development and progression of life.

In human physiology we attempt to explain the specific characteristics and mechanisms of the human body that make it living being.

Basic properties of life

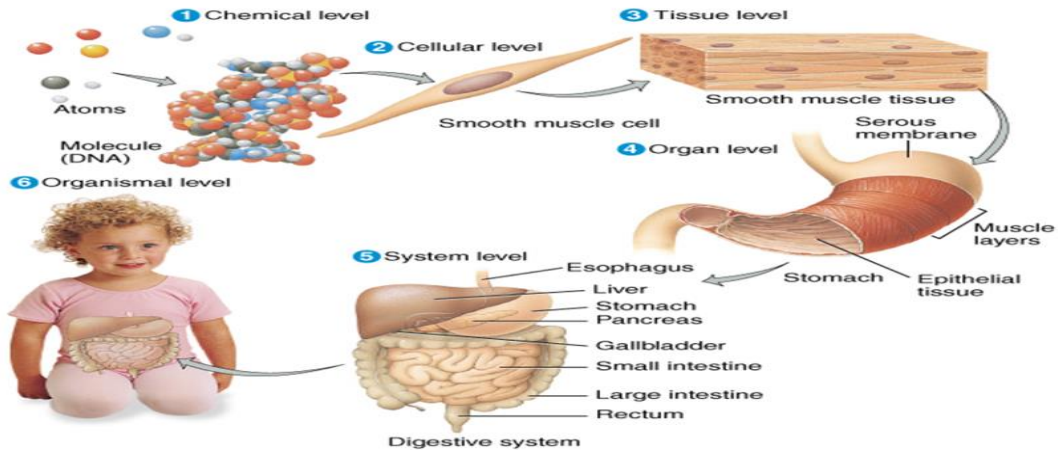
The seven properties of life: 1) Cellular organization, 2) Reproduction, 3) Metabolism, 4) Homeostasis, 5) Heredity, 6) Responsiveness, 7) Growth and development.

Function organization of the human body

The basic living unit of the body is the cell. All cells use oxygen as one of the major substances from which energy is divided; the oxygen combines with carbohydrates, fat or protein to release the energy required for cell function.

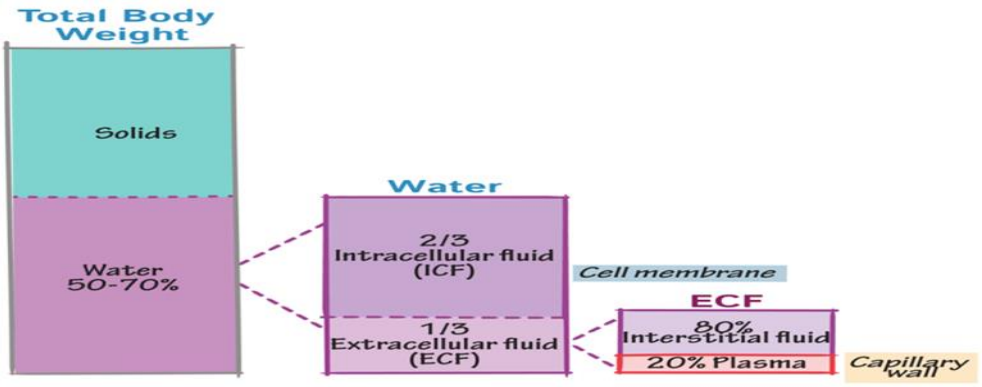
Levels of Organization

Atoms → molecules → macromolecules → organelles → cells → tissues→ organs → organ systems



Body fluids: About 60% of the adult human body is fluid, most of this fluid is inside the cells and is called intracellular fluid, about one-third of it is in the spaces outside the cells and is called extracellular fluid. This E.C.F is in constant motion throughout the body. It is rapidly mixed by the blood and the tissue fluids, and E.C.F are the ions and nutrients needed by the cells for maintenance of cellular function. Therefore all cells live in essentially the

same environment, that is the E.C.F, and for this reason is often called the internal environment of the body.



Although there is a constant change between E.C.F. and I.C.F., but there is a significant difference between the constituents of the two fluids.

The E.C.F. contains large amounts of sodium, chloride and bicarbonate ions, plus nutrients for cells, such as oxygen, glucose, fatty acids and amino acids …etc.

The I.C.F. differs significantly from the E.C.F. particularly, it contains large amount of potassium, magnesium and phosphate ions instead of the sodium and chloride found in E.C.F.

No		ICF	ECF
1	volume	40% 2:	20% 1
2	Chief kation	Potasium K^{+} Po4- Pln	Sodium Na^{++} Cl^{-} $HCO3^{-}$
3	PH	More acidic	Less acidic
4	Osmotic conc.	290mosm	290mosm

Homeostasis:

The term of homeostasis mean maintenance of state or constant conditions in the internal environment. Essentially all of the organs and tissues of the body perform functions. That helps to maintain constant conditions.

The process of homeostasis can be understood through the followings:

1. The E.C.F. is transported through all parts of the body in two different stages. The first entails movement of blood around the circulatory system & the second , movement of fluid between the blood capillaries and the cells. All the blood in the circulation transverses the entire of the circulation in an average once each minute when the body is at rest and as six times during activity. In general , no cell is located more than 25- 50 micrometers from a capillary.

2. Origin of nutrients in the E.C.F. :
   a. Respiratory system: the blood passes through the body and also flows through the lungs. The blood picks up oxygen in the alveoli, thus acquiring the oxygen needed by the cells.

   The membrane between the alveoli and the lumen of the pulmonary capillaries is only 0.4-2.0 micrometers in thickness.

   b. Gastrointestinal track: here, different dissolved nutrients including carbohydrates, fatty acids, amino acids and others are absorbed into the E.C.F.

      The liver changes the chemical composition of many of these to more usable forms.

   c. The muscloskeletal provides motility and energy.

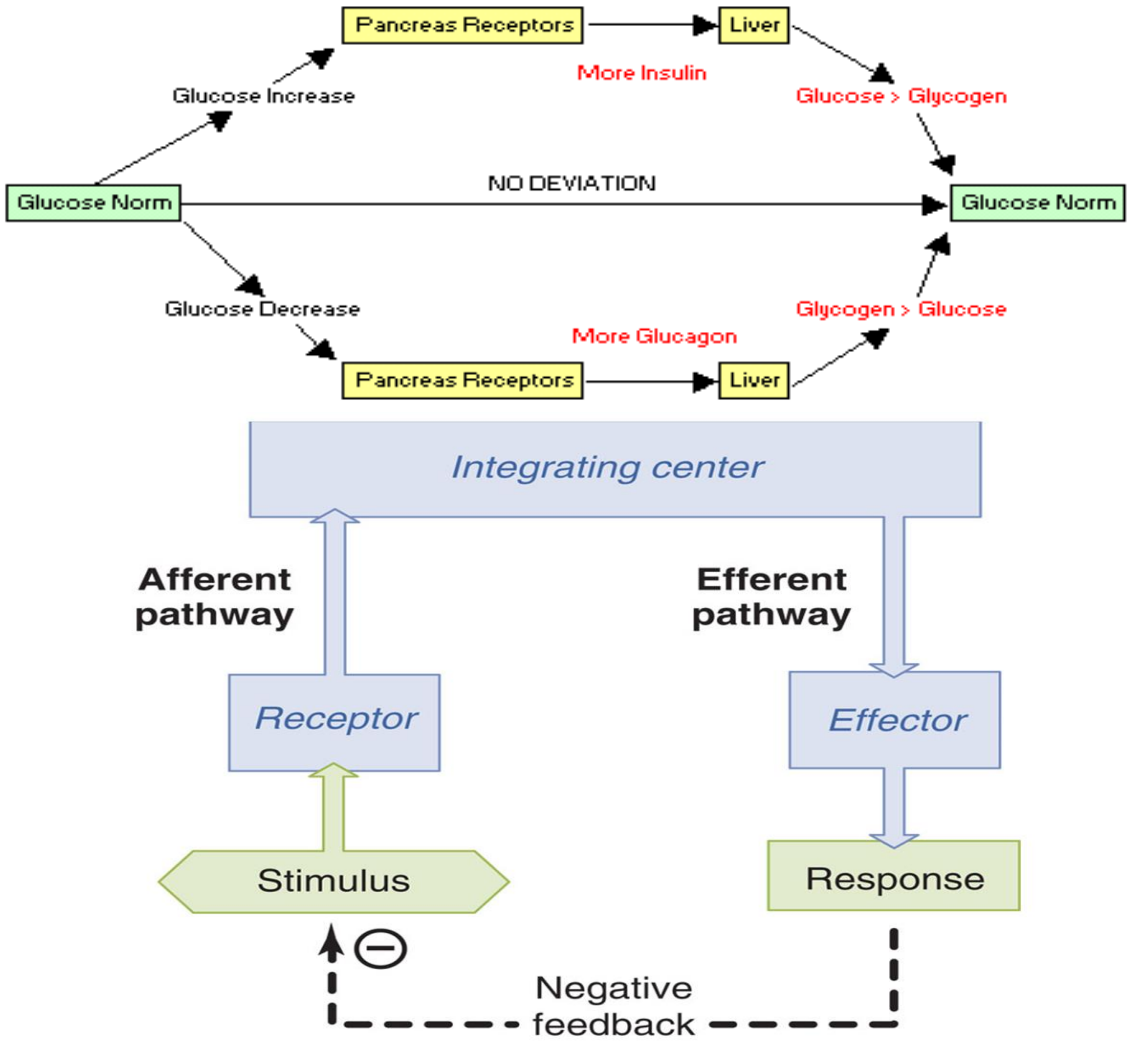
3. Removal of metabolic end products:
   a. Removal of carbon dioxide by the lungs.

   b. Kidney, regulation of blood fluid and excretion of excess substances.

4. Regulation of body functions:
   a. Nervous system: The nervous system is composed of three major parts:
      i. Sensory input portion.
      ii. Central nerve system.
      iii. Motor output portion.
   b. Hormonal system: Located in the body, are eight major endocrine glands that secrete chemical substances called hormones. Hormones are transported in the E.C.F. to all parts of the body to help regulate cellular function.
   c. Reproduction: Help to maintain static condition by generating new beings to take the phase of those that are dying.

Homeostasis: in a general sense refers to stability, balance or equilibrium. It is the body's attempt to maintain a constant internal environment. Maintaining a stable internal environment requires constant monitoring and adjustments as conditions change. This adjusting of physiological systems within the body is called homeostatic regulation.

Homeostatic regulation involves three parts or mechanisms: 1) the receptor, 2) the control center and 3) the effector. The receptor receives information that something in the environment is changing. The control center or integration center receives and processes information from the receptor. And lastly, the effector responds to the commands of the control center by either opposing or enhancing the stimulus. This is an ongoing process that continually works to restore and maintain homeostasis. For example, A) in regulating body temperature there are temperature receptors in the skin, which communicate information to the brain, which is the control center, and the effector is our blood vessels and sweat glands. Because the internal and external environment of the body are constantly changing and adjustments must be made continuously to stay at or near the set point, homeostasis can be thought of as a synthetic equilibrium. B) Glucose levels within the blood are constantly monitored by a sensor, the islets of Langerhans in the pancreas. When levels increase, the islets secrete the hormone insulin, which stimulates the uptake of blood glucose into muscles, liver, and adipose tissue. The islets are, in this case, the sensor and the integrating center. The muscles, liver, and adipose cells are the effectors, taking up glucose to control the levels. The muscles and liver can convert the glucose into the polysaccharide glycogen; adipose cells can convert glucose into fat. These actions lower the blood glucose and help to store energy in forms that the body can use later.



❖In emergencies, adrenaline is released by the body to override the homeostatic control of glucose. This is done to promote the breakdown of glycogen into glucose to be used in the emergency. These emergencies are often known as 'fight or flight reactions'. Adrenaline is secreted by the adrenal glands. The secretion of it leads to increased metabolism, breathing and heart rate. Once the emergency is over, and adrenaline levels drop, the homeostatic controls are once again back in place.

Feedback mechanisms regulate biological systems:

♦**Negative Feedback**: In negative feedback systems, the output shuts off the original stimulus . Most control systems of the body the acting stimulus. examples :

- Increased CO2 causes increased pulmonary ventilation, which decreases CO2.

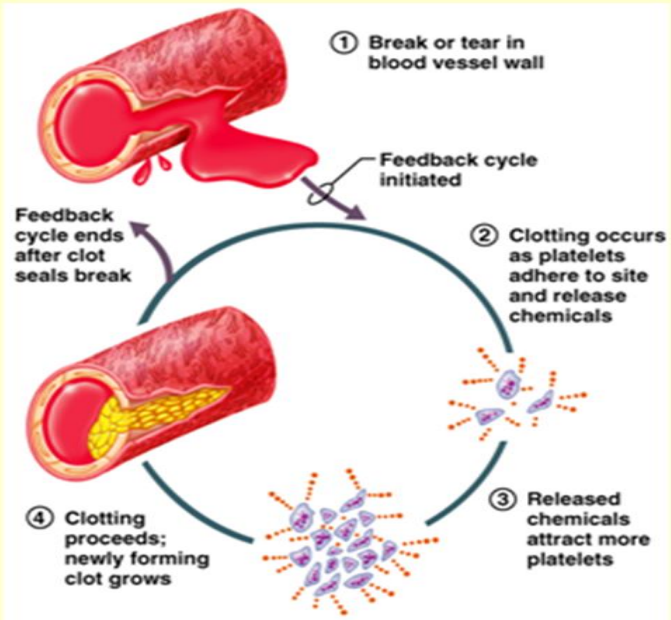
- Decreased arterial pressure activates the baroreceptor system which acts increase heart rate and arterial constriction, which increases arterial pressure
- thyroid stimulating hormone (TSH) released from pituitary gland stimulates thyroid gland which in turn secretes thyroxine. When thyroxin level increases in blood, it inhibits the secretion of TSH from pituitary so that, the secretion of thyroxine from thyroid gland decreases . On the other hand, if thyroxin secretion is less, it induces pituitary gland to release TSH. Now, TSH stimulates thyroid gland to secrete thyroxine
- Regulation of blood glucose levels (explained above)

The negative feedback system acts to maintain homeostasis

♦Positive Feedback : In positive feedback systems, the output enhances or overstates the original stimulus.in a positive feedback control system, a stimulus causes a responses that promotes the stimulus. In general, positive feedback systems lead to instability and therefore are not utilized as often as negative feedback systems. Examples:

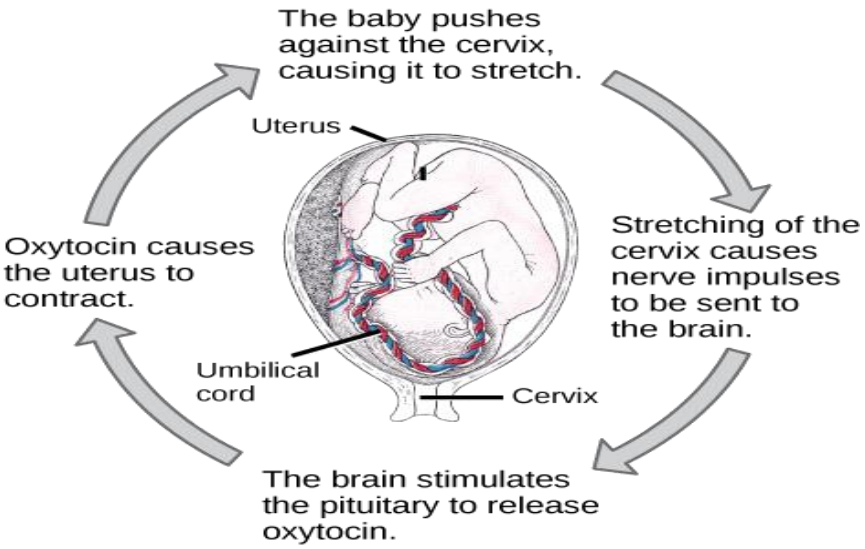
❖Regulation of blood clotting. A rupture in a blood vessel initiates a clot formation, and enzyme activation within the clot causes other enzymes in the blood to clot.

The cycle continues until the vessel in plugged and bleeding stops



❖Positive Feedback during Childbirth

- Stretch receptors in walls of uterus send signals to the brain
- Brain induces release of hormone (oxytocin) into bloodstream
- Uterine smooth muscle contracts more forcefully
- More stretch, more hormone, more contraction etc.
- Cycle ends with birth of the baby & decrease in stretch



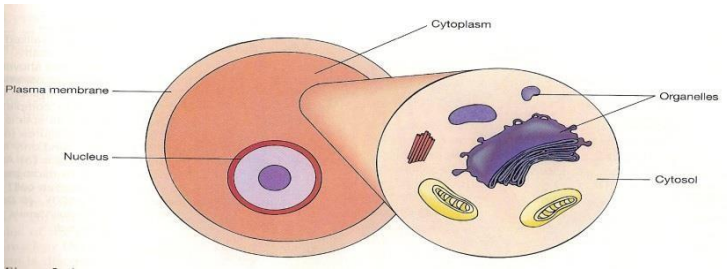
General Physiology Lect. 1

Function organization of the human body

The goal of physiology is to explain the physical and chemical factors that are responsible for the origin development and progression of life. Each life from the very simple virus up to the latest tree or the complicated human being has its own functional characteristics. Therefore, the vast field of physiology can be divided into viral physiology, plant physiology, human physiology and many more subdivisions

In human physiology we attempt to explain the specific characteristics and mechanisms of the human body that make it living being.

The basic living unit of the body is the cell. All cells use oxygen as one of the major substances from which energy is divided; the oxygen combines with carbohydrates, fat or protein to release the energy required for cell function.



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C. ***Reproduction:***

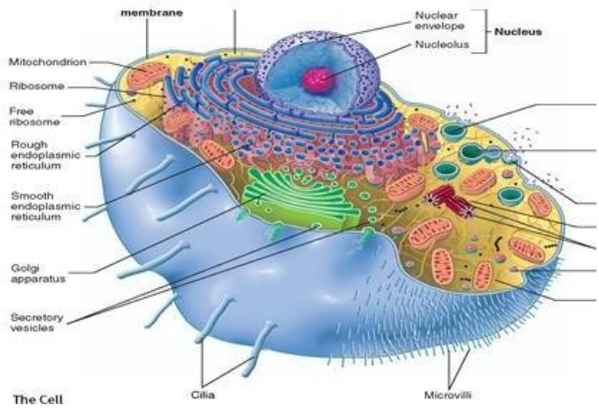
Help to maintain static condition by generating new beings to take the phase of those that are dying.

The human body has literally thousands of control systems in it. The most important of these are genetic control systems that operate in all cells to control I.C. function as well as E.C. function.

General physiology Lec. 2

Cell

Cell is defined as the structural and functional unit of the living body because it has all the characteristics of life



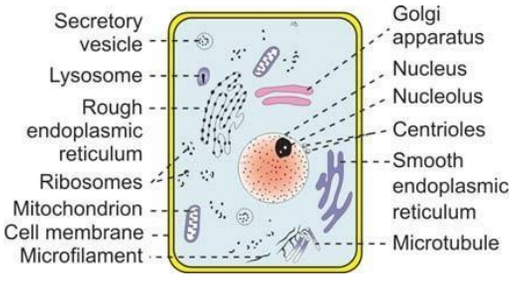
The cell membrane is a protective sheath that envelops the cell body. It separates the fluid outside the cell called extracellular fluid (ECF) and the fluid inside the cell called intracellular fluid (ICF). It is a semipermeable membrane and allows free exchange of certain substances between ECF and ICF

The cell membrane is composed of three types of substances

1. Proteins (55%)
2. Lipids (40%)
3. Carbohydrates (5%).

Each cell is formed by a cell body and a cell membrane or plasma membrane that covers the cell body. The important parts of the cell are

a. Cell membrane
b. Nucleus
c. Cytoplasm with organelles



The cell membrane is a unit membrane having the 'fluid mosaic model' i.e., the membrane is a fluid with mosaic of proteins (mosaic means pattern formed by arrangement of different colored pieces of stone, tile, glass or other such materials , lipids and carbohydrates. The electron microscopic study reveals three layers in the cell membrane namely, one electron lucent lipid layer in the center and two electron dense layers on either side of the central layer. Carbohydrate molecules are found on the surface of the cell membrane.

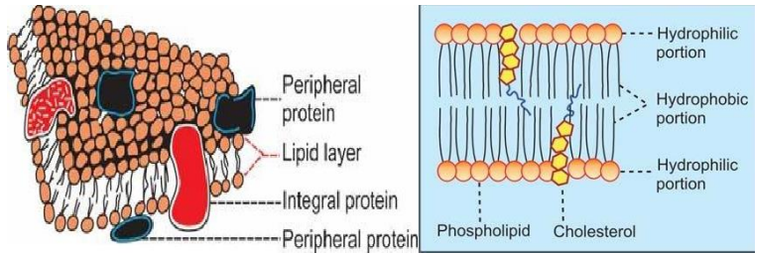
FUNCTIONS OF CELL MEMBRANE

1. Protective function: Cell membrane protects the cytoplasm and the organelles present in the cytoplasm.
2. Selective permeability: Cell membrane acts as a semipermeable membrane which allows only some substances to pass through it and acts as a barrier for other substances.
3. Absorptive function: Nutrients are absorbed into the cell through the cell membrane.
4. Excretory function: Metabolites and other waste products from the cell are excreted out through the cell membrane.
5. Exchange of gases: Oxygen enters the cell from the blood and carbon dioxide leaves the cell and enters the blood through the cell membrane.
6. Maintenance of shape and size of the cell: Cell membrane is responsible for the maintenance of shape and size of the cell.

Lipid Layer of Cell Membrane

It is a bilayered structure formed by a thin film of lipids. It is fluid in nature and the portions of the membrane along with the dissolved substances move to all areas of the cell membrane. The major lipids are:

a. Phospholipids
b. Cholesterol



Functions of lipid layer

The lipid layer is semi permeable in nature and allows only the fat soluble substances like oxygen, carbon dioxide and alcohol to pass through it. It does not allow the water soluble materials like glucose, urea and electrolytes to pass through it.

Protein Layers of the Cell Membrane

The protein layers of the cell membrane are the electron dense layers situated on either side of the central lipid layer. The protein substances present in these layers are mostly glycoproteins. These protein molecules are classified into two categories:

a. Integral proteins
b. Peripheral proteins.

Functions of protein layers

Functionally, the proteins in the cell membrane exist in different forms such as integral proteins, channel proteins, carrier proteins etc.

1. *Integral proteins* provide structural integrity of the cell membrane
2. *Channel proteins* provide route for diffusion of water soluble substances like glucose and electrolytes
3. *Carrier proteins* help in transport of substances across the cell membrane
4. *Receptor proteins* serve as receptor sites for hormones and neurotransmitters
5. *Enzymes:* some of the protein molecules form the enzymes which control

chemical reactions within the cell membrane

6. *Antigens:* Some proteins act as antigens and induce the process of antibody formation.

Carbohydrate of the Cell Membrane

Carbohydrate molecules form a thin loose covering over the entire surface of the cell membrane called glycocalyx. Some carbohydrate molecules are attached with proteins and form glycoproteins and some are attached with lipids and form glycolipids.

Functions of carbohydrates

1. The carbohydrate molecules are negatively charged and do not permit the negatively charged substances to move in and out of the cell.
2. The glycocalyx from the neighboring cells helps in the tight fixation of cells with one another.
3. Some of the carbohydrate molecules form the receptors for some hormones.

CYTOPLASM

The cytoplasm is the fluid present inside the cell. It contains a clear liquid portion called cytosol which contains various substances like proteins, carbohydrates, lipids and electrolytes. Apart from these substances, many organelles are also present in cytoplasm. The cytoplasm is distributed as peripheral ectoplasm just beneath the cell membrane and inner endoplasm between the ectoplasm and the nucleus.

ORGANELLES IN CYTOPLASM

All the cells in the body contain some common structures called organelles in the cytoplasm. Some organelles are bound by limiting membrane and others do not have limiting membrane .

1. ENDOPLASMIC RETICULUM

Endoplasmic reticulum is made up of tubules and microsomal vesicles. These structures form an interconnected network which acts as the link between the organelles and cell membrane.

The endoplasmic reticulum is of two types namely, rough endoplasmic reticulum and smooth endoplasmic reticulum.

Functions of rough endoplasmic reticulum

It is concerned with the protein synthesis in the cell, especially those secreted from the cell such as insulin from cells of islets of Langerhans in pancreas and antibodies in leukocytes.

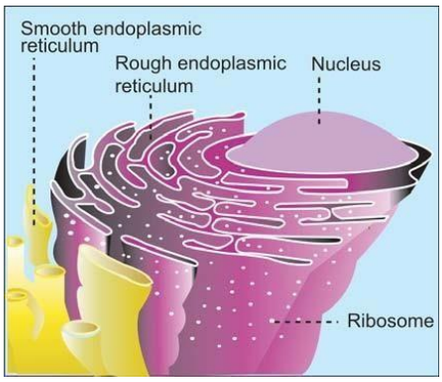
It also plays an important role in degradation of worn out cytoplasmic organelles like mitochondria. It wraps itself around the worn out organelles and forms a vacuole which is often called the autophagosome. It is digested by lysosomal enzymes

Functions of smooth endoplasmic reticulum

i. It is responsible for synthesis of cholesterol and steroid
ii. It is concerned with various metabolic processes of the cell because of the presence of many enzymes on the outer surface
iii. It is concerned with the storage and metabolism of calcium

iv. It is also concerned with catabolism and detoxification of toxic substances like some drugs and carcinogens (cancer producing substances) in liver.

Rough endoplasmic reticulum and smooth endoplasmic reticulum are interconnected and continuous with one another. Depending upon the activities of the cells, the rough endoplasmic reticulum changes to smooth endoplasmic reticulum and *vice versa*.

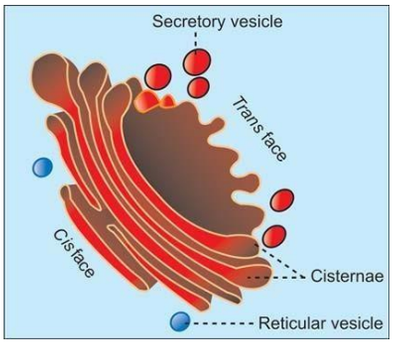


GOIGI APPARATUS

The Golgi apparatus is situated near the nucleus. It has two ends or faces namely, *cis* face and *trans* face. The *cis* face is positioned near the endoplasmic reticulum. The reticular vesicles from endoplasmic reticulum enter the Golgi apparatus through *cis* face. The *trans* face is situated near the cell membrane. The processed substances make their exit from Golgi apparatus through *trans* face.

Functions of Golgi Apparatus

i. It is concerned with the processing and delivery of substances like proteins and lipids to different parts of the cell.
ii. It functions like a post office because, it packs the processed materials into the secretory granules, secretory vesicles, and lysosomes
iii. It also functions like a shipping department of the cell because it sorts out and labels the materials for distribution to their proper destinations.



Lysosomes

These are small globular structures filled with enzymes. These enzymes are synthesized in rough endoplasmic reticulum and transported to the Golgi apparatus.

Lysosomes are of two types:

i. Primary lysosome which is pinched off from Golgi apparatus. It is inactive in spite of having the hydrolytic enzymes.
ii. Secondary lysosome which is active lysosome formed by the fusion of a primary lysosome with phagosome or endosome.

Functions of Lysosomes

i. Digestion of unwanted substances

With the help of hydrolytic enzymes like proteases, lipases, amylases and nucleases, lysosome digests and removes the unwanted substances.

ii. Removal of excess secretory products in the cells

Lysosomes in the cells of the secretory glands play an important role in the removal of excess secretory products by degrading the secretory granules.

iii. Secretory function – Secretory lysosomes

Recently, lysosomes having secretory function called secretory lysosomes are found in some of the cells, particularly in the cells of immune system. The conventional lysosomes are modified into secretory lysosomes by combining with secretory granules

Peroxisomes

Peroxisomes are otherwise called as microbodies. These are pinched off from endoplasmic reticulum. Peroxisomes contain some oxidative enzymes such as catalase, urate oxidase and D-amino acid oxidase.

Functions of Peroxisomes

i. Degrade the toxic substances like hydrogen peroxide and other metabolic products by means of detoxification
ii. Form the major site of oxygen utilization in the cells
iii. Break down the excess fatty acids
iv. Accelerate gluconeogenesis from fats
v. Degrade purine to uric acid
vi. Participate in the formation of myelin and bile acids.

Centrosome AND CENTRIOLES

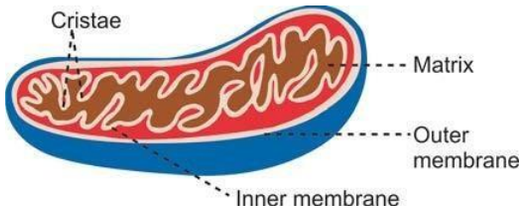
The centrosome is situated near the center of the cell close to the nucleus. It consists of two cylindrical structures called centrioles which are responsible for the movement of chromosomes during cell division.

Secretory VESICLES

The secretory vesicles are globular structures, formed in the endoplasmic reticulum, and processed and packed in Golgi apparatus. When necessary, the secretory vesicles rupture and release the secretory substances into the cytoplasm.

MITOCHONDRION

The mitochondrion is a rod or oval shaped structure with a diameter of 0.5 to 1 µ. It is covered by a double layered membrane .



Functions of Mitochondrion

i. The mitochondrion is called the 'power house of the cell' because it produces the energy required for the cellular functions. The energy is produced by oxidation of the food substances like proteins, carbohydrates and lipids by the oxidative enzymes in cristae. During oxidation, water and carbon dioxide are produced with release of energy. The released energy is stored in mitochondria and used later for synthesis of ATP.

ii. The components of respiratory chain in the mitochondrion are responsible for the synthesis of ATP by utilizing the energy through oxidative phosphorylation. The ATP molecules defuse throughout the cell from mitochondrion. Whenever energy is needed for cellular activity, the ATP molecules are broken down

iii. Apoptosis

ORGANELLES WITHOUT LIMITING MEMBRANE

RIBOSOMES

The ribosomes are small granular structures with a diameter of 15 nm. The ribosomes are made up of proteins (35%) and RNA (65%). The RNA present in ribosomes is called ribosomal RNA (rRNA).

Functions of Ribosomes

Ribosomes are called protein factories because of their role in the synthesis of proteins. Messenger RNA (mRNA) passes the genetic code for protein synthesis from nucleus to the ribosomes. The ribosomes, in turn arrange the amino acids into small units of proteins. The ribosomes attached with endoplasmic reticulum are involved in the synthesis of proteins like the enzymatic proteins, hormonal proteins, lysosomal proteins and the proteins of the cell membrane. The free ribosomes are responsible for the synthesis of proteins in hemoglobin, peroxisome and mitochondria.

Cytoskeleton

The cytoskeleton of the cell is a complex network that gives shape, support and stability to the cell. It is also essential for the cellular movements and the response of the cell to external stimuli. The cytoskeleton consists of three major protein components viz.

a. Microtubules
b. Intermediate filaments
c. **Microfilaments**

Microtubules

Microtubules are straight and hollow tubular structures formed by bundles of globular such as insulin from cells of islets of Langerhans in pancreas and antibodies in

Functions of microtubules

Microtubules:

i. Determine the shape of the cell
ii. Give structural strength to the cell
iii. Responsible for the movements of centrioles and the complex cellular structures like cilia
iv. Act like conveyer belts which allow the movement of granules, vesicles, protein molecules and some organelles like mitochondria to different parts of the cell
v. Form the spindle fibers which separate the chromosomes during mitosis

Intermediate Filaments

The intermediate filaments form a network around the nucleus and extend to the periphery of the cell. These filaments are formed by fibrous proteins and help to maintain the shape of the cell. The adjacent cells are connected by intermediate filaments by desmosomes.

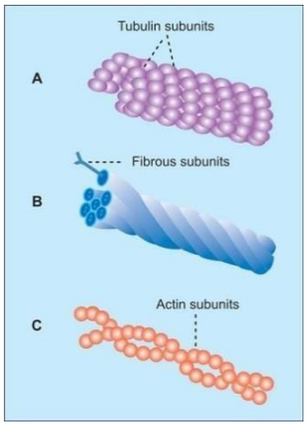
Microfilaments

Microfilaments are long and fine thread like structures which are made up of non tubular contractile proteins called actin and myosin. Actin is more abundant than myosin.

Functions of microfilaments

Microfilaments:

i. Give structural strength to the cell
ii. Provide resistance to the cell against the pulling forces
iii. Responsible for cellular movements like contraction, gliding and cytokinesis(partition of cytoplasm during cell division).



NUCLEUS

Nucleus is present in those cells which divide and produce enzymes. The cells with nucleus are called eukaryotes and those without nucleus are known as

prokaryotes (e.g. red blood cells). Prokaryotes do not divide or synthesize the enzymes.

Most of the cells have only one nucleus (uninucleated). Few types of cells like skeletal muscle cells have many nuclei (multinucleated). Generally the nucleus is located near the center of the cell. It is mostly spherical in shape. However, the shape and situation of nucleus vary in different cells.

Nuclear Membrane

The nucleus is covered by a double layered membrane called nuclear membrane. It encloses the fluid called nucleoplasm. Nuclear membrane is porous and permeable in nature and it allows nucleoplasm to communicate with the cytoplasm

Nucleoplasm

It is a gel like ground substance and contains large quantities of the genetic material in the form of DNA. The DNA is made up of chromatin threads. These chromatin threads become the rod shaped chromosomes just before the cell division.

Nucleoli

One or more nucleoli are present in each nucleus. The nucleolus contains RNA and some proteins, which are similar to those found in ribosomes. The RNA is synthesized by chromosomes and stored in the nucleolus.

FUNCTIONS OF NUCLEUS

1. Controls all the activities of the cell
2. Synthesizes RNA
3. Forms subunits of ribosomes
4. Sends genetic instruction to the cytoplasm for protein synthesis through mRNA
5. Controls the cell division through genes
6. Stores the hereditary information (in genes) and transforms this information from one generation of the species to the next.

Cell Junctions

The connection between the cells or the contact between the cell and extracellular matrix is called the cell junction. It is also called as membrane junction. It is generally classified into three types:

1. Occluding junction
2. Communicating junction
3. Anchoring junction

OCCLUDING JUNCTION

The junction which prevents the movement of ions and molecules from one cell to another cell is called the occluding junction.

Tight junctions belong to this category. It is formed by the tight fusion of the cell membranes from the adjacent cells. The area of the fusion is very tight and forms a ridge. This type of junction is present in the apical margins of epithelial cells in intestinal mucosa, wall of renal tubule, capillary wall and choroid plexus

Functions of Tight Junctions

1. The tight junctions hold the neighboring cells of the tissues firmly and thus provide strength and stability to the tissues.
2. It provides the barrier or gate function by which the interchange of ions, water and macromolecules between the cells is regulated.
3. It acts like a fence by preventing the lateral movement of integral membrane proteinsand lipids from cell membrane

4,By the fencing function, the tight junctions maintains the cell polarity by keeping the proteins in the apical region of the cell membrane.

5..Tight junctions in the brain capillaries form the blood-brain barrier (BBB) which prevents the entrance of many harmful substances from the blood into the brain tissues

COMMUNICATING JUNCTIONS

The junctions, which permit the movement of ions and molecules from one cell to another cell, are called communicating junctions. Gap junction and chemical synapse are the communicating junctions.

GAP JUNCTION OR NEXUS

The gap junction is also called nexus. It is present in heart, basal part of epithelial cells of intestinal mucosa, etc.

Functions of Gap Junction

1. The diameter of the channel in the gap junction is about 1.5 to 3 nm. So, the substances having molecular weight less than 1000 such as glucose also can pass through this junction easily

2. It helps in the exchange of chemical messengers between the cells

3. It helps in rapid propagation of action potential from one cell to another cell

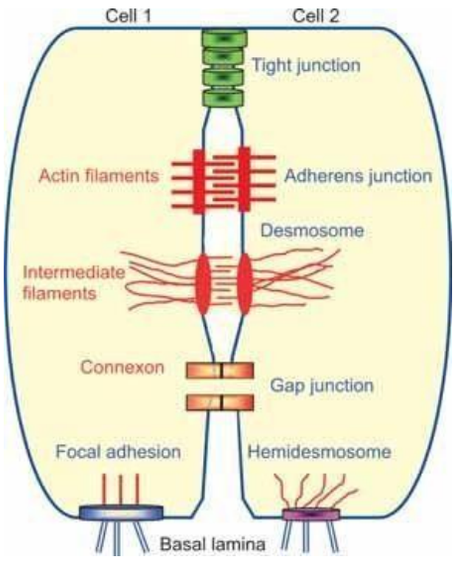
CHEMICAL SYNAPSE

Chemical synapse is the junction between a nerve fiber and a muscle fiber or between two nerve fibers, through which the signals are transmitted by the release of chemical transmitter

ANCHORING JUNCTIONS

Anchoring junctions are the junctions, which provide firm structural attachment between two cells or between a cell and the extracellular matrix. There are four types of anchoring junctions

i. Adherens junctions (cell to cell)
ii. Focal adhesions (cell to matrix)
iii. Desmosomes (cell to cell)
iv. Hemidesmosomes (cell to matrix)


Cell 1
Cell 2
Tight junction
Actin filaments
Adherens junction
Desmosome
Intermediate filaments
Connexon
Gap junction
Focal adhesion
Hemidesmosome
Basal lamina

General physiology Lec. 3

Homeostasis

Homeostasis" means the maintenance of constant internal environment. For the operation of homeostatic mechanism, the body must recognize the **deviation** of any physiological activity from the normal limits.

Fortunately, body is provided with appropriate detectors or sensors, which recognize the deviation and alert the integrating center. The integrating center immediately sends information to the concerned effectors to either accelerate or inhibit the activity so that the normalcy is restored.

Negative Feedback Mechanism

Negative feedback mechanism is the one by which a particular system reacts in such a way as to stop the change or reverse the direction of change. After receiving a message, the effectors send the inhibitory signals back to the system. Now, the system stabilizes its own function either by stopping the signals or by reversing the signals

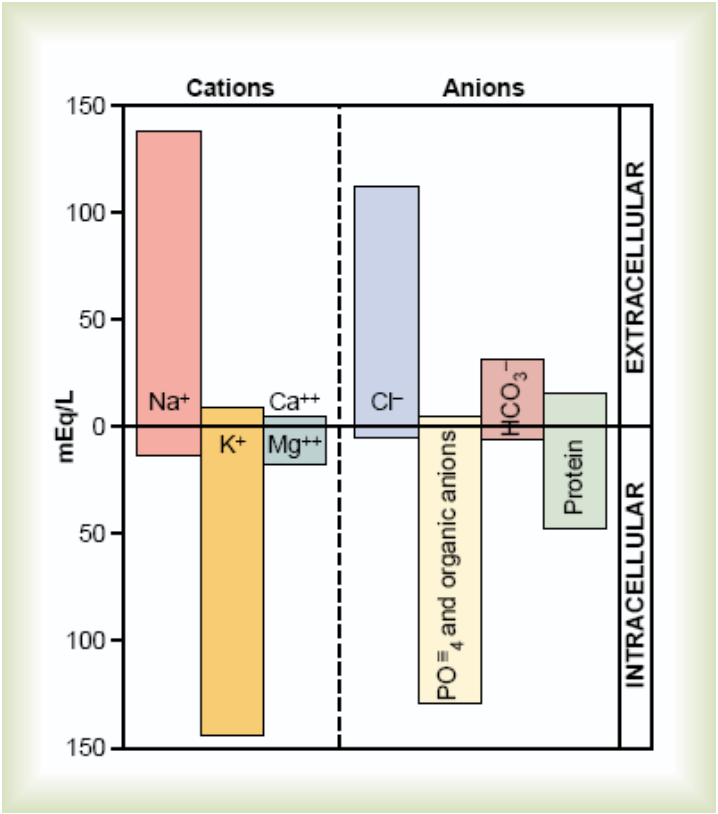
For example, thyroid stimulating hormone (TSH) released from pituitary gland stimulates thyroid gland which in turn secretes thyroxine. When thyroxin level increases in blood, it inhibits the secretion of TSH from pituitary so that, the secretion of thyroxine from thyroid gland decreases . On the other hand, if thyroxin secretion is less, it induces pituitary gland to release TSH. Now, TSH stimulates thyroid gland to secrete thyroxine

Positive Feedback Mechanism

Positive feedback mechanism is the one in which the system reacts in such a way as to amplify (increase the intensity of) the change in the same direction. Positive feedback is less common than the negative feedback. However, it has its own significance, particularly during emergency conditions.
One of the positive feedbacks occurs during the blood clotting. Blood clotting is necessary to arrest bleeding during injury and it occurs in three stages:
1.Formation of prothrombin activator
2.Conversion of prothrombin into thrombin
3.Conversion of fibrinogen into fibrin by thrombin.

Types of transports

1. Diffusion (passive)
2. Carrier-mediated transport (passive or active)
3. Vesicular transport (active



FACTORS AFFECTING RATE OF DIFFUSION

The rate of diffusion of substances through thecell membrane is directly proportional to the following factors:

1. Permeability of the cell membrane
2. Body temperature
3. Concentration gradient or electrical gradient of the substance across the cell membrane
4. Solubility of the Substance

The rate of diffusion of substances through the cell membrane is inversely proportional to the following factors:

1. Thickness of the cell membrane
2. Charge of the ions
3. Size of the molecule

- **"Active Transport" of Substances Through Membranes**

When a cell membrane moves molecules or ions "uphill" against a concentration gradient (or "uphill" against an electrical or pressure gradient), the process is called active transport. Different substances that are actively transported through at least some cell membranes include sodium ions, potassium ions, calcium ions, iron ions, hydrogen ions, chloride ions, iodide ions, urate ions, several different sugars, and most of the amino acids.

Active transport is divided into two types according to the source of the energy used to cause the transport: **primary active transport** and **secondary active transport**. In **primary active transport**, the energy is derived directly from breakdown of adenosine triphosphate (ATP) or of some other high-energy phosphate compound. In **secondary active transport,** the energy is derived secondarily from energy that has been stored in the form of ionic concentration differences of secondary molecular or ionic substances between the two sides of a cell membrane, created originally by primary active transport. In both instances, transport depends on **carrier proteins** that penetrate through the cell membrane, as is true for facilitated diffusion. However, in active transport, the carrier protein functions differently from the **carrier in facilitated diffusion because it is capable of imparting energy to the transported substance to move it against the electrochemical gradient**.

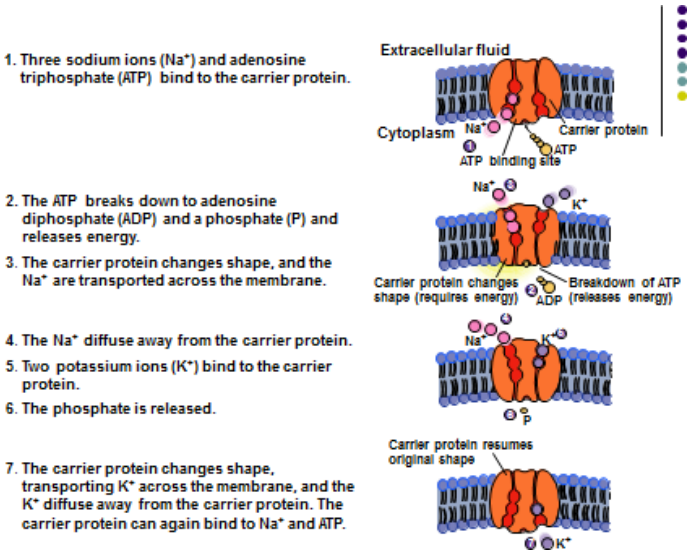
Sodium-Potassium Pump as an example of Primary Active Transport:

The active transport mechanism that has been studied in greatest detail is the **sodium-potassium (Na+-K+) pump**, a transport process that pumps sodium ions outward through the cell membrane of all cells and at the same time pumps potassium ions from the outside to the inside. This pump is responsible for maintaining the sodium and potassium concentration differences across the cell membrane, as well as for establishing a negative electrical voltage inside the cells. This pump is also the basis of nerve function, transmitting nerve signals throughout the nervous system. The carrier protein is a complex of two separate globular proteins: a larger one called the a subunit, and a smaller one called the b subunit, the larger protein has three specific features that are important for the functioning of the pump:

1. It has three **receptor sites for binding sodium ions** on the portion of the protein that protrudes to the inside of the cell.
2. It has two **receptor sites for potassium ions** on the outside.
3. The inside portion of this protein near the sodium binding sites has **ATPase activity**.

When two potassium ions bind on the outside of the carrier protein and three sodium ions bind on the inside, the ATPase function of the protein becomes activated. This then cleaves one molecule of ATP, splitting it to adenosine diphosphate (ADP) and liberating a high-energy phosphate bond of energy. This liberated energy is then believed to cause a chemical and conformational change in the protein carrier molecule, extruding the three

sodium ions to the outside and the two potassium ions to the inside. For some cells, such as electrically active nerve cells, 60 to 70 per cent of the cells' energy requirement may be devoted to pumping Na+ out of the cell and K+ into the cell.



Secondary Active Transport— Co-Transport and Counter-Transport

When sodium ions are transported out of cells by primary active transport, a large concentration gradient of sodium ions across the cell membrane usually develops—high concentration outside the cell and very low concentration inside. This gradient represents a storehouse of energy because the excess sodium outside the cell membrane is always attempting to diffuse to the interior. Under appropriate conditions, this diffusion energy of sodium can pull other substances along with the sodium through the cell membrane. This phenomenon is called **co-transport**; it is one form of **secondary active transport.**

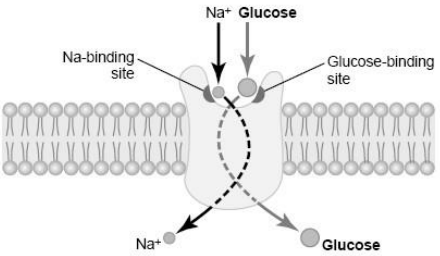
For sodium to pull another substance along with it, a coupling mechanism is required. This is achieved by means of still another carrier protein in the cell membrane.

The carrier in this instance serves as an attachment point for both the sodium ion and the substance to be co-transported. Once they both are attached, the energy gradient of the sodium ion causes both the sodium ion and the other substance to be transported together to the interior of the cell. In **counter-transport,** sodium ions again attempt to diffuse to the interior of the cell because of their large concentration gradient. However, this time, the substance to be transported is on the inside of the cell and must be transported to the outside. Therefore, the sodium ion binds to the carrier protein where it projects to the exterior surface of the membrane, while the substance to be counter-transported binds to the interior projection of the carrier protein. Once both have bound, a conformational

change occurs, and energy released by the sodium ion moving to the interior causes the other substance to move to the exterior.

Co-Transport of Glucose and Amino Acids Along with Sodium Ions

Glucose and many amino acids are transported into most cells against large concentration gradients; the mechanism of this is entirely by co-transport. Note that the transport carrier protein has two binding sites on its exterior side, one for sodium and one for glucose. Also, the concentration of sodium ions is very high on the outside and very low inside, which provides energy for the transport. A special property of the transport protein is that a conformational change to allow sodium movement to the interior will not occur until a glucose molecule also attaches. When they both become attached, the conformational change takes place automatically, and the sodium and glucose are transported to the inside of the cell at the same time. Hence, this is a **sodium-glucose co-transport** mechanism. **Sodium co-transport of the amino acids** occurs in the same manner as for glucose, except that it uses a different set of transport proteins. Five **amino acid transport proteins** have been identified, each of which is responsible for transporting one subset of amino acids with specific molecular characteristics. **Sodium co-transport of glucose and amino acids occurs especially through the epithelial cells of the intestinal tract and the renal tubules of the kid** **iese substances into the blood**. Other important co-t **ome** cells include co-transport of chloride ions, iodine i



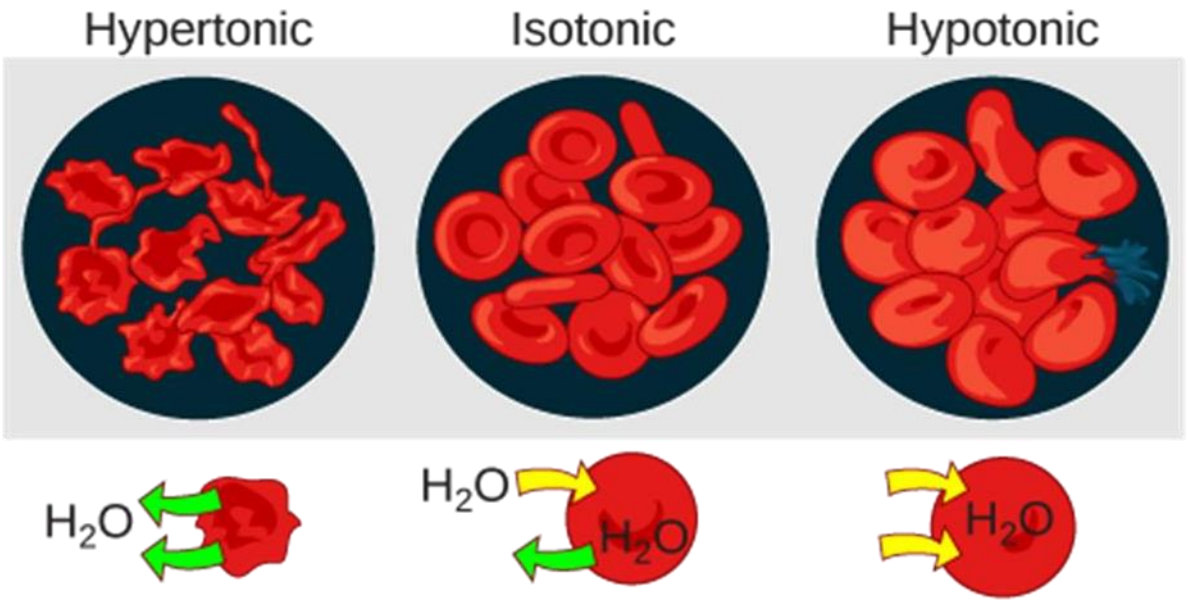
TONICITY OF FLUIDS

In clinical practice, the word tonicity always refers to tonicity of a solution with respect to that of plasma (290 mOsm). In other words, it is the red blood cell (RBC) membrane across which the tonicity is tested. Thus:

Isotonic fluids are those which have osmolality similar to plasma. RBCs neither shrink nor swell in such solution . A solution of 0.9% NaCl is isotonic with plasma.

Hypertonic fluids have osmolality higher than the plasma. The RBCs shrink in such solutions by losing water by osmosis .

Hypotonic fluids are those whose osmolality is lower than that of plasma. The RBCs swell up in hypotonic solutions by gaining water by osmosis .



Vesicular Transport

Materials move into or out of the cell by means of vesicles, also called **bulk transport**

1. Endocytosis (Clathrin-mediated)
2. Receptor mediated endocytosis
3. Pinocytosis
4. Phagocytosis
5. Exocytosis

ALL are active processes (require ATP) though they are not usually referred to as “active transport”

ENDOCYTOSIS

Endocytosis is the process in which the substance is trans ported into the cell by unfolding of the cell membrane around the substance and inter nailing it . It is further categorized into three types:

1. Pinocytosis, i.e. cell drinking refers to the process of engulfing liquid substances by the enfolding of cell membrane, e.g. reabsorption by renal tubular epithelial cells.

2. Phagocytosis, i.e. cell eating is the process of engulfing of solid particles, such as bacteria, dead tissue and for engulfing particles by the cells. The process of phagocytosis involves three steps:

   (i) the attachment stage,
   (ii) (ii) the engulfment stage and
   (iii) (iii) killing or degradation stage .

3. Receptor-mediated endocytosis. In this process the substance to be transported binds with the special receptor protein present on the cell surface. The receptor protein–substance complex is then engulfed by the cell membrane by the process of endocytosis. Transport of iron and cholesterol into the cells occurs by receptor mediated endocytosis

EXOCYTOSIS

Exocytosis is reverse of endocytosis, i.e. by this process the substances are expelled from the cell without passing through the cell membrane. In this process, the substances which are to be extruded are collected in the form of granules or vesicles which move towards the cell membrane. Their membrane then fuses to the cell membrane. The area of fusion breaks down releasing the con tents to the exterior and leaving the cell membrane intact. Release of hormones and enzymes by secretory cells of the body occurs by exocytosis. The process of exocytosis requires Ca2+ and energy along with docking proteins.

TRANSCYTOSIS

Vesicular transport within the cell is called transcytosis or cytopempsis. It is quite similar to exocytosis and endocytosis. Three basic steps involved in this process are: (i) vesicle formation, (ii) vesicle transportation and (iii) docking in the cell.

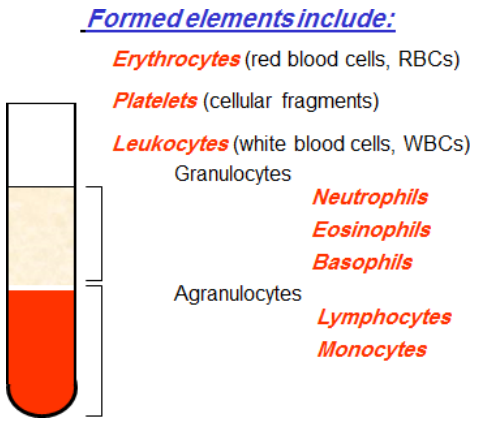
Blood

Blood is a viscous fluid which circulates through a closed system of blood vessels.

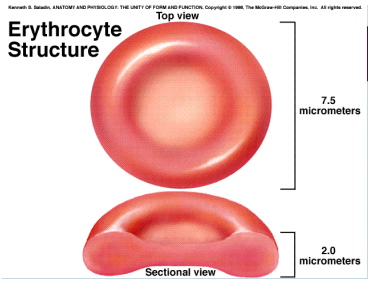
Composition of blood:

It consists of two parts, a fluid portion which is yellow in color called plasma and cellular elements which include different types of cells:

1. Red blood cells (Erythrocytes).
2. White blood cells (Leukocytes) of different types (Neutrophils, Eosinophils, Basophils, Monocytes and Lymphocytes).
3. Platelets (Thrombocytes).



The major function of R.B.C. is to transport hemoglobin which in turn carries oxygen from the lungs to the tissues. R.B.C. are biconcave discs having a mean diameter of about 7.5 micrometers and a thickness at the thickest point of 2.0 micrometers and in the center of 1 micrometers or less. The average volume is 90-95 mm^3.



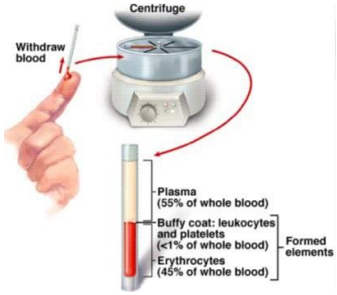
The shapes of R.B.C. , can change remarkably as the cells pass through capillaries. In normal men, the average number of R.B.C., per cubic millimeter is 5.4 millions (± 300,000) and in women is 4.8 millions (±300,000). This difference is due to the presence of testosterone hormone in male, this causes stimulation of the bone marrow which produces the R.B.C.

The concentration of Hb in R.B.C. , is about 34%, every 100 ml of R.B.C. contain 34 gm of Hb. Hemoglobin is a pigment in R.B.C.

The average concentration of Hb in the male is about (13- 18) gm/100 ml blood. In female is about (12-16) gm/100 ml blood, every 1 gm of Hb can combine with 1.39 ml of O2. In male each 100 ml of blood contain over 21 ml of O2 while in female it contains 19 ml of O2.

Hematocrit:

The ratio between plasma and cellular elements is 55% plasma to 45% cellular element (mainly R.B.C.) this ratio is called hematocrit or packed cell volume (P.C.V.) .When the percentage of R.B.C. is below 45% this causes anemia, while the percentage is above 45%, this causes polycythemia.



Plasma:

The fluid of blood, it contains protein, organic and inorganic substances of blood.

There are three types of protein in plasma:

1. Albumin, is present in the concentration of 4.5 gm/dl , its primary function is to cause osmotic pressure at the capillary membrane.
2. Globulin, is present in the concentration 2.5 gm/dl are divide into α , β and γ. α and β function in transporting substances by combining with them , γ to a lesser degree. β globulin play a special role in protecting the body against infection.
3. Fibrinogen, is present in the concentration of (0.3 gm/dl) it's of basic importance in blood clotting.

The total value of plasma protein is about 7 gm/100 ml plasma.

Blood functions:

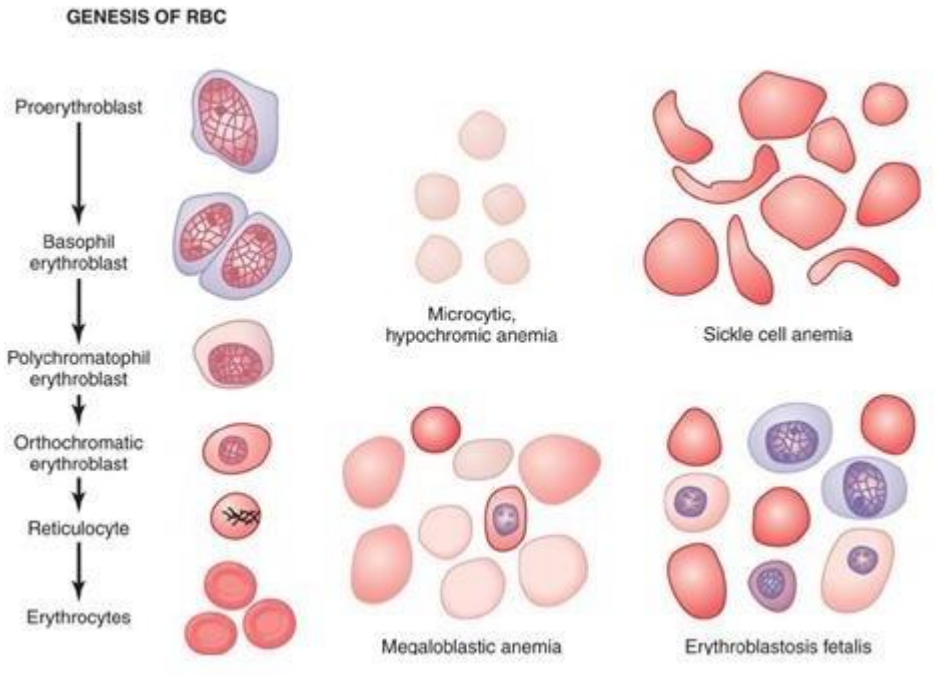
1. The main function of the blood is to transport gases O2 and CO2 . O2 is transported from lungs to the tissue of the body and CO2 is transported in opposite direction that is from the tissue to the lungs.
2. Is the delivery of nutrients, such as glucose, amino acids, fatty acids and vitamins to the tissue.
3. Distribution of heat, heat is generated by deep organs in the body, then it's distributed to all parts of the body.
4. Regulation of ions concentration and PH through the constant exchange of electrolytes between tissue fluids.
5. Protective function.

The W.B.C. play an important role in protection function of the blood in which they defend the body against infection of bacteria, viruses and other foreign bodies.

Genesis of R.B.C. :

R.B.C.s are derived from the cell known as Hemocytoblast which is formed from primodial stem cells located in bone marrow . The Hemocytoblast forms the Basophils erythrocytes (begins the synthesis of Hb). Then it becomes Polychromatophil erythroblast then the nucleus shrinks and the cell becomes Normoblast and then the nucleus extruded. At the same time endoplasmic reticulum reabsorbed and the cell called Reticulocyte when the reticulum is completely reabsorbed the cell then is a mature Erythrocyte.

R.B.C. are produced during early embryonic life by the yolk sac, the spleen and liver begin to produce R.B.C.s , during later embryonic life at age 20 , bone (whether flat or long) begins to produce R.B.C.s and flat bones produce R.B.C., such as bones of the skull, ribs and sternum. The increase of R.B.C.s count under normal value is called Polycythemia.



There are two types of polycythemia:

1. Physiological Polycythemia (secondary) :

   Whenever the tissue becomes hypotoxic because of too little oxygen in the atmosphere, such as at high altitudes, or because of failure of delivery of oxygen to tissues, as occurs in cardiac failure, the blood forming organs automatically produce large quantities of R.B.C.s , the blood count is generally 6-7 million/mm^3

2. Pathological Polycythemia (Vera):

   Which occur during the pathological condition such as cancerous conditions, in which cancer stimulates great number of R.B.C.s to be produced. The R.B.C. count may be 7-8 million/mm and the hematocrit 60-70%.

Anemia :

Anemia means a deficiency of R.B.C.s, which can be caused either by too rapid loss or by too slow production of R.B.C.s , There are different types of anemia:

1. ***Blood loss anemia:*** This s caused by loss of large volume of blood usually when there is a blood loss, the plasma is replaced quickly while the R.B.C.s , takes few weeks to be replaced. This is caused in some chronic blood such as (Hemorrhoid).

2. ***Bone marrow aplasia (aplastic anemia)::***
   This means the loss of function of bone marrow due to drug poisoning or Gamma-ray irradiation.

3. ***Hemolysis of R.B.C.s:*** Resulting from many of causes such as:
   - **a.** Drug poisoning.
   - **b.** Hereditary diseases such as (sickle cell diseases, spherocytosis, Hbs).
   - **c.** Erythroblastosis fetalis, a disease of the newborn in which antibodies from the mother destroy red cells in the baby.

4. ***Thalasemia (Cooly's anemia):***

It's also called Mediterranean anemia, there is a deficiency of globulin, for example: Deficiency of polypeptide chain which causes decrease in concentration of Hb.

5. ***Maturation failure or (pernicious anemia):***

Because of lack of vitamin B12 or folic acid. Vitamin B12 is an essential nutrients for all cells of the body and growth of tissues. Vitamin B12 is required for synthesis of DNA, lack of this causes failure of nuclear marutation and division and therefore inhibits R.B.C.s production.

When the vitamin B12 replaced by intestinal bacteria, is called extrinsic factor and there is other factor called intrinsic factor. B12 should combine with intrinsic factor, if the intrinsic factor is absent, then B12 will not absorbed this disease is called pernicious anemia, in which the

basic abnormality is an atrophic gastric mucosa. In pernicious anemia R.B.C.s are larger than the normal and undergo hemolysis easily.

Destruction of R.B.C.s

R.B.C.s are delivered from the bone marrow into the circulatory system an average of 120days, have no nucleus, endoplasmic reticulum and mitochondria, they have cytoplasmic enzymes that are capable of metabolizing glucose and forming small amount of ATP, which serves the red cell in:

1. Maintaining the pliability of the cell membrane.
2. Maintaining membrane transport of ions.
3. Keeping the iron of the cell hemoglobin in the ferrous form, rather than the ferric form.
4. Preventing oxidation of the proteins in the red cell.

These metabolic system of the red cell become progressively less active with time, and they become more and more fragile, because their life processes wear out.

- **Effect of anemia on circulatory system:**

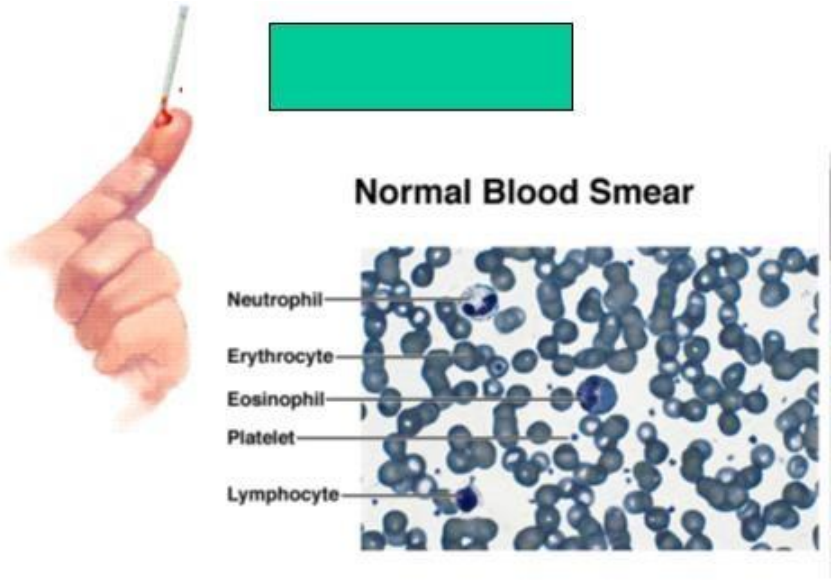
  It effects the viscosity of the blood from (3-1.5) and decrease resistance of blood flow in the peripheral blood vessels and also cardiac output increase 2 times. Hypoxia cause increase in return of blood to the heart, increasing the cardiac output to a still higher level.

- **Effect of polycythemia on circulatory system:**

  Here, increase blood volume, decrease in the rate of venous return to heart, sluggish blood flow through vessels, increase circulation time and increase in the deoxygenated Hb.

White blood cells

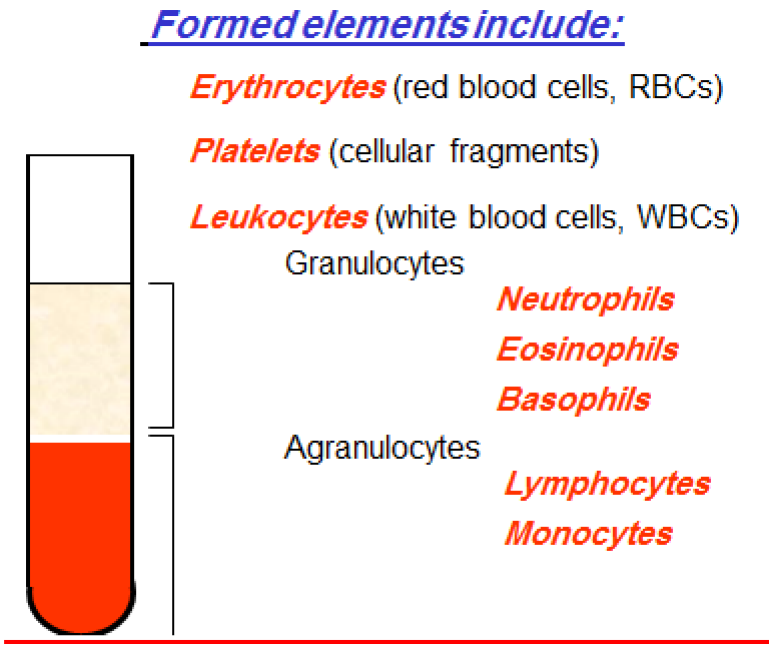
The W.B.C., count is from (4000-11000) cells/mm³, if the count less than 4000, the condition is called leukopenia, if it's more than 11000, the condition is leukocytosis. W.B.C. are involved in the body defense mechanism against mirco-organisms and other foreign materials. W.B.C. are classified according to the type of cytoplasm into the following:



1. ***Granular leukocytes***: in which the cytoplasm contain granules, these are classified into polymorphonuclear leukocytes which include:
   - **A.** ***Neutrophils:*** multilobed nucleus, 2-5 lobes depending on the age of the cell. The percent is 65%.
   - **B.** ***Eosinophils:*** multilobed nucleus (usually bilobed). The percent is 1-3%.
   - **C.** ***Basophils:*** in this type, the nucleus take the (S) shape. The percent less than 1%.

2. ***Agranular leukocytes:*** in which is no granules in the cytoplasm, these are classified into:
   - **A.** ***Monocytes:*** the nucleus is kidney shaped and they are the largest cells in the body. The percent is 7%.
   - **B.** ***Lymphocytes:*** they are large lymphocytes and a small lymphocytes which depend on the age, the percent is 30%.

The granulocytes and monocytes protect the body against invading organisms mainly by ingesting them, that is, by phagocytosis. The lymphocytes and plasma cell function mainly in connection with immune system.



Genesis of the leukocytes

The granulocytes and monocytes are formed only in the bone marrow, lymphocytes and plasma cells are produced mainly in the various lymphogenesis organs, including the lymph gland, spleen, thymus…etc.

Life span of the W.B.C.

The main reason W.B.C., are present in the blood is to be transported from the bone marrow or lymphoid tissue to the areas of the body where they are needed.

The life of the granulocytes, once released from the bone marrow is normally 4-8 hours, circulating in the blood and another 4-5 days in the tissues. In times of serious tissue infection, this total life span is often only a few hours, because the granulocytes proceed rapidly to the infected area.

The monocytes also have a short time, 10-20 hours, in the blood before wandering through the capillary membrane into the tissue. They can live for months or even years unless they

are destroyed by performing phagocytic function. The lymphocytes have life span of weeks, months, or even years, but this depends on the body's need for these cells.

Our bodies have a special system for combating the different infections and toxic agents. This composed of W.B.C., and tissue cells. These cells all work together to prevent diseases by actually destroying invading agents by phagocytosis and by forming antibodies and sensitized lymphocytes.

Phagocytosis:

The most important function of the neutrophils and macrophages is phagocytosis which mean cellular ingestion of the offending agent.

Phagocytes must be selective of the material that is phagocytosed, otherwise, some of the normal cells and structure of the body would be ingested. Whether or not phagocytosis will occur depends especially on three selective procedures:

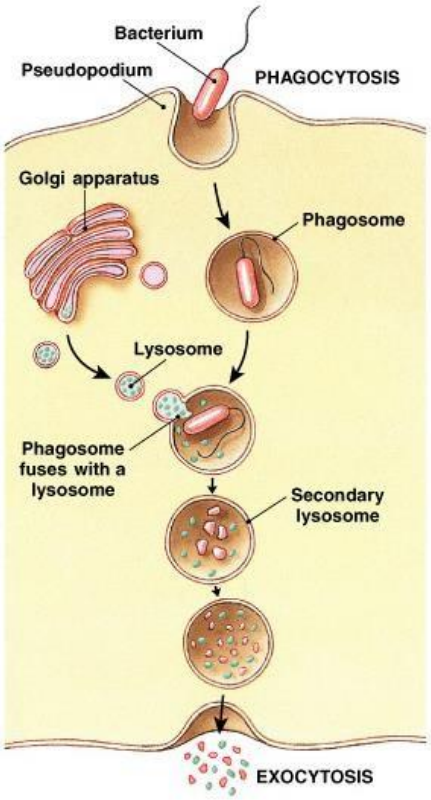
1. Most natural structures in tissue have smooth surface, which resist phagocytosis. But if the surface is rough, the likelihood of phagocytosis is increased.

2. Most natural substances of the body have protective protein coats that they repel the phagocytes, on the other hand, dead tissues and most foreign particles frequently have no protective coats, which also make the subject to phagocytosis.

3. The body has a specific means of recognizing certain foreign materials.

The immune system develops antibodies against infectious agents like bacteria. The antibodies adhere to the bacterial

membrane and there by make the bacteria especially susceptible to phagocytosis.



Inflammation:

When tissue injury occurs, whether caused by bacteria, trauma, chemicals, heat or any other phenomenon, multiple substances that cause dramatic secondary changes in the tissues are released by the injured tissues. The entire complex of tissue changes is called **INFLAMMATION**.

Inflammation is characterized by:

1. Vasodilation of the local blood vessels.
2. Increased permeability of the capillaries.
3. Often clotting of the fluid in the interstitial spaces because of the excessive amounts of fibrinogen and other protein leaking from the capillaries.

4. Migration of large number of granulocytes and monocytes in the tissue.
5. Swelling of the tissue cells.

Leukemias

Uncontrolled production of W.B.C. is caused by cancerous mutation myelogenous and lymphogenous cell.
Leukemias are divided into:
1. Lymphogenous leukemia.
2. Myelogenous leukemia.

The effect of leukemia is metastatic growth of leukemic cells in abnormal areas of the body. Almost all leukemias spread to the spleen, lymph nodes, liver, and other especially vascular regions. In myelogenous leukemia, the cancerous process produces partially differentiated cells, resulting in what might called:

1. Neutrophilic leukemia.
2. Eosinophilic leukemia.
3. Basophilic leukemia.
4. Monocytic leukemia.

More frequently, however, the leukemia cells are bizarre and undifferentiated and not identical to any of the normal W.B.C.. usually the more undifferentiated the cells, the more acute is the leukemia, often leading to death within few months if untreated.

Leukopenia or Agranulocytosis:

A clinical condition known as leukopenia occurs in which the bone marrow stops producing W.B.C. leaving the body unprotected against bacteria and other agents that might invade

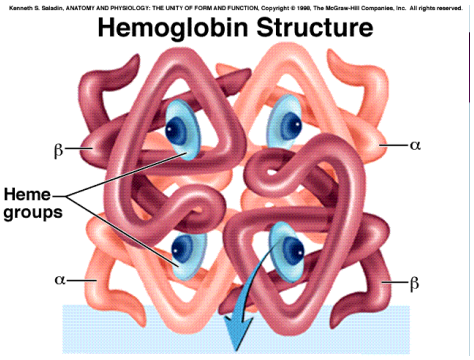
the tissues. Without treatment, death often is less that a week after acute total leukopenia begins. This result from different cases:

1. Irradiation of the body by gamma rays caused by a nuclear explosion.
2. Exposure to drugs and chemical that contain benzene or other is likely to cause aplasia of the bone marrow.

Hemoglobin

Hb is a pigment in R.B.C., it is a protein with molecular weights (64,458). The normal value of Hb is 14-16 gm/100ml blood, every 1 gm of Hb can combine with 1.39 ml O2 . Synthesis of Hb begins in the erythroblasts and continues through the normoblast and reticulocyte stage. Heme portion of Hb is synthesized mainly from acetic acid and glycine and that most of this synthesis occur in mitochondria. The chemical steps in formation of Hb. First, succinyl-CoA binds with glycine to form pyrrole. In turn, four pyrrole combine to form protoporphyrin 1x, which then combine with iron to form heme molecule. Finally, each heme molecule combine with long polypeptide chain, called globin, synthesized by the ribosomes, forming a subunit called Hb chain. Each chain has a molecular weight about 16.000, four of them turn, bind together loosely to form Hb.

1. 2 succinyl-coA+2 glycine → pyrrole
2. 4 pyrrole → protoporphyrin 1x
3. protoporphyrin 1x + Fe → heme
4. heme+polypeptide→hemoglobin chain(α or β)
5. 2 α chains + 2 β chains → hemoglobin A



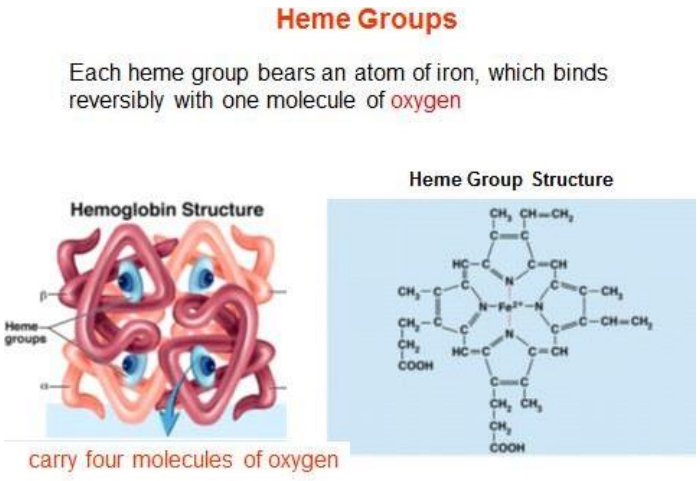
Formation of Hemoglobin

- Each erythrocyte contains about 280 million molecules of Hb. Hemoglobin consists of four protein chain called globins, two of these, the alpha chain (α), are 141 amino acids long, and other two, the beta (β) chains are 146 amino acids long. Each chain is conjugated with a nonprotein moiety called the heme group. Each heme can carry one molecule of O2, the Hb molecule as a whole can transport up to 4 O2 . About 20% of carbon dioxide in the bloodstream is also transported by Hb.

- Hemoglobin exists in several forms that display slight differences in the globin chains, the form adult Hb (HbA).

- About 2.5% of (HbA), however, is of a form called HbA2, which has a two delta (δ) chains in place of the β chains.

The fetus produces a form called fetal Hb or (HbF), which has two Gamma (γ) chains in the place of the adult β chains. HbF has a higher oxygen-binding capacity than adult HbA and enables the fetus to extract oxygen from the mother's bloodstream. The delta (δ) and gamma (γ) chains are the same length as the (β) chains, but differs in amino acid sequence. HbF is converted into HbA, but in some cases is not converted.



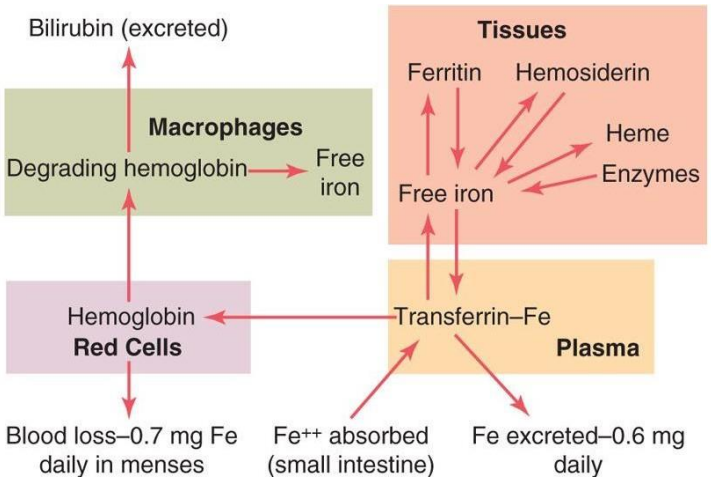
Iron Metabolism

- Because iron is important for formation of Hb, myoglobin and other substances such as cytochromes, cytochrome oxidase, peroxidase, and catalase, it is essential to understand the means by which iron is utilized in the body.
- The total quantity of iron in the body average 4-5 grams, about 65% of which is in the form of Hb.
- About 4% is in the form of myoglobin, 1% is in the form of the various heme compounds that promote intracellular oxidation, 0.1% is combined with the protein transferrin in the blood plasma, and 15-30% is stored mainly in the reticuloendothelial system and liver parenchymal cells, principally in the form of ferritin. A man excretes about 1 mg of iron each day, mainly into the feces

When iron is absorbed from the small intestine, it immediately combines in the blood plasma with beta globulin, apotransferria to form transferrin, which is then transported in the plasma.

The iron is loosely combined with the globulin molecule and consequently, can be released to any of tissue cells at any point in the body. Excess iron in the blood is deposited in all cells of the body, but especially in liver hepatocytes. In the cell cytoplasm, it combines mainly with a protein, apoferritin to form ferritin. The iron stored as ferritin is called ***storage iron***. Smaller quantities of the iron in the storage pool are stored, insoluble form called ***hemosiderin***. When the quantity of iron in plasma falls very low, iron is removed from ferritin quite easily, but much less easily from hemosiderin. When red blood cells have lived their life span and are destroyed, the Hb released

from the cells is ingested by the cells of the monocytes-macrophage system. There free iron is liberated, and it is mainly stored in the ferritin pool or formation of new Hb.



Hb Compounds

There are different compounds of Hb:

1. ***Oxyhemoglobin:*** this results from combination of O2 with Hb.

$$Hb + O2 \rightarrow HbO2$$

2. ***Carboxy Hb:*** this results from union of Co gas with Hb, Co gas is a very poisonous gas even if it is present in very small amount it displaces O2 in OxyHb so that carboxy Hb is produced, this is because of Co gas is about 250 times greater than O2 to Hb.

3. ***Sulfa Hb:*** this compound results from the combination of Hb with sulpher compounds.

4. ***Carbamino Hb:*** this results from the combination of CO2 gas with Hb.

$$Hb + CO2 \rightarrow HbCO2$$

5. ***Methemoglobin:*** if Hb subjected to O2 in the presence of an oxidizing agent, oxidation occurs and a new compound is produced is called Meth Hb.

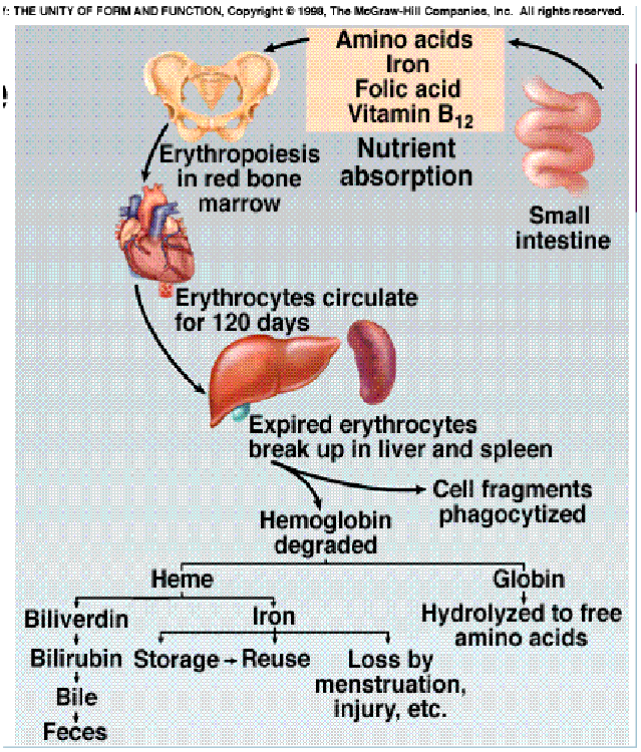
$$Met\ Hb\ Fe \rightarrow Fe + Hb \rightarrow HbFe$$

Destruction of Hb

The Hb released from the cells when they burst is phagocytosed almost immediately by macrophages in many parts of the body, but especially in liver (Kupffer cells), spleen and bone marrow. During the next few hours to days, the macrophage release the iron from the Hb back into the blood to be carried by transferrin either to bone marrow for production of new R.B.C. or to the liver and other tissues for storage in the form of ferritin. The porphyrin portion of the Hb molecule is converted by the macrophages, through a series of stages, into bile pigment bilirubin, which released into the blood and later secreted by the liver into the bile. A high level of bilirubin in the blood causes Jaundice, a yellowish cast in light-colored skin and the whites of eyes. Jaundice may be a sign of rapid hemolysis or a liver diseases. The normal plasma concentration of bilirubin is 0.5 mg/dl. The skin begins to appear jaundiced when concentration rise 1.5 mg/dl .

The common causes of jaundice are:

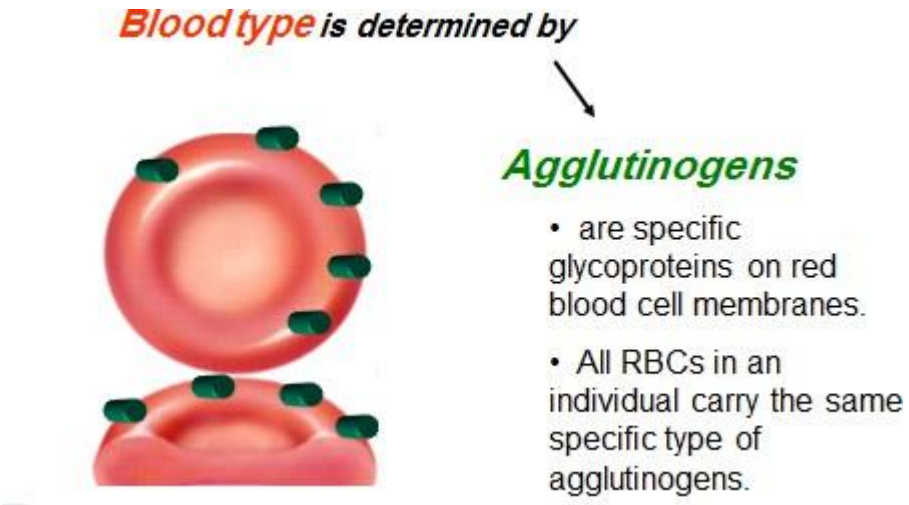
1. Increased destruction of R.B.C. with rapid release of bilirubin into blood.
2. Obstruction of the bile duct or damage to the liver cells.



Blood Groups

The ABO blood group consists of blood types A, B, AB and O, depending on the presence or absence of two antigens –type A and type B- occur on the surface of the R.B.C. it is also called (agglutinogens) because they often cause blood cell (agglutination) that cause blood transfusion. Because of the way these agglutinogens are inherited, people may have neither of them on their cells, they may have one, or they may have both simultaneously.

Type A: RBCs carry agglutinogen A.
Type B: RBCs carry agglutinogen B.
Type O: RBCs carry no A nor B agglutinogens.
Type AB: RBCs carry both A and B agglutinogens



Many genes have more than two alleles in a population. The ABO groups afford multiple alleles. Phenotypically, a person may have blood type A,B,AB and O owing to presence of three alleles in the population. Two of alleles are dominant and symbolized with a capital (I) (for immunoglobulin) and a superscript: I and I . there is one recessive allele, symbolized with a lower case i.

Genotype	Phenotype
I I	A
I i	A
I I	B
I i	B
I I	AB
i i	O

The essential function of DNA is to serve as a code for the structure of protein synthesized by a cell. A gene is a sequence of DNA nucleotides that code for a protein.

Agglutinins react against any AB agglutinogen expect those present on a person's own R.B.C. the agglutinin that reacts against antigen A is called α agglutinin, or anti-A, it is present in the plasma of people with type O or type B blood- that is , any one who does not possess agglutinogen A . the agglutinin that reacts against antigen B is β agglutinin, or anti-B, and is present in type O and A individuals – those

who don't possess agglutinogen B. Each agglutinin molecule has 10 binding sites where it can attach to an A or B agglutinogen. An agglutinin can therefore attach to several R.B.C. s at once and bind them together.

Agglutination

Is the process in which R.B.C. s adhere to each other in masses that are bound by these agglutinins.

Agglutinins

The agglutinins are gamma globulins, as other antibodies, and they are produced by the same cells that produce antibodies to any other antigens. Most of them are IgM and IgG immunoglobulin molecules. But why are these agglutinins produced in people who do not have the respective agglutinogens in their R.B.C.s? however, small amount of group A and B antigens enter the body in the food, in bacteria, and in other ways and these substances initiate the development of the anti-A or anti-B agglutinins.

Blood types	***Agglutinogens***	***Agglutinins***
A	**A**	**Anti B**
B	**B**	**Anti A**
AB	**A and B**	**———**
O	**———**	**Anti A and Anti B**

A person's ABO blood type can be determined by placing one drop of blood in a pool of anti-A serum and another drop in a pool of anti-B serum. Blood type AB will exhibit conspicuous agglutination in both antisera; type A or

B will agglutinate only in the corresponding antiserum; and type O will not agglutinate in.

Anti-A	Anti-B	Percentage %
Type A +	–	41%
Type B –	+	9%
Type AB +	+	3%
Type O –	–	47%

In giving transfusion, it is imperative that the donor's blood not agglutinate as it inters the recipient's blood stream. For example, if type B blood were transfused into type A recipient, the recipient's anti-B agglutinins would immediately agglutinate the donor's R.B.C.s. a mismatched transfusion causes a *Transfusion Reaction*. The agglutinated R.B.C.s block small blood vessels, hemolyze, and release their Hb over the next few hours to days. Free Hb can block the kidney tubules and cause death within a week or so from acute renal failure. For this reason, a person with type A (anti-B) blood must never be given a transfusion of type B or AB blood.

Type (AB) called the *Universal Recipient* while (O) *Universal Donor*.

The Rh Group

Along with the O-A-B blood group system, the Rh system is important in the transfusion of blood. In the O-A-B, the agglutinins responsible for causing transfusion reaction develop spontaneously, where as in the Rh system, spontaneous agglutinins almost never occur. There are 6 types of Rh antigens, each of which is called an Rh factor.

These types are C,D,E,c,d and e .A person who has a C antigen doesn't have c, but person missing the C antigen always has the c antigen. The same for D-d and E-e antigens. The type D is widely prevalent in the population. Therefore, anyone who has this type is said to be Rh+, where as a person who does not have type D is said to be Rh– .About 85% of people are Rh+ and 15% are Rh– .

Formation of Anti-Rh agglutinins:

When R.B.C.s containing Rh factor or even protein breakdown products of such cells are injected into a person whose blood does not contain the factor- that is, into the Rh– person anti-Rh agglutinins develop slowly and maximum concentration of agglutinins occurring about 2-4 months. On multiple exposure to Rh factor, the Rh– person become strongly (*sensitized*) to Rh factor.

Erythrobastosis Fetalis (Hemolytic disease of Newborn)

This disease of the fetus is characterized by agglutination and phagocytosis of R.B.C.s . In most instances of this diseases, the mother is Rh– and father is Rh+. The baby has inherited the Rh+ antigen from father, and mother has developed anti-Rh agglutinins from exposure to the baby's Rh antigen , in turn, the mother agglutinins diffuse through the placenta into the fetus to cause R.B.C.s agglutination.

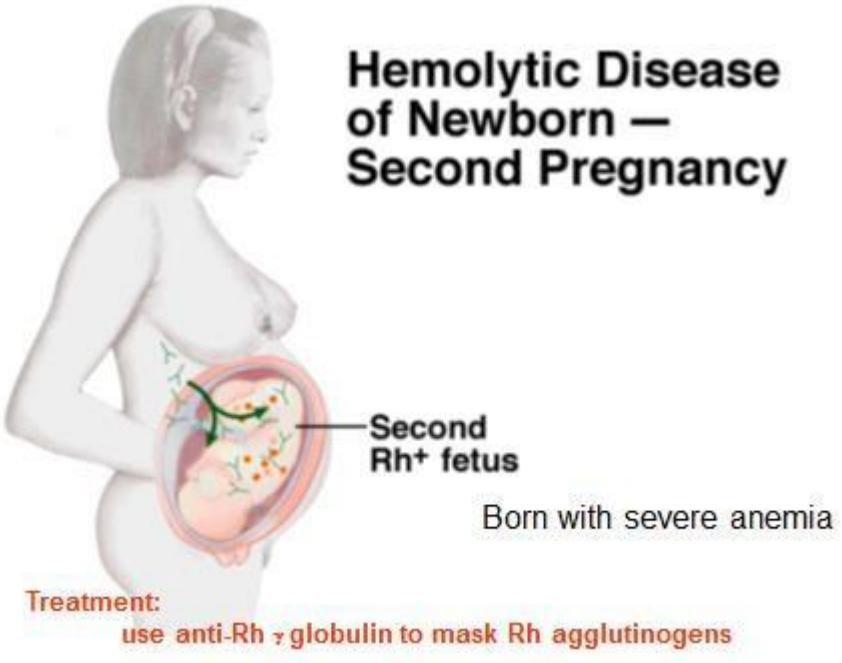
Effect of the Mother's Antibodies on the Fetus:

After anti-Rh antibodies have formed in the mother, they diffuse slowly through the placental membrane into the fetus's blood. There they cause agglutination of fetus's blood. The agglutinated R.B.C.s subsequently hemolyze, releasing Hb into the blood. The macrophages then convert the Hb into *Bilirubin*, which causes the skin to yellow (Jaundice). The antibodies can also attack and damage other cells of the body. The jaundiced erythroblastotic neonate is usually anemic at birth, and anti-Rh agglutinins from mother usually circulate in the infant's blood for 1-2 months after birth, destroying more and more R.B.C.s.

The usual treatment is to replace the neonate's blood with Rh– blood. About 400 milliliters of Rh– blood is infused over a period of 1.5 or more hours while the neonates own Rh+ blood is being removed. The Rh– cells are replaced with the baby own Rh+ cells.

Transfusion Reactions resulting from mismatched Blood Types

If donor's blood of one blood type is transfused to a recipient of another blood type, a transfusion reaction is likely in which the R.B.C.s of donor blood are agglutinated. It is rare that the transfused blood causes agglutination of the recipient's cells, the plasma portion of the donor's blood immediately becomes dilated by all the plasma of recipient, there by decreasing the titir of infused agglutinins to a level low to cause agglutination. On other hand, the infused blood does not dilute the agglutinins in the recipient's plasma to major extent. Therefore, the recipient's agglutinins can still agglutinate the donor's cells.



Nature of Antibodies

The antibodies are gamma globulins called immunoglobulin and they have molecular weights between 160,000-970,000. they always constitute about 20% of all the plasma protein.

It is composed of combinations of light and heavy polypeptide chains, most of combination are 2 light and 2 heavy chains.

This structure of the typical IgG, showing 2 heavy polypeptide chains and 2 light polypeptide chains. The antigen binds as two different sites on the variable portion of the chains. The end of each light and heavy called variable portion, the remainder of each chain is called constant portion.

Each antibody is specific for a particular antigen, this caused by the structural organization of amino acids in variable portion of both light and heavy.

There are many bonding sites that antibody-antigen coupling is nevertheless exceedingly strong, held together by:

1. **Hydrophobic bonding.**
2. **Hydrogen bonding.**
3. **Ionic attractions.**
4. **Van der walls forces.**

There are five general classes of antibodies, respectively IgM, IgG, IgA, IgD and IgE. The antibodies have 10 binding sites that make them exceedingly effective in protecting the body against invaders.

The antibodies acts mainly in two ways to protect the body invading agents by:

1. **direct attack on the invader and.**
2. **by activation of complement system.**

In the direct attack, the antibody like Y-shaped bars, reacting with antigens, because of bivalent nature of the antibodies and multiple antigen sites on most invading agents, the antibodies can inactivate the invading agents in several ways:

1. **Agglutination, in which multiple large particles with antigen on their surface.**
2. **Precipitation, in which the molecular complex of soluble antigen and antibody becomes so large that it is rendered insoluble and precipitates.**
3. **Neutralization, in which the antibodies cover the toxic sites of the antigenic agent.**

4. **Lysis, in which some potent antibodies are occasionally capable of directly attacking membranes of cellular agents and there by causing rupture of the cell.**

<u>The Activation of Complement:</u> **complement is a collective term describes a system of about 20 proteins, many of which are enzyme precursors.**

Hemostasis and Blood Coagulation

The term hemostasis means prevention of blood loss. This achieved by several mechanisms, including:

1. **Vascular spasm.**
2. **Formation of a platelets plug.**
3. **Formation of blood clot.**
4. **Growth of fibrous tissue into the blood clot to close the whole vessel permanently.**

Vascular Spasm

The most immediate protection against blood loss is vascular spasm, a prompt constriction of the broken vessel. Several things trigger this reaction. An injury stimulates with pain receptors, some of which directly innervate nearby blood vessels and cause them to constrict. Immediately after a blood vessel is cut or ruptured, the stimulus of the trauma to the vessel causes the wall of the vessel to contract due to nervous reflexes, local myogenic spasm and local humoral factors from blood platelets.

Formation of a Platelet Plug.

Platelets are not cells, but small fragments of megakaryote cytoplasm. Although they were once called thrombocytes. Platelets are small round or oval discs 2-4 µm in diameter.

They are formed in the bone marrow from megakaryocytes which are extremely large cells of the hemopoietic series in the bone marrow that fragment into platelets. The normal concentration of platelets in the blood is between 150,000 and 400,000 per µL.

Platelets have many functional, even through these do not have nuclei and can not reproduce. In their cytoplasm are such active factor as:

1. **They secrete growth factors that stimulate mitosis in fibroblasts and smooth muscle and help to maintain the linings of blood vessels.**

2. **They secrete vasoconstrictors that cause vascular spasm in broken vessels.**

3. **They form temporary platelet plugs to stop bleeding.**

4. **They phagocytize and destroy bacteria.**

5. **They secrete chemicals that attract neutrophils and monocytes to sites of inflammation.**

6. **They dissolve blood clots that have outlasted their usefulness.**

The cell membrane of the platelets is also important, on its surface is a coat of glycoproteins that causes it to avoid adherence to normal endothelium and yet to adhere to injured areas of the vessel wall.

Mechanism of the Platelet Plug

Platelet repair of vascular openings is based on several important functions of the platelet itself, when platelets come in contact with a damaged vascular surface, such as the collagen fibers in the vascular wall or damaged endothelial cells, they immediately change their characteristics. They begin to swell, they assume irregular forms and become sticky so that they stick to the collagen fibers, they secrete large quantities of ADP and their enzymes form thromboxane A2 in turn act on nearby platelets to activate them as well forming a platelet plug.

Formation of Blood Clot

The clot begins to develop in 15 seconds, if trauma of the vascular wall has been severe, and in 1-2 minutes if it is minor.

Mechanism of Blood Coagulation

The clotting takes place in three steps:

1. **In response to rupture of the vessel or damage to the blood, the complex of activated substances collectively called prothrombin activator.**
2. **The prothrombin activator catalyzes the conversion of prothrombin into thrombin.**
3. **The thrombin acts an enzyme to convert fibrinogen into fibrin fibers, that enmesh platelets, blood cells and plasma to form the clot.**

Conversion of Prothrombin to Thrombin :

Prothrombin is a plasma protein, an alpha 2- globulin, having a molecular weight of 68,700. it is present in normal plasma in a concentration 15 mg/dl. It is unstable protein that can easily split into thrombin which has a molecular weight 33,700 in presences of prothrombin activator and calcium ions.

Prothrombin is formed by the liver, vitamin K is required by the liver for normal formation of prothrombin.

Conversion of Fibrinogen to Fibrin

Fibrinogen is a high-molecular weight protein (340,000) that occurs in the plasma in quantities of 100-700 mg/dl. It's formed in the liver.
Thrombin is a protein enzyme with proteolytic capabilities, it act on fibrinogen to remove four low-molecular weight peptides from each

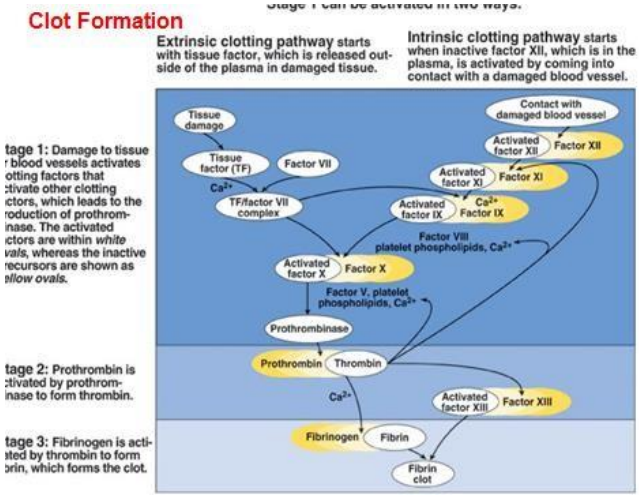
molecule of fibrinogen, forming a molecule of fibrin monomer that has the automatic capability of polymerizing with other fibrin molecule forming long fibrin fibers that form the reticulum of clot. There are two reaction pathways to coagulation, one of them, extrinsic mechanism, is initiated by clotting factors released by the damaged blood vessel and perivascular tissues. The reaction pathway it use only clotting factors found in the blood itself called intrinsic mechanim.

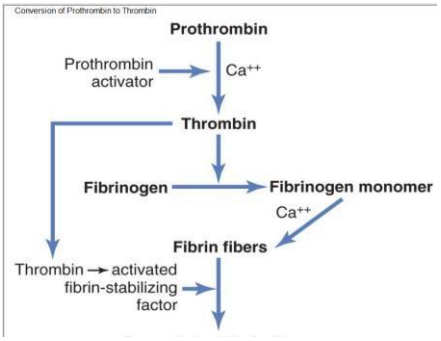
The extrinsic mechanism is the damage of blood vessel release lipoprotein mixture called thromboplastin (factor III) in the presences of Ca , thromboplatin activates factor VII, which then activates factor X. the extrinsic and intrinsic pathways differ only in how they arrive at active factor X.

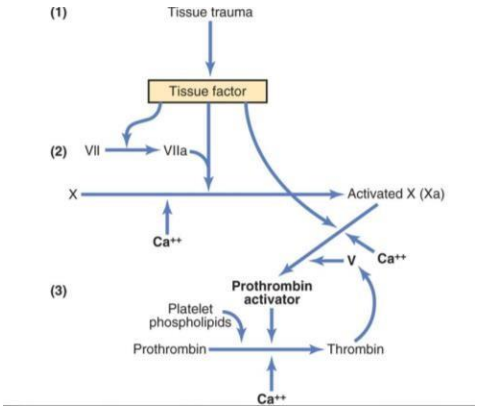
The intrinsic mechanism, when platelets degranulate, they release factor XII (Hageman factor) and then this leads to activated factors XI, IX and VIII, in that order, each serving as an enzyme that catalyzes the next step and finally to factor X. This pathway also requires calcium ions and platelet thomboplastic factor (PF3).

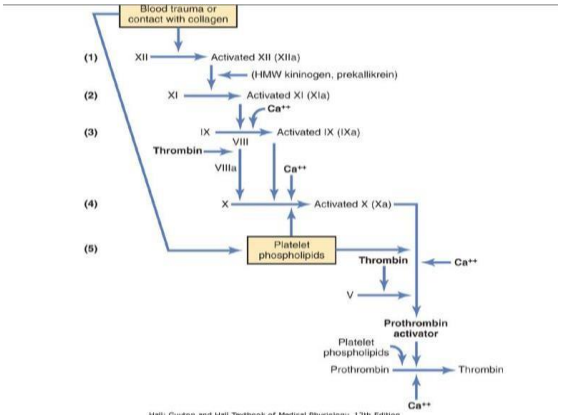
Once factor X is activated, the remaining events are identical in the intrinsic and extrinsic mechanisms. Factor X combines with factors III and V in the presence of (Ca and PF3) to produce an enzyme, prothombin activator, this enzyme acts on a globulin called prothrombin (factor II) , converting it to enzyme thrombin. Thrombin then converts fibrinogen to fibrin. Fibrin forms a loose mesh at first, but factor VIII causes the formation of covalent cross-links that convert this to fibrin polymer – a dense aggregation of fibers that forms the structural basis of the clot.

The especially important difference between extrinsic and intrinsic pathway is the extrinsic can explosive nature, once initiated, its speed of occurrence is limited only by the amount of tissue factor released from the traumatized tissues and by the quantities of factor X, VII and V in the blood. With severe trauma, clotting can occur in 15 seconds. While intrinsic usually 1-6 minutes to cause clotting.


Clot Formation
Extrinsic clotting pathway starts with tissue factor, which is released outside of the plasma in damaged tissue.
Intrinsic clotting pathway starts when inactive factor XII, which is in the plasma, is activated by coming into contact with a damaged blood vessel.
tage 1: Damage to tissue r blood vessels activates otting factors that ctivate other clotting ctors, which leads to the roduction of prothrom- inase. The activated ctors are within white vals, whereas the inactive recursors are shown as llow ovals.
tage 2: Prothrombin is ctivated by prothrom- inase to form thrombin.
tage 3: Fibrinogen is acti- ted by thrombin to form brin, which forms the clot.
Tissue damage
Contact with damaged blood vessel
Activated factor XII
Factor XII
Tissue factor (TF)
Factor VII
Activated factor XI
Factor XI
Ca2+
TF/factor VII complex
Activated factor IX
Ca2+
Factor IX
Factor VIII
platelet phospholipids, Ca2+
Activated factor X
Factor X
Factor V, platelet phospholipids, Ca2+
Prothrombinase
Prothrombin
Thrombin
Ca2+
Activated factor XIII
Factor XIII
Fibrinogen
Fibrin
Fibrin clot


Conversion of Prothrombin to Thrombin
Prothrombin
Prothrombin activator
Ca++
Thrombin
Fibrinogen
Fibrinogen monomer
Ca++
Fibrin fibers
Thrombin → activated fibrin-stabilizing factor


(1)
Tissue trauma
Tissue factor
(2)
VII
VIIa
X
Activated X (Xa)
Ca++
V
Ca++
(3)
Prothrombin activator
Platelet phospholipids
Prothrombin
Thrombin
Ca++


Blood trauma or contact with collagen
(1)
XII
Activated XII (XIIa)
(HMW kininogen, prekallikrein)
(2)
XI
Activated XI (XIa)
Ca++
(3)
IX
VIII
Activated IX (IXa)
Thrombin
VIIIa
Ca++
(4)
X
Activated X (Xa)
(5)
Platelet phospholipids
Thrombin
Ca++
V
Prothrombin activator
Platelet phospholipids
Prothrombin
Thrombin
Ca++

General Physiology Lec.9

Prevention of Clotting in the Normal Vascular System

The intravascular anticoagulants

1. **<u>Endothelial surface factor:</u>**

    a. **The smoothness of endothelium, which prevents contact activation of the intrinsic clotting system.**
    b. **Layer of glycocalyx, a mucopolysaccharides adsorbed to the inner surface of the endothelium, which repels the clotting factor and platelets.**
    c. **A protein bound with endothelial membrane, thrombin which bind thrombomodulin, this dulin-thrombin not only slows the clotting process, but also activates a plasma protein, protein C, that acts as an anticoagulant by inactivating activated factors V and VIII.**

2. **<u>Antithrombin factor:</u> the most important anticoagulants in the blood itself that remove thrombin from blood, the most powerful**

    1. **The fibrin fibers that themselves are formed during the process of clotting and**
    2. **an alpha- globulin called antithrombin III or antithrombin – heparin co factor, about 85-90% of thrombin formed adsorbed to the fibrin fibers as they develop. The thrombin that does not adsorb to fibrin fibers, soon combines with antithrombin III, which block the effect of the thrombin on the fibrinogen and inactivates it within 12-20 minutes.**

3. **<u>Heparin:</u> is a conjugated polysaccharide, formed by the basophilic mast cells located in the pericapillary connective tissue throughout the body. It prevents blood coagulation by combining with antithrombin-heparin co factor which makes this factor combine with thrombin. The antithrombin heparin complex removes several other activated coagulation factors in addition to thrombin from circulating blood, the others include factors XII, XI, IX and X.**

Prevention of Blood Coagulation outside the Body:

1. **Heparin: it prevents the blood coagulation when added to the sample of blood outside the body as well as in the body.**

2. **Calcium-deionizing agent used for preventing coagulation is sodium, ammonium, or potassium citrate. The citrate ion combines with Ca in the blood to cause an un-ionized Ca compound, and lack of Ca prevents coagulation.**

3. **Collecting of the blood in siliconized containers, which prevents contact activation of platelets and factor XII, which are effects that initiate the intrinsic clotting mechanism.**

4. **Coumarine derivates: these are used internally to prolong the coagulation time from the normal range of about 2-3 minutes to 10 minutes. Vitamin K is essential for the formation of prothrombin by the liver, these substances when given they interfere with action of Vit. K and this cause a decrease in the formation of prothrombin by the**

liver and this causes prolongation of coagulation time, and this prevents the occur of blood clots.

Blood Disease

1. **Decreased prothrombin, factor VII, IX and X caused by Vitamin K.**

Hepatitis , cirrhosis (replacement of liver cells by fibrous tissue), acute yellow atrophy and the presence of a stone in the common bile duct (in which bile does not reach the duodenum) and this effect on the absorption of vit. K . all these factors cause a severe tendency to bleed.
These liver diseases often cause decreased production of prothrombin and the other factor both because of poor vitamin K absorption and because of the diseased liver cells.

2. ***Hemophilia:*** **it is a hereditary disease which affects the male only, the female is not affected by the disease, because at least one of her two X chromosomes will have the appropriate genes. If one of her X chromosomes is deficient, she will be a hemophilia carrier.**

There are three types of Hemophilia:
1. **Classical hemophilia (hemophilia A):**

This is caused by the deficiency of factor VIII.
2. **Hemophilia B: this caused by deficiency of factor IX.**
3. **Hemophilia C: this caused by the deficiency of factor XI.**

The treatment by giving the patient deficient factor.

3. **Thrombocytopenia: this means the presence of a very low quantity of platelets in the circulating system, this caused**

by drugs, chemicals and sometimes due to unknown reason, in this case it's called idiopathic thrombocytopenia.

The treatment by giving the patient blood containing fresh blood platelets. (ordinary, bleeding does not occur until the number of platelets in the blood below 50,000 µl rather than normal 150,000-300,000 levels as low as 10,000 µl are frequently lethal.

Lect. Physiology

Digestive System

The major functions of the digestive system are as follows:

1. Ingestion is the introduction of solid or liquid food into the stomach.

2. Mastication is the process by which food taken into the mouth is chewed by the teeth. Digestive enzymes cannot easily penetrate solid food particles and can only work effectively on the surfaces of the particles. It's vital, therefore, to normal digestive function that solid foods be mechanically broken down into small particles. Mastication breaks large food particles into many smaller particles, which have a much larger total surface are a than do a few large particles.

3. Propulsion in the digestive tract is the movement of food from one end of the digestive tract to the other. The total time that it takes food to travel the length of the digestive tract is usually about 24-36 hours. Each segment of the digestive tract is specialized to assist in moving its contents from the oral end to the anal end. Deglutition, or swallowing, moves food and liquids, called a bolus, from the oral cavity into the esophagus. Peristalsis isresponsible for moving material through most of the digestive tract. Muscular contractions occur in peristaltic waves, consisting of a wave of relaxation of the circular muscles, which forms a leading wave of distention in front of the bolus, followed by a wave of strong contraction of the circular muscles behind the bolus, which forces thebolus along the digestive tube. Each peristaltic wave travels the length of the esophagus in about 10 seconds .Peristaltic waves in the small intestine usually only travel for short distances. In some parts of the large intestine, material is moved by mass movements, which are contractions that extend over much larger parts of the digestive tract than peristaltic movements.

4. Mixing. Some contractions don't propel food (chyme) from one end of the digestive tract to the other but rather move the food back and forth within the digestive tract to mix it with digestive secretions and to help break it into smaller pieces. Segmental contractions are mixing contractions that occur in the small intestine.

5. Secretion. As food moves through the digestive tract, secretions are added to lubricate, liquefy, and digest the food. Mucus, secreted along the entire digestive tract, lubricates the food and the lining of the tract. The muc us coats and protects the epithelial cells of the digestive tract from mechanical abrasion, from the damaging effect of acid in the stomach, and from the digestive enzymes of the digestive tract. The secretions also contain large amounts of water, which liquefies the food, thereby making it easier to digest and absorb. Water also moves into the intestine by osmosis. Liver secretions break large fat droplets into much smaller droplets, which makes possible the digestion and absorption of fats. Enzymes secreted by the oral cavity, stomach, intestine,and pancreas break large food molecules down into smaller molecules that canbe absorbed by the intestinal wall.

6. Digestion is the breakdown of large organic molecules into their component parts: carbohydrates into monosaccharides, proteins into amino acids, and triglycerides into fatty acids and glycerol.Digestio consists of mechanical digestion, which involves mastication and mixing of food, and chemical digestion, which is accomplished by digestive enzymes that are secreted along the digestive tract. Digestion of large molecules into their component parts must be accomplished before they can be absorbed by the digestive tract. Minerals and water are not broken down before being absorbed. Vitamins are also absorbed without digestion and lose their function if their structure is altered by digestion.

7. Absorption is the movement of molecules out of the digestive tract and into the circulation or into the lymphatic system. The mechanism by which absorption occurs depends on the type of molecule involved. Molecules pass out of the digestive tract by simple diffusion, facilitated diffusion, active transport, or cotransport.

8. Elimination is the process by which the waste products of digestion are removed from the body. During this process, occurring primarily in the large intestine, water and salts are absorbed and change the material in the digestive tract from a liquefied state to a semisolid state. These semisolid waste products, called feces, are then eliminated from the digestive tract by the process of defecation.

Stomach

The stomach is an enlarged segment of the digestive tract in the left superior part of the abdomen. Its shape and size vary from person to person; even within the same individual its size and shape change from time to time, depending on its food content and the posture of the body.

Secretions of the Stomach

Ingested food and stomach secretions mixed together, form a semifluid material called chyme. The stomach functions primarily as storage and mixing chamber for the chyme. Although some digestion and absorption occur in the stomach, they are not its major functions.

Stomach secretions include mucus, hydrochloric acid, gastrin, histamine, intrinsic factor, and pepsinogen. Pepsinogen is the inactive form of the protein-digesting enzyme pepsin.

The surface mucous cells and mucous neck cells secrete viscous and alkaline mucus that covers the surface of the epithelial cells and forms a layer 1-1.5 mm thick. The thick layer of mucus lubricates and protects the epithelial cells of the stomach wall from the damaging effect of the acidic chyme and pepsin. Irritation of the stomach mucosa results in stimulation of the secretion of a greater volume of mucus.

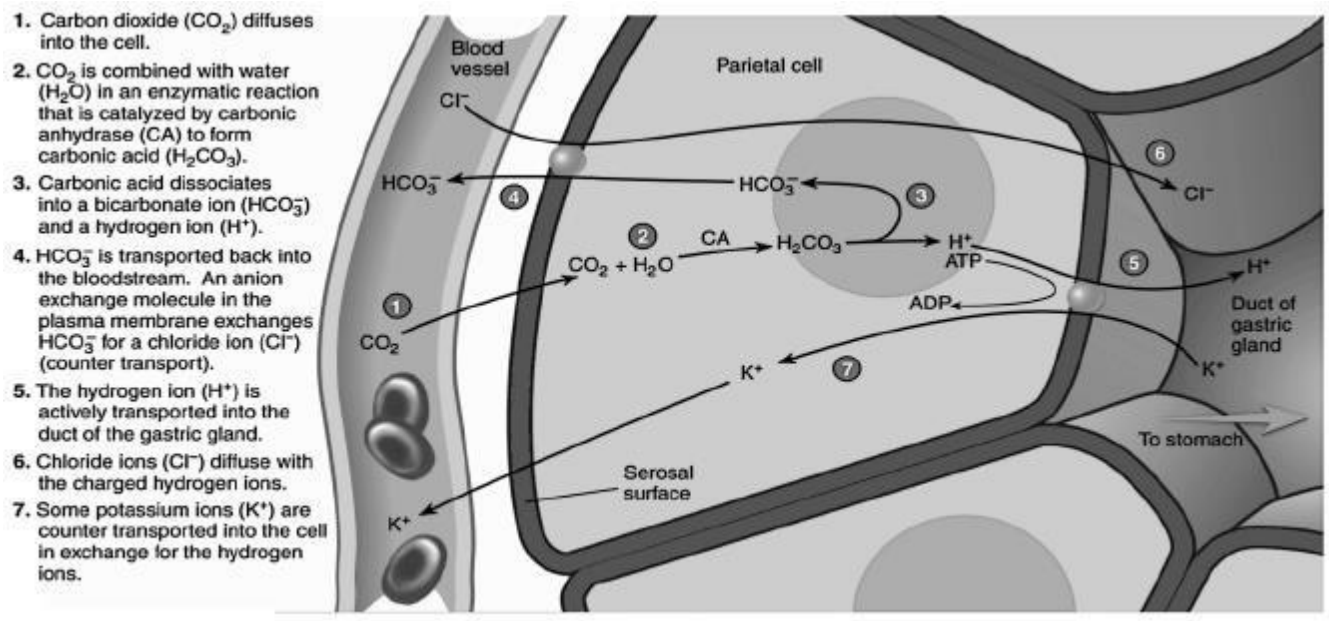
Parietal cells in the gastric glands of the pyloric region secrete intrinsic factor and a concentrated solution of hydrochloric acid. Intrinsic factor is a glycoprotein that binds with vitamin B_{12} and makes the vitamin more readily absorbed in the ileum. Vitamin B_{12} is important in deoxyribonucleic acid (DNA) synthesis.

Hydrochloric acid produces the low pH of the stomach, which is normally between 1 and 3. Although The hydrochloric acid secreted into the stomach has a minor digestive effect on ingested food, one of its main functions is to kill bacteria that are ingested with essentially everything humans put into their mouths. Some pathogenic bacteria may avoid digestion in the stomach, however, because they have an outer coat that resists stomach acids.

The low pH of the stomach also stops carbohydrate digestion by inactivating salivary amylase. Stomach acid also denatures many proteins so that proteolytic enzymes can reach internal peptide bonds, and it provides the proper pH environment for the function of pepsin.

Hydrogen ions are derived from carbon dioxide and water, which enter the parietal cell from its serosal surface, which is the side opposite the lumen of the gastric pit. Once inside the cell, carbonic anhydrase catalyzes the reaction between carbon dioxide and water to form carbonic acid. Some of the carbonic acid molecules then dissociate to form hydrogen ions and bicarbonate ions. The hydrogen ions are actively transported across the mucosal surface of the parietal cell into the lumen of the stomach; some potassium ions are moved into the cell in exchange for the hydrogen ions. Although hydrogen ions are actively transported against a steep concentration gradient, chloride ions diffuse with the hydrogen ions from the cell through the plasma membrane. Diffusion of chloride ions with the positively charged hydrogen ions reduces the amount of energy needed to transport the hydrogen ions against both a concentration gradient and an electrical gradient. Bicarbonate ions move down their concentration gradient from the parietal cell into the extracellular fluid. During this process, bicarbonate ions are exchanged for chloride ions through an anion exchange molecule, which is located in the plasma membrane, and the chloride ions subsequently move into the cell.

Chief cells within the gastric glands secrete pepsinogen. Pepsinogen is packaged in zymogen granules, which are released by exocytosis when pepsinogen secretion is stimulated. Once pepsinogen enters the lumen of the stomach, hydrochloric acid and previously formed pepsin molecules convert it to pepsin. Pepsin exhibits optimum enzymatic activity at a pH of 3 or less. Pepsin catalyzes the cleavage of some covalent bonds in proteins, thus breaking them into smaller peptide chains.



Hydrochloric Acid Production by Parietal Cells in the Gastric Glands of the Stomach

Regulation of Stomach Secretion

Approximately 2-3L of gastric secretions (gastric juice) is produced each day. The amount and type of food entering the stomach dramatically affects the secretion amount, but up to 700 mL is secreted as a result of a typical meal. Both nervous and hormonal mechanisms regulate gastric secretions. The neural mechanisms involve reflexes integrated within the medulla oblongata and local reflexes integrated within the enteric plexus of the GI tract. In addition, higher brain centers influence the reflexes. Chemical signals that regulate stomach secretions include the hormones gastrin, secretin, gastric-inhibitory polypeptide, and cholecystokinin, as well as the paracrine chemical signal histamine.

Regulation of stomach secretion is divided into three phases: cephalic, gastric, and intestinal.

1. Cephalic phase. In the cephalic phase of gastric regulation, the sensations of the taste and smell of food, stimulation of tactile receptors during the process of chewing and swallowing, and pleasant thoughts of food stimulate centers within the medulla oblongata that influence gastric secretions. Action potentials are sent from the medulla along parasympathetic neurons within the vagus (X) nerves to the stomach. Within the stomach wall, the preganglionic neurons stimulate postganglionic neurons in the enteric plexus. The postganglionic neurons, which are primarily cholinergic, stimulate secretory activity in the cells of the stomach mucosa.

Parasympathetic stimulation of the stomach mucosa results in the release of the neurotransmitter acetylcholine, which increases the secretory activity of both the parietal and chief cells and stimulates the secretion of gastrin and histamine from endocrine cells. Gastrin is released into the circulation and travels to the parietal cells, where it stimulates additional hydrochloric acid and pepsinogen secretion. In addition, gastrin stimulates endocrine cells to release histamine, which stimulates parietal cells to secrete hydrochloric acid. The histamine receptors on the parietal cells are called H_2 receptors, and are different from the H_1 receptors involved in allergic reactions. Drugs that block allergic reactions do not affect histamine-mediated stomach acid secretion and vice versa. Acetylcholine, histamine, and gastrin working together cause a greater secretion of hydrochloric acid than any of them does separately. Of the three, histamine has the greatest stimulatory effect.

2. Gastric phase. The greatest volume of gastric secretions is produced during the gastric phase of gastric regulation. The presence of food in the stomach initiates the gastric phase. The primary stimuli are distention of the stomach and the presence of amino acids and peptides in the stomach.

Distention of the stomach wall, especially in the body or fundus, results in the stimulation of mechanoreceptors. Action potentials generated by these receptors initiate reflexes that involve both the CNS and enteric reflexes, resulting in secretion of mucus, hydrochloric acid, pepsinogen, intrinsic factor, and gastrin. The presence of partially digested proteins or moderate amounts of alcohol or caffeine in the stomach also stimulates gastrin secretion.

When the pH of the stomach contents falls below 2, increased gastric secretion produced by distention of the stomach is blocked. This negative-feedback mechanism limits the secretion of gastric juice.

Amino acids and peptides released by the digestive action of pepsin on proteins directly stimulate parietal cells of the stomach to secrete hydrochloric acid. The mechanism by which this response is mediated is not clearly understood. It doesn't involve known neurotransmitters, and, when the pH drops below 2, the response is inhibited. Histamine also stimulates the secretory activity of parietal cells.

3. Intestinal phase. The entrance of acidic stomach contents into the duodenum of the small intestine controls the intestinal phase of gastric regulation.The presence of chyme in the duodenum activates both neural and hormonal mechanisms. When the pH of the chyme entering the duodenum drops to 2 or below, or if the chyme contains fat digestion products, gastric secretions are inhibited.

Acidic solutions in the duodenum cause the release of the hormone secretin into the circulatory system. Secretin inhibits gastric secretion by inhibiting both parietal and chief cells. Acidic solutions also initiate a local enteric reflex, which inhibits gastric secretions.

Fatty acids and certain other lipids in the duodenum and the proximal jejunum initiate the release of two hormones: gastric inhibitory polypeptide and cholecystokinin ,Gastric inhibitory polypeptide strongly inhibits gastric secretion, and cholecystokinin inhibits gastric secretions to a lesser degree. Hypertonic solutions in the duodenum and jejunum also inhibit gastric secretions. The mechanism appears to involve the secretion of a hormone referred to as enterogastrone, but the actual existence of this hormone has never been established.

Cephalic Phase

1. The taste or smell of food, tactile sensations of food in the mouth, or even thoughts of food stimulate the medulla oblongata (*green arrow*).
2. Parasympathetic action potentials are carried by the vagus nerves to the stomach (*pink arrow*).
3. Preganglionic parasympathetic vagus nerve fibers stimulate postganglionic neurons in the enteric plexus of the stomach.
4. Postganglionic neurons stimulate secretion by parietal and chief cells and stimulate gastrin secretion by endocrine cells.
5. Gastrin is carried through the circulation back to the stomach (*purple arrow*), where it stimulates secretion by parietal and chief cells.

(a)

Gastric Phase

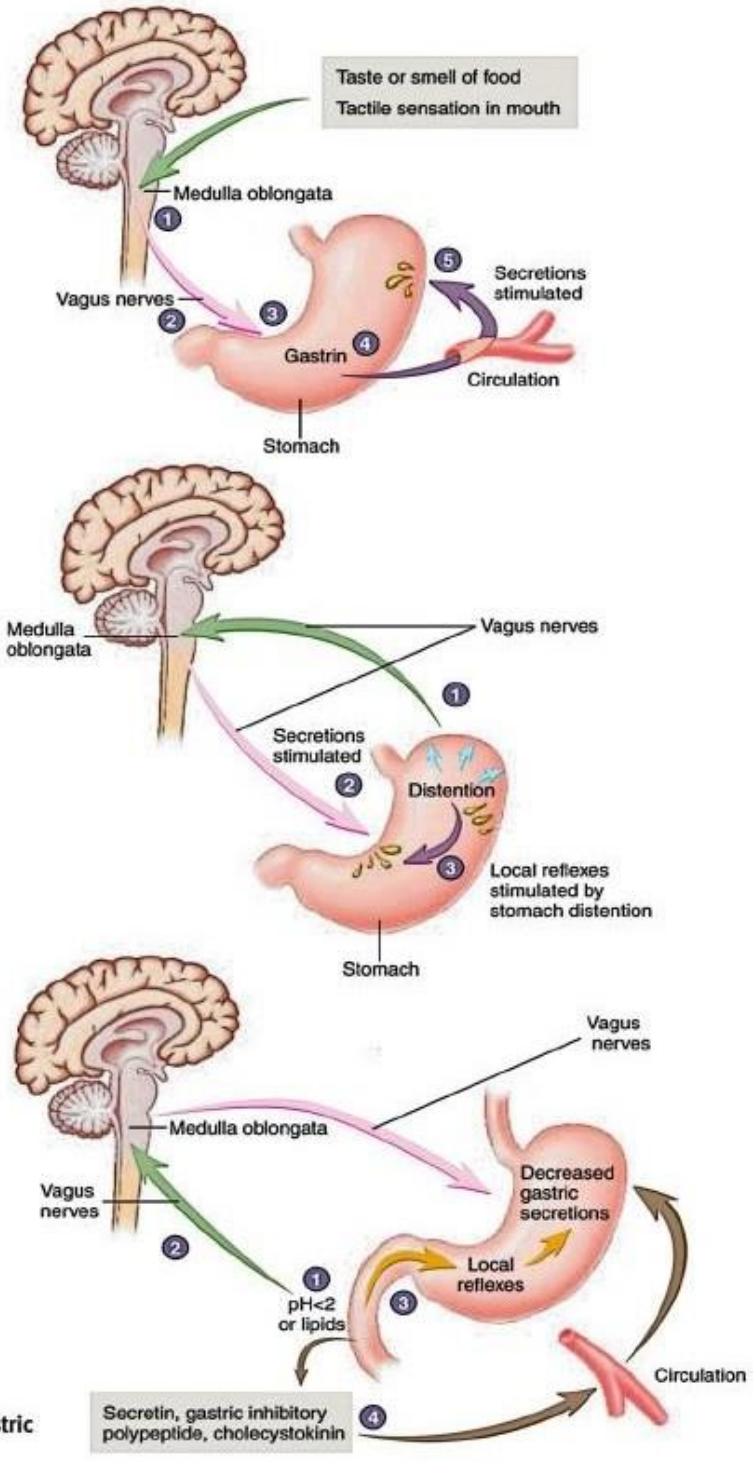
1. Distention of the stomach activates a parasympathetic reflex. Action potentials are carried by the vagus nerves to the medulla oblongata (*green arrow*).
2. The medulla oblongata stimulates stomach secretions (*pink arrow*).
3. Distention of the stomach also activates local reflexes that increase stomach secretions (*purple arrow*).

(b)

Intestinal Phase

1. Chyme in the duodenum with a pH less than 2 or containing fat digestion products (lipids) inhibits gastric secretions by three mechanisms (2–4).
2. Sensory vagal action potentials to the medulla oblongata (*green arrow*) inhibit motor action potentials from the medulla oblongata (*pink arrow*).
3. Local reflexes inhibit gastric secretion (*orange arrows*).
4. Secretin, gastric inhibitory polypeptide, and cholecystokinin produced by the duodenum (*brown arrows*) inhibit gastric secretions in the stomach.

(c)



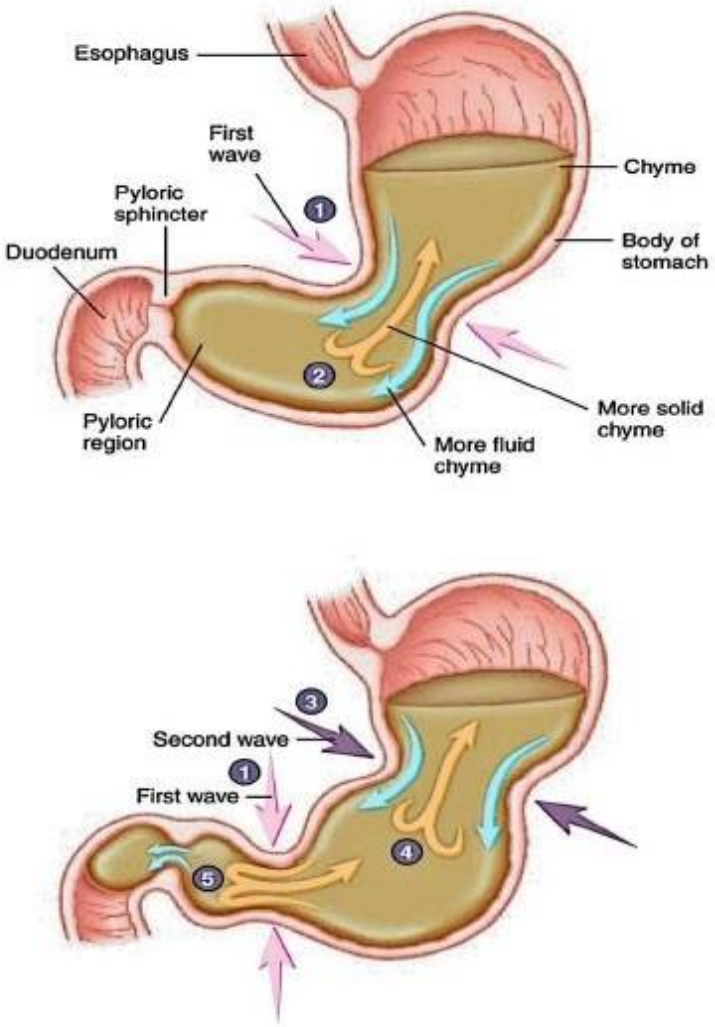
The Three Phases of Gastric Secretion

(*a*) Cephalic phase. (*b*) Gastric phase. (*c*) Intestinal phase.

Mixing of Stomach Contents

Ingested food is thoroughly mixed with the secretions of the stomach glands to form chyme. This mixing is accomplished by gentle mixing waves, which are peristaltic-like contractions that occur about every 20 seconds and proceed from the body toward the pyloric sphincter to mix the ingested material with the secretions of the stomach. Peristaltic waves occur less frequently, are significantly more powerful than mixing waves, and force the chyme near the periphery of the stomach toward the pyloric sphincter. The more solid material near the center of the stomach is pushed superiorly toward the cardiac region for further digestion. Roughly 80% of the contractions are mixing waves, and 20% are peristaltic waves.

1. Mixing waves initiated in the body of the stomach progress toward the pyloric region (*pink arrows directed inward*).
2. The more fluid part of the chyme is pushed toward the pyloric region (*blue arrows*), whereas the more solid center of the chyme squeezes past the peristaltic constriction back toward the body of the stomach (*orange arrow*).
3. Additional mixing waves (*purple arrows*) move in the same direction and in the same way as the earlier waves (**1**) that reach the pyloric region.
4. Again, the more fluid part of the chyme is pushed toward the pyloric region (*blue arrows*), whereas the more solid center of the chyme squeezes past the peristaltic constriction back toward the body of the stomach (*orange arrow*).
5. Some of the most fluid chyme is squeezed through the pyloric opening into the duodenum (*small blue arrows*), whereas most of the chyme is forced back toward the body of the stomach for further mixing (*orange arrows*).



Movements in the Stomach

Stomach Emptying

The amount of time food remains in the stomach depends on a number of factors, including the type and volume of food. Liquids exit the stomach within 11/2 - 21/2 hours after ingestion. After a typical meal, the stomach is usuallyempty within 3-4 hours. The pyloric sphincter usually remains partially closed because of mild tonic contraction.

Each peristaltic contraction is sufficiently strong to force a small amount of chyme through the pyloric opening and into the duodenum. The peristaltic contractions responsible for movement of chyme through the partially closed pyloric opening are called the pyloric pump.

Lec. 11

Saliva

Composition of Saliva

Mixed saliva contains 99.5% water and 0.5% solids.

Properties of Saliva

1. Volume: 1000 to 1500 mL of saliva is secreted per day and, it is approximately about 1 mL/ minute. Contribution by each major salivary gland is:

i. Parotid glands: 25%

ii. Submaxillary glands: 70%

iii. Sublingual glands: 5%.

2. Reaction: Mixed saliva from all the glands is slightly acidic with pH of 6.35 to 6.85.

3. Specific gravity: It ranges between 1.002 and 1.012.

4. Tonicity: Saliva is hypotonic to plasma.

Functions of Saliva

Saliva is a very essential digestive juice. Since it has many functions, its absence leads to many problems.

1. Preparation of food for swallowing

When food is taken into the mouth, it is moistened and dissolved by saliva. The mucous membrane of mouth is also moistened by saliva. It facilitates chewing. By the movement of the tongue, the moistened and masticated food is rolled into a bolus. The mucin of saliva lubricates the bolus and facilitates the swallowing.

2. Appreciation of taste

Taste is a chemical sensation. Saliva by its solvent action dissolves the solid food substances, so that the dissolved substances can stimulate the taste buds. The stimulated taste buds recognize the taste.

3. Digestive function

Saliva has three digestive enzymes namely, salivary amylase, maltase and lingual lipase.

Salivary Amylase

Salivary amylase is a carbohydrate digesting (amylolytic) enzyme. It acts on cooked or boiled starch and converts it into dextrin and maltose. Though starch digestion starts in the mouth, major part of it occurs in the stomach because, food stays only for a short time in the mouth. The optimum

pH necessary for the activation of salivary amylase is 6. The salivary amylase cannot act on cellulose.

Salivary maltase

The enzyme maltase is present only in traces in human saliva. It converts maltose into glucose.

Lingual Lipase

Lingual lipase is lipid digesting (lipolytic) enzymes. It digests milk fats (pre-emulsified fats). It hydrolyzes triglycerides into fatty acids and diacylglycerol.

Enzyme	Source of secretion	Activator	Action
1.Salivary amylase	All salivary glands	Acid medium	Converts cooked starch into maltose
2. Maltase	Major salivary glands	Acid medium	Converts maltose into glucose
3. Lingual lipase	Lingual glands	Acid medium	Converts triglycerides of milk fat into fatty acids and diacylglycerol

4. Cleansing and protective functions

i. Due to the constant secretion of saliva, the mouth and teeth are rinsed and kept free off food debris, shed epithelial cells and foreign particles. In this way, saliva prevents bacterial growth by removing materials, which may serve as culture media for the bacterial growth.

ii. The enzyme lysozyme of saliva kills some bacteria such as staphylococcus, streptococcus, and brucella.

iii. The proline-rich proteins and lactoferrin present in saliva possess antimicrobial property. These proteins also protect the teeth by stimulating enamel formation.

iv. Saliva also contains secretory immunoglobulin IgA which has antibacterial and antiviral actions.

v. Mucin present in the saliva protects the mouth by lubricating the mucous membrane of the mouth.

5. Role in speech

By moistening and lubricating soft parts of mouth and lips, saliva helps in speech. If the mouth becomes dry, articulation and pronunciation become difficult.

6. Excretory function

Many substances, both organic and inorganic, are excreted in saliva. It excretes substances like mercury, potassium iodide, lead, and thiocyanate. Saliva also excretes some viruses such as those causing rabies and mumps. In some pathological conditions, saliva excretes certain substances, which are not found in saliva under normal conditions such as glucose in diabetes mellitus. In certain conditions, some of the normal constituents of saliva are excreted in large quantities. For example, excess urea is excreted in saliva during nephritis, and excess calcium is excreted during hyperparathyroidism.

7. Regulation of body temperature

In dogs and cattle, excessive dripping of saliva during panting helps in loss of heat and regulation of body temperature. However, in human being sweat glands play major role in temperature regulation and saliva does not play any role in this function.

8. Regulation of water balance

When the body water content decreases, salivary secretion also decreases. This causes dryness of the mouth and induces thirst. When the water is taken, it reduces the thirst and restores the body water content.

Regulation of salivary secretion

Salivary secretion is regulated only by nervous mechanism. Autonomic nervous system is involved in the regulatory function.

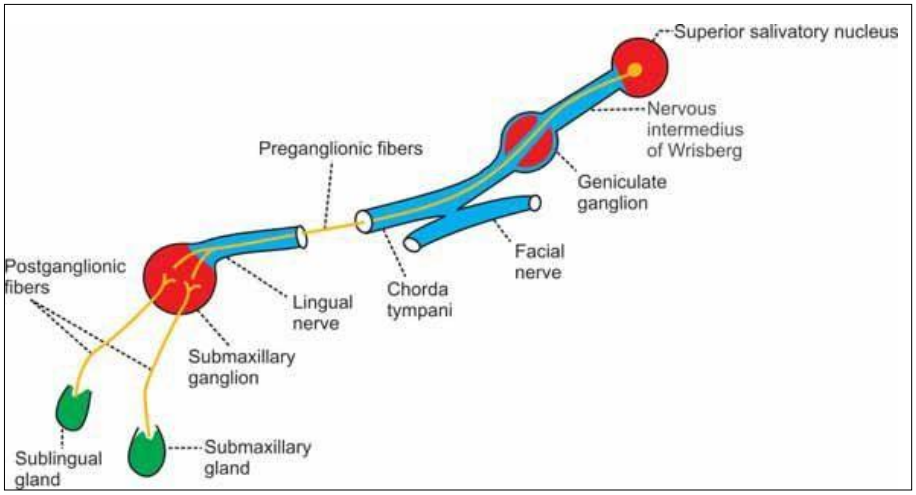
Nerve supply to salivary glands

Salivary glands are supplied by parasympathetic and sympathetic divisions of autonomic nervous system.

Parasympathetic fibers

Parasympathetic Fibers to Submandibular and Sublingual Glands

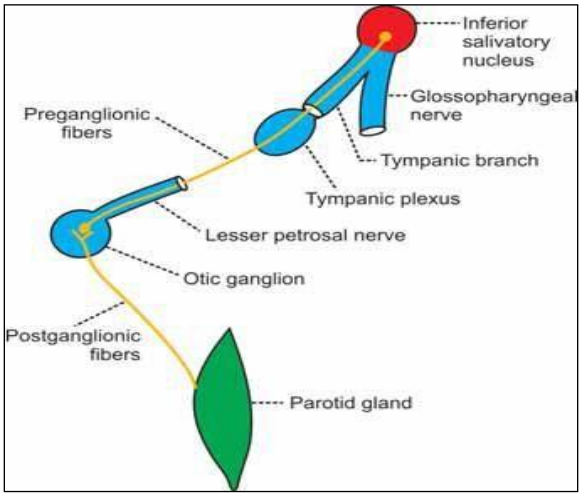
The parasympathetic preganglionic fibers to submandibular and sublingual glands arise from the superior salivatory nucleus situated in pons. After taking origin from this nucleus, the preganglionic fibers run through nervous intermedius of Wrisberg, geniculate ganglion, the motor fibers of facial nerve, chorda tympani branch of facial nerve and lingual branch of trigeminal nerve and finally reach the submaxillary ganglion. The postganglionic fibers arise from this ganglion and supply the submaxillary and sublingual glands.



Parasympathetic nerve supply to submaxillary and sublingual glands

Parasympathetic Fibers to Parotid Gland

The parasympathetic preganglionic fibers to parotid gland arise from inferior salivatory nucleus situated in the upper part of medulla oblongata. From here, the fibers pass through the tympanic branch of glossopharyngeal nerve, tympanic plexus and lesser petrosal nerve and end in otic ganglion . The postganglionic fibers arise from otic ganglion and reach the parotid gland by passing through the auriculotemporal branch in mandibular division of trigeminal nerve.



Parasympathetic nerve supply to parotid gland

Function of Parasympathetic Fibers

When the parasympathetic fibers of salivary glands are stimulated, a large quantity of watery saliva is secreted with less amount of organic constituents. It is because the parasympathetic fibers activate the acinar cells and dilate the blood vessels of salivary glands. The neurotransmitter is acetylcholine.

Sympathetic fibers

The sympathetic preganglionic fibers to salivary glands arise from the lateral horns of first and second thoracic segments of spinal cord. The fibers leave the cord through the anterior nerve roots and end in superior cervical ganglion of the sympathetic chain.

The postganglionic fibers from this ganglion are distributed to the salivary glands along the nerve plexus around the arteries supplying the glands.

Function of Sympathetic Fibers

The stimulation of sympathetic fibers causes less secretion of saliva, which is thick and rich in mucus. It is because these fibers activate the acinar cells and cause vasoconstriction by secreting noradrenaline.

Reflex regulation of salivary secretion

Salivary secretion is regulated by nervous mechanism through reflex action. Salivary reflexes are of two types:

1. Unconditioned reflex
2. Conditioned reflex.

1. Unconditioned Reflex

Unconditioned reflex is the inborn reflex that is present since birth. It does not need any previous experience. This reflex induces salivary secretion when any substance is placed in the mouth. It is due to the stimulation of nerve endings in the mucous membrane of the oral cavity. Examples:

i. When food is taken

ii. When any unpleasant or unpalatable substance enters the mouth

iii. When the oral cavity is handled with instruments by dentists.

2. Conditioned Reflex

Conditioned reflex is the one that is acquired by experience and it needs previous experience. Presence of food in the mouth is not necessary to elicit this reflex.The stimulus for this reflex is the sight, smell, hearing or thought of food. It is due to the impulses arising from eyes, nose, ear, etc.

General physiology

Effect of drugs and chemicals on salivary secretion

Substances which Increase the Salivary Secretion

1. Sympathomimetic drugs like adrenaline and ephedrine
2. Parasympathomimetic drugs like acetylcholine, pilocarpine, muscarine and physostigmine
3. Histamine.

Substances which Decrease the Salivary Secretion

1. Sympathetic depressants like ergotamine and dibenamine
2. Parasympathetic depressants like atropine, and scopolamine.

Applied physiology

Hyposalivation

The reduction in the secretion of saliva is called hyposalivation. It is of two types, namely, the temporary hyposalivation and the permanent hyposalivation.

1. Temporary hyposalivation occurs in:

i. Emotional conditions like fear

ii. Fever

iii. Dehydration.

2. Permanent hyposalivation occurs in:

i. Obstruction of salivary duct (sialolithiasis)

ii. Congenital absence or hypoplasia of salivary glands

iii. Paralysis of facial nerve (Bell's palsy).

Hypersalivation

The excess secretion of saliva is known as hypersalivation. The physiological condition when hypersalivation occurs is pregnancy. Hypersalivation in pathological conditions is called ptyalism, sialorrhea, sialism or sialosis. Hypersalivation occurs in the following conditions:

1. Decay of tooth or neoplasm (abnormal new growth or tumor) in mouth or tongue – due to continuous irritation of nerve endings in the mouth.
2. Disease of esophagus, stomach and intestine.
3. Neurological disorders such as mental retardation, cerebral stroke and parkinsonism.
4. Some psychological and psychiatric conditions.
5. Nausea and vomiting.

Other disorders

In addition to hyposalivation and hypersalivation, salivary secretion is affected by other disorders also which include:

1. Xerostomia

Xerostomia means dry mouth. It is also called pasties or cottonmouth. It is due to hyposalivation or absence of salivary secretion (aptyalism). Xerostomia causes difficulties in mastication, swallowing and speech. It also causes halitosis (bad breath).

The causes of this disease are:

i. Dehydration or renal failure

ii. Sjögren's syndrome

iii. Radiotherapy

iv. Trauma to salivary gland or their ducts

v. Side effect of drugs like antihistamines, antidepressants, and, antiparkinsonian drugs

vi. Shock

vii. After smoking marijuana (psychoactive compound from the plant cannabis).

2. Drooling

Uncontrolled flow of saliva outside the mouth is called drooling. It is often called ptyalism. Drooling occurs because of excess production of saliva in association with inability to retain saliva within the mouth. Drooling occurs in the following conditions:

i. During teeth eruption in children

ii. Upper respiratory tract infection or nasal allergies in children

iii. Difficulty in swallowing

iv. Tonsillitis

v. Peritonsillar abscess.

3. Chorda Tympani Syndrome

Chorda tympani syndrome is the condition characterized by sweating while eating. During trauma or surgical procedure some of the parasympathetic nerve fibers to salivary glands may be severed. And, during the regeneration some of these nerve fibers, which run along with chorda tympani branch of facial nerve may deviate and join with the nerve fibers supplying sweat glands. When the food is placed in the mouth, salivary secretion is associated with sweat secretion.

4. Mumps

Mumps is the acute viral infection affecting the parotid glands. The virus causing this disease is paramyxovirus. It is common in children who are not immunized. It occurs in adults also.

5. Sjögren's Syndrome

It is an autoimmune disorder in which the immune cells destroy exocrine glands such as lacrimal glands and salivary glands. Common symptoms of this syndrome are dryness of the mouth due to lack of saliva (xerostomia), persistent cough and dryness of eyes. In severe conditions the organs like kidneys, lungs, liver, pancreas, thyroid, blood vessels and brain are affected

Electrocardiogram (ECG)

Electrocardiography

is the technique by which the electrical activities of the heart are studied.

Electrocardiograph

is the instrument (ECG machine) by which the electrical activities of the heart are recorded.

Electrocardiogram

(ECG) is the record or graphical registration of electrical activities of the heart, which occur prior to the onset of mechanical activities--is the summed electrical activity of all the cardiac muscle fibers recorded from the surface of the body.

USES OF ECG- is useful in determining and diagnosing the following:

1. Heart rate
2. Heart rhythm3. Abnormal electrical conduction
4. Poor blood flow to heart muscle (ischemia)
5. Heart attack
6. Coronary artery disease
7. Hypertrophy of heart chambers.

ELECTROCARDIOGRAPHIC GRID

The paper that is used for recording ECG is called ECG paper. The electrocardiograph or ECG machine amplifies the electrical signals produced from the heart & records these signals on a moving ECG paper. **ECG grid** refers to the markings (lines)on ECG paper, has horizontal & vertical lines at regular intervals of 1 mm.

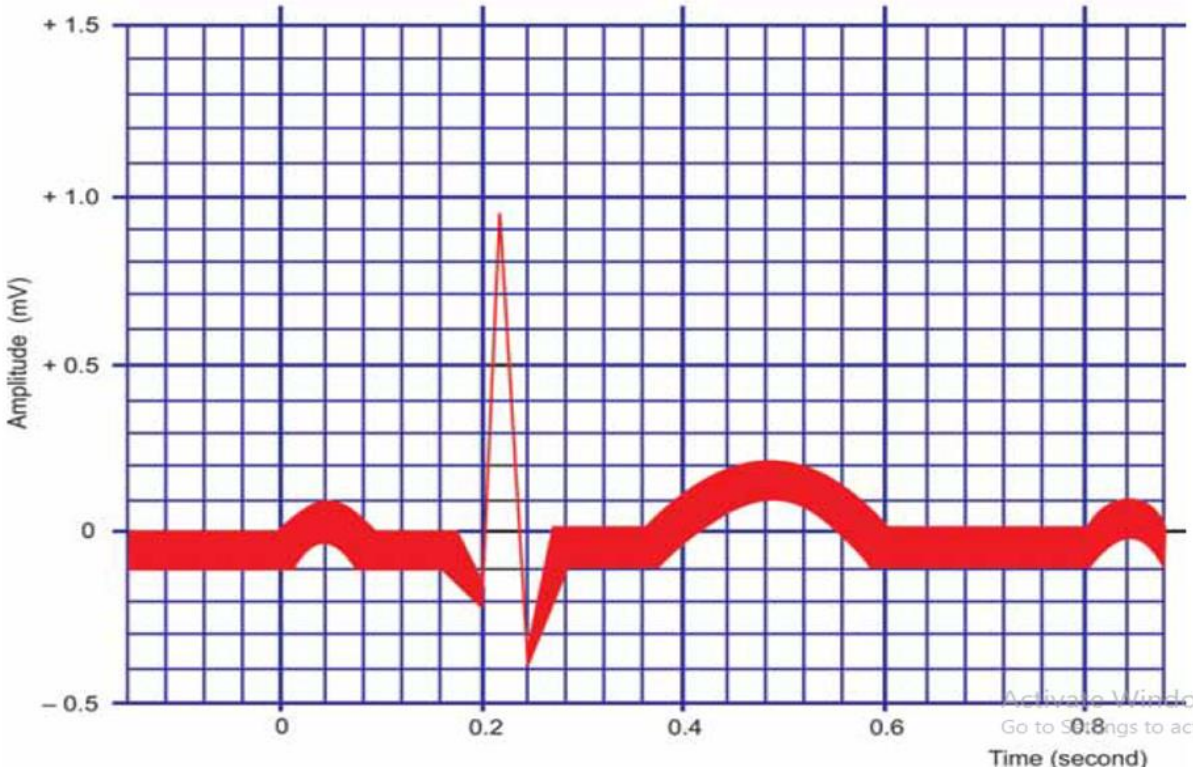
The duration of different ECG waves is denoted by the vertical lines.

Interval between 2 thick lines (5 mm) = 0.2 sec. Interval between 2 thin lines (1 mm) = 0.04 seconc

The amplitude of ECG waves is denoted by horizontal lines.

Interval between 2 thick lines (5 mm)= 0.5 mV.

Interval between two thin lines (1 mm)= 0.1 mV.



SPEED OF THE PAPER

The movement of paper can be adjusted in 2 speeds, 25 mm/second & 50 mm/second.

Usually, the speed of the paper during recording is fixed at 25 mm/second. If the heart rate is very high, the speed of the paper is changed to 50 mm/second.

ECG LEADS

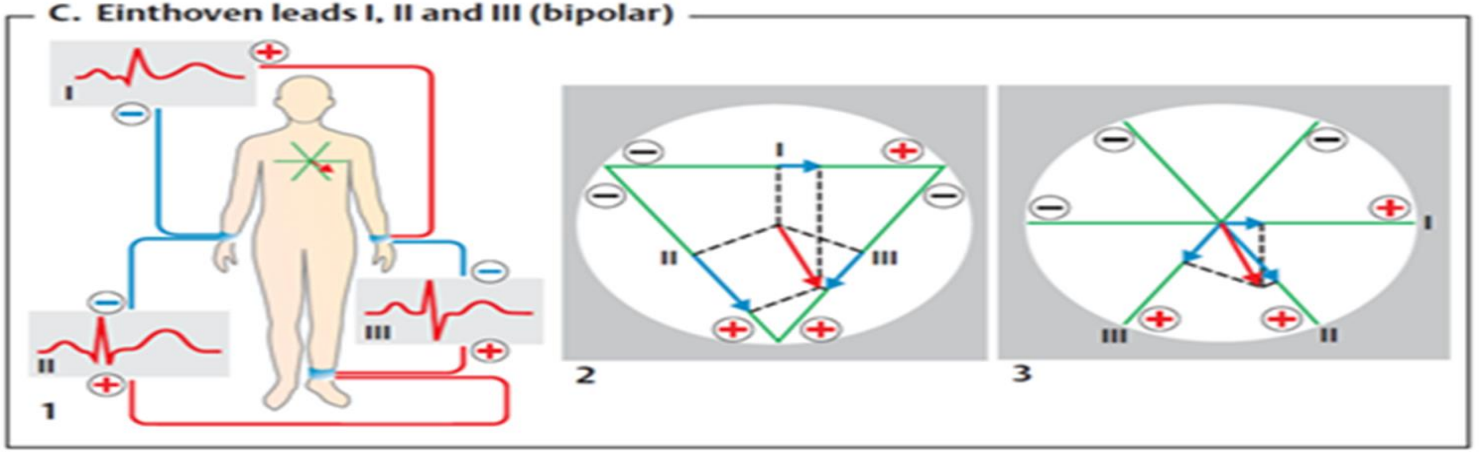
ECG is recorded by placing series of electrodes on the surface of body. These electrodes are= ECG leads & are connected to the ECG machine.

The electrodes are fixed on the limbs. The heart is said to be in the center of an imaginary equilateral triangle drawn by connecting the roots of these three limbs. This triangle is = Einthoven's triangle. The electrical potential generated from the heart appears simultaneously on the roots of these three limbs.

ECG is recorded in 12 leads which are generally classified into two categories.

A. Bipolar leads

B. Unipolar leads



BIPOLAR LIMB LEADS

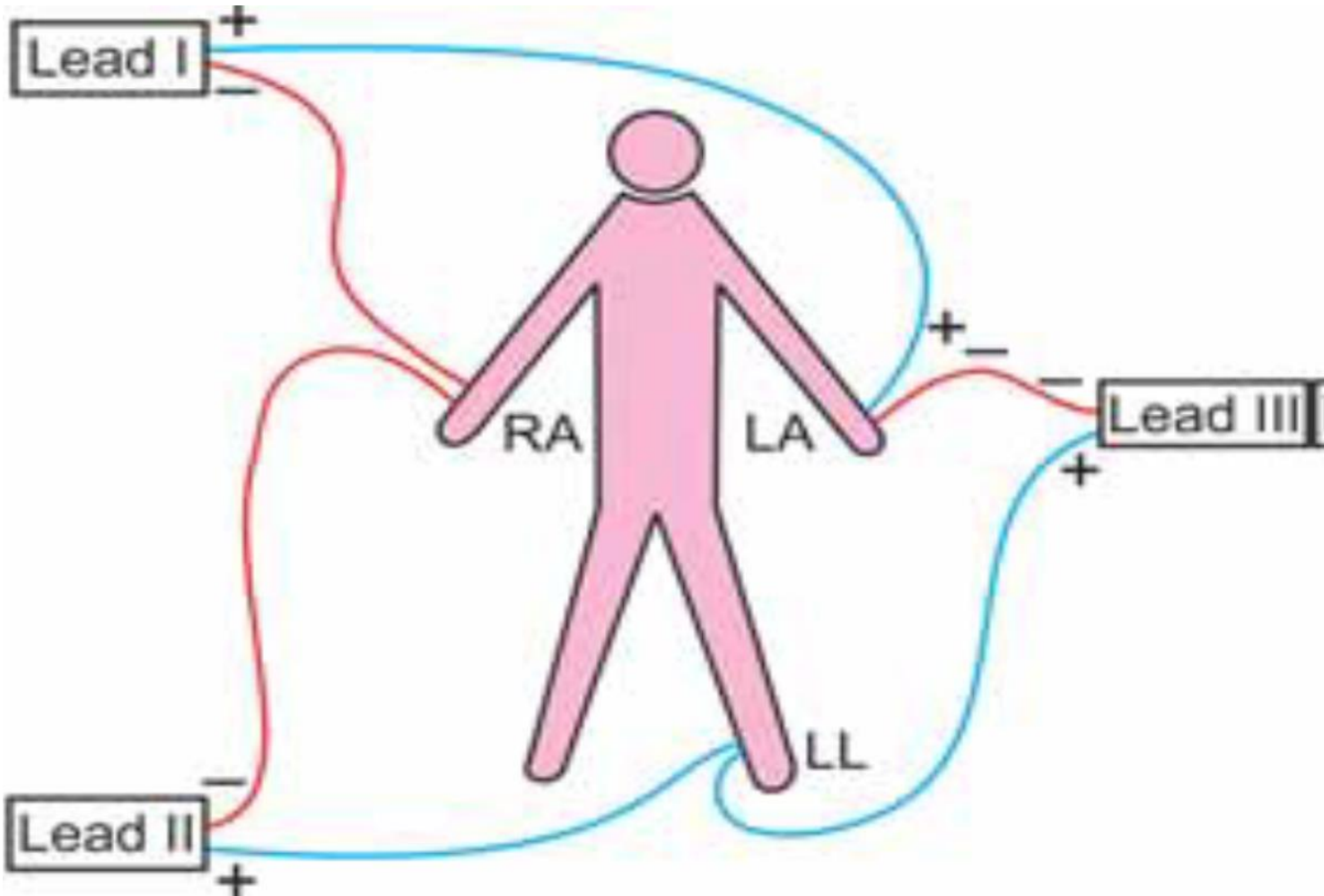
Bipolar limb leads = standard limb leads. Two limbs are connected to obtain these leads and both the electrodes are active recording electrodes, i.e. one electrode is positive and the other one is negative.

There are three standard limb leads:

Limb lead I

Limb lead II

Limb lead III



Lead I

Lead I is obtained by connecting right arm and left arm. The right arm is connected to the negative terminal of the instrument and the left arm is connected to the positive terminal.

Lead II

Lead II is obtained by connecting right arm and left leg. The right arm is connected to the negative terminal of the instrument and the left leg is connected to the positive terminal.

Lead III

Lead III is obtained by connecting left arm and left leg. The left arm is connected to the negative terminal of the instrument and the left leg is connected to the positive terminal.

UNIPOLAR LEADS

Here, one electrode is active electrode is positive and the other one is an indifferent electrode-is serving as a composite negative electrode. The unipolar leads are 2 types:

1. Unipolar limb leads

also called augmented limb leads. The active electrode is connected to one of the limbs. The indifferent electrode obtained by connecting the other two limbs through resistance.

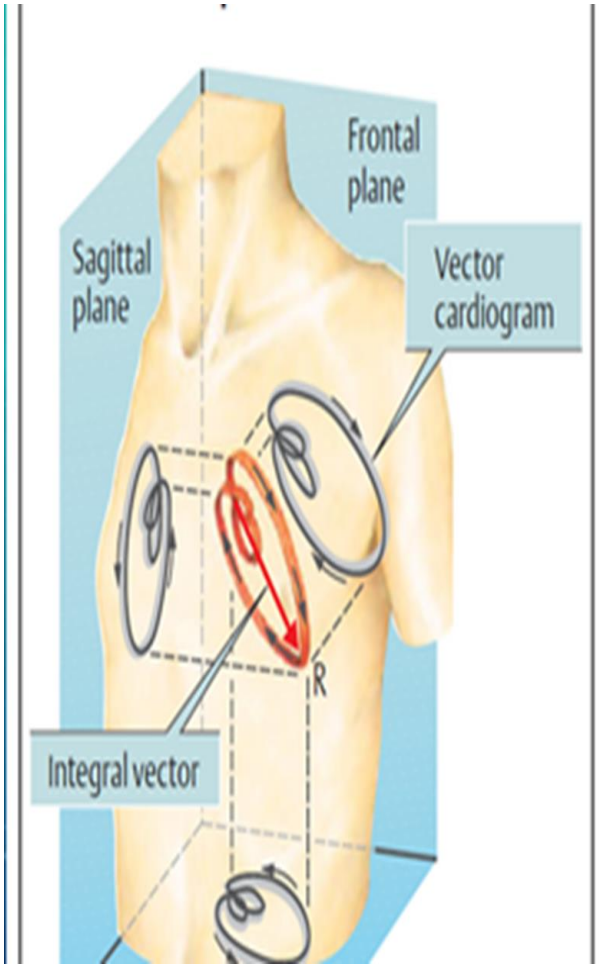
Unipolar limb leads are of 3 types:

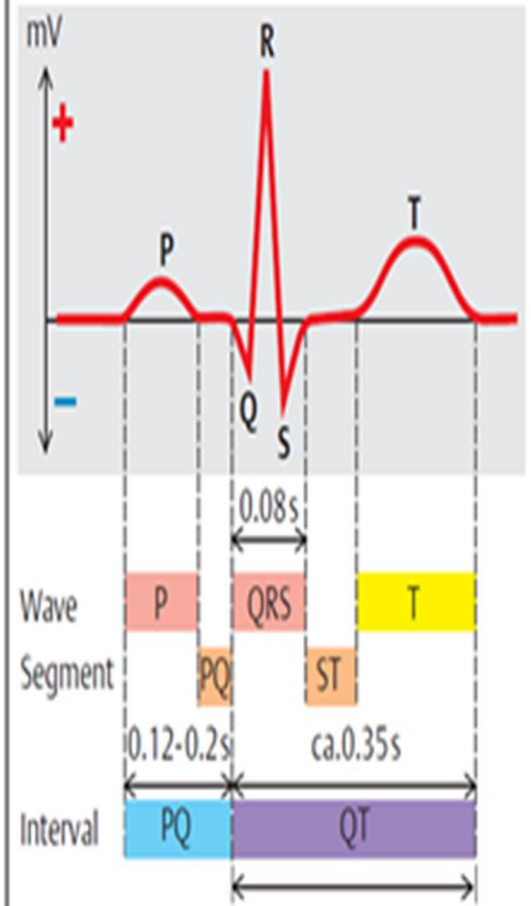
i. aVR lead in which the active electrode is from right arm

ii. aVL lead in which the active electrode is from left arm

iii. aVF lead in which the active electrode is from left leg (foot).

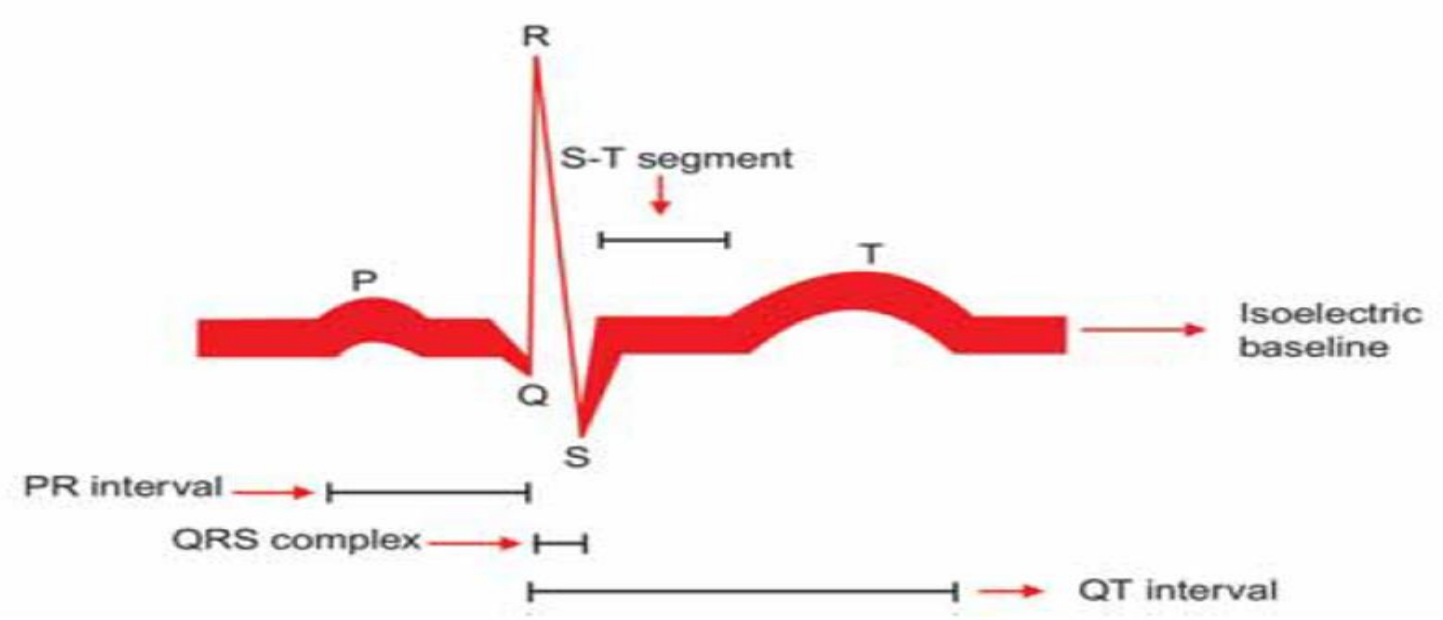
2. Unipolar chest leads.





WAVES OF NORMAL ELECTROCARDIOGRAM

A normal ECG consists of waves, complexes, intervals and segments, has the waves namely P, Q, R, S & T. Einthoven had named the waves of ECG starting from the middle of the English alphabets (P) instead of the beginning (A).



The major complexes in ECG are:

1. ‘P’ wave, the atrial complex produced due to the depolarization of atrial musculature.

Atrial repolarization is not recorded as a separate wave in ECG because it merges with QRS complex.

2. ‘QRS’ complex, the initial ventricular complex
3. ‘T’ wave, the final ventricular complex.
4. ‘QRST’, the ventricular complex.

‘QRS’ Complex

also called =the initial ventricular complex. ‘QRS’ complex is due to depolarization of ventricular musculature.

‘Q’ wave

is a small negative wave, is due to the depolarization of basal portion of interventricular septum.-continued as the tall ‘R’ wave,

‘R’ wave-

positive wave,is due to the depolarization of apical portion of interventricular septum and apical portion of ventricular. is followed by .

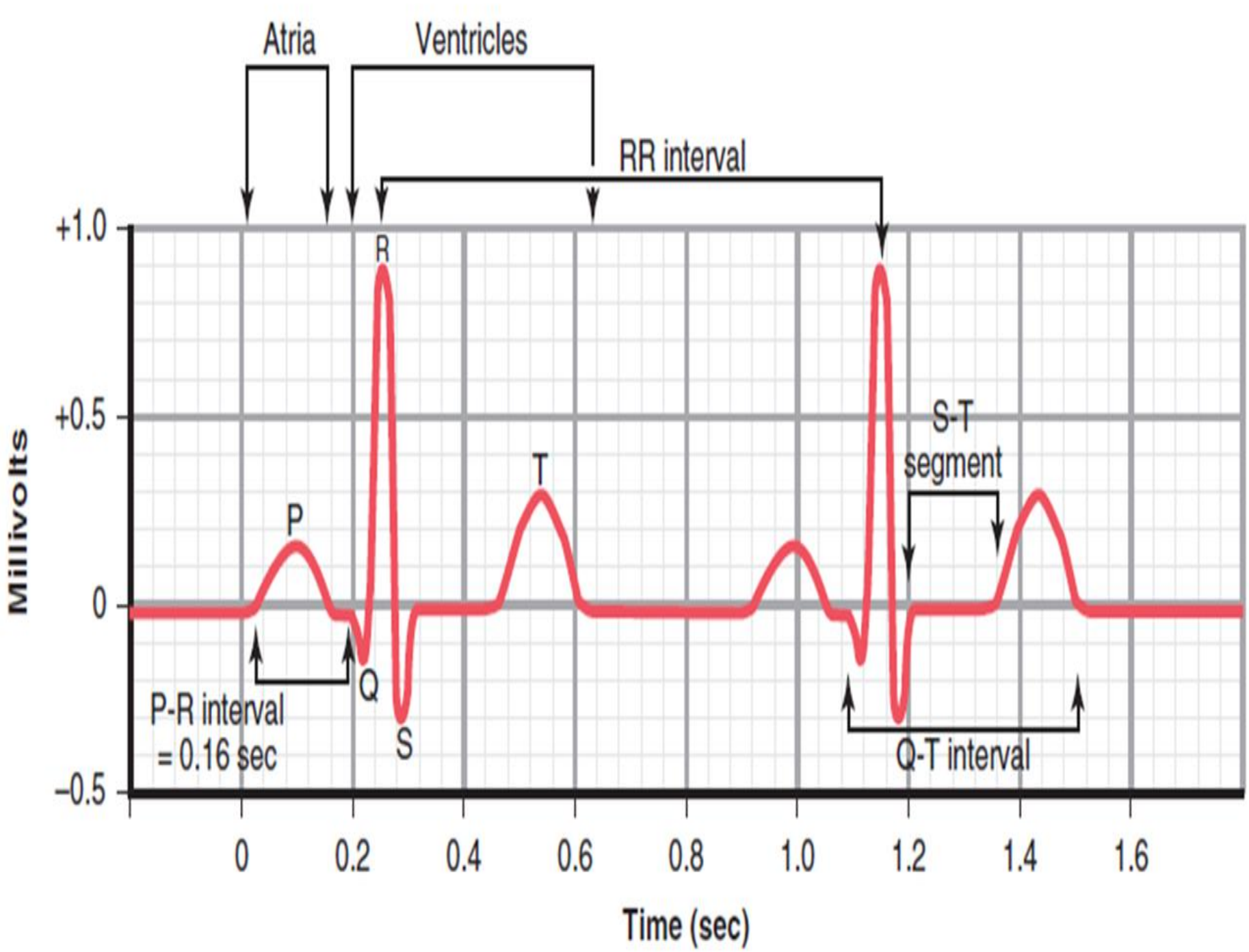
‘S’ wave--small negative wave, is due to the depolarization of basal portion of ventricular muscle near the atrioventricular ring.

‘T’ WAVE

It is the final ventricular complex & a positive wave,due to the repolarization of ventricular musculature

‘U’ WAVE

is not always seen. It is also an insignificant wave in ECG. It is supposed to be due to repolarization of papillary muscle.


Atria
Ventricles
RR interval
+1.0
+0.5
0
–0.5
Millivolts
R
P
T
S-T
segment
Q
S
P-R interval
= 0.16 sec
Q-T interval
0
0.2
0.4
0.6
0.8
1.0
1.2
1.4
1.6
Time (sec)

INTERVALS AND SEGMENTS OF ECG

‘P-R’ INTERVAL

It is the interval between the onset of ‘P’ wave & the onset of ‘Q’ wave.

it signifies the atrial depolarization & conduction of impulses through AV node. It shows the duration of conduction of the impulses from the SA node to ventricles through atrial muscle and AV node.

It is represented by the short isoelectric (zero voltage) period after the end of ‘P’ wave & onset of ‘Q’ wave. It denotes the time taken for the passage of depolarization within AV node.

The normal duration is 0.18 second & varies between 0.12 - 0.2 sec. If it is more than 0.2 second, signifies the delay in the conduction of impulse from SA node to the ventricles. Usually, the delay occurs in the AV node. So it is called= the AV nodal delay.

‘Q-T’ INTERVAL

the interval between the onset of ‘Q’ wave and the end of ‘T’ wave.

indicates the ventricular depolarization & ventricular repolarization, i.e. it signifies the electrical activity in ventricles. Duration--Between 0.4 and 0.42 second.

‘S-T’ SEGMENT

The time interval between the end of ‘S’ wave and the onset of ‘T’ wave is called ‘S-T’ segment. It is an isoelectric period.

Duration of ‘S-T’ Segment 0.08 second.

J Point

The point where ‘S-T’ segment starts is called ‘J’ point. It is the junction between the QRS complex and ‘S-T’ segment.

‘R-R’ INTERVAL

‘R-R’ interval is the time interval between two consecutive ‘R’ waves. signifies the duration of one cardiac cycle.

The normal duration of ‘R-R’ interval is 0.8 second.

Cardiovascular Adjustments during Exercise

During exercise, there is an increase in metabolic needs of body tissues, particularly the muscles. Various adjustments, which take place in the body, are aimed at

1. Supply of nutrients& oxygen to muscles &other tissues involved in exercise

2. Prevention of increase in body temperature.

TYPES OF EXERCISE

generally classified into2 types depending-- type of muscular contraction.

1. Dynamic exercise

involves isotonic muscular contraction and keeps the joints and muscles moving. Examples are swimming, bicycling, walking, etc. External work is involved in this type of exercise. The shortening of muscle fibers against load is called external work. In this type of exercise, the heart rate, force of contraction, cardiac output and systolic blood pressure increase. However, the diastolic blood pressure is unaltered or decreased-because= the peripheral resistance is unaltered or decreased.

2- STATIC EXERCISE

involves isometric muscular contraction without movement of joints. Example is pushing heavy object. (without the performance of external work). During this exercise, apart from increase in heart rate, force of contraction, cardiac output and systolic blood pressure, the diastolic blood pressure also increases-because of increase in peripheral resistance during static exercise.

Based on the type of metabolism (energy producing process) involved, exercise classified into 2types:

- ✓ Aerobic means ‘with air’ or ‘with oxygen’.

The energy is obtained by utilizing nutrients in the presence of oxygen- involves activities with lower intensity, which is performed for longer period. At the beginning, the body obtains energy by burning glycogen stored in liver. After about 20 minutes, when stored glycogen is exhausted, the body starts burning fat. Body fat is converted into glucose, which is utilized for energy.

Examples of aerobic exercise:

1. Fast walking 2. Jogging 3. Running 4. Bicycling
5. Skiing 6. Skating 7. Hockey 8. Soccer
9. Tennis 10. Badminton 11. Swimming 12. Rowing.

SEVERITY OF EXERCISE

The cardiovascular and other changes in the body depend upon the severity of exercise also.

Based on severity, the exercise is classified into three types:

- 1. MILD EXERCISE

It is the very simple form of exercise like slow walking. Little or no change occurs in cardiovascular system during mild exercise.

- 2. MODERATE EXERCISE

does not involve strenuous muscular activity,can be performed for a longer period. Exhaustion does not occur at the end of moderate exercise. The examples-- are fast walking and slow running.

- 3. SEVERE EXERCISE

involves strenuous muscular activity and it can be performed only for short duration. Fast running for a distance of 100 or 400 meters is the example. Complete exhaustion occurs at the end of severe exercise

EFFECTS OF EXERCISE ON CARDIOVASCULAR SYSTEM

- ON BLOOD

Red blood cell count increases because of release of erythropoietin from juxtaglomerular apparatus due to hypoxia. The pH of blood decreases due to increased carbon dioxide content.

- ON BODY FLUIDS

More heat is produced during exercise and the thermoregulatory system is activated. This in turn, causes secretion of large amount of sweat leading to:

i. Fluid loss

ii. Reduced blood volume

iii. Hemoconcentration

iv. Sometimes, severe exercise leads to dehydration.

- ON HEART RATE

Heart rate increases during exercise. Even the thought of exercise orpreparation for exercise-because of impulses from cerebral cortex to medullary centers, which reduces vagal tone.

In moderate exercise, the heart rate increases to 180 beats/minute.

In severe muscular exercise it reaches 240 to 260 beats/minute. The increased heart rate during exercise is mainly vagal with drawal and increase in sympathetic tone.

7. ON BLOOD PRESSURE

During **moderate isotonic exercise**, systolic pressure is increased-due to increase in heart rate & stroke volume. Diastolic pressure is not altered because peripheral resistance is not affected during moderate exercise.

In **severe exercise involving isotonic muscular contraction**, the systolic pressure increases but the diastolic pressure decreases-- because of the decrease in peripheral resistance-due to vasodilatation caused by metabolites.

During **exercise involving isometric contraction**, the peripheral resistance increases. So, the diastolic pressure also increases along with systolic pressure.

Blood Pressure after Exercise

After exercise, blood pressure falls below the resting level- because of vasodilatation caused by metabolic end products accumulated in muscles during exercise.-- the pressure returns to resting level quickly as soon as the metabolic end products are removed from muscles.

Cardiovascular physiology

HEART RATE

Normal heart rate is 72/minute. It ranges = 60 & 80 per minute.

TACHYCARDIA

is the increase in the heart rate above 100/minute.

Physiological conditions when tachycardia occurs are:

1. Childhood
2. Exercise
3. Pregnancy
4. Emotional conditions such as anxiety.

Pathological conditions when tachycardia occurs are:

1. Fever
2. Anemia
3. Hypoxia4. Hyperthyroidism
5. Hypersecretion of catecholamines
6. Cardiomyopathy
7. Valvular heart diseases.

BRADYCARDIA

is the decrease in the heart rate below 60/minute.

Physiological conditions when bradycardia occurs are:

1. Sleep
2. Athletic heart.

Pathological conditions when bradycardia occurs are:

1. Hypothermia
2. Hypothyroidism
3. Heart attack
4. Congenital heart disease
5. Degenerative process of aging
6. Obstructive jaundice
7. Increased intracranial pressure.

REGULATION OF HEART RATE

Heart rate is maintained within normal range constantly. It is subjected for variation during normal physiological conditions such as exercise, emotion, etc. However, under physiological conditions, the altered heart rate is quickly brought back to normal. Heart rate is regulated by the nervous mechanism which consists of three components:

I. Vasomotor center

II. Motor (efferent) nerve fibers to the heart

III. Sensory (afferent) nerve fibers from the heart.

Nerve supply to heart

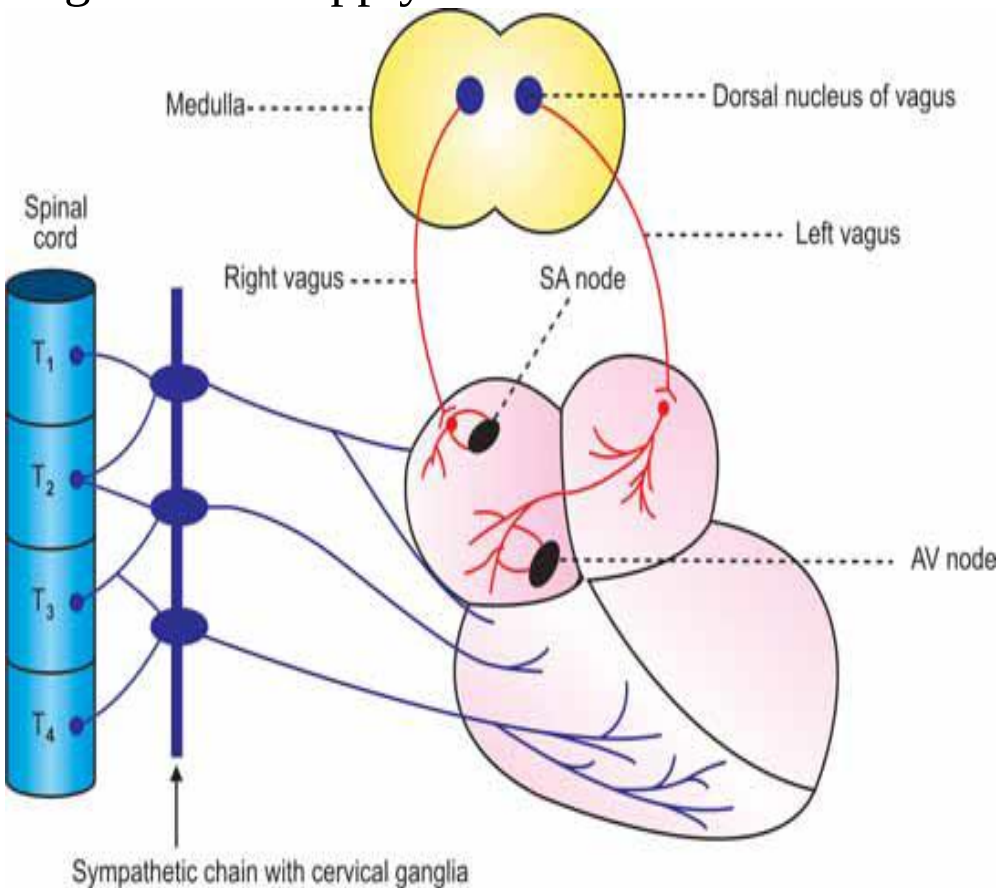
The parasympathetic nerve fibers supplying heart arise from the dorsal nucleus of vagus

The preganglionic parasympathetic nerve fibers from dorsal nucleus of vagus reach the heart and terminate on postganglionic neurons. The postganglionic fibers from these neurons innervate heart muscle. Most of the fibers from right vagus terminate in SA node. Remaining supply the atrial muscles and AV node.

Most of the fibers from left vagus supply AV node and some supply the atrial muscle and SA node. Ventricles do not receive the vagus nerve supply.

SYMPATHETIC NERVE FIBERS

The preganglionic fibers of the Sympathetic nerves to heart arise from lateral grey horns of the first 4 thoracic (T1 to T4) segments of thespinal cord. The sympathetic nerves are cardioaccelerator in function and carry cardioaccelerator impulsesfrom vasoconstrictor area to the heart.



FACTORS AFFECTING VASOMOTOR CENTER –

The vasomotor center regulates the cardiac activity by receiving impulses from different sources in the body. After receiving the impulses from different sources, the vasodilator area alters the vagal tone and modulates the activities of the heart. The various sources from which the impulses reach the vasomotor center are:

1. IMPULSES FROM HIGHER CENTERS(Cerebral Cortex, Hypothalamus)
2. IMPULSES FROM RESPIRATORY CENTERS
3. IMPULSES FROM BARORECEPTORS – MAREY'S REFLEX

The baroreceptors or pressoreceptors are the receptors, which give response to change in blood pressure. two types, carotid baroreceptors and aortic baroreceptors

The baroreceptors regulate the heart rate through a reflex called Marey's reflex. The stimulus for this reflex is increase in blood pressure.

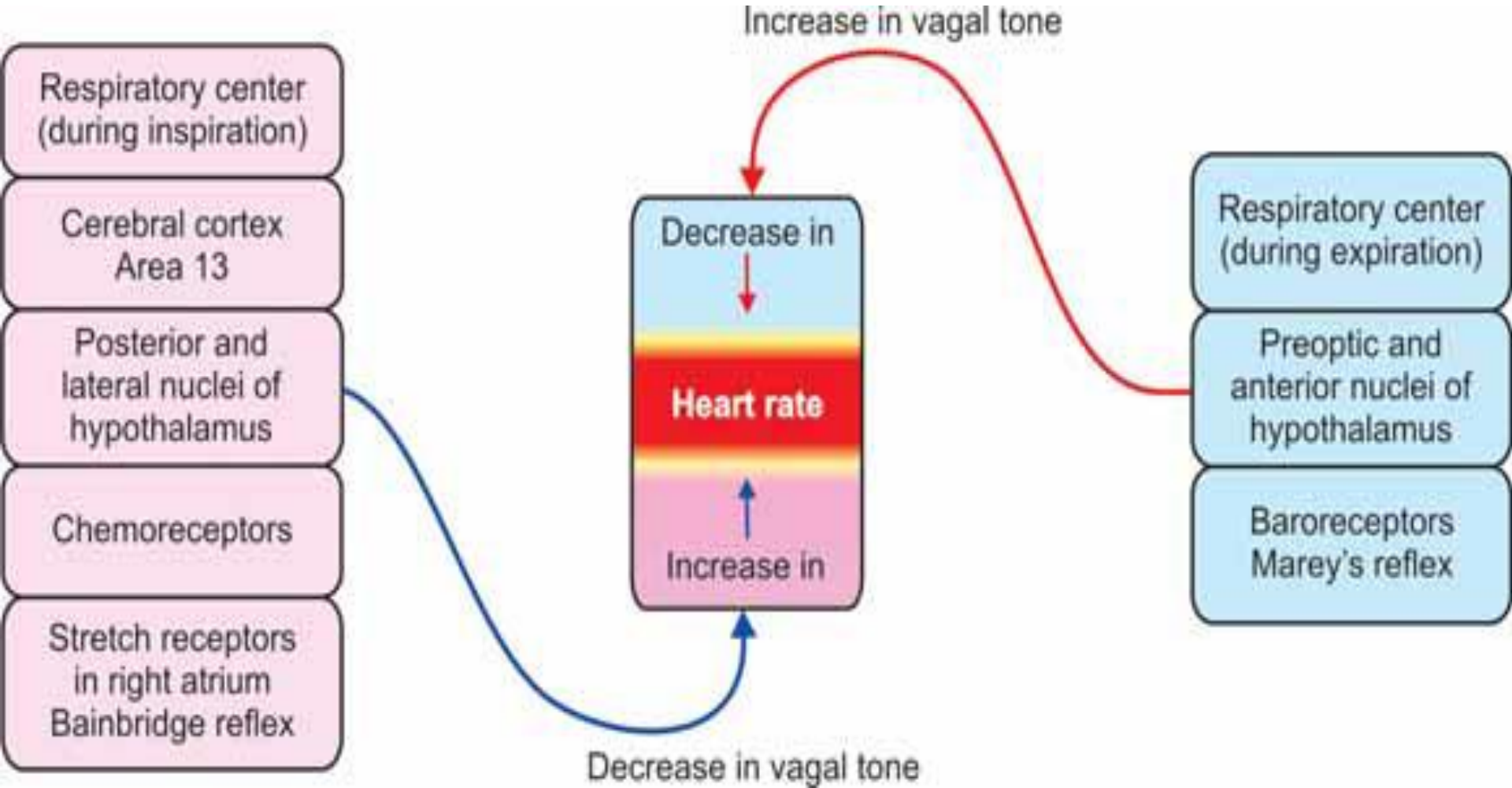
4. IMPULSES FROM CHEMORECEPTORS

Chemoreceptors are receptors giving response to change in chemical constituents of blood, particularly oxygen, carbon dioxide and hydrogen ion concentration.

Peripheral chemoreceptors are situated in thecarotid body and aortic body adjacent to baroreceptors.

5. IMPULSES FROM RIGHT ATRIUM – BAINBRIDGE REFLEX
6. IMPULSES FROM OTHER AFFERENT NERVES

Factors regulating vagal tone and heart rate



Arterial blood pressure

is the lateral pressure exerted by the column of blood on the wall of arteries. is expressed in four different terms:

1. Systolic blood pressure
2. Diastolic blood pressure
3. Pulse pressure
4. Mean arterial blood pressure.

Systolic blood pressure (systolic pressure) is the maximum pressure exerted in the arteries during systole of the heart. The normal systolic pressure is 120 mm Hg. It ranges = 110 & 140 mm Hg.

Diastolic blood pressure (diastolic pressure) is the minimum pressure in the arteries during diastole of the heart. The normal diastolic pressure is 80 mm Hg. It varies between 60 and 80 mm Hg.

Pulse pressure is the difference between systolic pressure and diastolic pressure. Normally, it is 40 mm Hg (120 to 80).

PHYSIOLOGICAL VARIATIONS

1. Age2. Sex

In females, up to the period of menopause, the arterial pressure is about 5 mm Hg less than in males of same age. After menopause, the pressure in females becomes equal to that in males of same age.

3. Body Built

The pressure is more in obese persons than in lean persons.

4. Diurnal Variation

In early morning, the pressure is slightly low. It gradually increases and reaches the maximum at noon. It becomes low in evening.

5. After Meals

The arterial blood pressure is increased for few hours after meals due to increase in cardiac output.

6. During Sleep

Usually, the pressure is reduced up to 15 to 20 mm Hg during deep sleep. However, it increases slightly during sleep associated with dreams.

7. Emotional Conditions

During excitement or anxiety, the blood pressure is increased due to release of adrenaline.

8. After Exercise

After moderate exercise, systolic pressure increases by 20 to 30 mm Hg above the basal level due to increase in force of contraction and stroke volume. Normally, diastolic pressure is not affected by moderate exercise. It is because the diastolic pressure depends upon peripheral resistance, which is not altered by moderate exercise.

After severe muscular exercise, the systolic pressure rises by 40 to 50 mm Hg above the basal level. But, the diastolic pressure reduces because the peripheral resistance decreases in severe muscular exercise.

DETERMINANTS OF ARTERIAL BLOOD PRESSURE – FACTORS MAINTAINING ARTERIAL BLOOD PRESSURE

Some factors are necessary for maintenance of normal blood pressure, which are called local factors, mechanical factors or determinants of blood pressure. These factors are divided into 2 types:

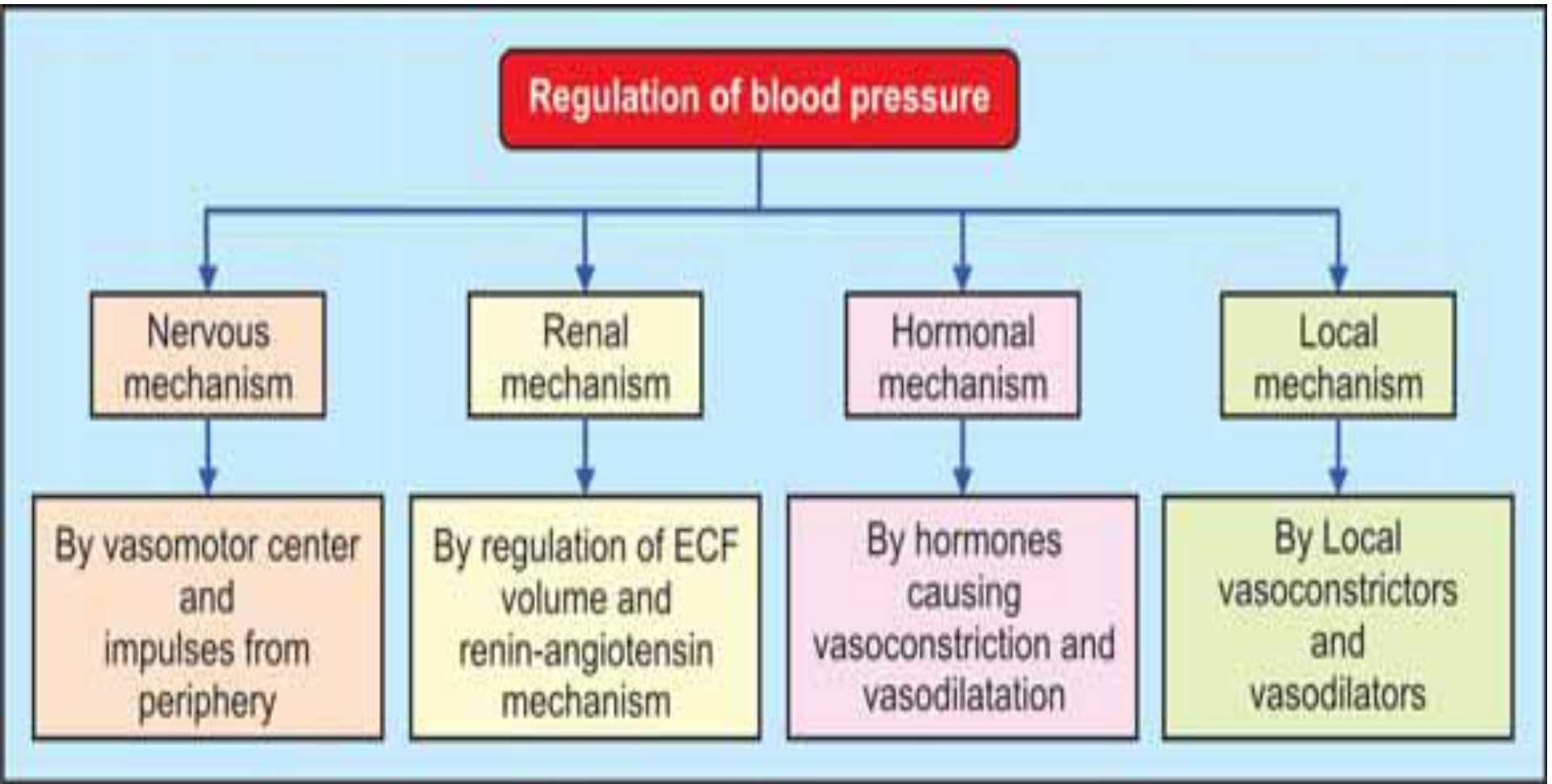
I. Central factors -pertaining to the heart:(Cardiac output& Heart rate).

II. Peripheral factors-- pertaining to blood and blood vessels:

1. Peripheral resistance
2. Blood volume
3. Venous return
4. Elasticity of blood vessels
5. Velocity of blood flow
6. Diameter of blood vessels
7. Viscosity of blood.

REGULATION OF ARTERIAL BLOOD PRESSURE

Arterial blood pressure varies even under physiological conditions. immediately it is brought back to normal level because of the presence of well organized regulatory mechanisms in the body. Body has four such regulatory mechanisms.



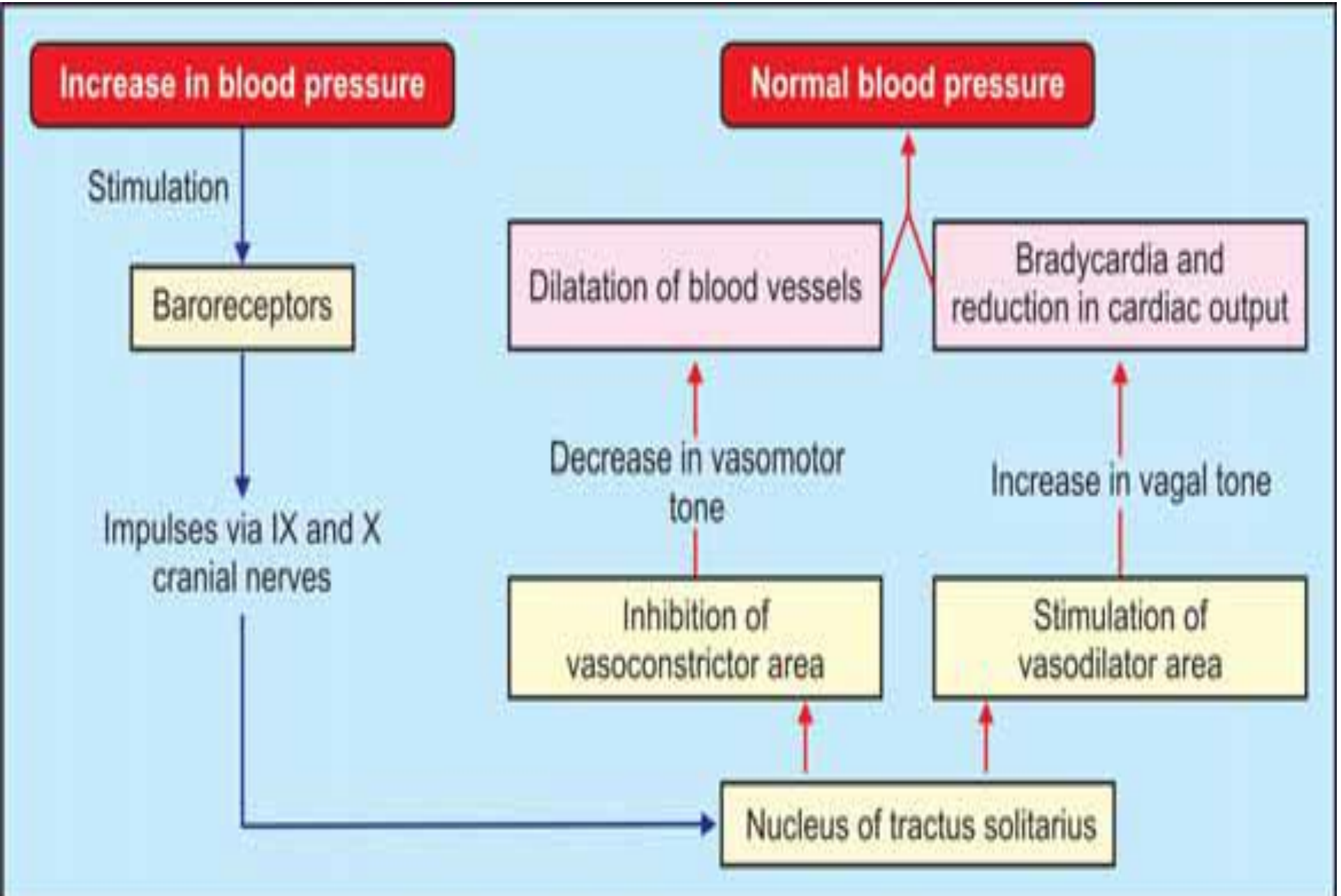
The nervous regulation is rapid among all the mechanisms involved in regulation of ABP. When BP alters, nervous system brings the pressure back to normal within few minutes. Although nervous mechanism is quick in action, it operates only for a short period & then it adapts to the new pressure= called short-term regulation.

The nervous mechanism regulating ABP operates through the vasomotor system. The vasomotor system includes three components:

1. Vasomotor center
2. Vasoconstrictor fibers
3. Vasodilator fibers.

The vasomotor center regulates ABP by causing vasoconstriction or vasodilatation, its actions depend upon the impulses it receives from other structures such as baroreceptors, chemoreceptors, higher centers and respiratory centers. --baroreceptors and chemoreceptors play a major role in the short-term regulation of blood pressure.

Regulation of blood pressure by baroreceptor mechanism



2. Chemoreceptor Mechanism

Chemoreceptors are receptors giving response to change in chemical constituents of blood. Peripheral chemoreceptors influence the vasomotor center.

Peripheral chemoreceptors are sensitive to lack of oxygen, excess of carbon dioxide and hydrogen ion concentration in blood. Whenever

blood pressure decreases, the blood flow decreases resulting in decreased oxygen content and excess of carbon dioxide and hydrogen ion.

These factors stimulate the chemoreceptors, which send impulses to stimulate the vasoconstrictor center. The blood pressure rises and blood flow increases.

Chemoreceptors play a major role in maintaining respiration rather than blood pressure.

Sinoaortic mechanism

Mechanism of action of baroreceptors and chemoreceptors in carotid and aortic region. The nerves from the baroreceptors and chemoreceptors are called buffer nerves because these nerves regulate the heart rate, blood pressure and respiration.

RENAL MECHANISM FOR REGULATION OF B P – LONG-TERM REGULATION

kidneys play an important role in the long term regulation of ABP. by 2 ways:

1. By regulation of ECF volume
2. Through renin-angiotensin mechanism.

BY REGULATION OF EXTRACELLULAR FLUID VOLUME

When the BP increases, kidneys excrete large amounts of water & salt, particularly sodium by means of pressure diuresis & pressure natriuresis. Pressure diuresis is the excretion of large quantity of water in urine because of increased BP

Even a slight increase in BP doubles the water excretion.

Pressure natriuresis is the excretion of large quantity of sodium in urine.

Because of diuresis & natriuresis, there is decrease in the ECF volume &blood volume, which in turn brings the ABP back to normal level.

When blood pressure decreases, the reabsorption of water from renal tubules is increased. This in turn, increases ECF volume, blood volume & cardiac output resulting in restoration of BP.

Actions of Angiotensin II

When BP & ECF volume decrease, renin secretion from kidneys is increased. It converts angiotensinogen into angiotensin I. This is converted into angiotensin II by ACE (angiotensin converting enzyme). Angiotensin II acts in 2 ways to restore the BP:

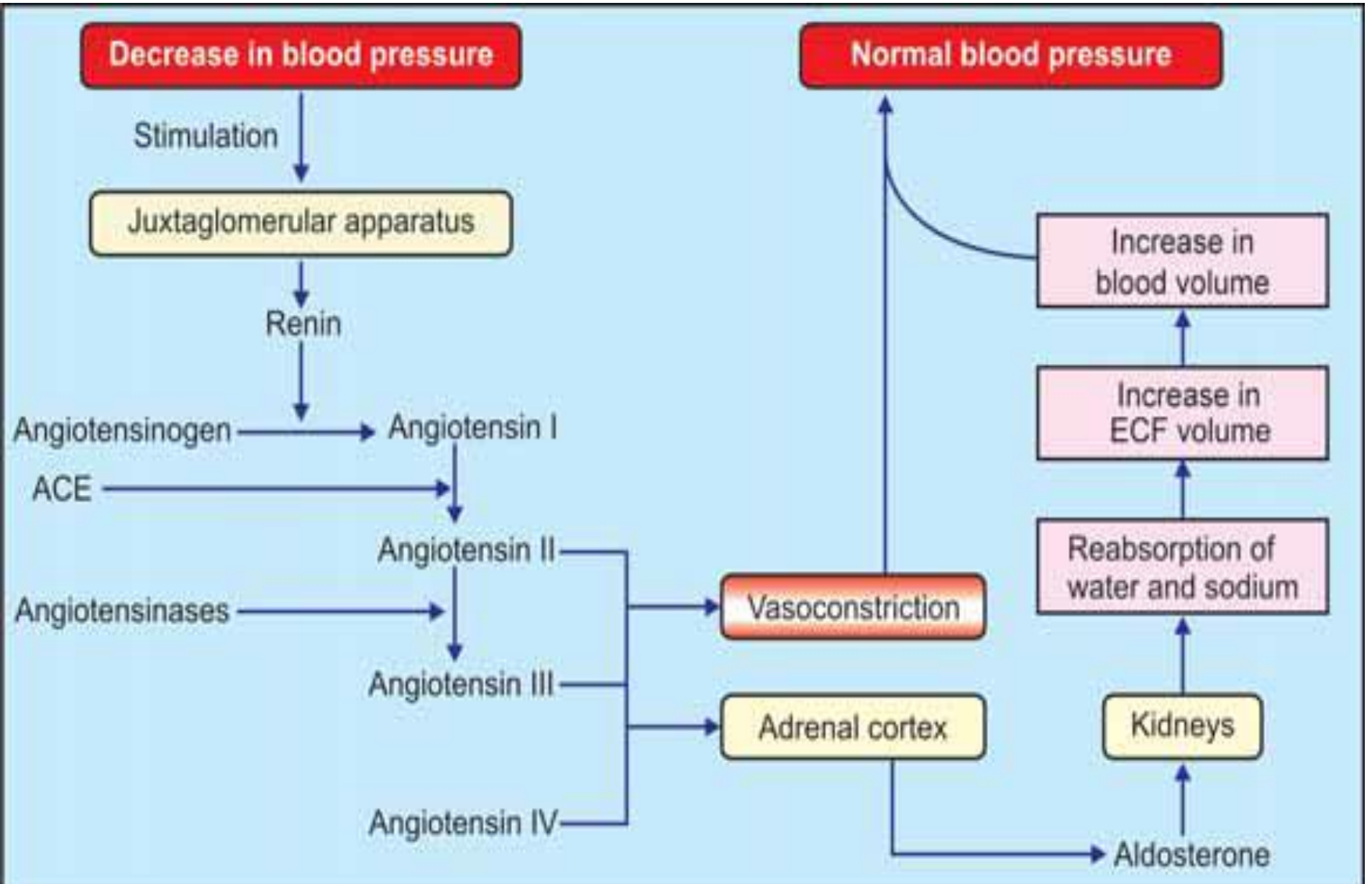
i. It causes constriction of arterioles in body so that the peripheral resistance is increased, & BP rises. In addition, angiotensin II causes constriction of afferent arterioles in kidneys so that the glomerular filtration reduces.

This results in retention of water & salts. This increases ECF volume to normal level. This in turn increases the BP to normal level.

ii. Simultaneously, angiotensin II stimulates the adrenal cortex to secrete aldosterone.

This hormone increases reabsorption of sodium from renal tubules. Sodium reabsorption is followed by water reabsorption resulting in increased ECF volume & blood volume. It increases the BP to normal level.

Regulation of blood pressure by renin-angiotensin mechanism.
ACE = Angiotensin converting enzyme



HORMONAL MECHANISM FOR REGULATION Of BP

Hormones which **Increase** the Blood Pressure

1. Adrenaline
2. Noradrenaline
3. Thyroxine
4. Aldosterone
5. Vasopressin
6. Angiotensin
7. Serotonin.

Hormones which **Decrease** the Blood Pressure

1. Vasoactive intestinal polypeptide (VIP)
2. Bradykinin
3. Prostaglandin
4. Histamine
5. Acetylcholine
6. Atrial natriuretic peptide
7. Brain natriuretic peptide
8. C-type natriuretic peptide.

LOCAL MECHANISM FOR REGULATION OF BP

some local substances also regulate the BP.-- by vasoconstriction or vasodilatation.

LOCAL VASOCONSTRICTORS

The local vasoconstrictor substances are of vascular endothelial origin= known as endothelins (ET). Endothelins are produced by stretching of blood vessels. These peptides act by activating phospholipase, which activates the prostacyclin & thromboxane A2. These two substances cause constriction of blood vessels & increase in blood pressure.

LOCAL VASODILATORS

The local vasodilators are of two types:

1. Vasodilators of metabolic origin such as carbon dioxide, lactate, hydrogen ions & adenosine
2. Vasodilators of endothelial origin such as nitric oxide (NO).

HYPERTENSION

the persistent high blood pressure. Clinically, systolic pressure remains elevated above 150 mm Hg & diastolic pressure remains elevated above 90 mm Hg, it is considered as hypertension. If there is increase only in systolic pressure, it is called systolic hypertension.

Types of Hypertension

1. **Primary hypertension or essential hypertension**

Primary hypertension is the elevated blood pressure in the absence of any underlying disease- called essential hypertension.

The arterial blood pressure is increased because of increased peripheral resistance, which occurs due to some unknown cause.

2**. Secondary hypertension**

is the high blood pressure due to some underlying disorders. The different forms of secondary hypertension are:

- i. Cardiovascular hypertension that is produced due to the cardiovascular

disorders such as atherosclerosis(hardening of blood vessels by fat deposition) and coarctation (narrowing) of aorta

- ii. Endocrine hypertension which is due to hyperactivity of some endocrine glands such as pheochromocytoma, hyperaldosteronism and Cushing's syndrome
- iii. Renal hypertension that is caused by renal diseases like glomerulonephritis and stenosis of renal arteries
- iv. Neurogenic hypertension which is developed by nervous disorders such as increased intracranial pressure and lesion in tractus solitarius
- v. Hypertension during pregnancy which is due to toxemia of pregnancy.

HYPOTENSION

is the low BP. When the systolic pressure is less than 90 mm Hg, considered as hypotension. Types

1. Primary hypotension

is the low BP that develops in the absence of any underlying disease & develops due to some unknown cause. It is also called essential hypotension. Frequent fatigue and weakness are the common symptoms of this condition. However, the persons with primary hypotension are not easily susceptible to heart or renal disorders.

2. Secondary hypotension

occurs due to some underlying diseases. The diseases which cause hypotension are:

- i. Myocardial infarction
- ii. Hypoactivity of pituitary gland
- iii. Hypoactivity of adrenal glands
- iv. Tuberculosis
- v. Nervous disorders.

General physiology
Nutrition and Metabolism

Nutritional Requirements

- Living tissue is maintained by constant expenditure of energy (ATP).
  - Indirectly from glucose, fatty acids, ketones, amino acids, and other organic molecules.
- Energy of food is commonly measured in kilocalories.
  - One kilocalorie is = 1000 calories.
- One calorie = amount of heat required to raise the temperature of 1 cm^3 of H_20 from 14.5° to 15.5° C.
  - The amount of energy released as heat when food is combusted in vitro = amount of energy released within cells through aerobic respiration.

Metabolic Rate and Caloric Requirements

- Metabolic rate is the total rate of body metabolism.
  - Metabolic rate measured by the amount of oxygen consumed by the body/min.
- BMR:
  - Oxygen consumption of an awake relaxed person 12–14 hours after eating and at a comfortable temperature.
- BMR determined by:
  - Age.
  - Gender.
  - Body surface area.
  - Thyroid secretion.

Anabolic Requirements

- Anabolism:
  - Food supplies raw materials for synthesis reactions.
- Synthesize:
  - DNA and RNA.
  - Proteins.
  - Triglycerides.
  - Glycogen.
- Must occur constantly to replace molecules that are hydrolyzed.

Aerobic Requirements (continued)

- Catabolism:
  - Hydrolysis (break down monomers down to $C0_2$ and H_20.):
    - Hydrolysis reactions and cellular respiration.
    - Gluconeogenesis.
    - Glycogenolysis.
    - Lipolysis.

Turnover Rate

- Rate at which a molecule is broken down and resynthesized.
- Average daily turnover for carbohydrates is 250 g/day.
  - Some glucose is reused to form glycogen.
    - Only need about 150 g/day.
- Average daily turnover for protein is 150 g/day.
  - Some protein may be reused for protein synthesis.
    - Only need 35 g/day.
      - 9 essential amino acids.
- Average daily turnover for fats is 100 g/day.
  - Little is actually required in the diet.
    - Fat can be produced from excess carbohydrates.
      - Essential fatty acids:
        - Linoleic and linolenic acids.

Vitamins and Minerals

- Vitamins:
  - Small organic molecules that serve as coenzymes in metabolic reactions or have highly specific functions.
- Must be obtained from the diet because the body does not produce them, or does so in insufficient amounts.
- 2 classes of vitamins:
  - Fat-soluble:
    - A,D, E, and K.
  - Water-soluble:
    - B_1, B_2, B_3, B_6, B_{12}, pantothenic acid, biotin, folic acid, and vitamin C.

Vitamins

- Water-soluble vitamins:
  - Serve as coenzymes in the metabolism of carbohydrates, lipids, and proteins.
  - May serve as antioxidants.
- Fat-soluble vitamins:
  - Bind to nuclear receptors.
  - Serve as antioxidants.
  - Assist in regulation of fetal development.
  - Regulate Ca^{2+} balance.

Minerals

- Needed as cofactors for specific enzymes and other critical functions.
- Trace elements:
  - Required in small amounts from 50 μg to 18 mg/day.

Free Radicals and Antioxidants

- Electrons are located in orbitals.
  - Each orbital contains a maximum of 2 electrons.
- Free radical:
  - When an orbital has an unpaired electron.
  - Highly reactive in the body.
  - Oxidize or reduce other atoms.
- Major free radicals called:
  - Reactive oxygen or nitrogen species:
    - Oxygen or nitrogen as unpaired electron.

Free Radicals and Antioxidants

(continued)

- Functions of free radicals:
  - Help to destroy bacteria.
  - Produce vasodilation.
- Exert oxidative stress contributing to disease states.
  - Excess production of free radicals can damage lipids, proteins, and DNA.
  - Promotes apoptosis, contributes to aging, inflammatory disease, heart disease, CVA, and degenerative disease.
  - Promotes malignant growth.
- Protective mechanism against oxidative stress.
  - Can react with free radicals by picking up unpaired electrons.
    - Glutathione, vitamin C, and vitamin E.

Regulation of Energy Metabolism

- Energy reserves:
  - Molecules that can be oxidized for energy are derived from storage molecules (glycogen, protein, and fat).
- Circulating substrates:
  - Molecules absorbed through small intestine and carried to the cell for use in cell respiration.

Eating

- Eating behaviors partially controlled by hypothalamus.
- Lesions in vetromedial area produce hyperphagia (obesity).
- Lesions in lateral hypothalamus produces hypophagia (weight loss).
- Endorphins, NE, serotonin, and CCK affect hunger and satiety.

Regulatory Functions of Adipose Tissue

- Adipocytes store fat within large vacuoles.
  - May secrete hormones involved in regulation of metabolism.
  - Leptin:
    - Hormone that signals the hypothalamus to indicate the level of fat storage.
    - Involved in long-term regulation of eating.
      - Satiety factor in obese have decreased sensitivity to leptin in the brain.
  - Neuropeptide Y:
    - Potent stimulator of appetite.
    - Functions as a NT within the hypothalamus.
      - These neurons are inhibited by leptin.
  - TNFα:
    - Acts to reduce the sensitivity of cells to insulin.
      - Increased in obesity.
    - May contribute to insulin resistance.

Obesity

- Obesity is often diagnosed by using a body mass index (BMI).
- $$BMI = \frac{w}{h^2}$$
  - w = weight in kilograms
  - h = height in meters
- Healthy weight as BMI between 19 – 25.
- Obesity defined as BMI > 30.
  - Obesity in childhood is due to an increase in both the size and the # of adipocytes.
  - Weight gains in adulthood is due to increase in adipocyte size in intra-abdominal fat.

Calorie Expenditures

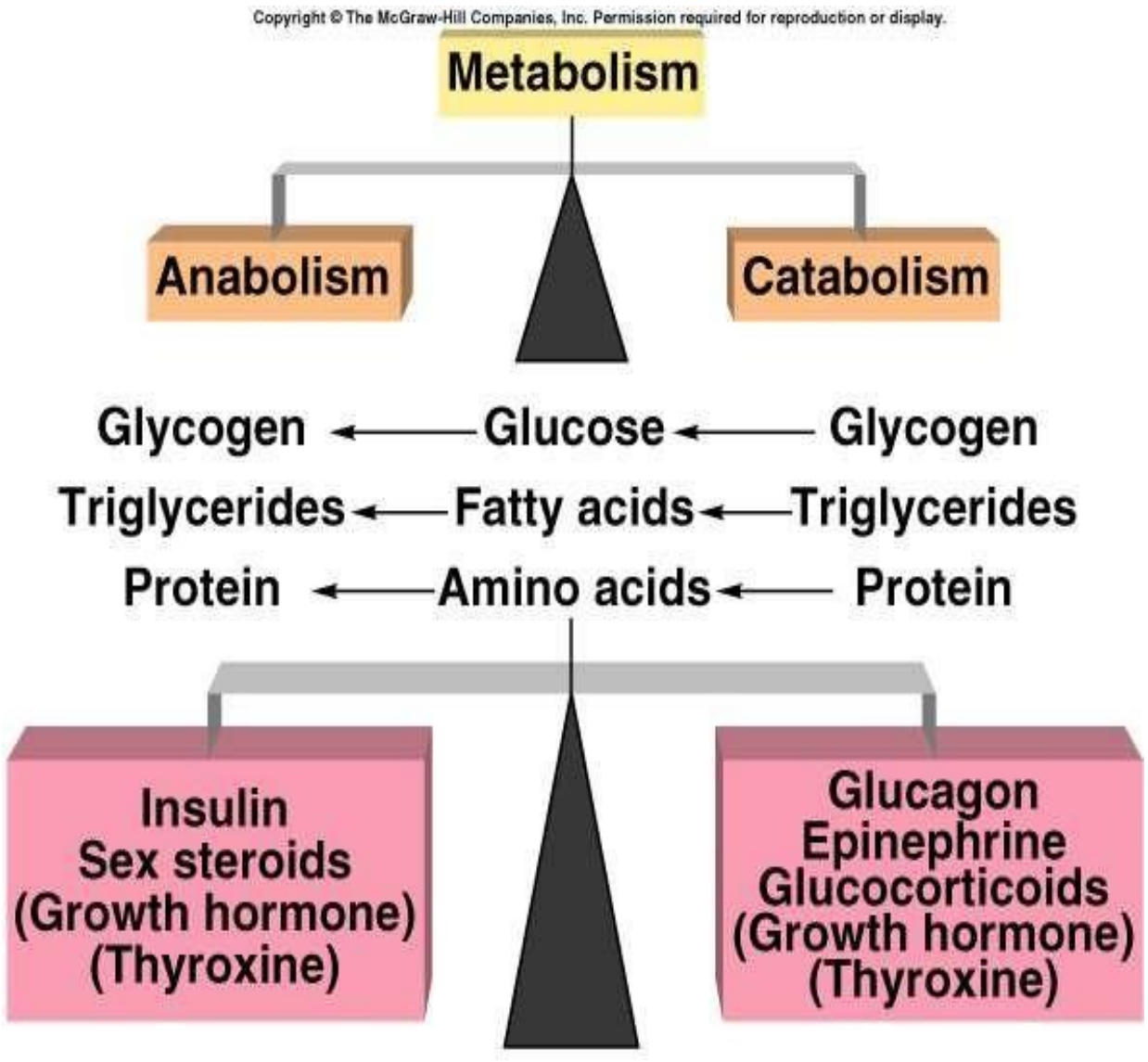
- 3 components:
  - Basal metabolic rate (BMR):
    - 60% total calorie expenditure.
  - Adaptive thermogenesis:
    - 10% total calorie expenditure.
  - Physical activity:
    - Contribution variable.

Hormonal Regulation of Metabolism

- Absorptive state:
  - Absorption of energy.
  - 4 hour period after eating.
  - Increase in insulin secretion.
- Postabsorptive state:
  - Fasting state.
  - At least 4 hours after the meal.
  - Increase in glucagon secretion.

Balance Between Anabolism and Catabolism

- The rate of deposit and withdrawal of energy substrates, and the conversion of 1 type of energy substrate into another; are regulated by hormones.



Energy Regulation of Pancreas

- Islets of Langerhans contain 3 distinct cell types:
  - α cells:
    - Secrete glucagon.
  - β cells:
    - Secrete insulin.
  - Δ cells:
    - Secrete somatostatin.

Regulation of Insulin and Glucagon

- Mainly regulated by blood [glucose].
- Lesser effect: blood [amino acid].
  - Regulated by negative feedback.
- Glucose enters the brain by facilitated diffusion.
- Normal fasting [glucose] is 65–105 mg/dl.

Regulation of Insulin and Glucagon (continued)

- When blood [glucose] increases:
  - Glucose binds to GLUT2 receptor protein in β cells, stimulating the production and release of insulin.
- Insulin:
  - Stimulates skeletal muscle cells and adipocytes to incorporate GLUT4 (glucose facilitated diffusion carrier) into plasma membranes.
    - Promotes anabolism.

Absorptive State

- Insulin is the major hormone that promotes anabolism in the body.
- When blood [insulin] increases:
  - Promotes cellular uptake of glucose.
  - Stimulates glycogen storage in the liver and muscles.
  - Stimulates triglyceride storage in adipose cells.
  - Promotes cellular uptake of amino acids and synthesis of proteins.

Postabsorptive State

- Maintains blood glucose concentration.
- When blood [glucagon] increased:
  - Stimulates glycogenolysis in the liver (glucose-6-phosphatase).
  - Stimulates gluconeogenesis.
  - Skeletal muscle, heart, liver, and kidneys use fatty acids as major source of fuel (hormone-sensitive lipase).
  - Stimulates lipolysis and ketogenesis.

Thyroxine

- Active form is T_3.
- Stimulates cellular respiration by:
  - Production of uncoupling proteins.
- Stimulation of active transport Na^+/K^+ pumps:
  - Lowers cellular [ATP].
- Increases metabolic heat.
- Increases metabolic rate.
- Contributes to proper growth and development of CNS in children.

Growth Hormone (Somatotropin)

- Inhibited by somatostatin.
- Stimulates growth in children and adolescents.
- Stimulated by:
  - GHRH.
  - Increase in blood [amino acids].
  - Decrease in blood [glucose].
- Pulsatile, increasing during sleep, decreasing during day.

Growth Hormone (continued)

- IGF-1:
  - Liver produces and secretes IGF-1 in response to GH.
  - Stimulates cell division and growth of cartilage.
- IGF-2:
  - Has more insulin-like actions.
- Promotes anabolism and catabolism.
  - Stimulates cellular uptake of amino acids and protein synthesis.
  - Decreases glucose utilization by the tissues.
    - Raises blood [glucose].

Effects of Growth Hormone on Body Growth

- Gigantism:
  - Excess GH secretion in children.
    - Maintain normal body proportions.
- Acromegaly:
  - Excess GH secretion in adults after the epiphyseal discs are sealed.
    - No increase in height.
  - Growth of soft tissue.
    - Elongation of jaw, deformities in hands, feet, and bones of face.
- Dwarfism:
  - Inadequate secretion of GH during childhood.

Progression of Acromegaly

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Muscle Physiology

Graded potential

is a mild local change in the membrane potential that develops in receptors, synapse or neuromuscular junction when stimulated- also called graded membrane potential or graded depolarization.

The graded potential is distinct from the action potential and the properties of these two potentials are given in Table 23-1. In most of the cases, the graded potential is responsible for the generation of action potential. However, in some cases the graded potential hyperpolarizes the membrane potential (more negativity than resting membrane potential).

The graded potentials include:

1. End plate potential in neuromuscular junction
2. Receptor potential
4. Excitatory postsynaptic potential
5. Inhibitory postsynaptic potential

MOLECULAR CHANGES DURING MUSCULAR CONTRACTION ACTOMYOSIN COMPLEX

In the relaxed state of the muscle, the thin actin filaments from the opposite ends of sarcomere are away from each other leaving abroad ‘H’ zone.

During the contraction of the muscle, the actin(thin) filaments glide over the myosin (thick) filaments and form actomyosin complex.

MOLECULAR BASIS OF MUSCULAR CONTRACTION

The molecular mechanism is responsible for formation of actomyosin complex that results in muscular contraction. It includes three stages:

1. Excitation contraction coupling
2. Role of troponin and tropomyosin
3. Sliding mechanism

Excitation Contraction Coupling

is the process that occurs in between the excitation and contraction of muscle.

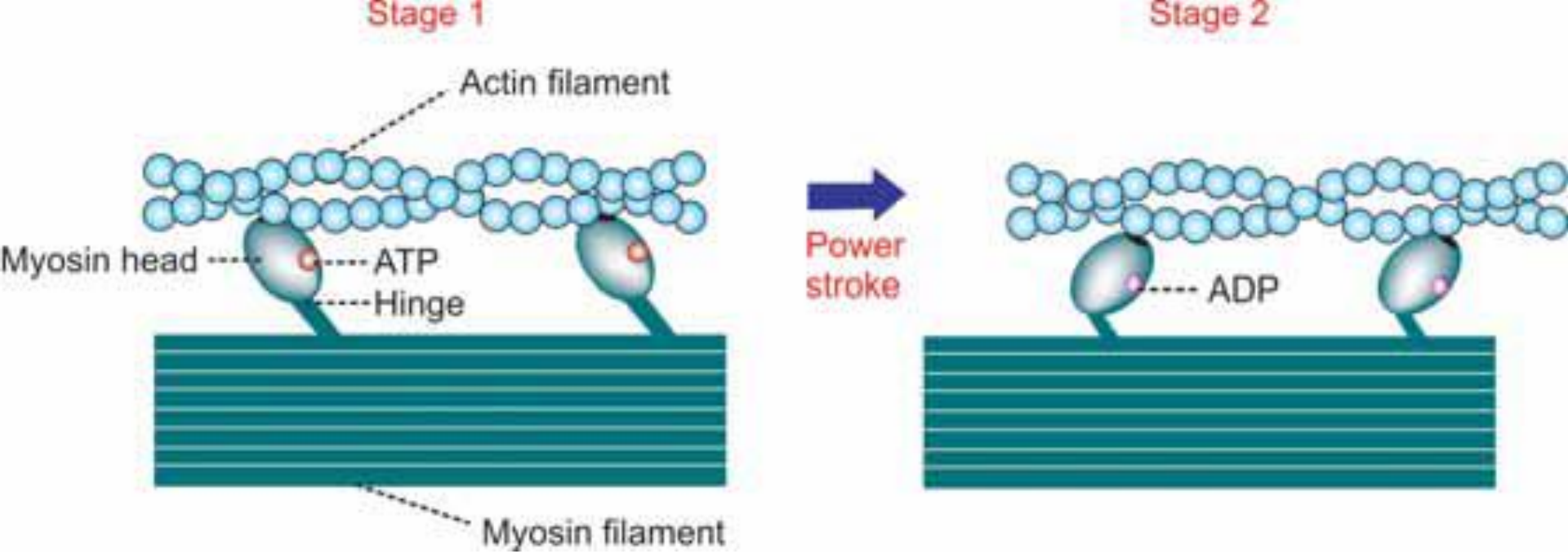
This process involves series of activities which are responsible for the contraction of the excited muscle.

Stages of excitation contraction coupling -When the impulse passes through a motor neuron and reaches the neuromuscular junction, acetylcholine is released from motor endplate. causes opening of ligand gate sodium channels.

So, sodium ions enter neuromuscular junction. leads to development of endplate potential--causes generation of action potential in muscle fiber & spreads over sarcolemma & into muscle fiber through‘ T’ tubules- are responsible for the rapid spread of action potential into muscle fiber.

When the action potential reaches the cisternae of ‘L’ tubules, these cisternae are excited. Now, the calcium ions stored in the cisternae are released into the sarcoplasm. The calcium ions from the sarcoplasm move towards the actin filaments to produce the contraction. Thus, the calcium ion forms the link or coupling material between the excitation and the contraction of muscle.

Hence, the calcium ions are said to form the basis of excitation contraction coupling.



Stage 1: Myosin head binds with actin;
Stage 2: Tilting of myosin head (power stroke) drags the actin filament

Sliding Mechanism and Formation of Actomyosin Complex – Sliding Theory

Sliding theory explains how the actin filaments slide over myosin filaments and form the actomyosin complex during muscular contraction.

After binding with active site of F actin, the myosin head is tilted towards the arm so that

This tilting of head is called power stroke. After tilting, the head immediately breaks a way from the active site and returns to the original position. Now, it combines with a new active site on the actin molecule. And, tilting movement occurs again. Thus, the head of cross bridge bends back and forth and pulls the

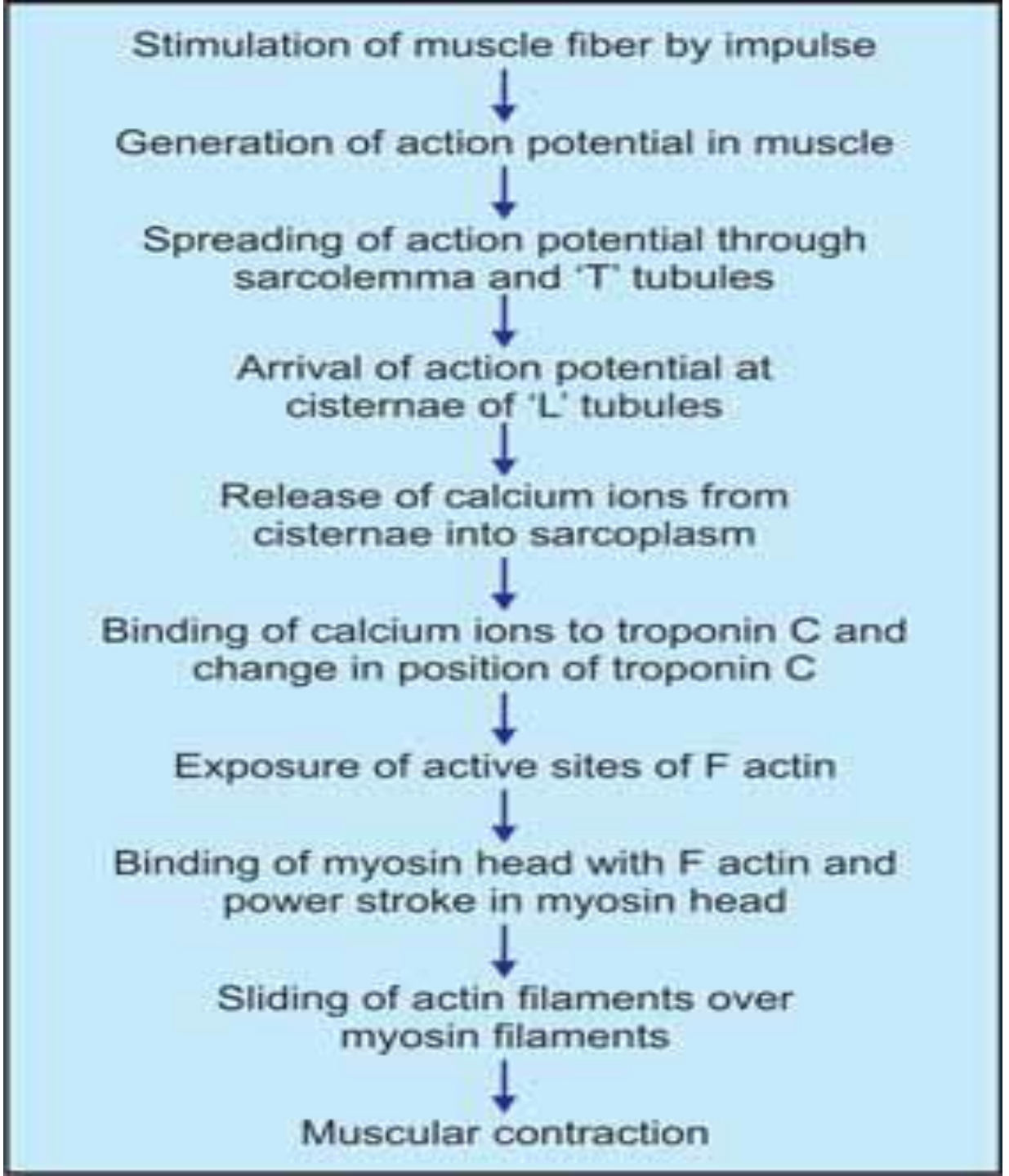
actin filament towards the center of sarcomere.

In this way, all the actin filaments of both theends of sarcomere are pulled. So, the actin filaments of opposite sides overlap and form actomyosin complex.

Formation of actomyosin complex results in contraction of the muscle.

When the muscle shortens further, the actin filaments from opposite ends of the sarcomere approach each other. So, the ‘H’ zone becomes narrow. And, the two ‘Z’ lines come closer with reduction in length of the sarcomere. However, the length of ‘A’ band is not altered. But, the lengtho f ‘I’ band decreases.

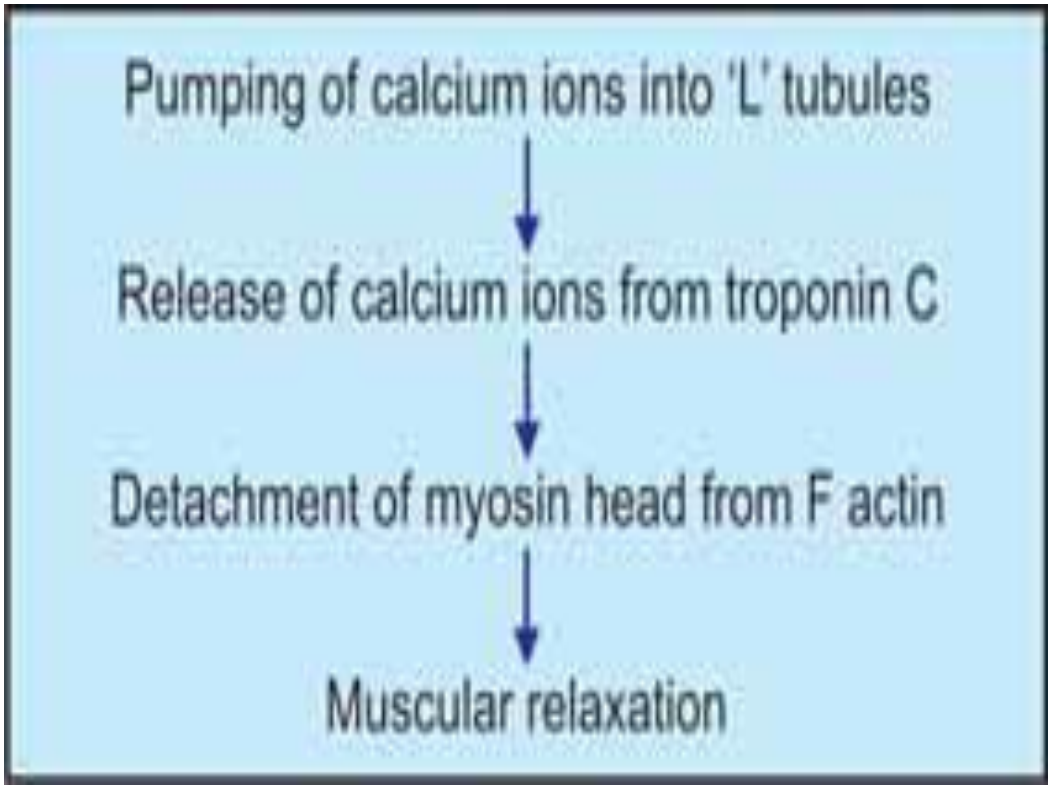
Sequence of events during muscular contraction



Relaxation of the Muscle

occurs when the calcium ions are pumped back into the L tubules.

When calcium ions enter the L tubules, calcium content in sarcoplasm decreases leading to the release of calcium ions from the troponin. It causes detachment of myosin from actin followed by relaxation of the muscle . The detachment of myosin from actin obtains energy from breakdown of ATP. Thus, the chemical process of muscular relaxation is an active process although the physical process is said to be passive



Energy Sources

ATP provides immediate energy for M. contraction from 3 sources:

Creatine phosphate(during resting conditions stores energy to synthesize ATP.

Anaerobic respiration (occurs in absence of oxygen and results in breakdown of glucose to yield ATP and lactic acid

Aerobic respiration (requires oxygen and breaks down glucose to produce ATP, carbon dioxide and water / , more efficient than anaerobic .

Effects of aging on Skeletal Muscle

Reduced muscle mass

Increased time for muscle to contract in response to nervous stimuli

Reduced stamina

Increased recovery time

Loss of muscle fibers

Decreased density of capillaries in muscle

Neuromuscular junction

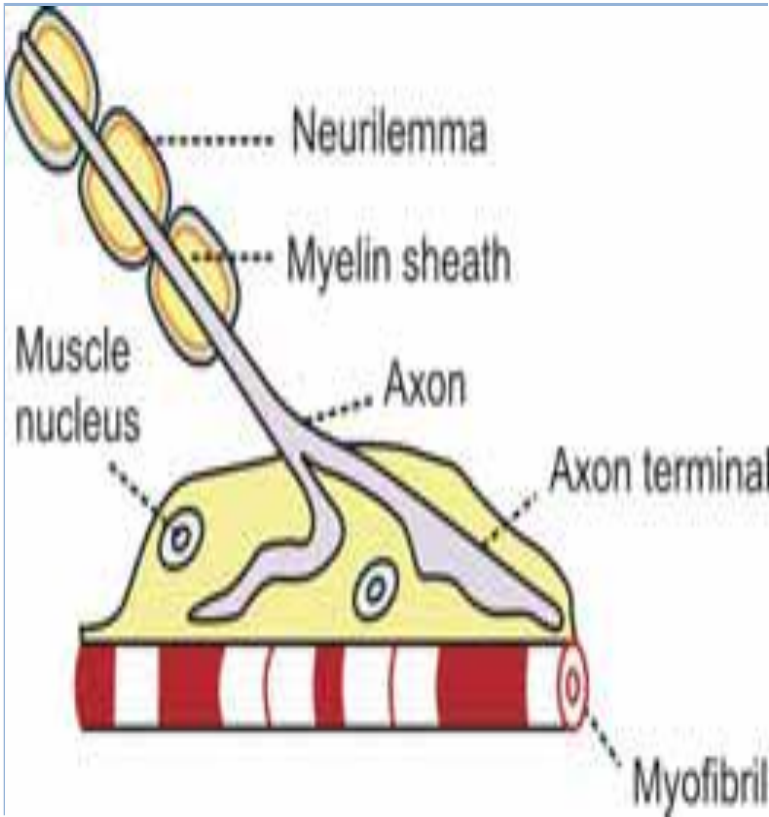
is the junction between the terminal branch of the nerve fiber and muscle fiber.

STRUCTURE

Skeletal muscle fibers are innervated by the motor nerve fibers. Each nerve fiber (axon) divides into many terminal branches. Each terminal branch innervates one muscle fiber through the neuromuscular junction

Terminal branch of nerve fiber called axon terminal. When the axon comes close to the muscle fiber loses myelin sheath. So, the axis cylinder is exposed.

This portion of the axis cylinder is expanded like a bulb called **motor endplate.**



Synaptic Trough or Gutter

motor endplate invaginates inside muscle fiber& forms a depression known as synaptic trough or synaptic gutter. The membrane of muscle fiber below the motor endplate is thickened.

Synaptic Cleft

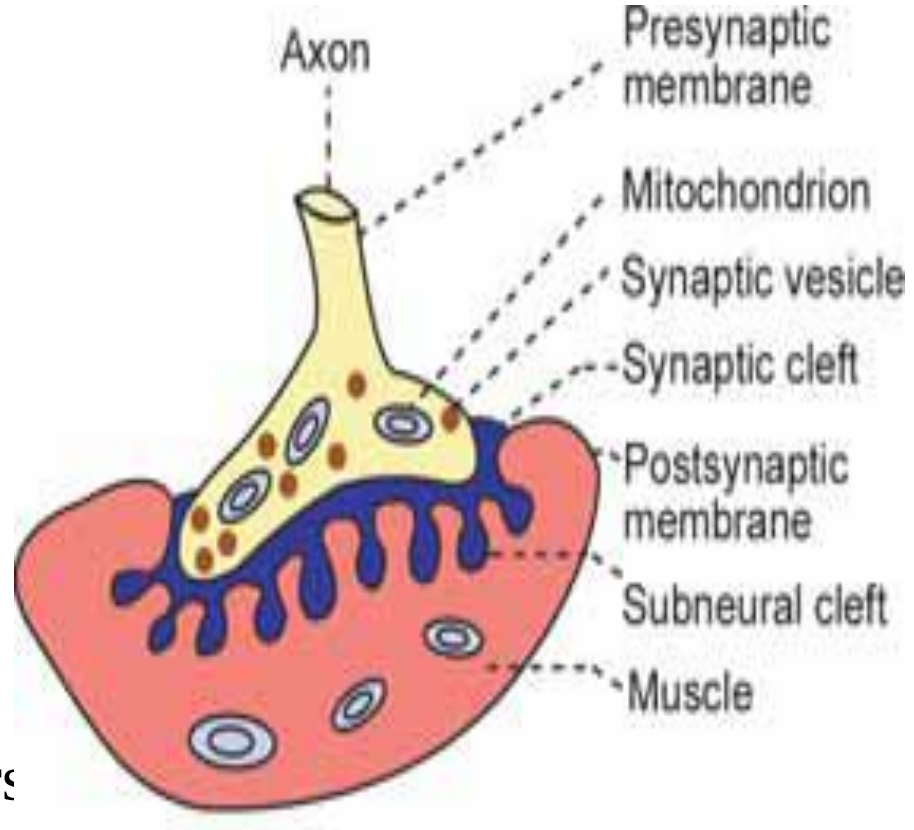
The membrane of the nerve ending called presynaptic membrane. The membrane of the muscle fiber is called postsynaptic membrane.

The space between these two is called synaptic cleft.

The postsynaptic membrane is membrane of the muscle fiber.

It is thrown into numerous folds called subneural clefts.

The postsynaptic membrane contains the receptors called nicotinic acetylcholine receptors

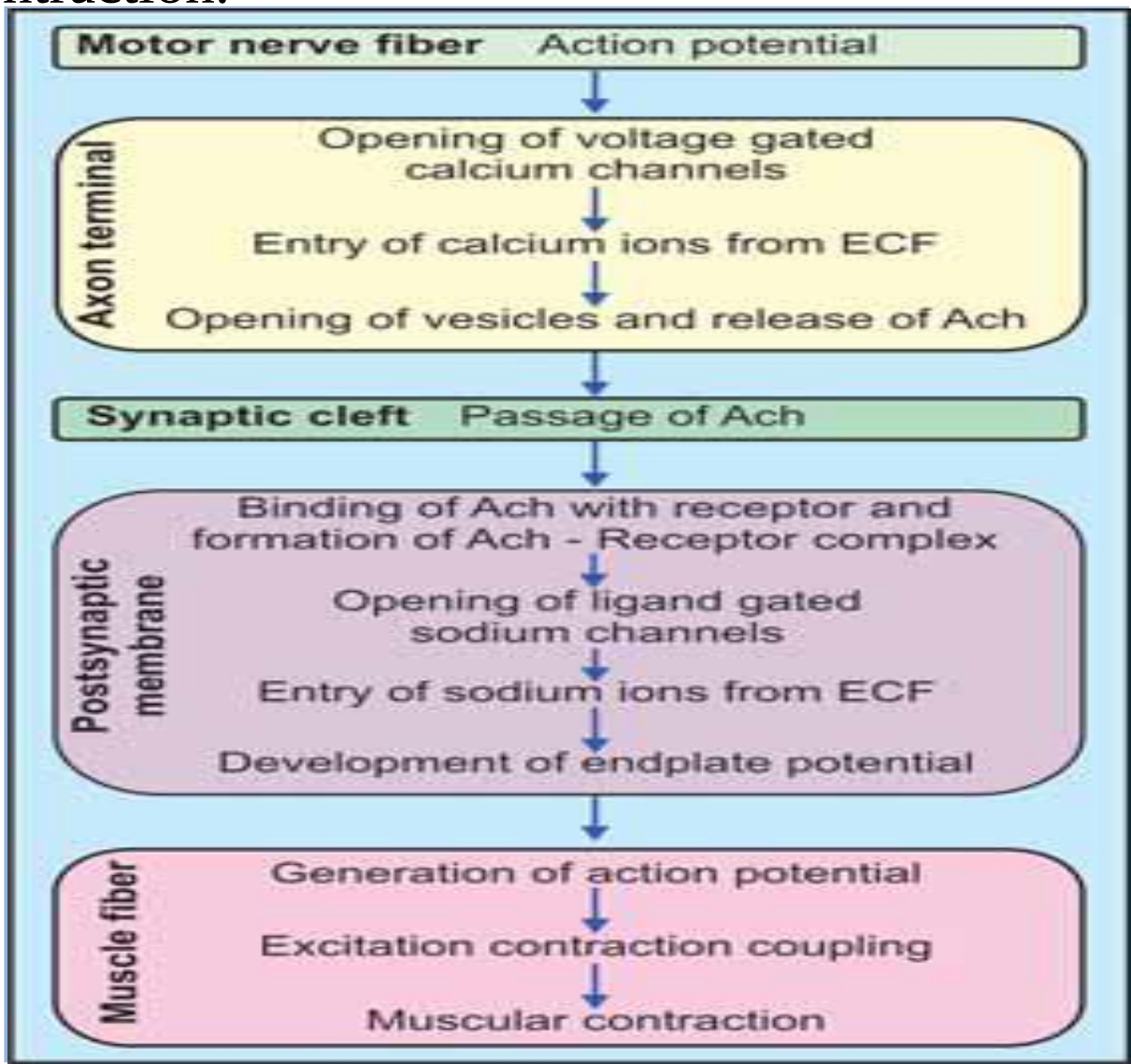


NEUROMUSCULAR TRANSMISSION

transfer of information from motor nerve ending to the muscle fiber through neuromuscular junction. mechanism by which the motor nerve impulses initiate muscle contraction.

Sequence of events during Neuromuscular transmission.

1. Release of acetylcholine
2. Action of acetylcholine
3. Development of endplate potential
4. Development of miniature endplate potential
5. Destruction of acetylcholine



NEUROMUSCULAR BLOCKERS

are the drugs, which can prevent the transmission of impulses from nerve fiber to the muscle fiber through the neuromuscular junctions.

MOTOR UNIT

- DEFINITION

The single motor neuron, its axon terminals and the muscle fibers innervated by it are together called motor unit. Each motor neuron activates a group of muscle fibers through the axon terminals. Stimulation of a motor neuron causes contraction of all the muscle fibers innervated by that neuron.

DISORDERS OF NEUROMUSCULAR JUNCTION

The disorders of neuromuscular junction includes:

- **Myasthenia gravis**

is an autoimmune disorder of neuromuscular junction caused by antibodies to cholinergic receptors. It is characterized by grave weakness of the muscle due to the inability of neuromuscular junction to transmit impulses from nerve to the muscle.

- **Eaton-Lambert syndrome**

is also an autoimmune disorder of neuromuscular junction. It is caused by antibodies to calcium channels in axon terminal.

This disease is characterized by features of myasthenia gravis. In addition the patients have blurred vision and dry mouth.

Motor units

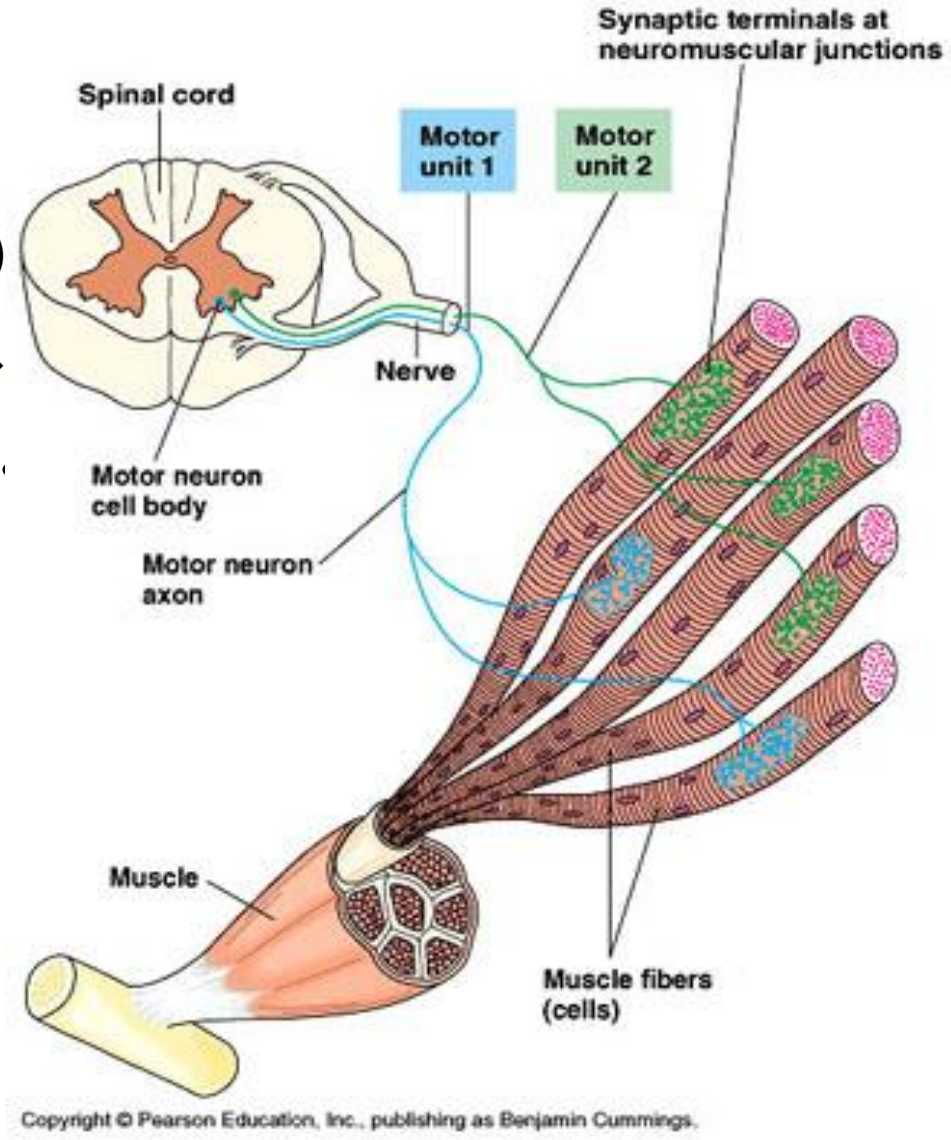
Motor unit: Composed of one motor neuron and all the muscle fibers that it innervates

There are many motor units in a muscle

The number of fibers innervated by a single motor neuron varies (from a few to thousand)

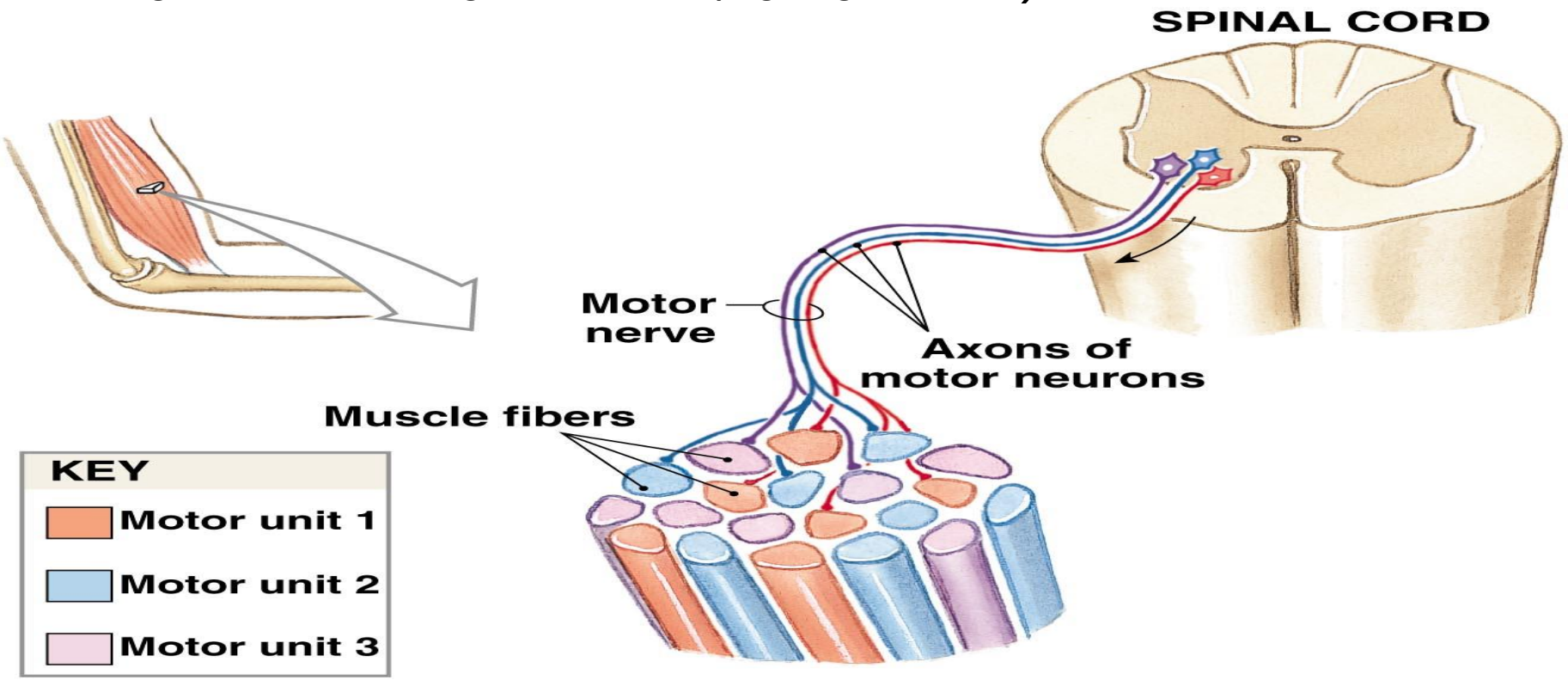
The fewer the number of fibers per neuron → the finer the movement (more brain power)

Which body part will have the largest motor units? The smallest?



- Skeletal muscles are made up of thousands of muscle fibers

- A single motor neuron may directly control a few fibers within a muscle, or hundreds to thousands of muscle fibers
  - All of the muscle fibers controlled by a single motor neuron constitute a ***motor unit***
  - The size of the motor unit determines how fine the control of movement can be –
    - small motor units → precise control (e.g. eye muscles
    - large motor units →gross control (e.g. leg muscles)



General physiology
High altitude and deep-sea physiology

High altitude and deep-sea physiology

- High altitude
- Any altitude above 8000 ft from mean sea level is called high altitude. People can ascend up to this level without any adverse effect. At high altitudes, the barometric pressure is low. However, the amount of oxygen available in the atmosphere is same as it is at the sea level. Due to low barometric pressure, the partial pressure of gases, particularly oxygen decreases leading to hypoxia. The carbon dioxide in high altitude is very much negligible and it does not create any problem.

- **Barometric pressure and partial pressure of oxygen at different altitudes**

- The barometric pressure decreases at different altitudes and, accordingly the partial pressure of oxygen also decreases leading to various effects on the body. Barometric pressure and partial pressure of oxygen at different altitudes and their common effects on the body are given in table.

Altitude (feet)	Barometric pressure (mm Hg)	Partial pressure of oxygen (mm Hg)	Common effects
Sea Level	760	159	———
5,000	600	132	No hypoxia
10,000	523	110	Mild symptoms of hypoxia start appearing
15,000	400	90	Moderate hypoxia develops with following symptoms: — Reduction in visual acuity — Effects on mental functions: — Improper judgment and — Feeling of over confidence
20,000	349	73	Severe hypoxia appears with cardiorespiratory symptoms such as: — Increase in heart rate and cardiac output — Increase in respiratory rate and respiratory minute volume This is the highest level for permanent inhabitants
25,000	250	62	This is the critical altitude for survival — Hypoxia becomes severe — Breathing oxygen becomes essential
29,628	235	49	This is the height of Mount Everest
30,000	226	47	Symptoms become severe even with oxygen
50,000	87	18	Hypoxia becomes more severe even with pure oxygen

Changes in the body at high altitude

When a person is exposed to high altitude particularly by rapid ascent, the various systems in the body cannot deal with the lowered oxygen tension and, the effects of hypoxia start. Besides, hypoxia, other factors such as expansion of gases, fall in atmospheric temperature and light rays are also responsible for the changes in the functions of the body at high altitude.

- **Mountain sickness**

- **Definition**

- Mountain sickness is the condition characterized by adverse effects of hypoxia at high altitude. It is commonly developed in persons going to high altitude for the first time. It occurs within a day in these persons before they get adapted to the altitude.

Symptoms

In mountain sickness, the symptoms occur mostly in digestive system, cardiovascular system, respiratory system and nervous system. The symptoms of mountain sickness are:

1. **Digestive system**: Loss of appetite, nausea and vomiting occur because of expansion of gases in the gastrointestinal tract.

2. **Cardiovascular system**: Heart rate increases.

3. **Respiratory system**: Pulmonary blood pressure increases due to increased blood flow. Blood flow increases because of vasodilatation induced by hypoxia. Increased pulmonary blood pressure results in pulmonary edema which casus breathlessness.

4. **Nervous system**: The symptoms of nervous system are headache, depression, disorientation, irritability, lack of sleep, weakness and fatigue.

Treatment: Mountain sickness is treated by oxygen therapy.

Acclimatization

Definition

Acclimatization refers to the adaptations or the adjustments by the body in high altitude. While staying at high altitudes for several days to several weeks, a person slowly gets adapted or adjusted to the low oxygen tension so that, hypoxic effects are reduced. It enables the person to ascent further.

Changes during Acclimatization

The various changes during acclimatization help the body to cope with the adverse effects of hypoxia at high altitude. Following changes occur in the body during acclimatization:

1. Changes in blood During acclimatization, the RBC count increases and packed cell volume rises from the normal value of 45% to about 59%. The hemoglobin content in the blood rises from 15 g% to 20 g%. So, the oxygen carrying capacity of the blood is increased. Thus, more oxygen can be carried to tissues in spite of hypoxia. Increase in RBC count, packed cell volume and hemoglobin content is due to erythropoietin that is released from juxtaglomerular apparatus of kidney

2. Changes in cardiovascular system Overall activity of cardiovascular system is increased in high altitude. There is increase in rate and force of contraction of heart, cardiac output and blood pressure. Hypoxia induced vasodilatation increases the vascularity in the body. So, blood flow to the vital organs such as heart, brain, muscles, etc. increases.

3. Respiratory system

i. Pulmonary ventilation increases up to 65% due to the stimulation of chemoreceptors. This helps the person to ascend several thousand feet

ii. Pulmonary hypertension develops due to increased cardiac output, and pulmonary blood flow

iii. Diffusing capacity of gases increases in the alveoli due to the increase in pulmonary blood flow and pulmonary ventilation. It enables more diffusion of oxygen in blood.

4. Changes in tissues

Both in human beings and animals residing at high altitudes permanently, the cellular oxidative enzymes involved in metabolic reactions are more than in the inhabitants at sea level. Even, when a sea level inhabitant stays at high altitude for certain period, the amount of oxidative enzymes is not increased. So, the elevation in the amount of oxidative enzymes occurs only in fully acclimatized persons. An increase in the number of mitochondria is observed in these persons.

Deep Sea Physiology

In high altitude, the problem is with low atmospheric (barometric) pressure. In deep sea or mines, the problem is with high barometric pressure. The increased pressure decreases the volume of gases and produces compression effect on the body and internal organs.

Barometric pressure at different depths

At sea level, the barometric pressure is 760 mm Hg, which is referred as 1 atmosphere. At the depth of every 33 feet (about 10 m), the pressure increases by one atmosphere. Thus, at the depth of 33 feet, the pressure is two atmospheres. It is due to the air above water and the weight of water itself.

Effect of high barometric pressure — nitrogen narcosis

Narcosis refers to unconsciousness or stupor (lethargy with suppression of sensations and feelings) produced by drugs. Nitrogen narcosis means narcotic effect produced by nitrogen at high pressure. Nitrogen narcosis is common in deep sea divers who breathe compressed air (air under high pressure). Breathing compressed air (air under high pressure) is essential for a deep sea diver or an underwater tunnel worker. It is to equalize the surrounding high pressure acting on thoracic wall and abdomen.

Symptoms

The first symptom starts appearing at a depth of 120 feet. The person becomes very cheerful and careless without understanding the seriousness of the conditions.

Mechanism

Nitrogen is soluble in fat. During compression by high barometric pressure in deep sea, nitrogen escapes from blood vessels and gets dissolved in the fat present in various parts of the body, especially the neuronal membranes. The dissolved nitrogen acts like an anesthetic agent suppressing the neuronal excitability. Nitrogen remains in dissolved form in the fat till the person remains in the deep sea. When he ascends up, decompression sickness develops.

Effects of Exposure to Cold and Heat

Effects of exposure to cold

During exposure to cold, the body temperature is maintained by two mechanisms

A. Heat production

B. Prevention of heat loss.

Heat production

When the body is exposed to cold, the heat is produced by the following activities:

1. By Increased Metabolic Activities

The heat gain center in hypothalamus is stimulated during exposure to cold. It causes secretion of adrenaline and noradrenaline by activating sympathetic centers. These hormones, especially adrenaline increase heat production by accelerating cellular metabolic activities.

2. By Shivering

Shivering is the increased involuntary muscular activity with slight vibration of the body in response to fear, onset of fever or exposure to cold. Shivering occurs when the body temperature falls to about 25°C (77°F). During exposure to cold, the heat gain center activates the motor center for shivering situated in posterior hypothalamus and, shivering occurs. Enormous heat is produced during shivering due to severe muscular activities.

Prevention of heat loss

When the body is exposed to cold, the heat gain center in the posterior nucleus of hypothalamus is stimulated. It activates the sympathetic centers in posterior hypothalamus resulting in cutaneous vasoconstriction and decrease in blood flow. Due to decrease in cutaneous blood flow, sweat secretion is decreased and heat loss is prevented.

Effects of exposure to severe cold

Exposure of body to severe cold leads to death if quick remedy is not provided. The survival time depends upon the temperature of the environment. If a person is exposed to ice cold water, i.e. 0°C for 20 to 30 minutes, the body temperature falls below 25°C (77°F) and the person can survive if he is placed immediately in hot water tub with a temperature of 43°C (110°F). The survival time at 9°C (28°F) is about 1 hour and the survival time at 15.5°C (60°F) is about 5 hours.

The effects of exposure of body to extreme cold are:

1. Loss of temperature regulating capacity

2. Frostbite.

Loss of Temperature Regulating Capacity

The temperature regulating capacity of hypothalamus is affected when the body temperature reduces to about 34.4°C (94°F). The hypothalamus totally looses the power of temperature regulation when body temperature falls below 25°C (77°F). Shivering does not occur. In addition to loss of hypothalamic function, the metabolic activities are also suppressed. Sleep or coma develops due to depression of the central nervous system.

Frostbite

Frostbite is the freezing of the surface of the body when it is exposed to cold. It occurs due to sluggishness of blood flow. Most commonly exposed areas such as ear lobes and digits of hands and feet are affected. Frostbite is common in mountaineers. Prolonged exposure will lead to permanent damage of the cells followed by thawing and gangrene (death and decay of tissues) formation.

Effects of exposure to heat

Heat exhaustion

Heat exhaustion is the body's response to excess loss of water and salt through sweat caused by exposure to hot environmental conditions. In fact it is the warning that body is getting too hot. Heat exhaustion results in loss of consciousness and collapse.

Dehydration exhaustion

Prolonged exposure to heat results in dehydration. It is due to excessive sweating. Dehydration

leads to fall in cardiac output, and blood pressure. Collapse occurs if treatment is not given immediately.

Heat cramps

Severe painful cramps occur due to reduction the quantity of salts and water as a result of increased sweating during the continuous exposure to heat.

HEATSTROKE

Heatstroke

Heatstroke is an abnormal increase in body temperature that occurs during exposure to extreme heat. It is characterized by increase in body temperature above 41°C (106°F) accompanied by some physical and neurological symptoms. Compared to other effects of exposure to heat such as heat exhaustion and heat cramps, heatstroke is very severe and often becomes fatal if not treated immediately. The hypothalamus looses the power of regulating body temperature. Sunstroke is the heatstroke that is caused by prolonged exposure to sun during summer in desert or tropical areas.

- **Features**

- The common features of heatstroke are nausea, vomiting, dizziness, headache, abdominal pain,

- difficulty in breathing, vertigo, confusion, muscle cramps, convulsions, paralysis and unconsciousness. If immediate and vigorous treatment is not given, the damage of brain tissues occurs, resulting in coma and death.

- **Treatment**

- The person affected by heatstroke must be treated before the damage of organs.

- Immediate cooling of the body is the usual treatment.

Nervous system
NEURON

Nervous system

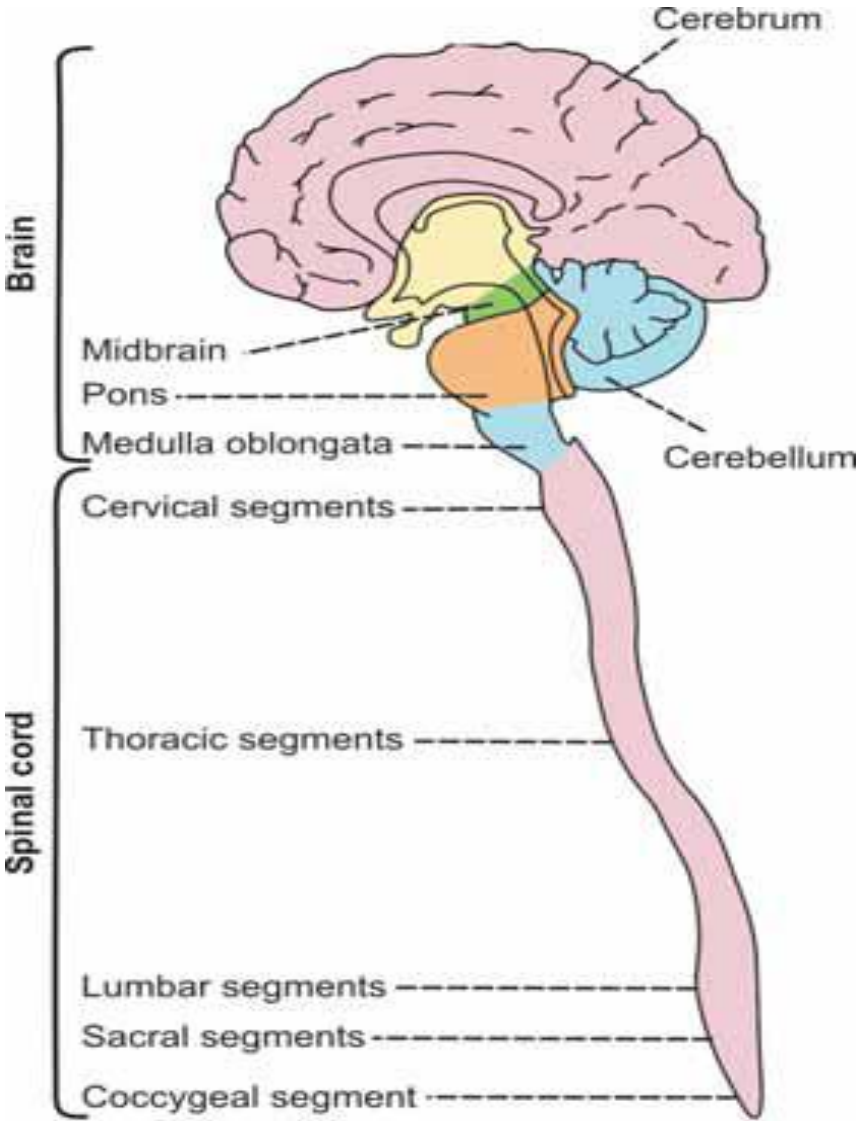
controls all the activities of the Body-quicker than the other control system in body namely, the endocrine system. Primarily, the nervous system is divided into two parts.

1. Central nervous system (CNS)

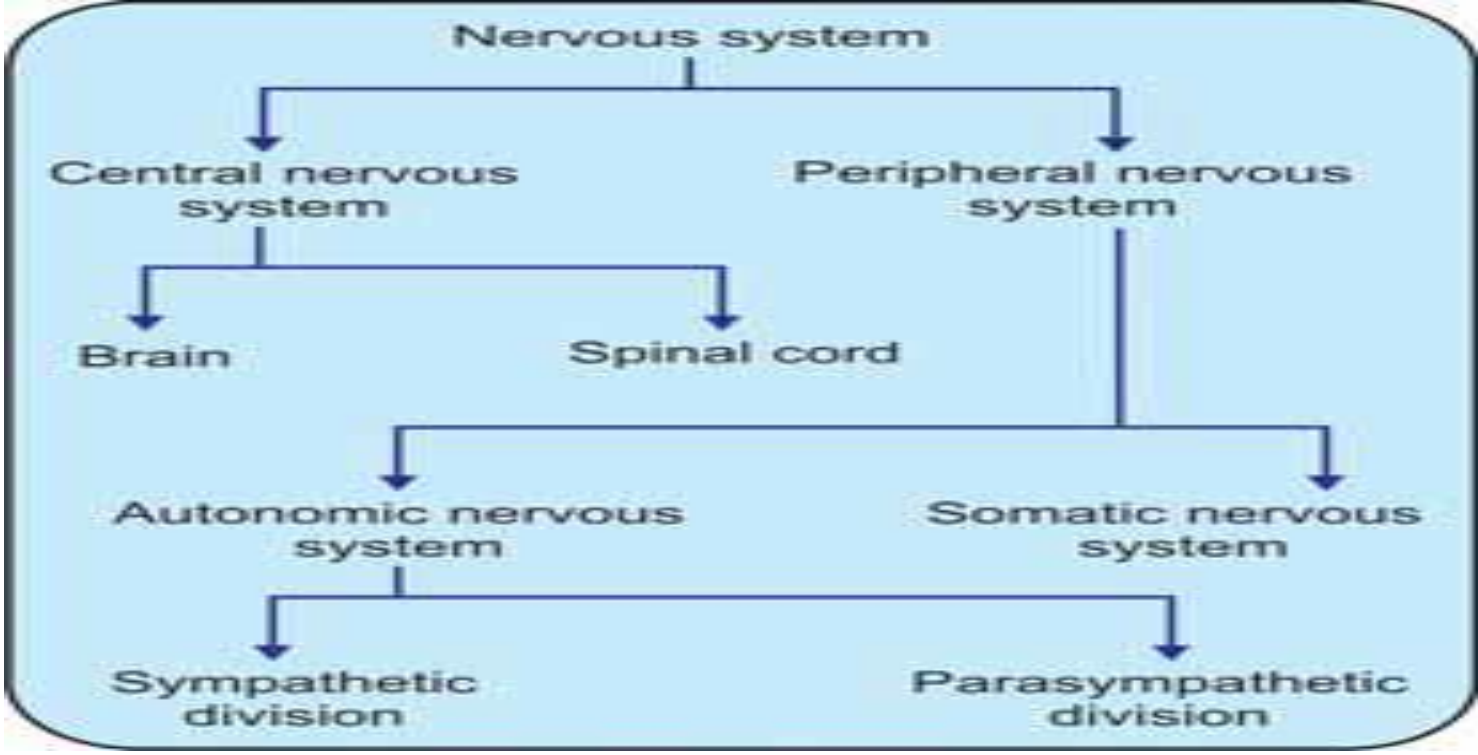
includes brain & spinal cord.

formed by neurons & supporting cells called neuroglia.

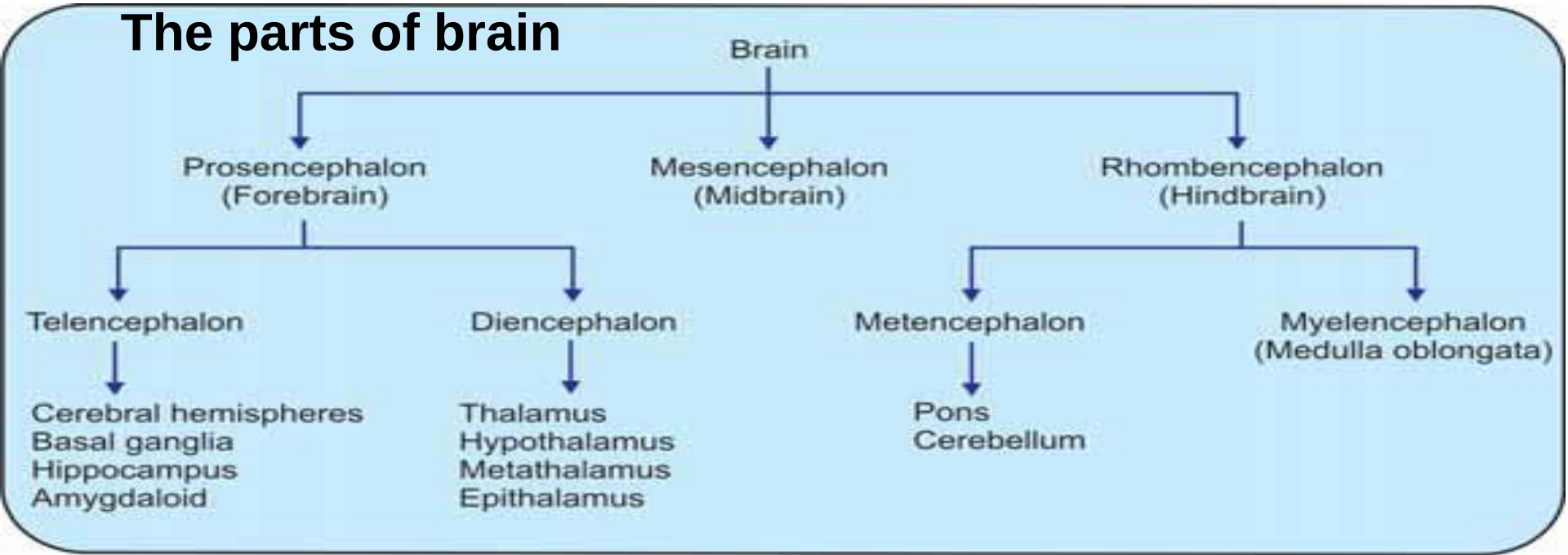
2. Peripheral nervous system.



Organization of nervous system



The parts of brain



2. Peripheral nervous system (PNS)

formed by the neurons & their processes present in all regions of & body. consists of cranial nerves arising from brain & spinal nerves arising from the spinal cord. It is again divided into two subdivisions:

1. Somatic nervous system: concerned with somatic functions- includes the nerves supplying skeletal muscles-- controls the movements of the body by acting on the skeletal muscles.

2. Autonomic nervous system : is concerned with regulation of visceral or vegetative functions. So, otherwise called vegetative or involuntary nervous system. The autonomic nervous system consists of two divisions, sympathetic & parasympathetic divisions.

NEURON

the structural & functional unit of the nervous system. otherwise called nerve cell--like any other cell in the body having nucleus & all the organelles in the cytoplasm. However, it is different from other cells by two ways:

1. Neuron has branches or processes called axon & dendrites
2. Neuron does not have centrosome; so it cannot undergo division.

 CLASSIFICATION OF NEURON

The neurons are classified by three different methods.

I. Depending upon number of poles

II. Depending upon function

III. Depending upon length of the axon.

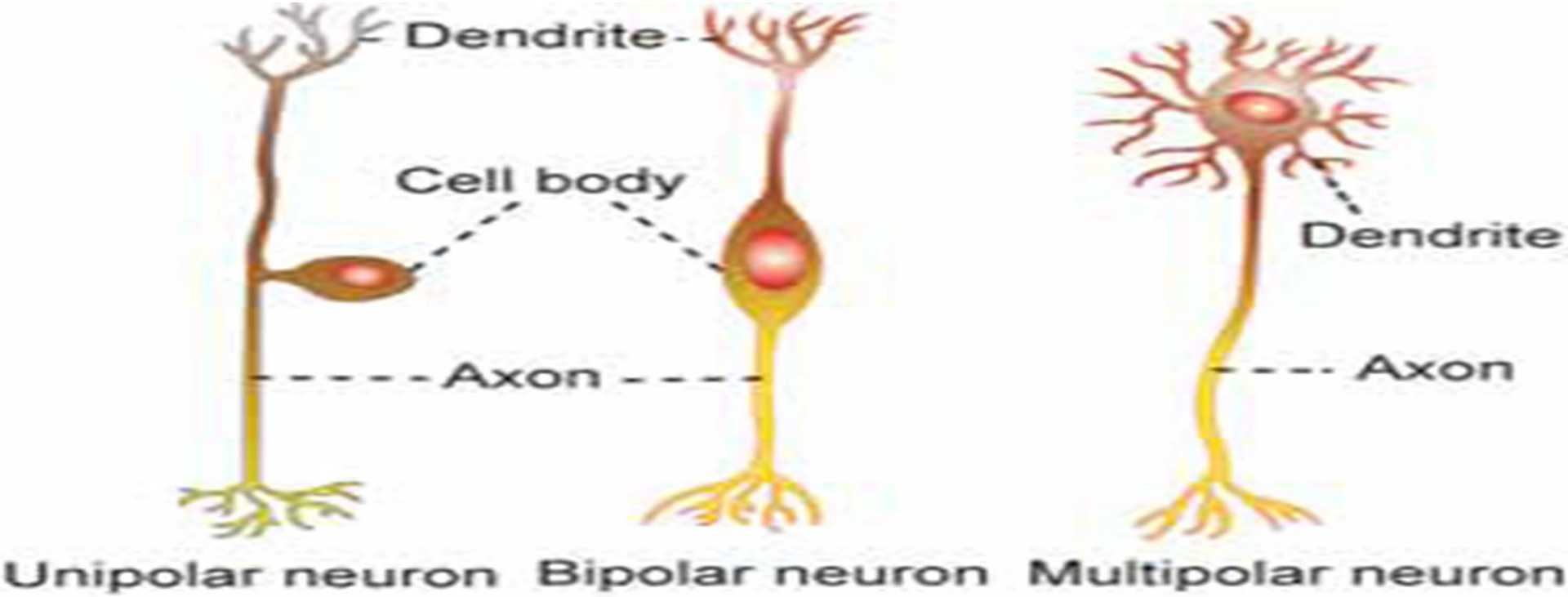
Depending upon Number of Poles

Based on the number of poles from which the nerve fibers arise:

1. Unipolar neurons that have only one pole from which, both the axon & dendrite arise

2. Bipolar neurons which have two poles. Axon arises from one pole & dendrites arise from the other pole.

3. Multipolar neurons which have many poles. One of the poles gives rise to the axon &, all the other poles give rise to dendrites.



Depending upon Function

On the basis of function, the nerve cells are classified into two types:

1. Motor neurons or efferent neurons

which carry the motor impulses from central nervous system to the peripheral effector organs like muscles, glands, blood vessels, etc.

2. Sensory neurons or afferent neurons

which carry the sensory impulses from periphery to the central nervous system.

The Neurons

Function- send impulses to & from CNS & PNS & the effectors(muscles, gland, receptor, nerve endings).

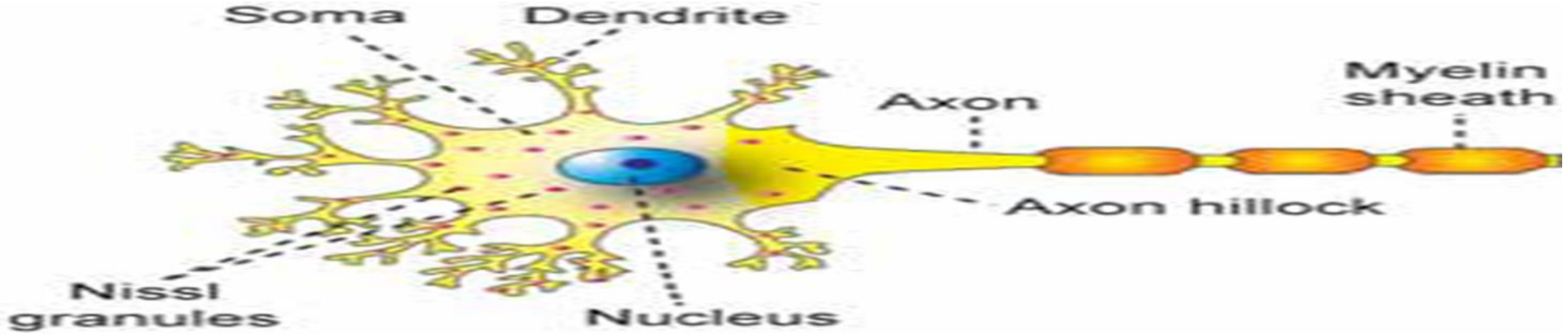
Receive, integrate , & transmit information

Operate through electrical impulses

Communicate with other neurons through chemical signals

The transmission of information along the length of the neuron is electrochemical in nature.

Neurons do not actually touch each other, instead, there is a space between the end of one & the beginning of the next (continuity without contact). neurotransmitter- is required to cross the gap between one neuron and the next.



STRUCTURE OF NEURON

Each neuron is made up of three parts:

1. Nerve cell body

also known as soma or perikaryon. is constituted by a mass of cytoplasm called neuroplasm.

The nucleus does not contain centrosome. So, the nerve cell cannot

multiply like other cells. Neurofibrils are thread like structures present in form of network in soma & nerve processes. Presence of neurofibrils is another characteristic feature of neurons.

2. Dendrite

is the branched process of neuron & it is branched repeatedly. The dendrite may be present or absent. If present, it may be one or many in number. Dendrite is conductive in nature- transmits impulses towards the nerve cell body.

3. Axon.

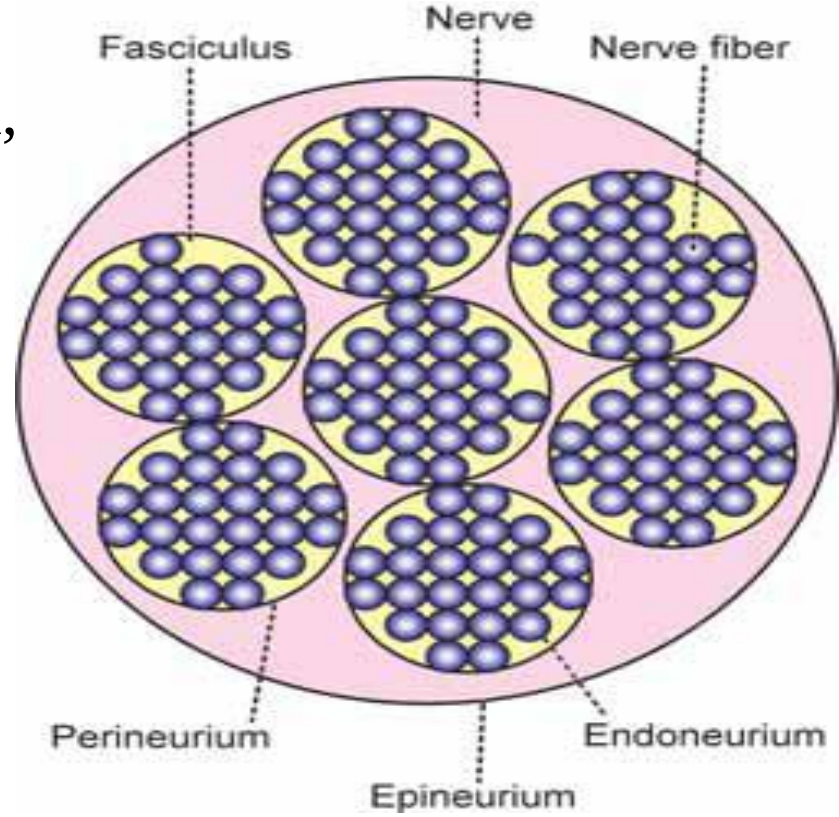
Axon

is longer than dendrite. Each neuron has only one axon, extends for a long distance away from the nerve cell body. The length of the longest axon is about one meter.

Organization of nerve

Many axons together form a bundle called fasciculus. Many fasciculi together form a nerve.

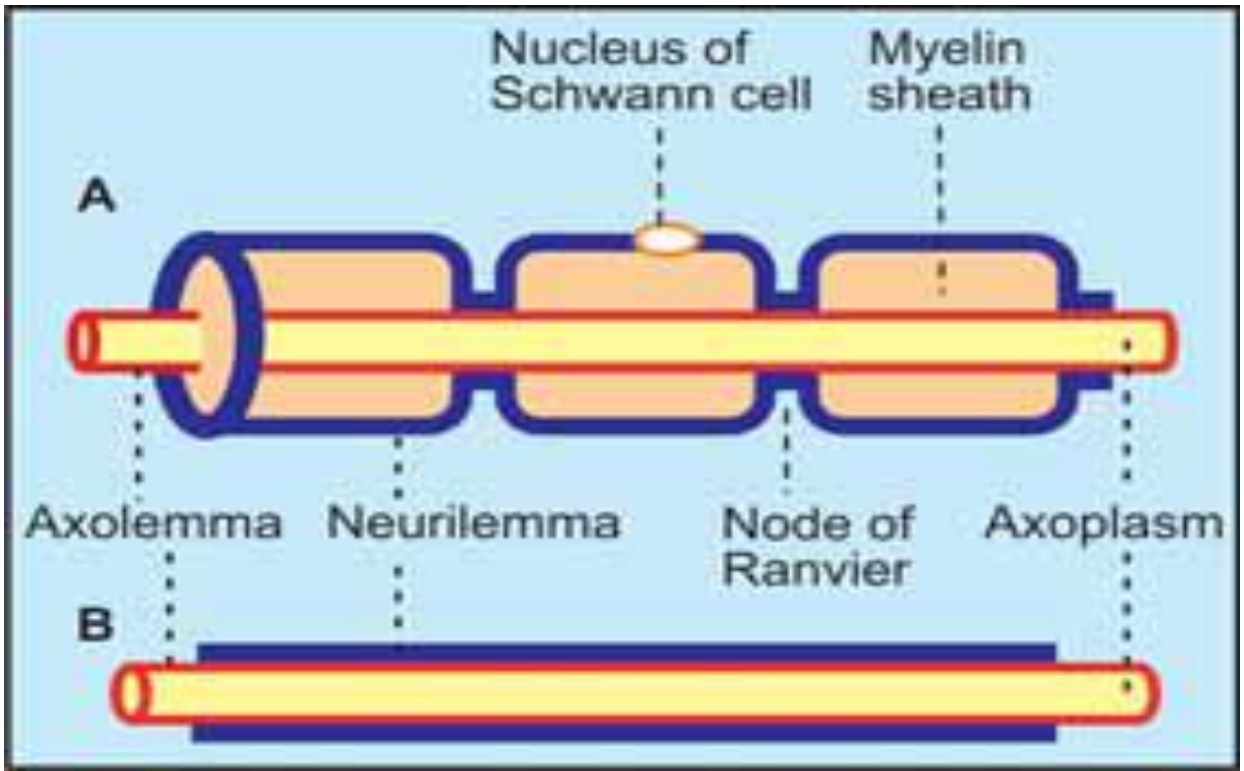
whole nerve is covered by tubular sheath, called epineurium. Each fasciculus is covered by perineurium & each nerve fiber(axon) is covered by endoneurium



Cross section of a nerve

The axon has long central core of cytoplasm called axoplasm- is covered by axolemma which is the continuation of the cell membrane of nerve cell body. The axoplasm along with the axolemma is called the **axis cylinder of the nerve fiber-** is covered by a membrane called neurilemma.

The nerve fibers which are insulated by myelin sheath are called myelinated nerve fibers- responsible for the white color of nerve fibers.



Myelinated nerve fiber

formation of myelin sheath around the axon is called **myelinogenesis**. It is formed by Schwann cells in neurilemma.

Functions of myelin sheath

1. Faster conduction:

Myelin sheath is responsible for faster conduction of impulse through the nerve fibers. - the impulses jump from one node to another node by saltatory conduction.

2. Insulating capacity:

Myelin sheath has a high insulating capacity. Because of this quality, the myelin sheath restricts the nerve impulse within the single nerve fiber, and prevents the stimulation of neighboring nerve fibers.

CLASSIFICATION OF NERVE FIBERS

1. Depending upon structure (i. Myelinated nerve fibers

ii. Nonmyelinated nerve fibers)

2. Depending upon distribution (Somatic nerve fibers ii. Visceral or autonomic nerve fibers)

3. Depending upon origin(i. Cranial nerves ii. Spinal nerves arising)

4. Depending upon function(i. Sensory - afferent nerve fibers ii. Motor or efferent nerve fibers)

5. Depending upon secretion of neurotransmitter(i. Adrenergic nerve fibers ii. Cholinergic nerve fibers)

6. Depending upon diameter & conduction of impulse (Erlanger-Gasser classification).

1. Type A nerve fibers 2. Type B nerve fibers 3. Type C nerve fibers.

Type A nerve fibers are divided into 4 subtypes. Except ‘C’ type of fibers, all the nerve fibers are myelinated. The velocity of impulse through a nerve fiber is directly proportional to the thickness of the fibers.

PROPERTIES OF NERVE FIBERS

Excitability is as the physiochemical change that occurs in a tissue when a stimulus is applied.

The stimulus is an external agent, which produces excitability in the tissues. When the nerve fiber is stimulated action potential develops.

Conductivity

the ability of nerve fibers to transmit the impulse from the area of stimulation to other areas. The action potential is transmitted through the nerve fiber as nerve impulse.

Normally in the body, action potential is transmitted through the nerve fiber in only one direction.

Mechanism of conduction of action potential

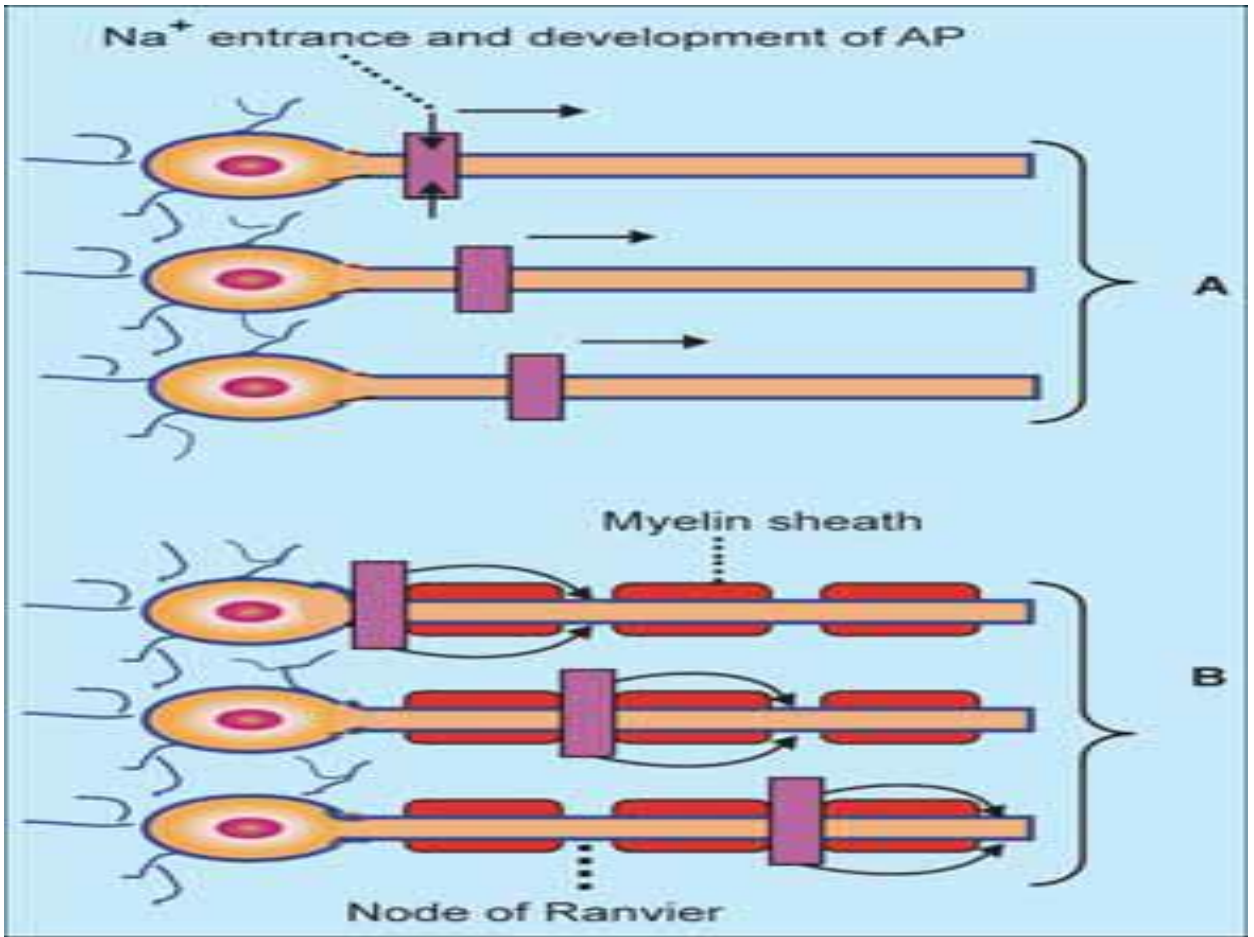
The depolarization occurs first at the site of stimulation in nerve fiber. It causes depolarization of the neighboring areas. Like this, depolarization travels throughout the nerve fiber. is followed by repolarization.

Conduction through myelinated nerve fiber — Saltatory conduction

is form of conduction of nerve impulse in which, impulse jumps from one node to another. Conduction of impulse through a myelinated nerve fiber is about 50 times faster than through a nonmyelinated fiber.

because the action potential jumps from one node to another node of Ranvier instead of travelling through the entire nerve fiber

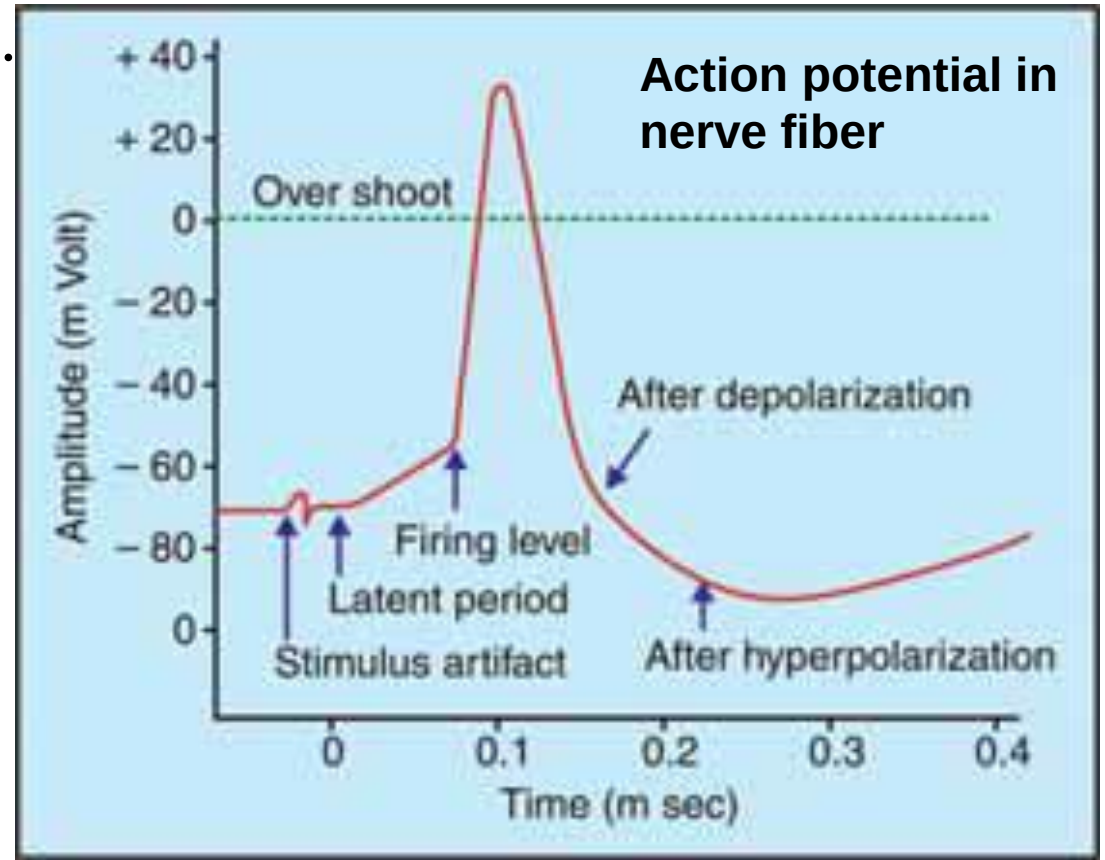
Mode of conduction through nerve fibers



Mechanism of saltatory conduction

The myelin sheath is not permeable to ions. So, the entry of sodium from extracellular fluid into nerve fiber occurs only in the node of Ranvier, where myelin sheath is absent. It causes depolarization in the node, and not in the internode.

Thus, the depolarization occurs at successive nodes. So, the action potential jumps from one node to another. Hence, it is called saltatory conduction (saltare = jumping).



Summation

When one subliminal stimulus is applied, it does not produce any response in the nerve fiber because, the subliminal stimulus is very weak.

However, if two or more subliminal stimuli are applied within a short interval of about 0.5 m sec,

the response is produced--because the subliminal stimuli are summed up together to become strong enough to produce the response.

Adaptation

While stimulating a nerve fiber continuously, the excitability of nerve fiber is greater in beginning. Later the response decreases slowly & finally the nerve fiber does not show any response at all. This is known **as adaptation or accommodation--** causes for adaptation are:

1. When a nerve fiber is stimulated continuously, depolarization occurs continuously

2. The continuous depolarization inactivates the sodium pump & increases the efflux of potassium ions.

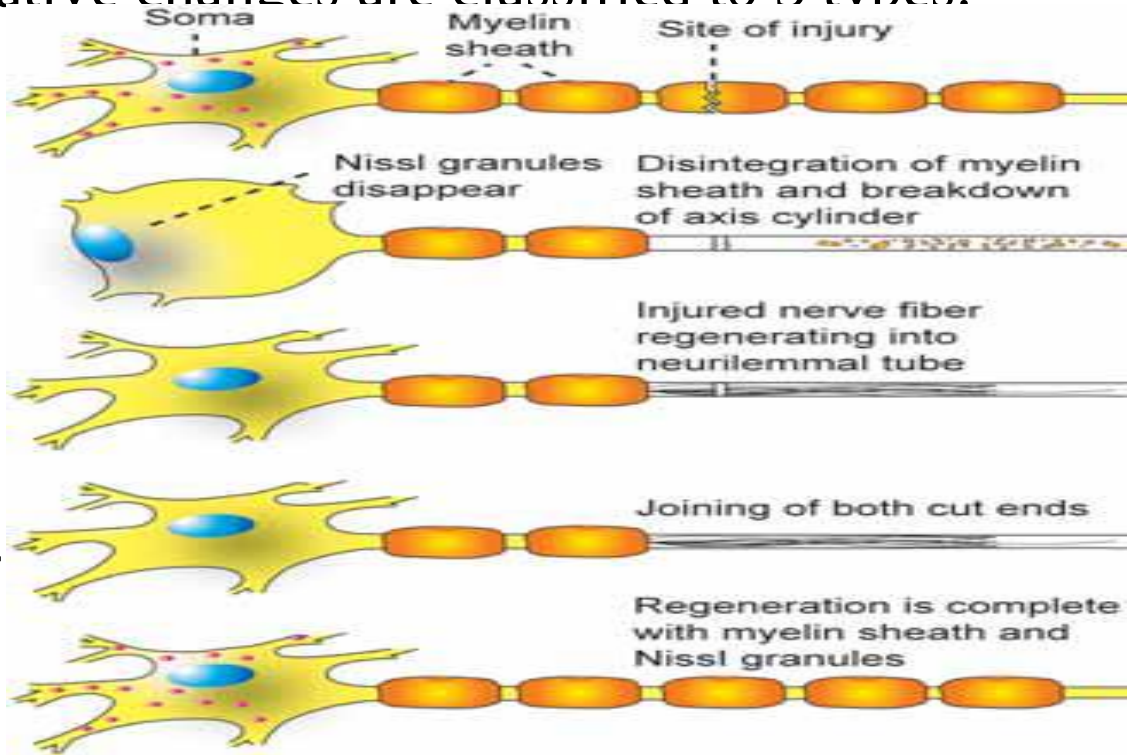
DEGENERATION OF NERVE FIBERS

When a nerve fiber is injured, various changes occur in nerve fiber & nerve cell body-called degenerative changes.-occurs due to obstruction of blood flow, local injection of toxic substances, crushing of nerve fiber or the transection of the fiber.

Degenerative Changes in the Neuron

refers to deterioration or impairment or pathological changes of an injured tissue. When a peripheral nerve fiber is injured, degenerative changes occur in the nerve cell body & nerve fiber same neuron and the adjoining neuron. the degenerative changes are classified to 3 types:

1. Wallarian degeneration
2. Retrograde degeneration
3. Transneural degeneration.



Degeneration & regeneration of nerve fiber

Neuroglia or the glia (glia = glue)

is the supporting cell of nervous system== non-excitable and do not transmit nerve impulse (action potential). So, also called non-neural cells or glial cells.

 CLASSIFICATION OF NEUROGLIAL CELLS

The neuroglial cells are distributed in CNS as well as PNS.

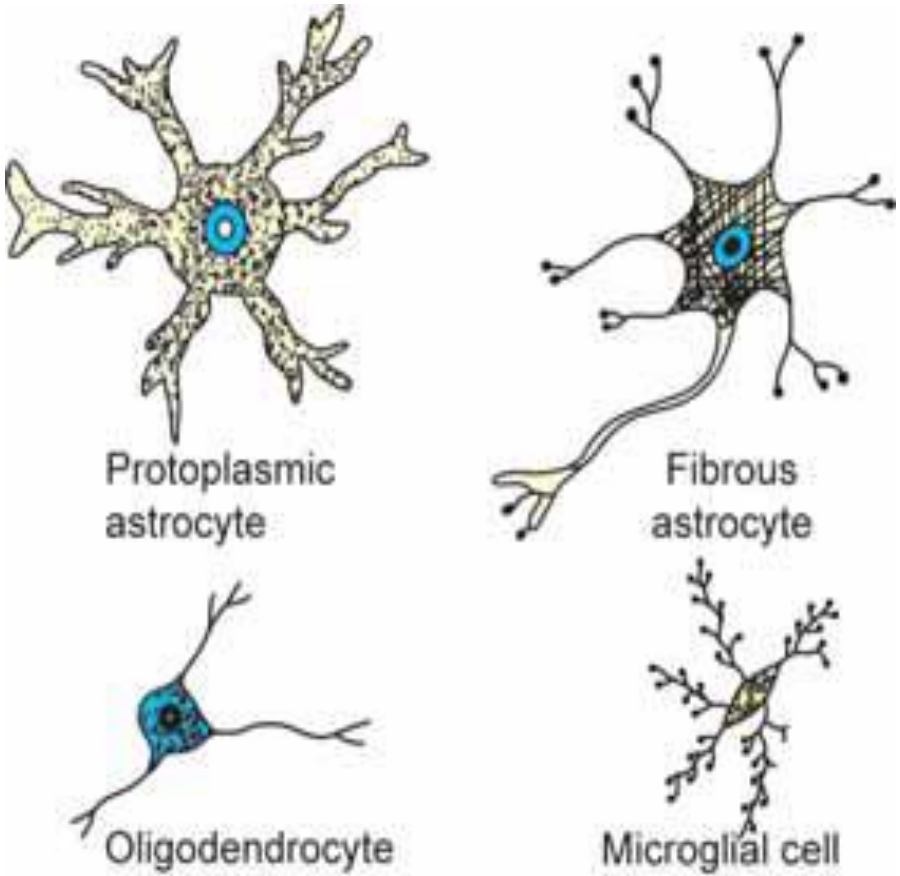
Central Neuroglial Cells

1. Astrocytes
2. Microglia
3. Oligodendrocytes.

Peripheral Neuroglial Cells

neuroglial cells in PNS are two types:

1. Schwann cells
2. Satellite cells



Receptors

are the sensory (afferent) nerve endings that terminate in the periphery as bare unmyelinated nerve endings or in the form of specialized capsulated structures. When stimulated, receptors produce a series of impulses which are transmitted through the afferent nerves.

Actually receptors function like a transducer.

Transducer is a device, which converts one form of energy into another.

So, the receptors are often defined as the biological transducers which convert various forms of energy (stimuli) in the environment into

action potentials in nerve fiber. Generally, the receptors are classified into two types:

I. Exteroceptors

II. Interoceptors.

EXTEROCEPTORS

are the receptors which give response to stimuli arising from outside the body-- are divided into three groups.

1. Cutaneous Receptors

The receptors situated in the skin, also called mechanoreceptors because of their response to mechanical stimuli such as touch, pressure and pain.

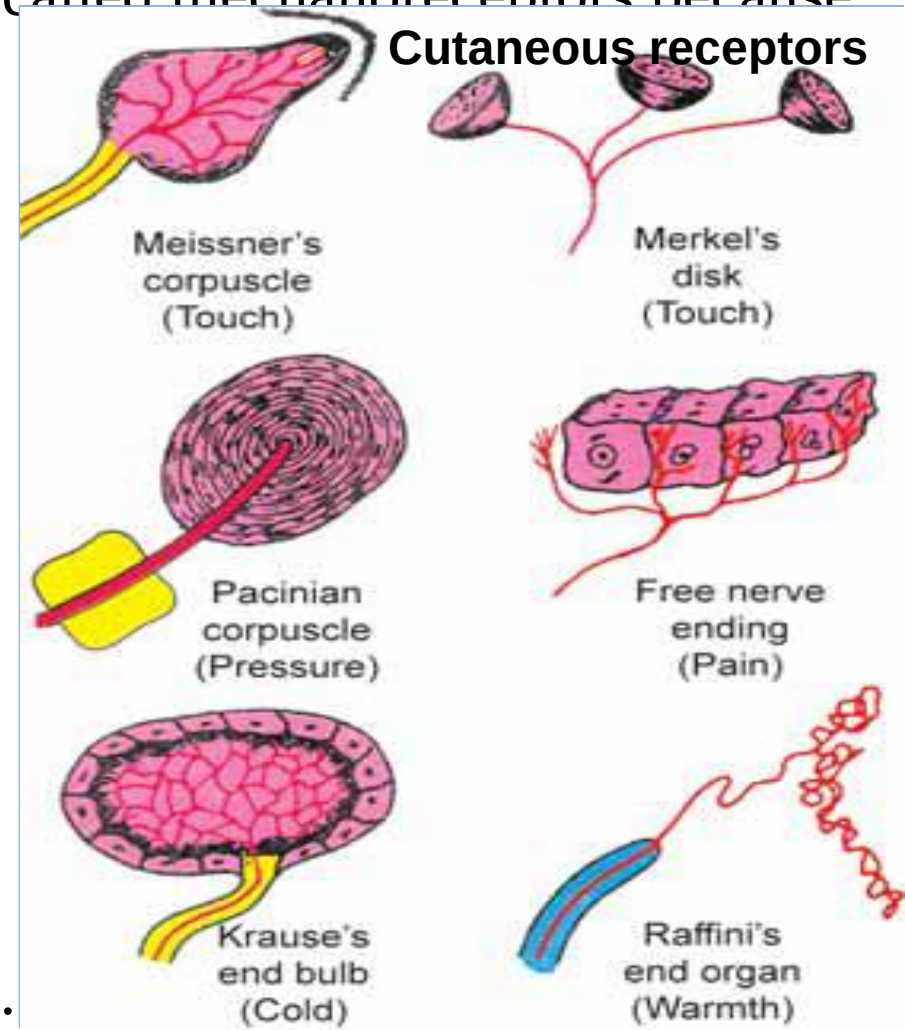
Touch and pressure receptors give response to vibration also.

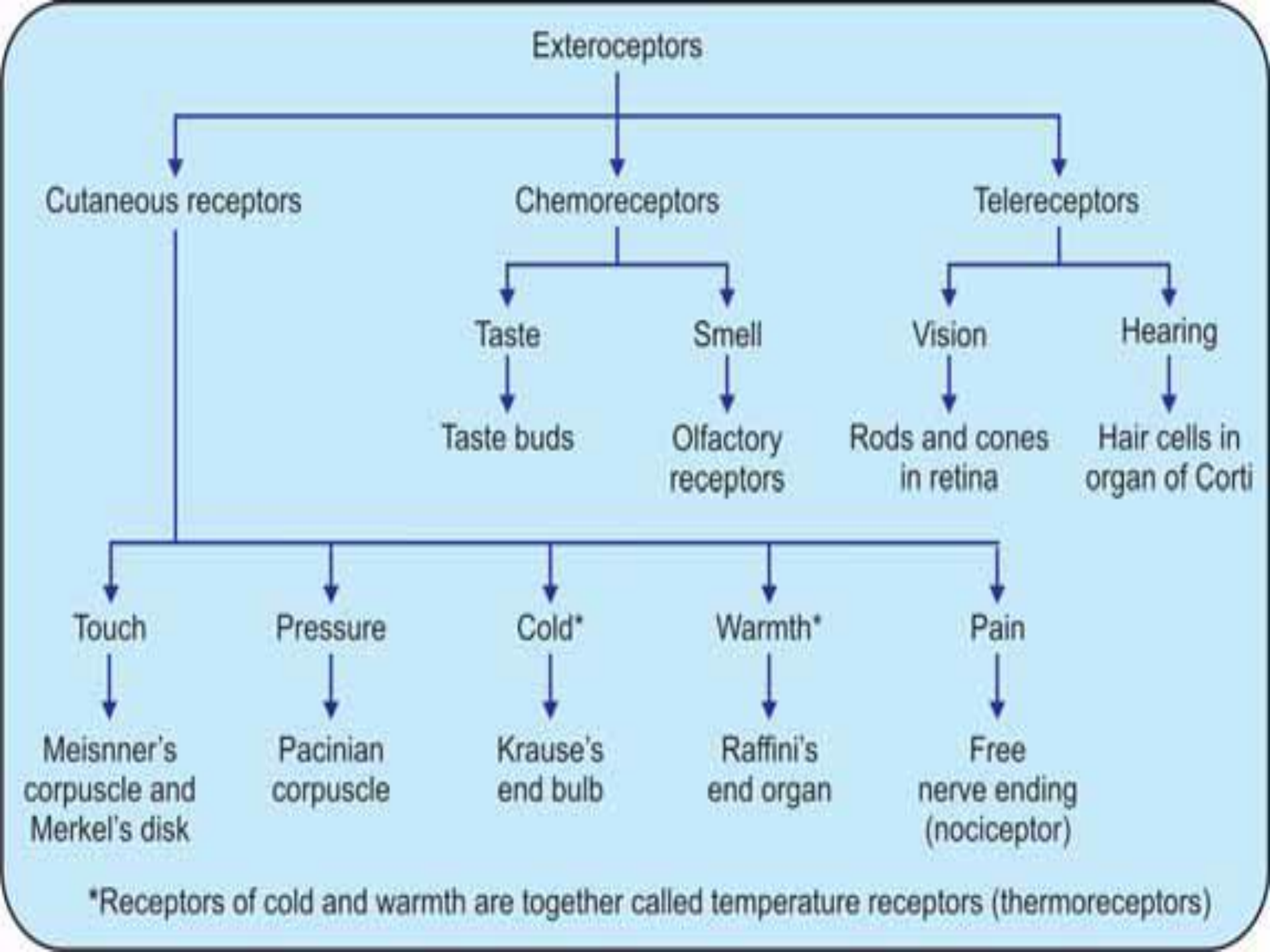
2. Chemoreceptors

The receptors, which give response to chemical stimuli

3. Telereceptors

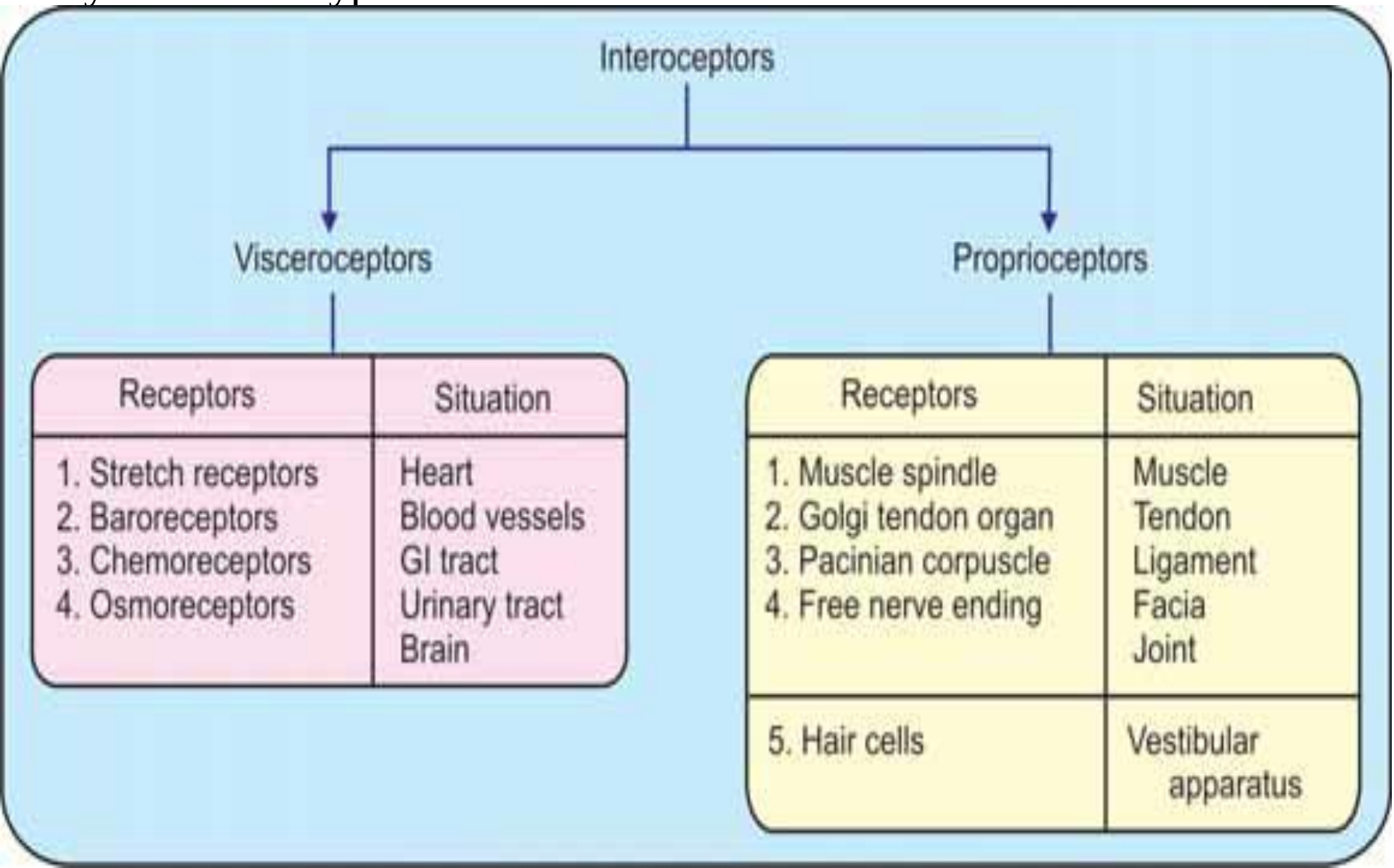
are the receptors that give response to stimuli arising away from the body. also called the distance receptors.




Exteroceptors
Cutaneous receptors
Chemoreceptors
Telereceptors
Taste
Smell
Vision
Hearing
Taste buds
Olfactory receptors
Rods and cones in retina
Hair cells in organ of Corti
Touch
Pressure
Cold*
Warmth*
Pain
Meisnner's corpuscle and Merkel's disk
Pacinian corpuscle
Krause's end bulb
Raffini's end organ
Free nerve ending (nociceptor)
*Receptors of cold and warmth are together called temperature receptors (thermoreceptors)

INTEROCEPTORS

the receptors which give response to stimuli arising from within the body.are of two types:



Body Fluid

Human beings' body composed of fluids and solids. Fluid part is more than two third of the whole body. The maintenance of a relatively constant volume and a stable composition of the body fluids are essential for homeostasis. Water forms most of the fluid part of the body, it is the main constituent of cells, tissues and organs; and is vital for life. Drinking enough water is essential for physiological processes such as circulation, metabolism, temperature regulation, and waste removal.

The total body water in human varies from 45-75% of body weight. This percentage depends on **age, gender, and degree of obesity (percentage of body fat).** In a normal young **adult male, body contains 60- 65%** of water. In a normal young **adult female**, **the water is 50-55%,** the water is less because of more amount of subcutaneous adipose tissue present in female. In thin persons, water content is more than that in obese persons. As a person grows older, the percentage of total fluid gradually decreases, due in part to the fact that aging is usually associated with an increased percentage of the body weight being fat, which decreases the percentage of water in the body. In premature and newborn babies, the total body water ranges from 70- 75% of body weight. Total quantity of body water in an average human being weighing about 70 kg is about 40 L.

Total body fluid has been divided into two compartments:

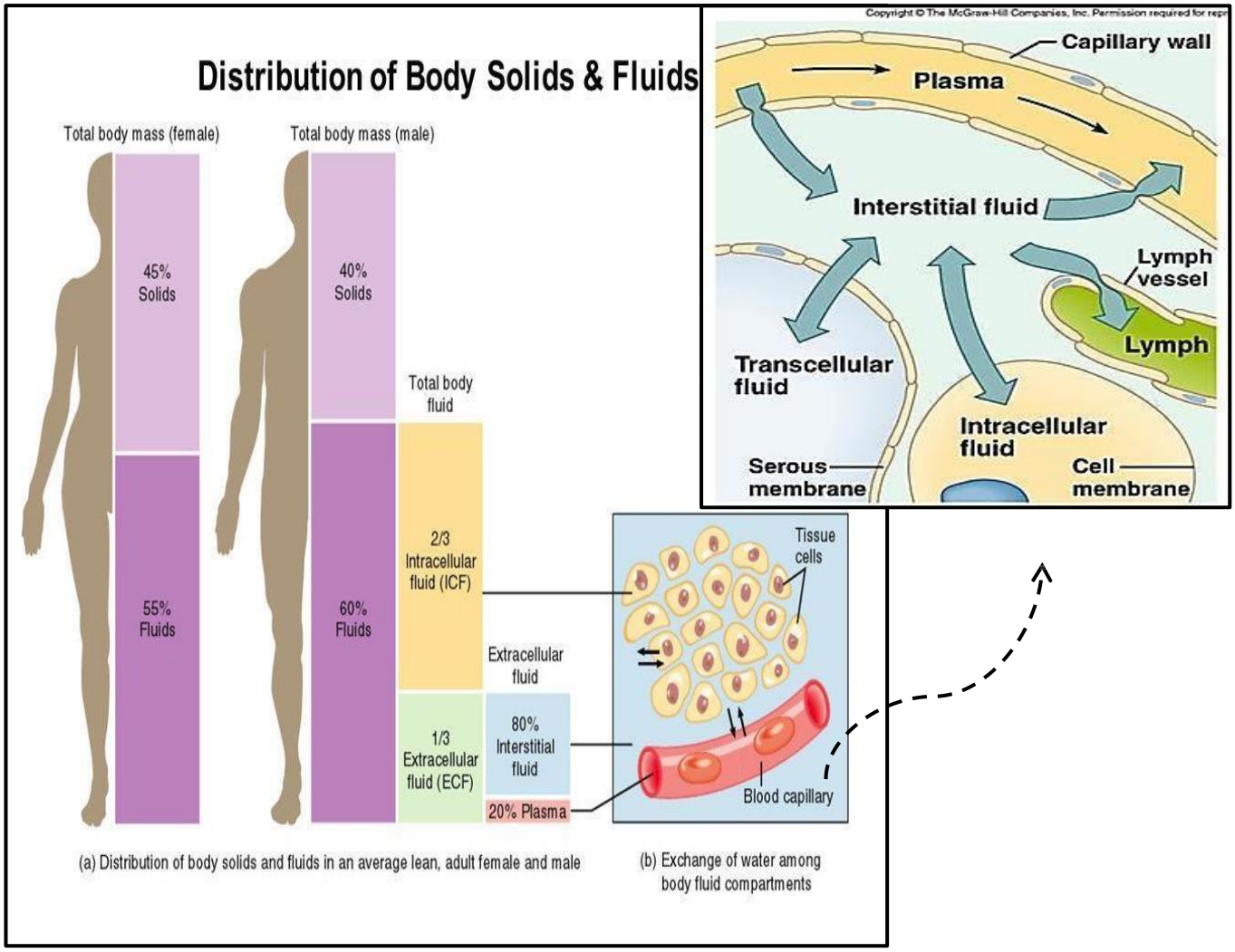
1- Intracellular fluid (ICF)

About 40% of total body weight (28 from 42 liters of total body weight) are inside the cells and are collectively called the intracellular fluid. The fluid of each cell contains its individual mixture of different constituents, but the concentrations of these substances are similar from one cell to another.

2- Extracellular fluid (ECF)

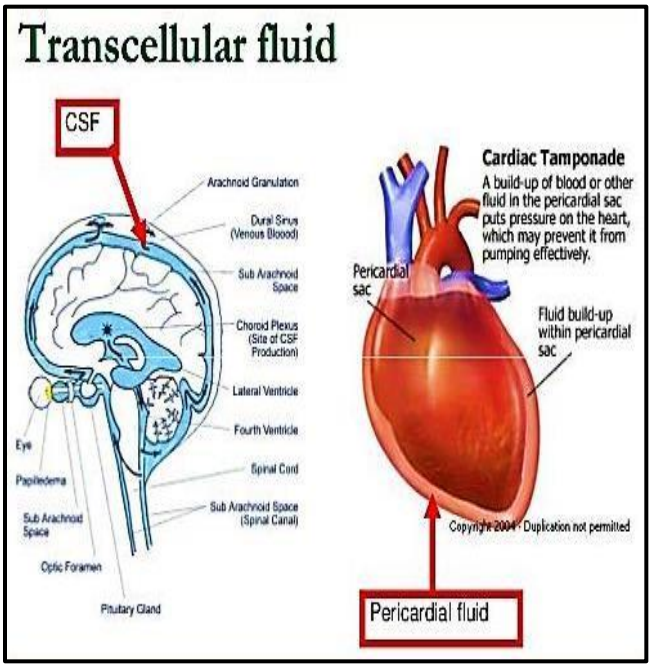
All the fluids outside the cells are collectively called the extracellular fluid. Together these fluids account for about 20% of total body weight, or about 14 liters in a 70-kg man. The two largest compartments of the extracellular fluid are:

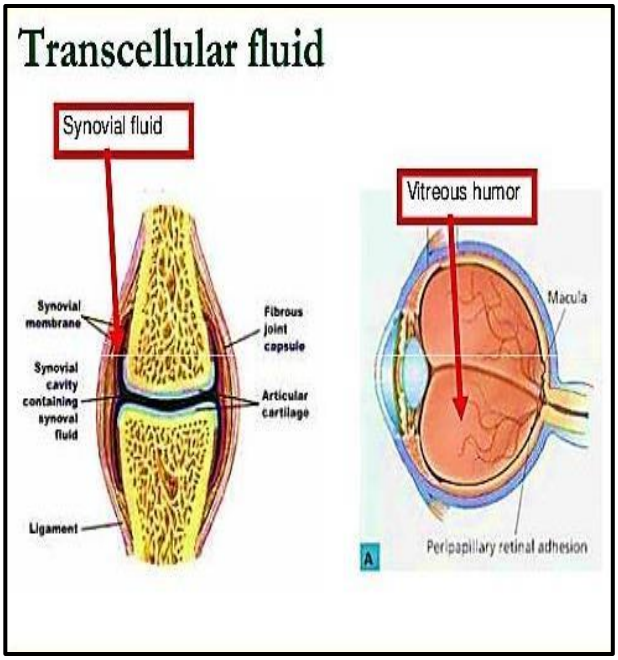
1) ***The interstitial fluid***, which makes up more than three fourths (3/4) or (11 liters) of the extracellular fluid.
2) ***The plasma***, which makes up almost one fourth (1/4) of the extracellular fluid, or about 3 liters. The plasma is the non-cellular part of the blood; it exchanges substances continuously with the interstitial fluid through the pores of the capillary membranes. These pores are highly permeable to almost all solutes in the extracellular fluid except the proteins.



3- **Also,** there is another small compartment of fluid that is referred to as ***transcellular fluid*;** constitute about 1 to 2 liters. This compartment includes fluid in:

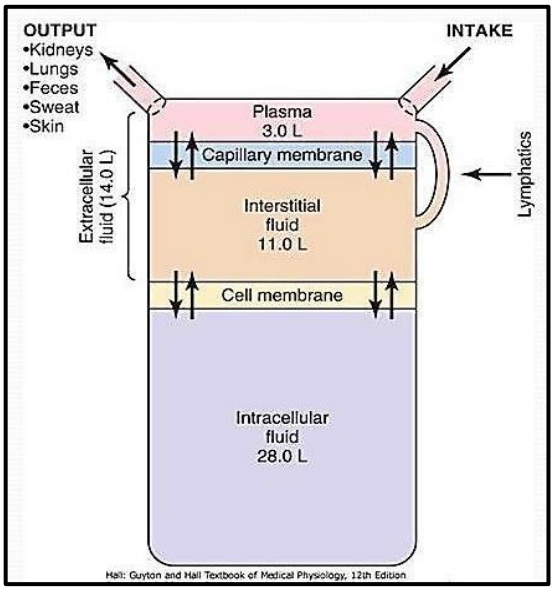
a) The synovial.
b) Peritoneal.
c) Pericardial.
d) Intraocular spaces (Vitreous humor)
e) The cerebrospinal fluid (CSF).





Barriers separate ICF and ECF

a. Cell membrane: Separates intra cellular fluid (ICF) from extra cellular fluid (ECF) including surrounding interstitial fluid.
b. Blood vessel wall: Separate interstitial fluid from plasma



Daily intake of water

Water is added to the body by two major sources:

1. It is ingested in the form of liquids or water in food, which together normally adds about 2100 ml/day to the body fluids.
2. It is synthesize in the body by oxidation of carbohydrates, adding about 200 ml/day.

These mechanisms provide a total water intake of about 2300 ml/day. However, intake of water is highly variable among different people and even within the same person on different days, depending on climate, habits, and level of physical activity.

Daily loss of body water

1- ***Insensible Water Loss*:** Some water losses cannot be specifically regulated. Ex: humans experience a continuous loss of water by evaporation from the respiratory tract and diffusion through the skin, which together account for about 700 ml/day of water loss under normal conditions. Insensible water loss through skin occurs independently of sweating and is present even in people who are born without sweat gland. This loss is minimized by the cornified layer of skin, which provides a barrier against excessive loss by diffusion.

2- ***Water Loss in Sweat*:** The amount of water lost by sweating is highly variable, depending on physical activity and environmental temperature. The volume of sweat normally is about (100 ml/day), but in very hot weather or during heavy exercise fluid loss in sweat occasionally increases to 1-2 L/hour.

3- ***Water Loss in Feces*:** Only a small amount of water (100 ml/day) normally is lost in the feces. This loss can increase to several liters a day in people with severe diarrhea.

4- ***Water Loss by the Kidneys*:** The remaining water loss from the body occurs in the urine excreted by the kidneys. Multiple mechanisms control the rate of urine excretion. In fact, the most important means by which the body maintains a balance between water and electrolytes in the body, intake and output, are by controlling the rates of excretion by the kidneys.

Constituents of extracellular and intracellular fluids

Extracellular fluid constituents

Ionic composition of plasma and interstitial fluid is similar, because highly permeable capillary membranes separate them. The most important difference between these two compartments is the higher concentration of protein in the plasma; because the capillaries have a low permeability to the plasma proteins, only small amounts of proteins are leaked into the interstitial spaces.

The composition of extracellular fluid is carefully regulated by various mechanisms, but especially by the kidneys. This regulation allows the cells to remain continually bathed in a fluid that contains the proper concentration of electrolytes and nutrients for optimal cell function. The extracellular fluid, including the plasma and the interstitial fluid, contains large amounts of sodium (Na^+) and chloride ions (Cl^-), reasonably large amounts of bicarbonate ions ($HCO3^-$), but only small quantities of potassium (K^+), calcium (Ca^{++}), magnesium (Mg^{++}), phosphate, (Po_4^{-3}) and organic acid ions.

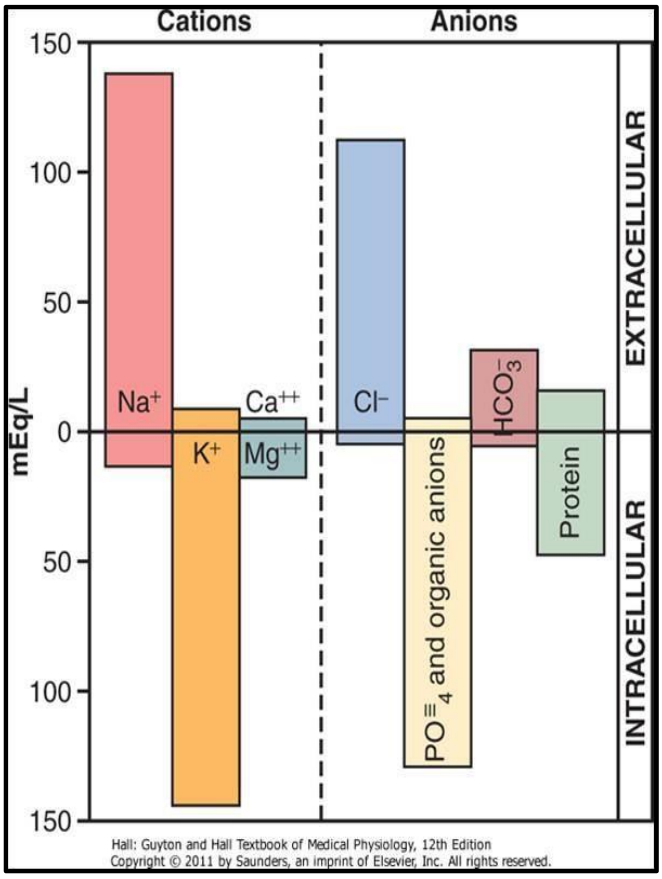
Intracellular fluid constituents

The intracellular fluid is separated from the extracellular fluid by a cell membrane that is highly permeable to water but is not permeable to most of the electrolytes in the body.

In contrast to the extracellular fluid, the intracellular fluid contains only small quantities of Na^+ and Cl^- ions and almost no Ca^{++} ions. Instead, it contains large amounts of K^+ and Po_4^{-3} ions plus moderate quantities of Mg^{++} and So_4^{-2} ions, all of which have low concentrations in the extracellular fluid. Also, ***cells contain large amounts of protein- almost 4 times as much as in the plasma.***

Most body fluids are neutral in charge. Thus, cations, or positively charged ions, and anions, or negatively charged ions, are balanced in fluids. Na^+ and Cl^- ions are concentrated in the ECF of the body, whereas K^+ and Po_4^{-3} ions are concentrated inside cells (ICF).

Intracellular Fluid	**Extracellular Fluid**
Major Cations	**Major Cations**
Potassium (K^+)	Sodium (Na^+)
Magnesium (Mg^{++})	Potassium (K^+)
Sodium (Na^+)	Magnesium (Mg^{++})
	Calcium (Ca^{++})
Major Anions	**Major Anions**
Phosphate (Po_4^{-3})	Chloride (Cl^-)
Chloride (Cl^-)	Bicarbonate (HCO_3^-)
Bicarbonate (HCO_3^-)	Phosphate (Po_4^{-3})
Sulfate (So_4^{-2})	



Differences between ECF and ICF

ECF	ICF
Most abundant cation - Na+	***Most abundant cation - K+***
Muscle contraction Impulse transmission Fluid and electrolyte balance	Resting membrane potential Action potentials Maintains intracellular volume Regulation of pH
Most abundant anion – Cl^-	***Anion are proteins and phosphates (Po_4^{-3})***
Regulates osmotic pressure Forms HCl in gastric acid	

Two major factors contribute to the movement of fluid from one compartment to another: **1- Hydrostatic pressure, and 2- Osmotic pressure**

1-Hydrostatic pressure: The pressure (or force) exerted by a fluid against a wall at equilibrium, at a given point within the fluid, due to the force of gravity causes movement of fluid between compartments. Hydrostatic pressure increases in proportion to depth measured from the surface because of the increasing weight of fluid exerting downward force from above. ***The hydrostatic pressure of blood is the pressure exerted by blood against the walls of the blood vessels by the pumping action of the heart.***

2- Osmotic pressure: It is the minimum pressure, which needs to be applying to a solution to prevent the inward flow of its pure solvent across a semipermeable membrane.

- In blood vessels, fluids leave the plasma at the arteriolar ends of capillaries and enter the interstitial spaces because of the net outward force of hydrostatic pressure (blood pressure). Fluid returns to the plasma from the interstitial spaces at the venular ends of capillaries because of the net inward force of colloid osmotic pressure due to the plasma proteins.

Specialized Fluids of the Body

1- **Lymph**: Clear and colorless fluid 96% water and 4% solids
2- **Milk**: It is secrete by mammary glands; complete natural food. Contain 83-87%.
3- **Cerebrospinal fluid**: Clear, colorless liquid formed within the cavities of brain and around spinal cord
4- **Amniotic fluid**: Liquid produced by membranes and fetus. Its volume increases with gestational age
5- **Aqueous humor**: It is a clear fluid filling the space in the front of the eyeball between the lens and cornea. Blockade in the flow of aqueous humor causes glaucoma due to increased intraocular pressure.
6- **Sweat**: It is secretion of sweat gland, regulates body temperature by cooling and evaporation. Water content of sweat varies from 99.2-99.7%
7- **Tears**: Tears are fluid produced by lachrymal glands. It is isotonic but becomes hypertonic due to evaporation as fluid passes over the cornea.

Edema

Different pathological conditions induces abnormalities in fluid balance, which are either an overload of fluid called *Edema* or a decrease in effective fluid referred to as *Dehydration*.

Edema refers to the disturbance of water balance in which there is an excess fluid in the body tissues. In most instances, edema occurs mainly in the extracellular fluid compartment, but it can involve intracellular fluid as well.

Types of Edema

1- Intracellular Edema

Three conditions are especially prone to cause intracellular swelling:

(1) Hyponatremia.

(2) Lack of adequate nutrition to the cells.

(3) Depression of the metabolic systems of the tissues.

When blood flow to a tissue is decreased, the delivery of oxygen and nutrients is reduced. If the blood flow becomes too low to maintain normal tissue metabolism, the cell membrane ionic pumps become depressed.

When the pumps become depressed, Na^+ that normally leak into the interior of the cell can no longer be pumped out of the cells and the excess intracellular Na^+ cause osmosis of water into the cells. Sometimes this process can increase intracellular volume of a tissue area to 2 to 3 times than normal. When such an increase in intracellular volume occurs, it is usually introduction to death of the tissue.

Note: Intracellular edema can also occur in inflamed tissues. Inflammation usually increases cell membrane permeability, allowing Na^+ and other ions to diffuse into the interior of the cell, with subsequent osmosis of water into the cells.

2- Extracellular Edema

Extracellular fluid edema occurs when excess fluid accumulates in the extracellular spaces. ***There are two general causes of extracellular edema:***

(1) Abnormal leakage of fluid from the plasma to the interstitial spaces across the capillaries, causing interstitial fluid accumulation because of excessive capillary fluid filtration.

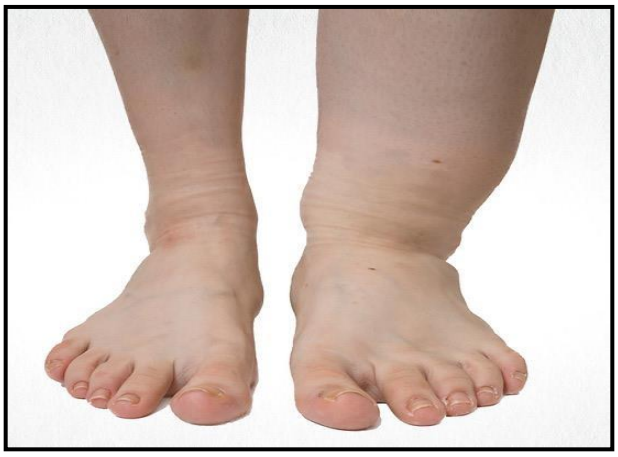
(2) Failure of the lymph vessels to return fluid and protein from the interstitium back into the circulation, often called **lymphedema**. Edema can become especially severe because plasma proteins that leak into the interstitium have no other way to be removed. The rise in protein concentration raises the colloid osmotic pressure of the interstitial fluid, which draws even more fluid out of the capillaries.

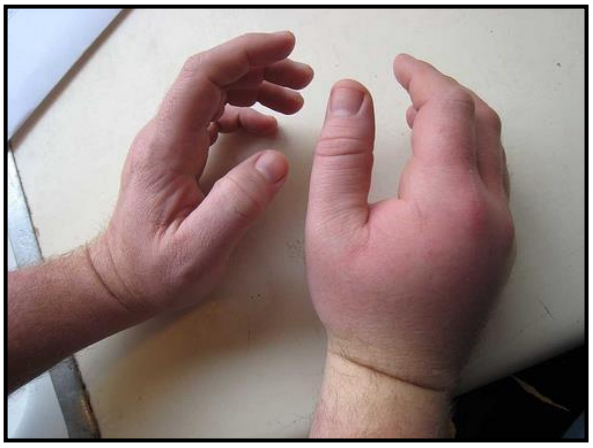
Types of extracellular edema

1- ***Peripheral edema***: This usually affects the legs, feet, and ankles, but it can also happen in the arms. It could be a sign of problems with circulatory system, lymph nodes, or kidneys. Edema demonstrates in the soft tissues as swelling of the limbs and face with a subsequent increase in size and tightness of the skin.

2- ***Pedal edema***: This happens when fluid gathers in the feet and lower legs. It's more common in older persons or pregnant.

3- ***Lymphedema***: This swelling in the arms and legs is most often caused by damage lymph nodes or tissues that help filter germs and waste from the body. The damage may be the result of cancer treatments like surgery and radiation. The cancer itself can also block lymph nodes and lead to fluid buildup. Blockage of lymph flow can be especially severe with infections of the lymph nodes, such as infection by filaria nematodes (*Wuchereria bancrofti*), which live in the lymph system.

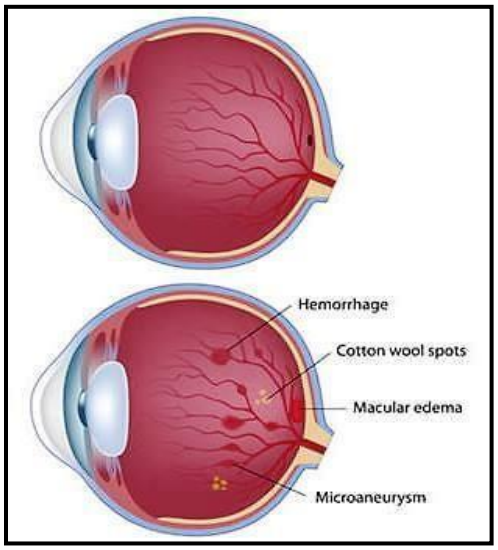




4- ***Pulmonary edema***: When fluid collects in the air sacs in the lungs. That makes it hard to breathe, and it's worse when the patient lie down. Which may leads to a fast heartbeat, feel suffocated, and cough up foamy spittle, sometimes with blood. This may occur, where excess fluid swells into interstitial tissues of the lung, which is associated with cardiac failure and renal failure.

5- ***Cerebral edema***: This is a very serious condition in which fluid builds up in the brain. It can happen in case of hit the head hard, if a blood vessel gets blocked or bursts, or there is a tumor or allergic reaction.

6- Macular edema: This happens when fluid builds up in a part of the eye called macula, which is in the center of the retina, the light-sensitive tissue at the back of the eye. It happens when damaged blood vessels in the retina leak fluid into the area.



Causes of extracellular edema

A large number of conditions can cause fluid accumulation in the interstitial spaces by abnormal leaking of fluid from the capillaries or by preventing the lymphatics from returning fluid from the interstitium back to the circulation. The following is a partial list of conditions that can cause extracellular edema by these two types of abnormalities:

1) ***Increase in capillary hydrostatic pressure (at arterial or venous side).***
   A. In acute or chronic kidney failure.
   B. In heart failure.
   C. In excessive body heat and vasodilator drugs.

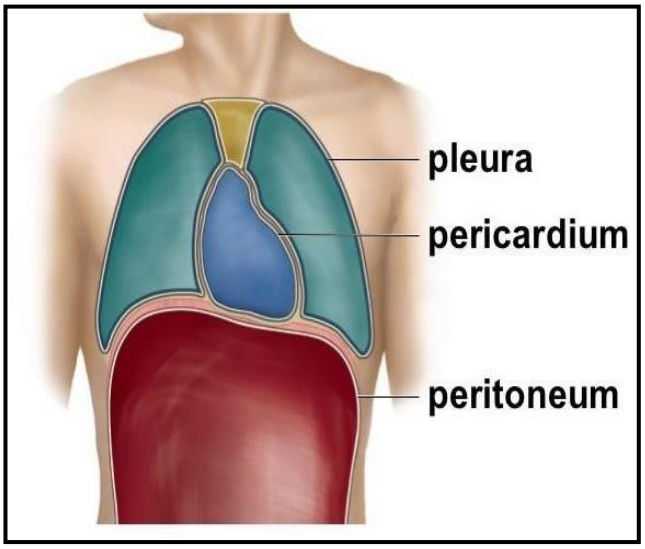
2) ***Increased capillary permeability***
   A. Immune reactions that cause release of histamine and other immune products.
   B. Toxins
   C. Bacterial infections
   D. Vitamin deficiency, especially vitamin C
   E. Prolonged ischemia
   F. Burns

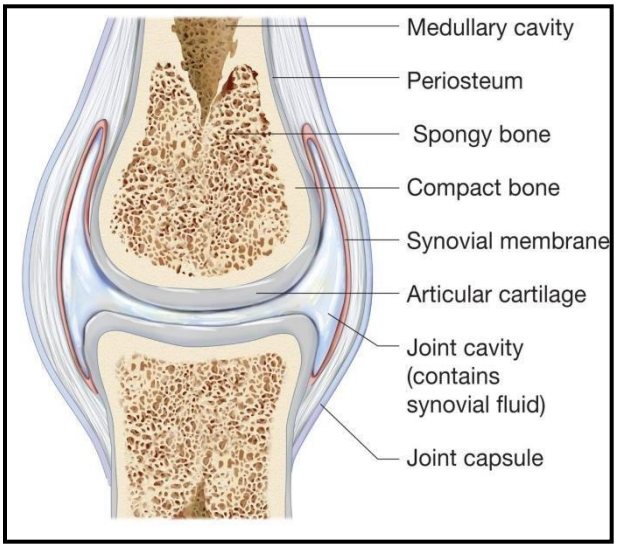
3) ***Decreased plasma proteins***
   A. Loss of proteins in urine (nephrotic syndrome).
   B. Loss of protein from denuded skin areas in burns and wounds.
   C. Failure to produce proteins; like in liver disease.

4) ***Blockage of lymph return***
   A. Cancer
   B. Infections (e.g., filaria nematodes)
   C. Surgery
   D. Congenital absence or abnormality of lymphatic vessels.

Fluid in the "Potential Spaces" of the body

Some examples of "potential spaces" are the thoracic cavity [include pleural cavity and pericardial cavity], peritoneal cavity, and synovial cavities. Virtually all these potential spaces have surfaces that almost touch each other, with only a thin layer of fluid in between.





The abdominal cavity is especially prone to collect body fluid; the other potential spaces, such as the pleural cavity, pericardial cavity, and joint spaces, can become seriously swollen when generalized edema is present. Injury or local infection in any one of the cavities often blocks the lymph drainage, causing isolated swelling in the cavity.

Measurement of body fluid volume

Volume of different compartments of the body fluid is measured by ***indicator dilution method*** or by ***dye dilution method***. The volume of a fluid compartment in the body can be measured by placing an indicator substance in the compartment, allowing it to disperse evenly throughout the compartment's fluid, and then analyzing the extent to which the substance becomes diluted.

- **Measurement of Extracellular Fluid Volume:** The volume of extracellular fluid can be estimated using any of several substances that disperse in the plasma and interstitial fluid but do not readily permeate the cell membrane. They include radioactive sodium, radioactive chloride, radioactive iothalamate, thiosulfate ion, and inulin. When any one of these substances is injected into the blood, it usually disperses almost completely throughout the extracellular fluid within 30 to 60 minutes.

- **Measurement of Total Body Water:** Radioactive water (tritium, $3H_2O$) or heavy water (deuterium, $2H_2O$) can be used to measure total body water. These forms of water mix with the total body water within a few hours after being injected into the blood, and the dilution principle can be used to calculate total body water

  Calculation of Intracellular Volume: The intracellular volume cannot be measured directly. However, it can be calculated as

  Intracellular volume = Total body water - Extracellular volume

- **Measurement of Plasma Volume:** To measure plasma volume, a substance must be used that does not readily penetrate capillary membranes but remains in the vascular system after injection.

  Calculation of Interstitial Fluid Volume: Interstitial fluid volume cannot be measured directly, but it can be calculated as

  Interstitial fluid volume = Extracellular fluid volume - Plasma volume

Dehydration

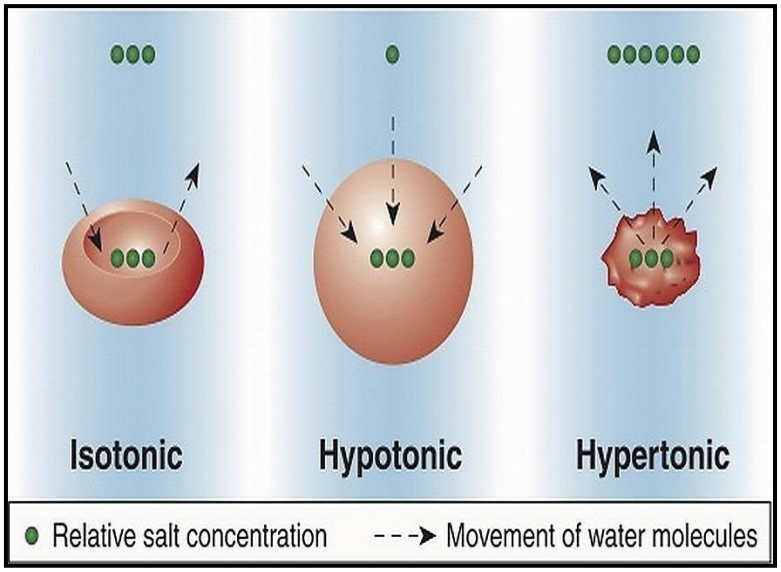
Dehydration is significant decrease in total body water content due to pathologic fluid losses, reduced fluid intake, or a combination of both so that the body begins to lose its ability to function normally. It is a condition that can occur when the loss of body fluids, mostly water, is more than the amount that is taken in. More water is moving out of cells and then out of the body than the amount of water that is taken in.

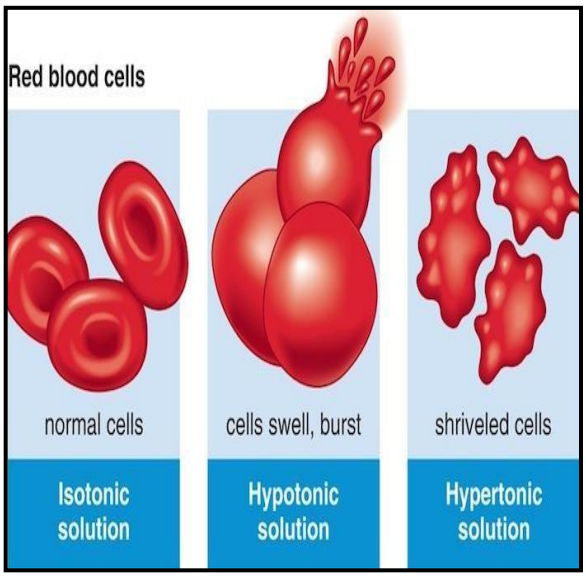
Depletion or reduction of intravascular fluid can take three forms depending on the proportion of water and sodium lost:

1- ***Hypertonic dehydration*** is depletion in total body water due to pathologic fluid losses, reduced water intake, or a combination of both. This leads to ***hypernatremia*** in the extracellular fluid compartment, which then draws water from the intracellular fluids. Since the water loss is shared by all body fluid compartments and leads to relatively little reduction in extracellular fluids, the individual's circulation is not compromised unless the loss is very great. This is also known as ***intracellular or hypernatremic dehydration***.

2- ***Hypotonic dehydration*** of extracellular, which is a fluid depletion where more sodium than water is lost (***hyponatremia)***, and extracellular fluid become depleted.

3- Isotonic or (isonatremic) dehydration, which is a balanced depletion of both water and sodium, also leads to a loss of extracellular fluid. This is also known as ***isotonic fluid volume depletion.***





Classification of Dehydration

Basically dehydration is of three types:

1. Mild dehydration when fluid loss is about 5% of total body fluids.
2. Moderate dehydration when fluid loss is about 10%.
3. Severe dehydration when fluid loss is about 15%.

Causes of Dehydration

1- ***Severe Diarrhea*** - the most common cause of dehydration and related deaths. The large intestine absorbs water from food matter, and diarrhea prevents this from happening. The body excretes too much water, leading to dehydration.

2- ***Vomiting*** - leads to a loss of fluids and makes it difficult to replace water by drinking it.

3- ***Excess Sweating*** - the body's cooling mechanism releases a significant amount of water. Hot and humid weather and vital physical activity can further increase fluid loss from sweating. Similarly, a fever can cause an increase in sweating and may dehydrate the patient, especially if there is also diarrhea and vomiting.

4- ***Diabetes*** - high blood sugar levels cause increased urination and fluid loss.

5- ***Frequent urination*** - usually caused by uncontrolled diabetes, but also can be due to alcohol and medications.

6- ***Burns*** - blood vessels can become damaged, causing fluid to leak into the surrounding tissues.

Signs and Symptoms of Dehydrations:

Mild to moderate dehydration

1. Excess thirst is the first sign of dehydration.
2. Dryness of the mouth, headaches, tiredness and a lack of energy.
3. Decrease in sweating.
4. Decrease in urine formation, which is darker yellow in color than usual.
5. Pale and dry skin.
6. Decreased tears
7. Loose of 3-5 % of body weight in mild dehydration and 5-9% of body weight in moderate dehydration.

Severe dehydration

Beside the previous signs become more intensity and getting worse:

1. Decrease in blood volume and cardiac output.
2. Cardiac shock.
3. Deep breath with rapid breath and pulse.
4. Minimum urination
5. Become confused or disorientated; also feel irritable.
6. Loose of 10% of body weight.

Very severe dehydration

1. Damage of organs like brain, liver and kidneys
2. Mental depression and confusion
3. Renal failure
4. Coma.

Respiratory pressures

Two types of pressures are exerted in the thoracic cavity and the lungs during the process of respiration:

1. Intrapleural pressure or intrathoracic pressure.
2. Intra-alveolar pressure or intrapulmonary pressure.

Intrapleural pressure

It is the pressure existing in pleural cavity, that is, in between the visceral and parietal layers of pleura. It is exerted by the suction of the fluid that lines the pleural cavity. It is also called intrathoracic pressure since it is exerted in the whole of thoracic cavity. Intrapleural pressure is always negative.

***Importance of Intrapleural Pressure*:**

1) Throughout the respiratory cycle intrapleural pressure remains lower than intra-alveolar pressure; this keeps the lungs always inflated.
2) It prevents the collapsing tendency of lungs.
3) It causes dilatation of vena cava and larger veins in thorax.

Intra-alveolar pressure

It is the pressure existing in the alveoli of the lungs. Normally, intra-alveolar pressure becomes negative during inspiration and positive during expiration.

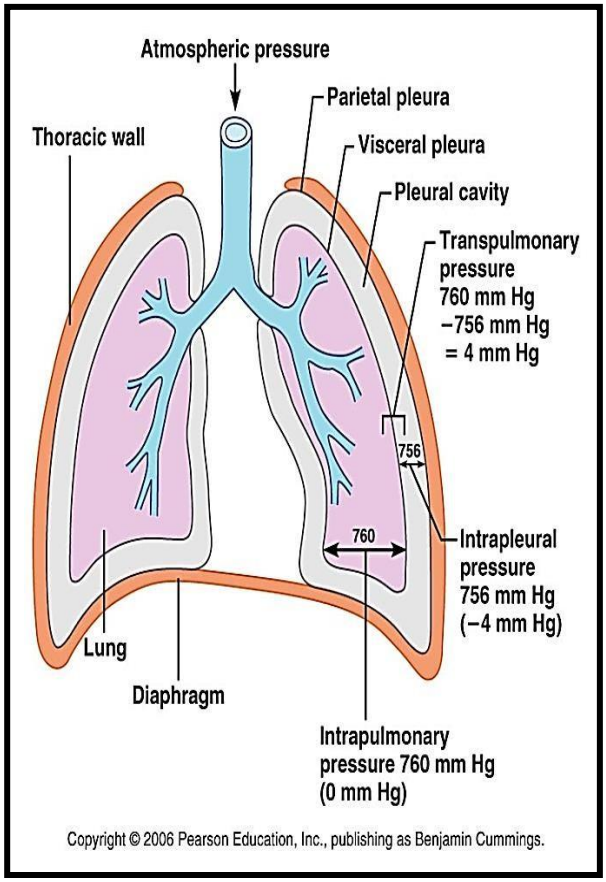
Importance of Intra-alveolar Pressure

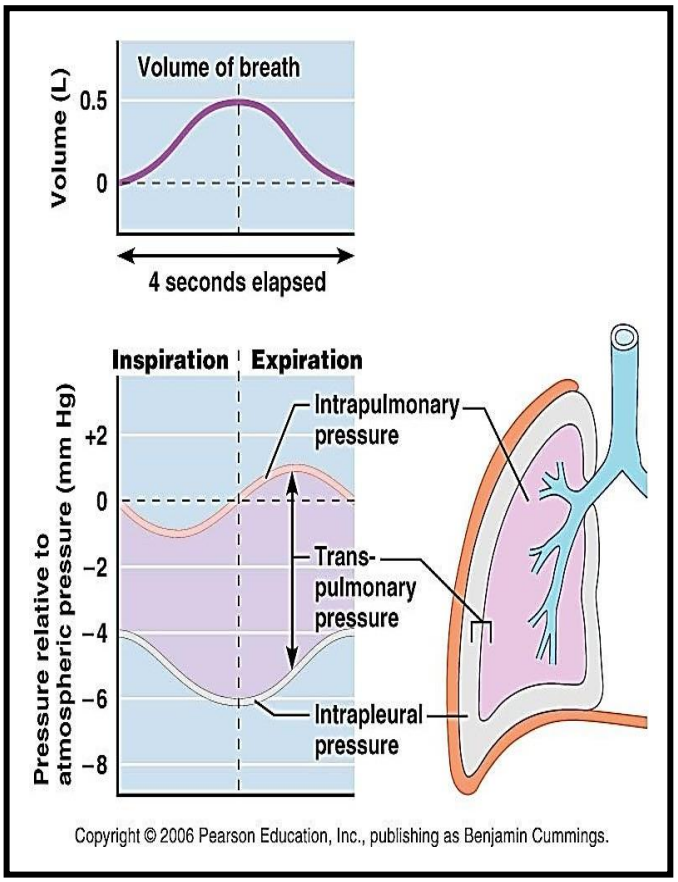
1) It causes flow of air in and out of alveoli. During inspiration, the intra-alveolar pressure becomes negative, so the atmospheric air enters the alveoli. And, during expiration, the air is expelled out of alveoli
2) It also helps in the exchange of gases between the alveolar air and the blood.

1- Transpulmonary Pressure

It is the difference between intra-alveolar pressure and intrapleural pressure.

Changes in respiratory pressures during inspiration and expiration '0' indicate the normal atmospheric pressure (760 mm Hg).





Factors causing collapsing tendency of lungs

Two factors are responsible for the collapsing tendency of lungs

1. Elastic property of lung tissues which show constant recoiling tendency and try to collapse the lungs.
2. Surface tension exerted on the surface of the alveolar membrane by the fluid secreted from alveolar epithelium.

Fortunately, there are some factors which save the lungs from collapsing.

Factors preventing collapsing tendency of lungs

Two factors preventing collapsing tendency of lungs. In spite of the elastic property of the lungs and the surface tension in the alveoli of lungs, the collapsing tendency of lungs is prevented by two factors:

1. Intrapleural pressure which is always negative. Because of negativity, it keeps the lungs expanded and prevents the collapsing tendency of lungs produced by the elastic tissues.
2. Surfactant secreted in alveolar epithelium. It is surface acting materials that decrease surface tension on the alveolar membrane and prevents the collapsing tendency produced by surface tension.

Compliance

Compliance is the ability of the lungs and thorax to expand. It is defined as the change in volume per unit change in the respiratory pressure. Determination of compliance is useful as it is the measure of stiffness of lungs. Stiffer the lungs, less is the compliance.

If lungs are removed from thorax, the expansibility (compliance) of lungs alone is doubled. It is because of the absence of the inactivity and the restriction exerted by the structures of thoracic cage, which interfere with expansion of lungs.

Variation in Compliance

Compliance decreases in pathological conditions such as:

1. Deformities of thorax.
2. Paralysis of respiratory muscles.
3. Pleural effusion.
4. Fibrosis
5. Abnormal thorax.

Compliance increases in physiological and pathological conditions.

1. In old age, lung compliance increases due to loss of elastic property of lung tissues.
2. In emphysema, lung compliance increases because of damage of alveolar membrane.

The work of breathing

It is the work done by the respiratory muscles during breathing to overcome the resistance in the thorax and respiratory tract.

During the respiratory processes, inspiration is active process and the expiration is a passive process. So, during quiet breathing, the respiratory muscles perform the work only during inspiration and not during expiration.

During normal quiet breathing, all respiratory muscle contraction occurs during inspiration; expiration is almost entirely a passive process caused by elastic recoil of the lungs and chest cage. Thus, under resting conditions, the respiratory muscles normally perform "work" to cause inspiration but not to cause expiration.

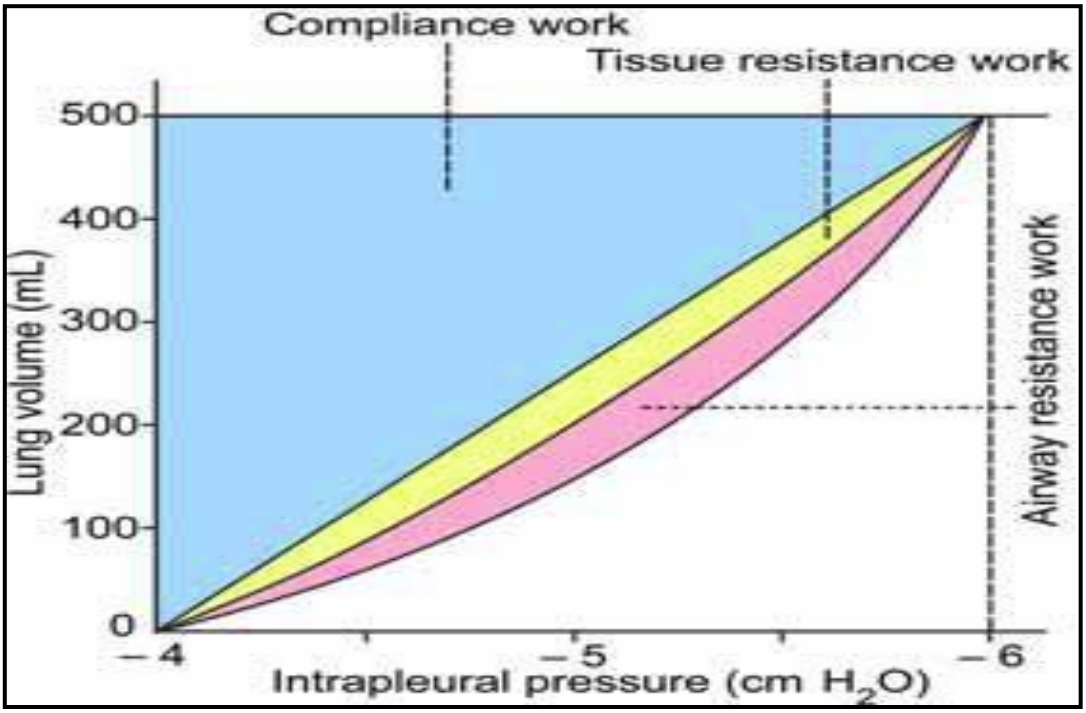
The resistance and work of breathing

The energy obtained during the work of breathing is utilized to overcome three types of resistance:

1. **Airway resistance (airway resistance work)**
   Airway resistance is the resistance offered to the passage of air through respiratory tract. Resistance increases during bronchiolar constriction, which increases the work done by the muscles during breathing. Work done to overcome the airway resistance is called airway resistance work.
2. **Elastic resistance of lungs and thorax (compliance work).**
   Energy is required to expand lungs and thorax against the elastic force. Work done to overcome this elastic resistance is called compliance work.

3. Non-elastic viscous resistance (tissue resistance work).

Energy is also required to overcome the viscosity of lung tissues and tissues of thoracic cage. Work done to overcome this viscous resistance is called tissue resistance work.



Work of breathing

Dead space

Dead space is defined as the part of the respiratory tract, where gaseous exchange does not take place. The air present in the dead space is called dead space air.

Dead space is of two types:

I. Anatomical dead space.

II. Physiological dead space.

Physiological Dead Space

Physiological dead space includes anatomical dead space plus two additional volumes:

1. The air in the alveoli, which are nonfunctioning. In some of the respiratory diseases, alveoli do not function because of dysfunction or destruction of alveolar membrane
2. The air in the alveoli, which do not receive adequate blood flow. Gaseous exchange does not take place during inadequate blood supply.

Normal value and measurement of dead space

Under normal conditions, the physiological dead space is equal to anatomical dead space. It is because, all the alveoli are functioning and all alveoli receive adequate blood flow in normal conditions. *The volume of normal dead space is 150 ml.*

In respiratory disorders, which affect the pulmonary blood flow or the alveoli, the dead space increases. It is associated with reduction in alveolar ventilation. *The dead space is measured by single breath nitrogen washout method.*

Respiratory Protective Reflexes

Respiratory protective reflexes are the reflexes that protect the lungs and air passage from foreign particles. The respiratory protective reflexes are:

1- Cough Reflex

Cough is a modified respiratory process characterized by forced expiration. It is the protective reflex that occurs because of irritation of respiratory tract and some other areas such as external auditory canal. Cough begins with deep inspiration followed by forced expiration with closed glottis. This increases the intrapleural pressure above 100 mm Hg. Then, glottis opens suddenly with explosive outflow of air.

2- Sneezing Reflex

Sneezing is also a modified respiratory process characterized by forced expiration. It is the protective reflex caused by irritation of nasal mucous membrane. This irritation occurs because of dust particles, debris, mechanical obstruction of the airway, and excess fluid accumulation in the nasal passages. Sneezing starts with deep inspiration, followed by forceful expiratory effort with opened glottis resulting in exclusion of irritant agents out of respiratory tract.

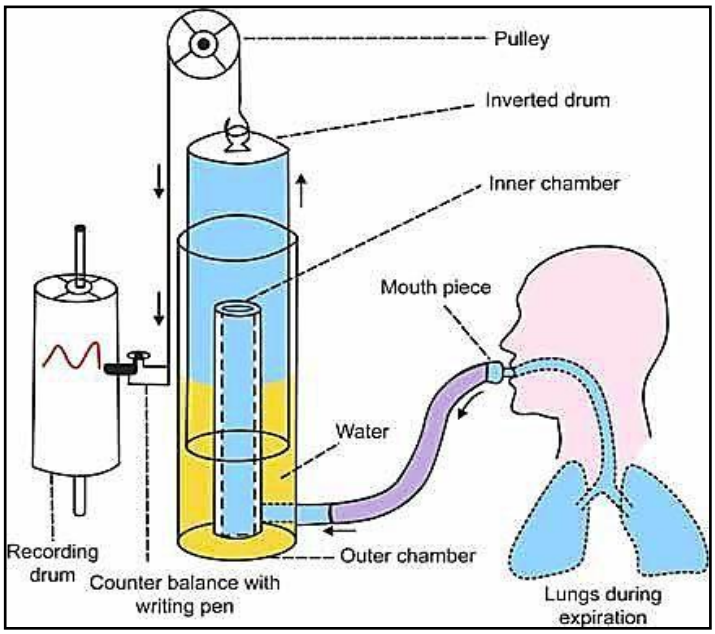
3- Swallowing Reflex (Deglutition)

Swallowing is a respiratory protective reflex that prevents entrance of food particles into the air passage during swallowing. While swallowing of the food, the respiration is arrested for a while. The temporary arrest of respiration is called apnea. The arrest of breathing during swallowing is called swallowing apnea or deglutition apnea.

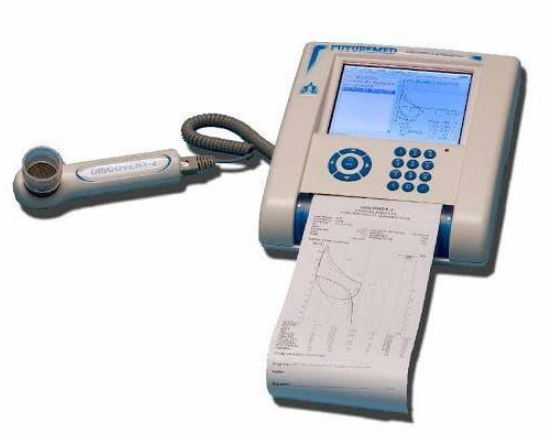
Lung volumes and capacities

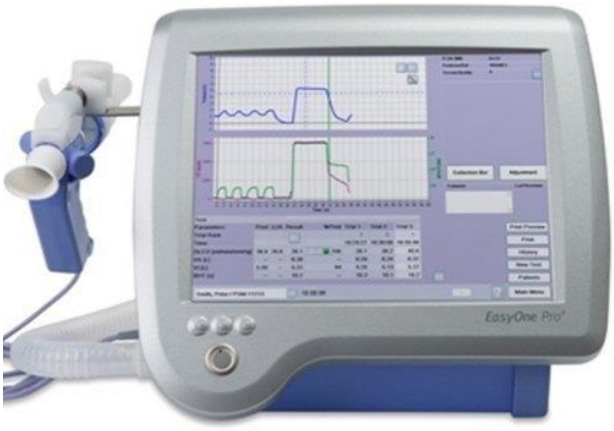
Pulmonary function tests

Pulmonary or lung function tests are useful in assessing the functional status of the respiratory system. These tests involve measurement of lung volumes and capacities. Pulmonary ventilation can be studied by recording the volume movement of air into and out of the lungs, a method called ***spirometry***. Pulmonary function tests are carried out mostly by using spirometer. The graphical recording of lung volumes and capacities is called ***spirogram***.



Spirometer: During expiration, the air enters the spirometer from lungs. The inverted drum moves up and the pen draws a downward curve on the recording drum.





The air in lung is classified into two divisions:

1. Lung volumes. 2. Lung capacities.

Lung volume

Lung volumes are the static volumes of air breathed by an individual. The lung volumes are of four types:

1. **Tidal volume (TV)**

   Tidal volume is the volume of air breathed in and out of lungs in a single normal quiet respiration. Tidal volume signifies the normal depth of breathing.

   Normal value = 500 mL (0.5 L).

2. **Inspiratory reserve volume (IRV)**

   Inspiratory reserve volume is an additional volume of air that can be inspired forcefully after the end of normal inspiration.

   Normal value = 3300 mL (3.3 L).

3. **Expiratory reserve volume (ERV)**

   Expiratory reserve volume is the additional volume of air that can be expired out forcefully, after normal expiration.

   Normal value = 1000 mL (1 L).

4. **Residual volume (RV)**

   Residual volume is the volume of air remaining in the lungs even after forced expiration. Normally, lungs cannot be emptied completely even by forceful expiration. Some quantity of air always remains in the lungs even after the forced expiration. Normal value = 1200 mL (1.2 L).

Lung capacity

Lung capacities are the combination of two or more lung volumes. Lung capacities are of four types:

1. Inspiratory capacity (IC)

Inspiratory capacity is the maximum volume of air that is inspired after normal expiration. It includes tidal volume and inspiratory reserve volume.

IC = TV + IRV = 500 + 3300 = 3800 mL.

2. Vital capacity (VC)

It is the maximum volume of air that can be expelled out forcefully after a deep (maximal) inspiration. Vital capacity includes tidal volume, inspiratory reserve volume and expiratory reserve volume.

VC = TV + IRV + ERV = 500 + 3300 + 1000 = 4800 mL.

3. Functional residual capacity (FRC)

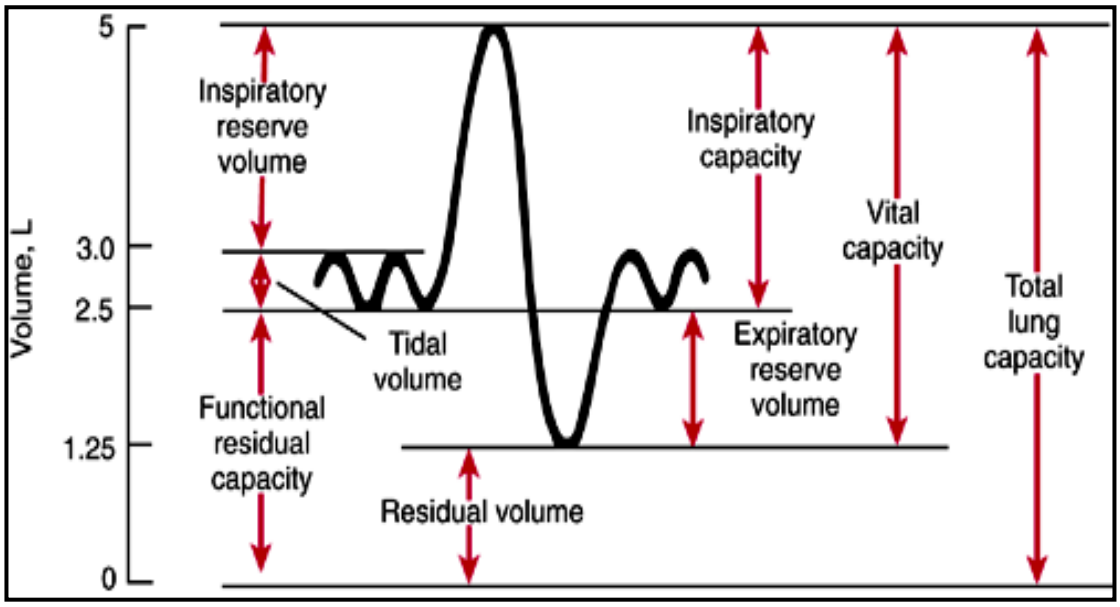
It is the volume of air remaining in the lungs after normal expiration (after normal tidal expiration). Functional residual capacity includes expiratory reserve volume and residual volume.

FRC = ERV + RV = 1000 + 1200 = 2200 mL.

4. Total lung capacity (TLC)

Total lung capacity is the volume of air present in the lungs after a deep (maximal) inspiration. It includes all the volumes.

TLC = IRV + TV + ERV + RV = 3300 + 500 + 1000 + 1200 = 6000 mL.



Respiratory volume and capacity

Ventilation

Pulmonary ventilation

It is the volume of air moving in and out of lungs per minute in quiet breathing. It is also called *respiratory minute volume (RMV).*

Normal value and calculation

Normal value of pulmonary ventilation is 6 L/minute. It is the product of tidal volume (TV) and the rate of respiration (RR). It is calculated by the formula:

Pulmonary ventilation = Tidal volume × Respiratory rate

= 500 mL × 12/minute

= 6,000 mL = 6 L/minute.

Factors affecting pulmonary ventilation:

1. Surface tension of alveolar fluid (Surfactant)
2. Lung compliance:
    a. Elasticity.
    b. Surface tension
3. Airway resistance.

Alveolar ventilation

Alveolar ventilation is the amount of air utilized for gaseous exchange every minute. Alveolar ventilation is different from pulmonary ventilation. In pulmonary ventilation, six (6) L of air moves in and out of lungs in every minute. But the whole volume of air is not utilized for exchange of gases. *The volume of air subjected for exchange of gases is the alveolar ventilation*. The air trapped in the respiratory passage (dead space) does not take part in gaseous exchange. Normal value of alveolar ventilation is 4,200 mL (4.2 L)/ minute.

Regulation of Respiration

Respiration is a reflex process. But it can be controlled voluntarily also. Voluntary arrest of respiration (voluntary apnea) is possible only for a short period of about 40 seconds. However, by practice, breathing can be withheld for a long period. At the end of that period, the person is forced to breathe. Though, normally, the quiet regular breathing takes place because of regulatory mechanisms.

Respiration is regulated by two mechanisms:

A. ***Nervous or neural mechanism:*** Nervous mechanism that regulates respiration includes respiratory centers, afferent nerves and efferent nerves. The nervous system normally adjusts the rate of alveolar ventilation almost exactly to the demands of the body, even during heavy exercise and most other types of respiratory stress.

Respiratory center

Respiratory centers are group of neurons, which control the rate, rhythm and force of respiration. These centers are bilaterally situated in reticular formation of brainstem, receive afferent impulses from different parts of the body and, modulate the movements of thoracic cage and lungs accordingly through efferent nerve fibers.

The respiratory center is composed of several groups of neurons. It is divided into three major collections of neurons:

1. **A dorsal respiratory group**, located in the dorsal portion of the medulla, which mainly causes inspiration. Its control inspiration and respiratory rhythm
2. **A ventral respiratory group,** located in the ventrolateral part of the medulla, which mainly causes expiration. Functions in both inspiration and expiration. The function of this neuronal group differs from that of the dorsal respiratory group in several important ways.
3. **The pneumotaxic center**, located dorsally in the superior portion of the pons, which mainly controls rate and depth of breathing. The function of this center is primarily to limit inspiration. This has a secondary effect of increasing the rate of breathing because limitation of inspiration also shortens expiration and the entire period of each respiration.

B. Chemical mechanism:

The chemical mechanism of respiratory regulation is operated through the chemoreceptors which give response to chemical changes in blood such as:

1. Hypoxia {decreased partial pressure of O_2 in blood (PO_2)}
2. Hypercapnea {increased partial pressure of CO_2 in blood (PCO_2)}
3. Increased hydrogen ion concentration.

Types of Chemoreceptors

Chemoreceptors are classified into two groups:

1. **Central chemoreceptors:** The chemoreceptors are present in the brain, situated in medulla oblongata, close to dorsal respiratory group of neurons. The main stimulant for the central chemoreceptors is the increased hydrogen ion concentration.

If hydrogen ion concentration increases in the blood, it cannot stimulate the central chemoreceptors because, the hydrogen ions from blood cannot cross the blood-brain barrier and blood cerebrospinal fluid barrier.

On the other hand, if carbon dioxide increases in the blood, it can easily cross the blood-brain barrier and blood cerebrospinal fluid barrier and enter the interstitial fluid of brain or the cerebrospinal fluid. There, the carbon dioxide combines with water to form carbonic acid. Since carbonic acid is unstable, it immediately dissociates into hydrogen ion and bicarbonate ion.

The hydrogen ions stimulate the central chemoreceptors. Chemoreceptors in turn send stimulatory impulses to dorsal respiratory group of neurons causing increased ventilation (increased rate and force of breathing). Because of this, the excess carbon dioxide is washed out and the respiration is brought back to normal.

2. **Peripheral chemoreceptors:** Chemoreceptors present in the carotid and aortic region of brain are called peripheral chemoreceptors. Reduction in PO_2 is the most potent stimulant for the peripheral chemoreceptors; but these receptors are mildly sensitive to the increased PCO_2 and increased hydrogen ion concentration.

The relationship between oral health and respiratory disease

The relationship between oral health and systemic conditions, including the association between poor oral hygiene, periodontal disease, and respiratory disease, has been increasingly debated over recent decades. Oral bacteria and, especially, periodontal pathogens have been implicated as important agents with regard to causing other illnesses including respiratory diseases

Four possible mechanisms to explain the biological plausibility of an association between oral conditions and nosocomial respiratory infections have been described:

1. Oral pathogens directly aspirated into the lungs.

   The most common respiratory pathogens are found within the dental plaque inside the oral cavity. These bacteria, once established in the mouth, can be aspirated into the lungs and cause infection.

2. Salivary enzymes associated with periodontal disease modify respiratory tract mucosal surfaces and promote adhesion and colonization by respiratory pathogens, with consequent aspiration into the lungs thereby causing infection.

3. Hydrolytic enzymes from periodontopathic bacteria may destroy the salivary film that protects against pathogenic bacteria. This may reduce the ability of mucins to adhere to pathogens, thus leaving them free to adhere to mucosal receptors in the respiratory tract.

4. The presence of a large variety of cytokines and other biologically active molecules continually released from periodontal tissues and peripheral mononuclear cells, in case of untreated periodontitis, may alter the respiratory epithelium and promote colonization by respiratory pathogens, thereby resulting in infection.

Temperature of the Body

Normal body Temperatures

Body temperature or ***Core temperature*** is the average temperature of structures present in deeper part of the body; it is always more than oral or rectal temperature. It is about 37.8°C (100°F) and it's usually remains very constant, within ±1°F (±0.6°C), except when a person has a febrile illness. ***The skin temperature***, in contrast to the core temperature, rises and falls with the temperature of the surroundings.

The normal body temperature in human is 37°C (98.6°F) when measured by placing the clinical thermometer in the mouth ***(oral temperature).*** *It varies between 35.8°C and 37.3°C (96.4° and 99.1°F).*

Variations of body temperature

Physiological Variations

1. ***Age:*** In infants, the body temperature varies in accordance to environmental temperature for the first few days after birth. It is because the temperature regulating system does not function properly during infancy. In children the temperature is slightly (0.5°C) more than in adults because of more physical activities. In old age, since the heat production is less, the body temperature decreases slightly.
2. ***Sex:*** In females, the body temperature is less because of low basal metabolic rate as compared to that of males.
3. ***Diurnal variation:*** In early morning, the temperature is 1°C less than normal. In the afternoon, it reaches the maximum (about 1°C more than normal).
4. ***After meals:*** The body temperature rises slightly (0.5°C) after meals.
5. ***Exercise:*** During exercise, the temperature raises due to production of heat in muscles.
6. ***Sleep:*** During sleep, the body temperature decreases by 0.5°C.
7. ***Emotion:*** During emotional conditions, the body temperature increases.
8. ***Menstrual cycle:*** In females, immediately after ovulation, the temperature rises (0.5° to 1°C) sharply. It decreases (0.5°C) during menstrual phase.

Heat Balance

Regulation of body temperature depends upon the balance between heat produced in the body and the heat lost from the body.

Heat gain or heat production in the body

The various mechanisms involved in the production of heat in the body are:

1. ***Metabolic Activities:*** The major portion of heat produced in the body is due to the metabolism of food. Heat production is more during metabolism of fat (about 9 calories/ liter). Then less calories of heat is produced during carbohydrate metabolism (4.7 calories). Protein metabolism produces heat the less of all (4.5 calories).

2. ***Muscular Activity:*** Heat is produced in the muscle both at rest and during activities. During rest, heat is produced by muscle tone. About 80% of heat of activity is produced by the activity of skeletal muscles.

3. ***Role of Hormones:*** Thyroxin (T_4) and adrenaline increase the heat production by accelerating the metabolic activities.

4. ***Radiation of Heat from the Environment:*** Body gains heat by radiation. It occurs when the environmental temperature is higher than the body temperature.

5. ***Shivering:*** Shivering refers to shaking of the body caused by rapid involuntary contraction or twitching of the muscles during exposure to cold.

Heat loss from the body

Maximum heat is lost from the body through skin and small amount of heat is lost through respiratory system, kidney and gastrointestinal tract. When environmental temperature is less than body temperature, heat is lost from the body.

Heat loss occurs by the following methods:

1. ***Conduction:*** Only minute quantities of heat, about 3%, are normally lost from the body by direct conduct from the surface of the body to solid objects, such as a chair or a bed. Loss of heat by conduction to air, however, represents a large proportion of the body's heat loss (about 15%) even under normal conditions.

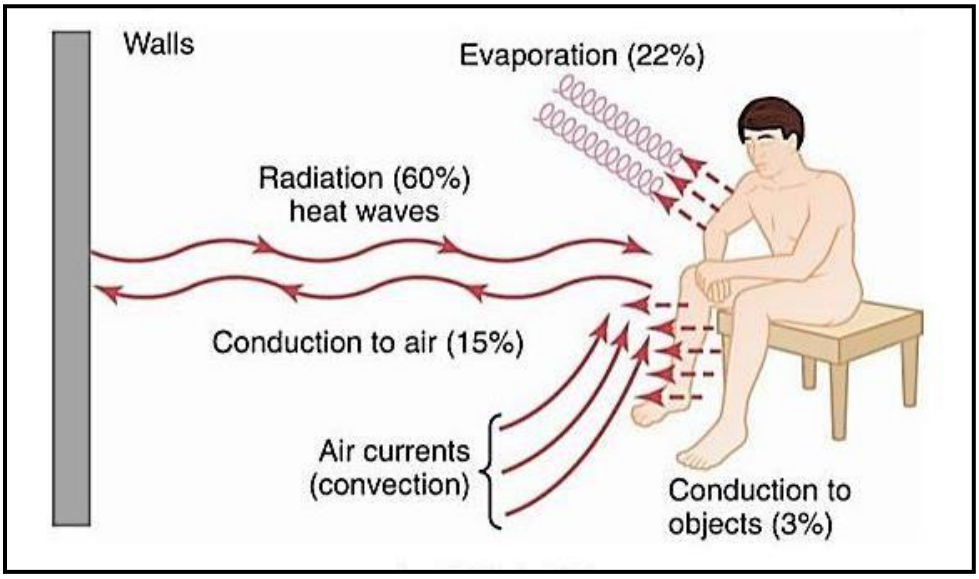
   Once the temperature of the air adjacent to the skin equals the temperature of the skin, no further loss of heat occurs in this way because now an equal amount of heat is conducted from the air to the body.

2. ***Radiation:*** 60% of heat is lost by means of radiation, transfer of heat by infrared ray (electromagnetic ray) radiation from body to other objects through the surrounding air. The human body radiates heat rays in all directions. Heat rays are also being radiated from the walls of rooms and other objects toward the body. If the temperature of the body is greater than the temperature of the surroundings, a greater quantity of heat is radiated from the body than is radiated to the body.

3. ***Convection:*** A small amount of heat convection almost always occurs around the body, about 15% of total heat loss occurs by conduction to the air and then by air convection away from the body. Heat is conducted to the air surrounding the body and then carried away by air currents. The heat from the skin is first conducted to the air and then carried away by the convection air currents.

4. ***Evaporation – Insensible Perspiration:*** Normally, a small quantity of water is continuously evaporated from skin and lungs (22%). So it is called insensible perspiration or insensible water loss. It is about 50 mL/hour. When body temperature increases, more heat is lost by evaporation of more water.

   Insensible evaporation through the skin and lungs cannot be controlled for purposes of temperature regulation because it results from continual diffusion of water molecules through the skin and respiratory surfaces.

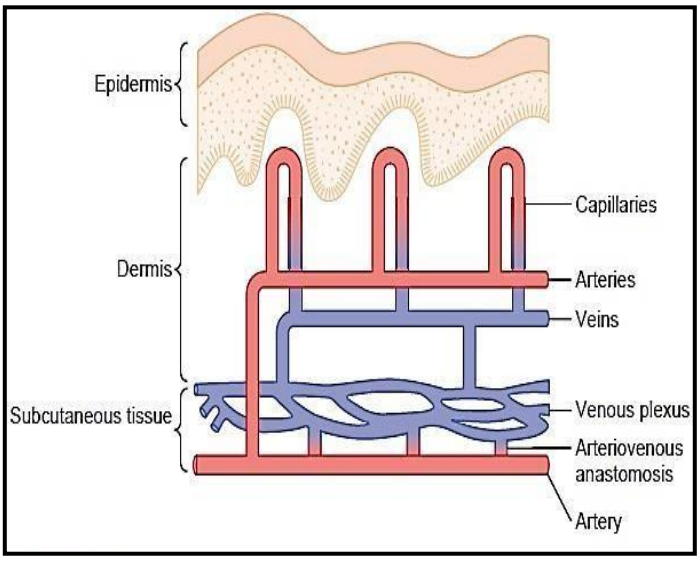


Insulator System of the Body

The skin, the subcutaneous tissues, and especially the fat of the subcutaneous tissues act together as a heat insulator for the body. The fat is important because it conducts heat only one third as readily as other tissues. The insulation beneath the skin is an effective means of maintaining normal internal core temperature, even though it allows the temperature of the skin to approach the temperature of the surroundings.

Blood flow to the skin from the body core provides heat transfer

Blood vessels are distributed profusely beneath the skin. Especially important is a continuous venous plexus that is supplied by inflow of blood from the skin capillaries. In the most exposed areas of the body (the hands, feet, and ears) blood is also supplied to the plexus directly from the small arteries.



The environmental air temperature is affect quantitatively on conductance of heat from the core to the skin surface and then conductance into the air, an approximate eightfold increase in heat conductance between the fully vasoconstricted state and the fully vasodilated state. Therefore, the skin is an effective controlled "***heat radiator***" system, and the flow of blood to the skin is a most effective mechanism for heat transfer from the body core to the skin.

Detection of temperature by receptors in the skin and deep body tissues

Although the signals generated by the temperature receptors of the hypothalamus are extremely powerful in controlling body temperature; receptors in other parts of the body play additional roles in temperature regulation. This is especially true of temperature receptors in the skin and in a few specific deep tissues of the body. The skin has far more cold receptors than warmth receptors in fact, 10 times as many in many parts of the skin. Therefore, peripheral detection of temperature mainly concerns detecting cool and cold instead of warm temperatures. When the skin is chilled over the entire body, immediate reflex effects are invoked and begin to increase the temperature of the body in several ways.

Deep body temperature receptors are found mainly in the spinal cord, in the abdominal viscera, and in or around the great veins in the upper abdomen and thorax. These deep receptors function differently from the skin receptors because they are exposed to the body core temperature rather than the body surface temperature. Yet, like the skin temperature receptors, they detect mainly cold rather than warmth. It is probable that both the skin and the deep body receptors are concerned with preventing hypothermia.

Regulation of body temperature

1- Role of sympathetic nervous system

Heat conduction to the skin is controlled by the sympathetic nervous system.

- Heat conduction to the skin by the blood is controlled by the degree of vasoconstriction of the arterioles and the arteriovenous anastomoses that supply blood to the venous plexus of the skin.
- This vasoconstriction is controlled entirely by the sympathetic nervous system in response to changes in body core temperature and changes in environmental temperature.

2- Role of Hypothalamus in regulation of body temperature

The temperature of the body is regulated almost entirely by ***nervous feedback mechanisms***, and almost ***all these mechanisms operate through temperature regulating centers located in the hypothalamus***. For these feedback mechanisms to operate, there must also be ***temperature detectors*** to determine when the body temperature becomes either too high or too low. The set point under normal physiological conditions is 37°C.

Hypothalamus has two centers which regulate the body temperature:

1- Heat loss center- Anterior Hypothalamic- Preoptic Area

2- Heat gain center- Posterior Hypothalamus.

Heat loss center- Anterior Hypothalamic- Preoptic Area

This center is situated in preoptic area of anterior hypothalamus and contains large numbers of ***heat-sensitive neurons***, which are called thermo-receptors, as well as about one third as many ***cold-sensitive neurons***. These neurons are believed to function as temperature sensors for controlling body temperature. Stimulation of preoptic area results in cutaneous vasodilatation and sweating.

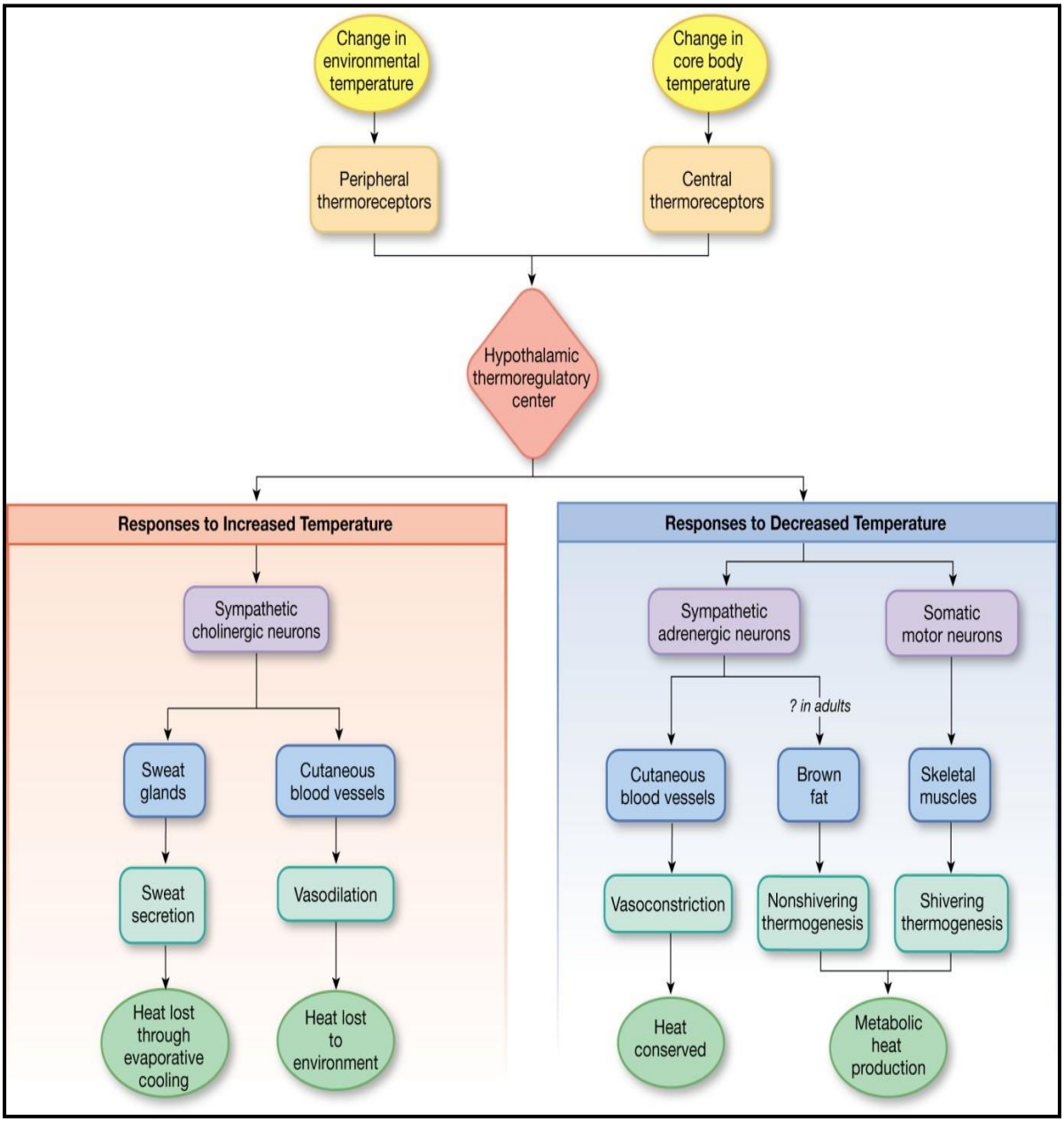
Therefore, it is clear that the hypothalamic-preoptic area has the capability to serve as a thermostatic body temperature control center. So, **when the preoptic area is heated the response to control the body temperature:**

1- The skin all over the body immediately breaks out in a profuse sweat.
2- The skin blood vessels over the entire body become greatly dilated. This response is an immediate reaction to cause the body to lose heat, thereby helping to return the body temperature toward the normal level.
3- In addition, any excess body heat production is inhibited. Therefore, it is clear that the hypothalamic-preoptic area has the capability to serve as a thermostatic body temperature control center.

2- Heat gain center- Posterior Hypothalamus

It is otherwise known as *heat production center*, it is situated in posterior hypothalamic area. Stimulation of posterior hypothalamus causes shivering. The temperature sensory signals from the anterior hypothalamic preoptic area are also transmitted into this posterior hypothalamic area. Here the signals from the preoptic area and signals from elsewhere in the body is combined and integrated to control heat-producing and heat-conserving reactions of the body.

Figure: Response of hypothalamic thermoregulatory center to temperature change (Sympathetic cholinergic &adrenergic neurons)



Mechanisms that decrease or increase body temperature

When the hypothalamic temperature centers detect that the body temperature is either too high or too low, they institute appropriate temperature-decreasing or temperature-increasing procedures:

Temperature-decreasing mechanisms when body temperature increases

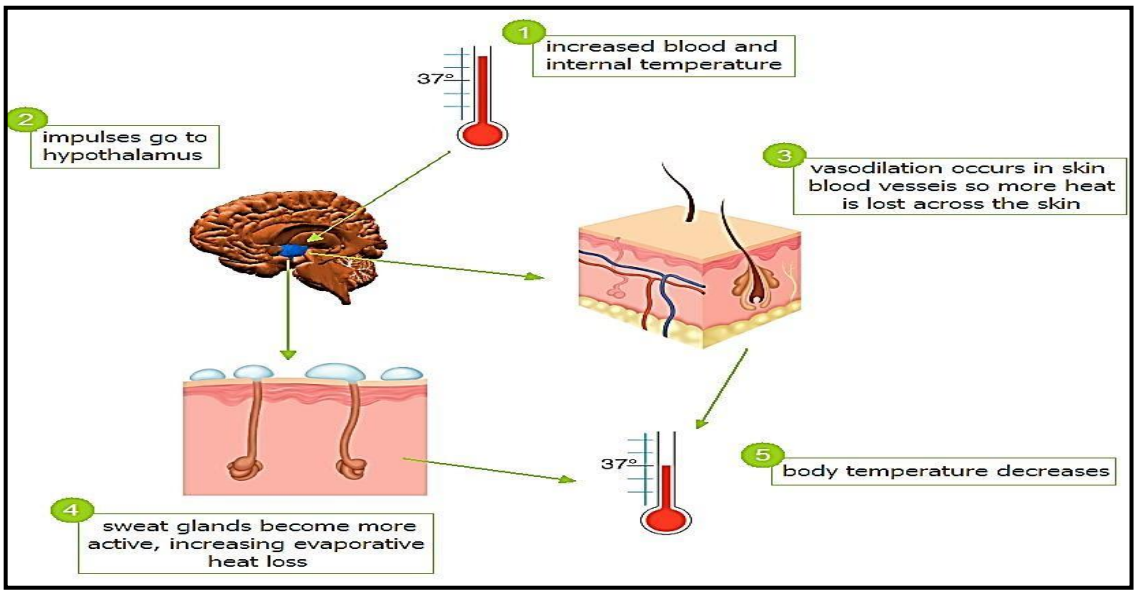
When body temperature increases, blood temperature also increases. When blood with increased temperature passes through hypothalamus, it stimulates the thermoreceptors present in the heat loss center in preoptic area. Now, the heat loss center brings the temperature back to normal ***by promotion of heat loss and prevention of heat production*** through theses mechanisms:

1) Heat loss center promotes heat loss from the body by:

   A- ***Vasodilation of skin blood vessels***- In almost all areas of the body, the skin blood vessels becomes extremely dilated. Full vasodilation can increase the rate of heat transfer to the skin as much as eightfold.

   B- ***Increasing the secretion of sweat***- When sweat secretion increases, more water is lost from skin along with heat.

2) ***Decrease in heat production***- The mechanisms that cause excess heat production, such as shivering and chemical thermogenesis, is strongly inhibited.



Temperature-increasing mechanisms when body temperature decreases

When the body is too cold, the temperature controls system institutes exactly opposite procedures, it is brought back to normal ***by prevention of heat loss and promotion of heat production*** through theses mechanisms:

1. ***Prevention of heat loss by Skin vasoconstriction throughout the body-*** This vasoconstriction is caused by stimulation of the posterior hypothalamic sympathetic centers, (when body temperature decreases, the preoptic thermoreceptors are not activated). The blood flow to skin decreases, and so the heat loss is prevented.

2. ***Increase in thermogenesis (heat production)*** by two ways:

   A- ***Shivering:*** The primary motor center for shivering is situated in posterior hypothalamus. When body temperature is low, this center is activated by heat gain center and, shivering occurs. Enormous heat is produced during shivering due to severe muscular activities.

   B- ***Increased metabolic reactions:*** The sympathetic centers, which are activated by heat gain center, stimulate secretion of adrenaline and noradrenaline. These hormones, particularly adrenaline increase heat production by accelerating cellular metabolic activities. At the same time, hypothalamus secretes thyrotropic releasing hormone (TRH). It causes release of thyroid stimulating hormone (TSH) from pituitary. It in turn increases release of thyroxin (T_4) from thyroid. T_4 accelerates the metabolic activities in the body and increases heat production.

Sympathetic "Chemical" Excitation of heat production

An increase in either sympathetic stimulation or circulating adrenaline and noradrenaline in the blood can rapidly increase the rate of cellular metabolism. This effect is called chemical thermogenesis, or non-shivering thermogenesis.

Chemical thermogenesis: It is the process in which heat is produced in the body by metabolic activities induced by hormones.

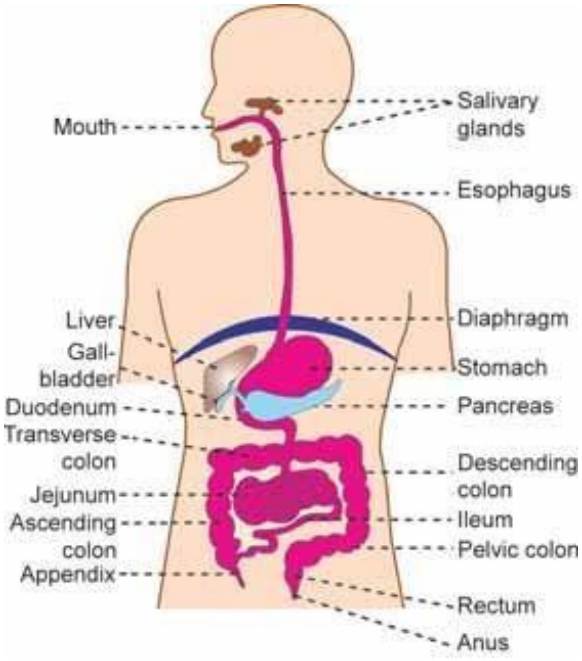
Lect. Physiology

Digestive System

Digestion is defined as the process by which food is broken down into simple chemical substances that can be absorbed and used as nutrients by the body. Most of the substances in the diet cannot be utilized as such. These substances must be broken into smaller particles. Then only these substances can be absorbed into blood and distributed to various parts of the body for utilization. The digestive system is responsible for these functions .

Digestive system is made up of gastrointestinal tract (GI tract) or alimentary canal and accessory organs , which help in the process of digestion and absorption. GI tract is a tubular structure extending from the mouth up to anus structure extending from the mouth up to anus external environment on both ends. GI tract is formed by two types of organs

1. Primary digestive organs
2. Accessory digestive organs



1. Primary Digestive Organs

Primary digestive organs are the organs where actual digestion takes place. These organs are:

1. Mouth
2. Pharynx
3. Esophagus
4. Stomach
5. Small intestine
6. Large intestine.

2. Accessory Digestive Organs

Accessory digestive organs are the organs which help the primary digestive organs in the process of digestion. These organs are:

1. Teeth
2. Tongue
3. Salivary glands
4. Exocrine part of pancreas
5. Liver
6. Gallbladder.

WALL OF GASTROINTESTINAL TRACT

In general, the wall of the GI tract is formed by four layers which are from inside out:

1. Mucus layer
2. Sub mucus layer
3. Muscular layer
4. Serous or fibrous layer.

1. MUCUS LAYER

- The mucus layer is the innermost layer of the wall of GI tract. It is also called gastrointestinal mucosa or mucous membrane. It faces the cavity of GI tract.

  The mucosa has three layers of structures:

  A. Epithelial lining which is in contact with contents of GI tract

B. Lamina propria formed by connective tissue

C. Muscularis mucosa formed by smooth muscle fibers

2. SUBMUCUS LAYER

This is present in all parts of GI tract except This is present in all parts of GI tract except mouth and pharynx. This layer contains loose collagen fibers, elastic fibers, reticular fibers and few cells of connective tissue. Blood vessels , lymphatic vessels and nerve plexus arepresent in this layers.

3. MUSCULAR LAYER

This layer in lips, cheeks and wall of pharynx have skeletal muscle fibers . The esophagus has both skeletal and smooth muscle fibers . Wall of the stomach and intestine is formed by smooth muscle fibers.

The smooth muscle fibers in stomach are arranged in three layers:

A. Inner oblique layer

B. Middle circular layer

C. Outer longitudinal layer.

The smooth muscle fibers in the intestine are arranged in two layers:

i. Inner circular layer
ii. Outer longitudinal layer.

The smooth muscle fibers present in inner circular layer of anal canal constitute internal anal sphincter. The external anal sphincter isformed by skeletal muscle fibers .

4. SEROUS OR FIBROUS LAYER

Outermost layer of the wall of GI tract is either serous or fibrous in nature . The serous layer is formed by connective tissue and mesoepithelial cells. It is also called serosa or serous mem- brane. It covers stomach, small intestine and large intestine.

The fibrous layer is otherwise called fibrosa. It is formed by connective tissue. It covers pharynx and esophagus.

NERVE SUPPLY TO GASTROINTESTINAL TRACT

GI tract has two types of nerve supply:

I. Intrinsic nerve supply
II. Extrinsic nerve supply.

The enteric nervous system is present within the wall of GI tract from esophagus to anus. The nerve fibers of this system are interconnected and form two major networks called

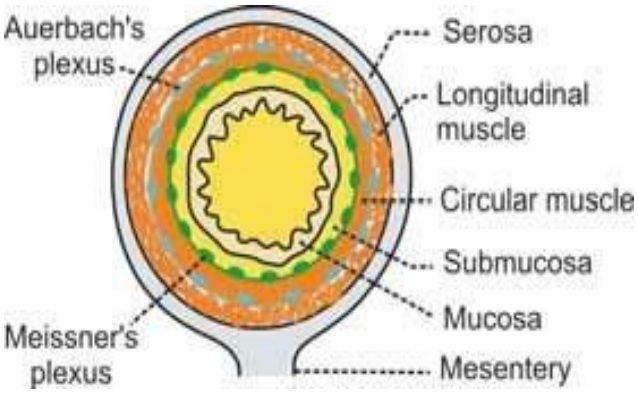
1. Auerbach's Plexus

It is also known as myenteric nerve plexus. It is present in between the inner circular muscle layer and the outer longitudinal muscle layer . The major function of this plexus is to regulate the movements of GI tract.

2.Meissner's Nerve Plexus

Meissner's plexus is otherwise called sub mucus nerve plexus. It is situated in between the muscular layer and sub mucosal layer of GI tract.

The function of Meissner's plexus is the regulation of secretory functions of GI tract.



EXTRINSIC NERVE SUPPLY

The extrinsic nerves that control the enteric nervous system are from autonomic nervous system. Both sympathetic and parasympathetic divisionsof autonomic nervous system innervate the GI tract .

Sympathetic Nerve Fibers

Preganglionic sympathetic nerve fibers to GI tract arise from lateral horns of spinal cord between fifth thoracic and second lumbar segments (T5 – L2).

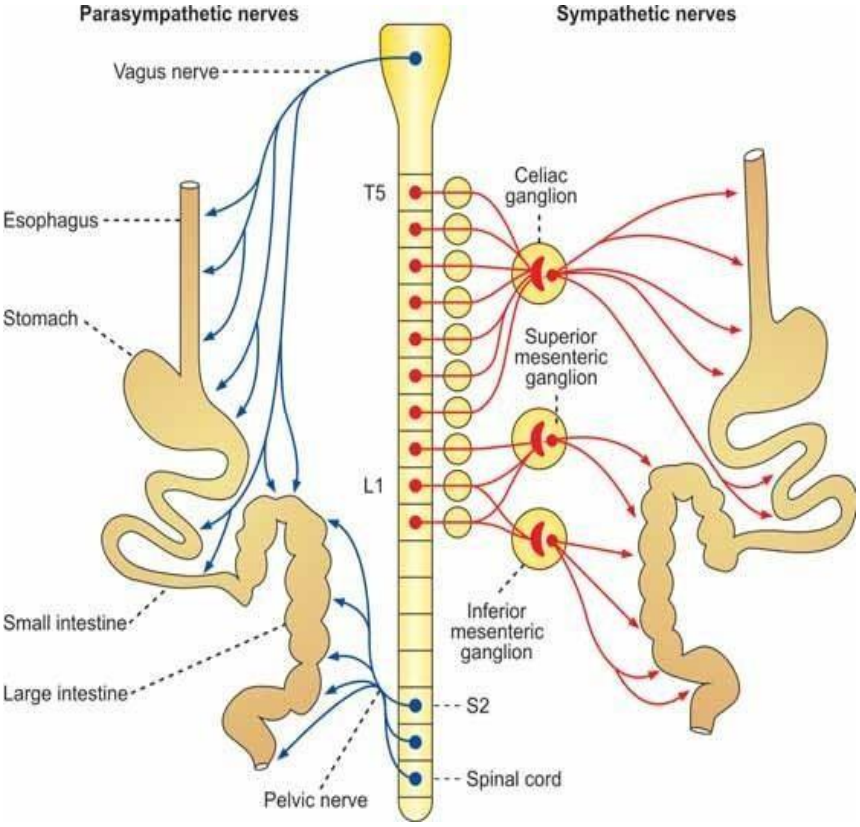
From here, the fibers leave the spinal cord, pass through the ganglia of sympathetic chain without having any synapse and then terminate in the celiac and mesenteric ganglia. The postganglionic fibers from these ganglia are distributed throughout the GI tract.

The function of Sympathetic nerve fibers inhibit the movements and decrease the secretions of GI tract by secreting the neurotransmitter noradrenaline. It also causes constriction of sphincters.

Parasympathetic Nerve Fibers

Parasympathetic nerve fibers to GI tract pass through some of the cranial nerves and sacral nerve. The preganglionic and postganglionic parasympathetic nerve fibers to mouth and salivary glands pass through facial and glossopharyngeal nerves.

The functions of parasympathetic nerve fibers accelerate movements and increase the secretions of GI tract. The neurotransmitter secreted by the parasympathetic nerve fibers is acetylcholine .


Parasympathetic nerves
Sympathetic nerves
Vagus nerve
Esophagus
Stomach
Small intestine
Large intestine
Pelvic nerve
T5
L1
S2
Spinal cord
Celiac ganglion
Superior mesenteric ganglion
Inferior mesenteric ganglion

Lect. Physiology

Digestive System

The major functions of the digestive system are as follows:

1. Ingestion is the introduction of solid or liquid food into the stomach.

2. Mastication is the process by which food taken into the mouth is chewed by the teeth. Digestive enzymes cannot easily penetrate solid food particles and can only work effectively on the surfaces of the particles. It's vital, therefore, to normal digestive function that solid foods be mechanically broken down into small particles. Mastication breaks large food particles into many smaller particles, which have a much larger total surface are a than do a few large particles.

3. Propulsion in the digestive tract is the movement of food from one end of the digestive tract to the other. The total time that it takes food to travel the length of the digestive tract is usually about 24-36 hours. Each segment of the digestive tract is specialized to assist in moving its contents from the oral end to the anal end. Deglutition, or swallowing, moves food and liquids, called a bolus, from the oral cavity into the esophagus. Peristalsis isresponsible for moving material through most of the digestive tract. Muscular contractions occur in peristaltic waves, consisting of a wave of relaxation of the circular muscles, which forms a leading wave of distention in front of the bolus, followed by a wave of strong contraction of the circular muscles behind the bolus, which forces thebolus along the digestive tube. Each peristaltic wave travels the length of the esophagus in about 10 seconds .Peristaltic waves in the small intestine usually only travel for short distances. In some parts of the large intestine, material is moved by mass movements, which are contractions that extend over much larger parts of the digestive tract than peristaltic movements.

4. Mixing. Some contractions don't propel food (chyme) from one end of the digestive tract to the other but rather move the food back and forth within the digestive tract to mix it with digestive secretions and to help break it into smaller pieces. Segmental contractions are mixing contractions that occur in the small intestine.

5. Secretion. As food moves through the digestive tract, secretions are added to lubricate, liquefy, and digest the food. Mucus, secreted along the entire digestive tract, lubricates the food and the lining of the tract. The muc us coats and protects the epithelial cells of the digestive tract from mechanical abrasion, from the damaging effect of acid in the stomach, and from the digestive enzymes of the digestive tract. The secretions also contain large amounts of water, which liquefies the food, thereby making it easier to digest and absorb. Water also moves into the intestine by osmosis. Liver secretions break large fat droplets into much smaller droplets, which makes possible the digestion and absorption of fats. Enzymes secreted by the oral cavity, stomach, intestine,and pancreas break large food molecules down into smaller molecules that canbe absorbed by the intestinal wall.

6. Digestion is the breakdown of large organic molecules into their component parts: carbohydrates into monosaccharides, proteins into amino acids, and triglycerides into fatty acids and glycerol.Digestio consists of mechanical digestion, which involves mastication and mixing of food, and chemical digestion, which is accomplished by digestive enzymes that are secreted along the digestive tract. Digestion of large molecules into their component parts must be accomplished before they can be absorbed by the digestive tract. Minerals and water are not broken down before being absorbed. Vitamins are also absorbed without digestion and lose their function if their structure is altered by digestion.

7. Absorption is the movement of molecules out of the digestive tract and into the circulation or into the lymphatic system. The mechanism by which absorption occurs depends on the type of molecule involved. Molecules pass out of the digestive tract by simple diffusion, facilitated diffusion, active transport, or cotransport.

8. Elimination is the process by which the waste products of digestion are removed from the body. During this process, occurring primarily in the large intestine, water and salts are absorbed and change the material in the digestive tract from a liquefied state to a semisolid state. These semisolid waste products, called feces, are then eliminated from the digestive tract by the process of defecation.

Stomach

The stomach is an enlarged segment of the digestive tract in the left superior part of the abdomen. Its shape and size vary from person to person; even within the same individual its size and shape change from time to time, depending on its food content and the posture of the body.

Secretions of the Stomach

Ingested food and stomach secretions mixed together, form a semifluid material called chyme. The stomach functions primarily as storage and mixing chamber for the chyme. Although some digestion and absorption occur in the stomach, they are not its major functions.

Stomach secretions include mucus, hydrochloric acid, gastrin, histamine, intrinsic factor, and pepsinogen. Pepsinogen is the inactive form of the protein-digesting enzyme pepsin.

The surface mucous cells and mucous neck cells secrete viscous and alkaline mucus that covers the surface of the epithelial cells and forms a layer 1-1.5 mm thick. The thick layer of mucus lubricates and protects the epithelial cells of the stomach wall from the damaging effect of the acidic chyme and pepsin. Irritation of the stomach mucosa results in stimulation of the secretion of a greater volume of mucus.

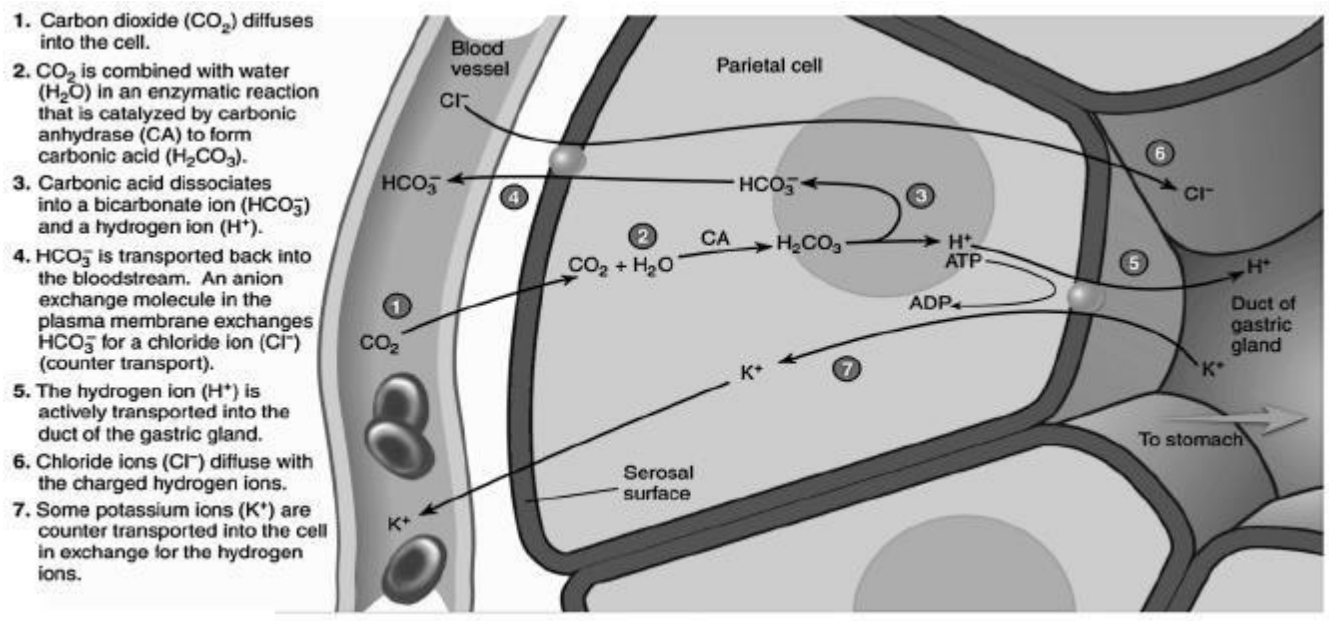
Parietal cells in the gastric glands of the pyloric region secrete intrinsic factor and a concentrated solution of hydrochloric acid. Intrinsic factor is a glycoprotein that binds with vitamin B_{12} and makes the vitamin more readily absorbed in the ileum. Vitamin B_{12} is important in deoxyribonucleic acid (DNA) synthesis.

Hydrochloric acid produces the low pH of the stomach, which is normally between 1 and 3. Although The hydrochloric acid secreted into the stomach has a minor digestive effect on ingested food, one of its main functions is to kill bacteria that are ingested with essentially everything humans put into their mouths. Some pathogenic bacteria may avoid digestion in the stomach, however, because they have an outer coat that resists stomach acids.

The low pH of the stomach also stops carbohydrate digestion by inactivating salivary amylase. Stomach acid also denatures many proteins so that proteolytic enzymes can reach internal peptide bonds, and it provides the proper pH environment for the function of pepsin.

Hydrogen ions are derived from carbon dioxide and water, which enter the parietal cell from its serosal surface, which is the side opposite the lumen of the gastric pit. Once inside the cell, carbonic anhydrase catalyzes the reaction between carbon dioxide and water to form carbonic acid. Some of the carbonic acid molecules then dissociate to form hydrogen ions and bicarbonate ions. The hydrogen ions are actively transported across the mucosal surface of the parietal cell into the lumen of the stomach; some potassium ions are moved into the cell in exchange for the hydrogen ions. Although hydrogen ions are actively transported against a steep concentration gradient, chloride ions diffuse with the hydrogen ions from the cell through the plasma membrane. Diffusion of chloride ions with the positively charged hydrogen ions reduces the amount of energy needed to transport the hydrogen ions against both a concentration gradient and an electrical gradient. Bicarbonate ions move down their concentration gradient from the parietal cell into the extracellular fluid. During this process, bicarbonate ions are exchanged for chloride ions through an anion exchange molecule, which is located in the plasma membrane, and the chloride ions subsequently move into the cell.

Chief cells within the gastric glands secrete pepsinogen. Pepsinogen is packaged in zymogen granules, which are released by exocytosis when pepsinogen secretion is stimulated. Once pepsinogen enters the lumen of the stomach, hydrochloric acid and previously formed pepsin molecules convert it to pepsin. Pepsin exhibits optimum enzymatic activity at a pH of 3 or less. Pepsin catalyzes the cleavage of some covalent bonds in proteins, thus breaking them into smaller peptide chains.



Hydrochloric Acid Production by Parietal Cells in the Gastric Glands of the Stomach

Regulation of Stomach Secretion

Approximately 2-3L of gastric secretions (gastric juice) is produced each day. The amount and type of food entering the stomach dramatically affects the secretion amount, but up to 700 mL is secreted as a result of a typical meal. Both nervous and hormonal mechanisms regulate gastric secretions. The neural mechanisms involve reflexes integrated within the medulla oblongata and local reflexes integrated within the enteric plexus of the GI tract. In addition, higher brain centers influence the reflexes. Chemical signals that regulate stomach secretions include the hormones gastrin, secretin, gastric-inhibitory polypeptide, and cholecystokinin, as well as the paracrine chemical signal histamine.

Regulation of stomach secretion is divided into three phases: cephalic, gastric, and intestinal.

1. Cephalic phase. In the cephalic phase of gastric regulation, the sensations of the taste and smell of food, stimulation of tactile receptors during the process of chewing and swallowing, and pleasant thoughts of food stimulate centers within the medulla oblongata that influence gastric secretions. Action potentials are sent from the medulla along parasympathetic neurons within the vagus (X) nerves to the stomach. Within the stomach wall, the preganglionic neurons stimulate postganglionic neurons in the enteric plexus. The postganglionic neurons, which are primarily cholinergic, stimulate secretory activity in the cells of the stomach mucosa.

Parasympathetic stimulation of the stomach mucosa results in the release of the neurotransmitter acetylcholine, which increases the secretory activity of both the parietal and chief cells and stimulates the secretion of gastrin and histamine from endocrine cells. Gastrin is released into the circulation and travels to the parietal cells, where it stimulates additional hydrochloric acid and pepsinogen secretion. In addition, gastrin stimulates endocrine cells to release histamine, which stimulates parietal cells to secrete hydrochloric acid. The histamine receptors on the parietal cells are called H_2 receptors, and are different from the H_1 receptors involved in allergic reactions. Drugs that block allergic reactions do not affect histamine-mediated stomach acid secretion and vice versa. Acetylcholine, histamine, and gastrin working together cause a greater secretion of hydrochloric acid than any of them does separately. Of the three, histamine has the greatest stimulatory effect.

2. Gastric phase. The greatest volume of gastric secretions is produced during the gastric phase of gastric regulation. The presence of food in the stomach initiates the gastric phase. The primary stimuli are distention of the stomach and the presence of amino acids and peptides in the stomach.

Distention of the stomach wall, especially in the body or fundus, results in the stimulation of mechanoreceptors. Action potentials generated by these receptors initiate reflexes that involve both the CNS and enteric reflexes, resulting in secretion of mucus, hydrochloric acid, pepsinogen, intrinsic factor, and gastrin. The presence of partially digested proteins or moderate amounts of alcohol or caffeine in the stomach also stimulates gastrin secretion.

When the pH of the stomach contents falls below 2, increased gastric secretion produced by distention of the stomach is blocked. This negative-feedback mechanism limits the secretion of gastric juice.

Amino acids and peptides released by the digestive action of pepsin on proteins directly stimulate parietal cells of the stomach to secrete hydrochloric acid. The mechanism by which this response is mediated is not clearly understood. It doesn't involve known neurotransmitters, and, when the pH drops below 2, the response is inhibited. Histamine also stimulates the secretory activity of parietal cells.

3. Intestinal phase. The entrance of acidic stomach contents into the duodenum of the small intestine controls the intestinal phase of gastric regulation.The presence of chyme in the duodenum activates both neural and hormonal mechanisms. When the pH of the chyme entering the duodenum drops to 2 or below, or if the chyme contains fat digestion products, gastric secretions are inhibited.

Acidic solutions in the duodenum cause the release of the hormone secretin into the circulatory system. Secretin inhibits gastric secretion by inhibiting both parietal and chief cells. Acidic solutions also initiate a local enteric reflex, which inhibits gastric secretions.

Fatty acids and certain other lipids in the duodenum and the proximal jejunum initiate the release of two hormones: gastric inhibitory polypeptide and cholecystokinin ,Gastric inhibitory polypeptide strongly inhibits gastric secretion, and cholecystokinin inhibits gastric secretions to a lesser degree. Hypertonic solutions in the duodenum and jejunum also inhibit gastric secretions. The mechanism appears to involve the secretion of a hormone referred to as enterogastrone, but the actual existence of this hormone has never been established.

Cephalic Phase

1. The taste or smell of food, tactile sensations of food in the mouth, or even thoughts of food stimulate the medulla oblongata (*green arrow*).
2. Parasympathetic action potentials are carried by the vagus nerves to the stomach (*pink arrow*).
3. Preganglionic parasympathetic vagus nerve fibers stimulate postganglionic neurons in the enteric plexus of the stomach.
4. Postganglionic neurons stimulate secretion by parietal and chief cells and stimulate gastrin secretion by endocrine cells.
5. Gastrin is carried through the circulation back to the stomach (*purple arrow*), where it stimulates secretion by parietal and chief cells.

(a)

Gastric Phase

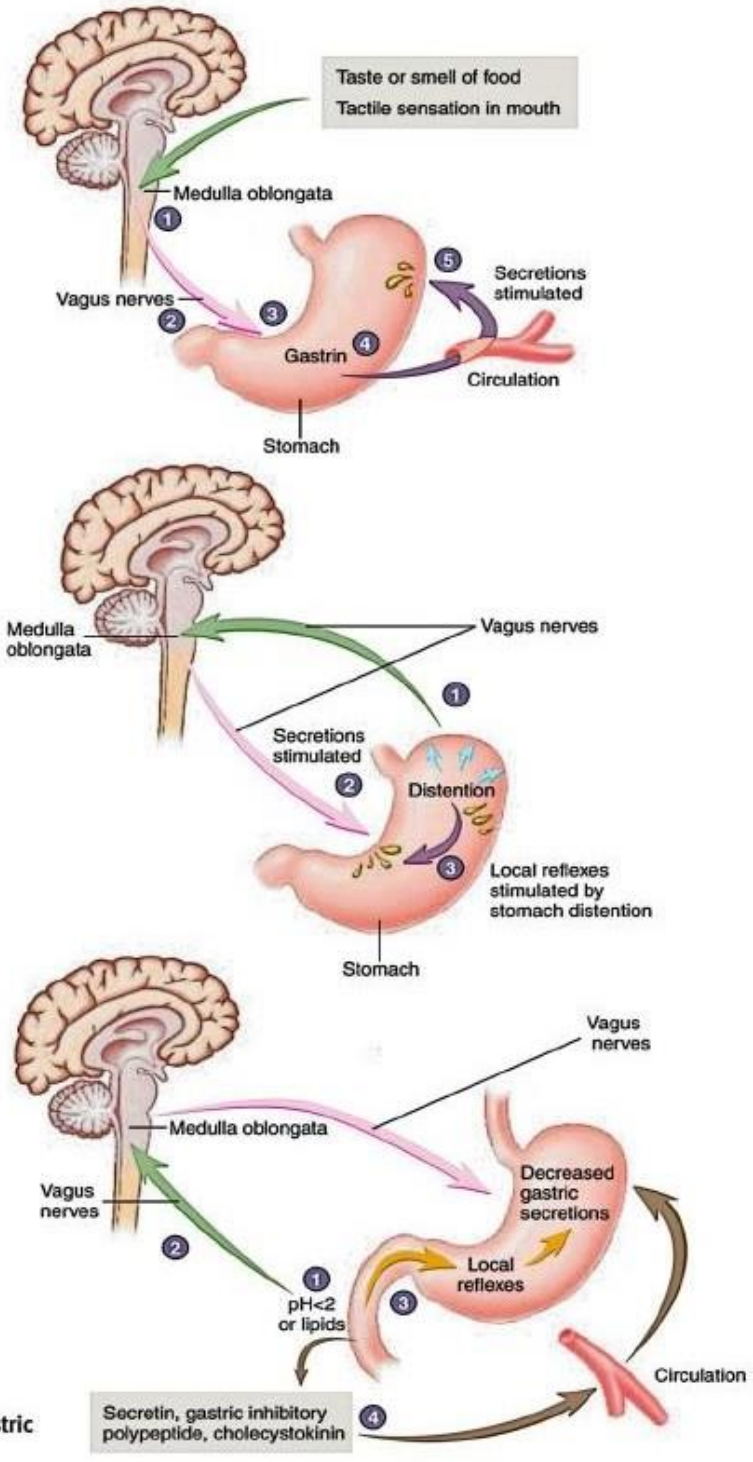
1. Distention of the stomach activates a parasympathetic reflex. Action potentials are carried by the vagus nerves to the medulla oblongata (*green arrow*).
2. The medulla oblongata stimulates stomach secretions (*pink arrow*).
3. Distention of the stomach also activates local reflexes that increase stomach secretions (*purple arrow*).

(b)

Intestinal Phase

1. Chyme in the duodenum with a pH less than 2 or containing fat digestion products (lipids) inhibits gastric secretions by three mechanisms (2–4).
2. Sensory vagal action potentials to the medulla oblongata (*green arrow*) inhibit motor action potentials from the medulla oblongata (*pink arrow*).
3. Local reflexes inhibit gastric secretion (*orange arrows*).
4. Secretin, gastric inhibitory polypeptide, and cholecystokinin produced by the duodenum (*brown arrows*) inhibit gastric secretions in the stomach.

(c)



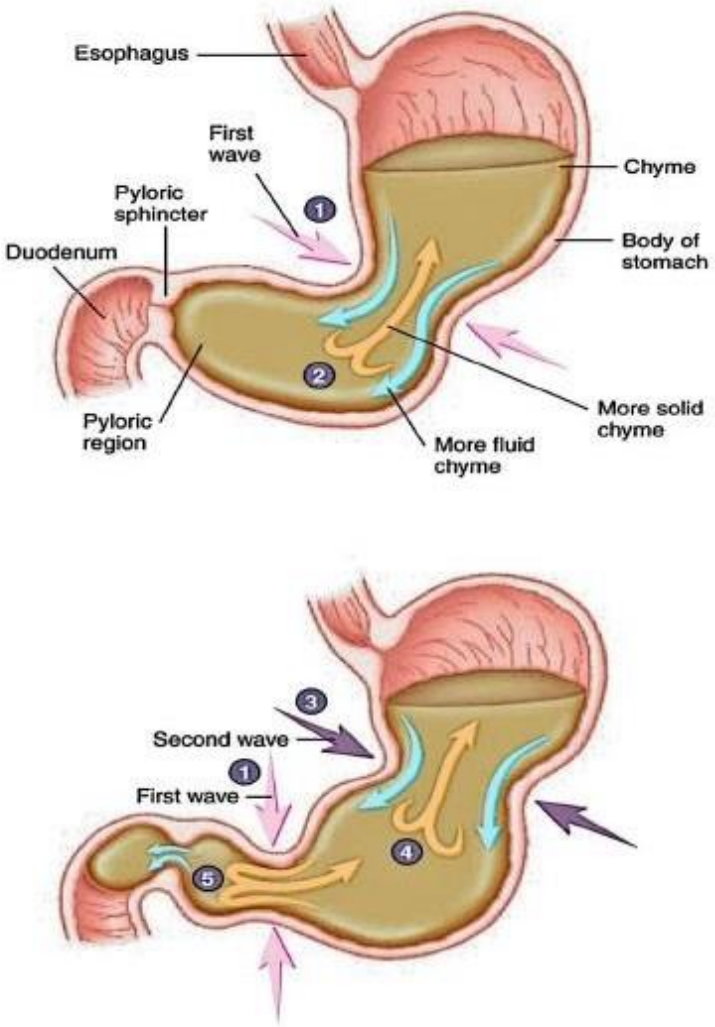
The Three Phases of Gastric Secretion

(*a*) Cephalic phase. (*b*) Gastric phase. (*c*) Intestinal phase.

Mixing of Stomach Contents

Ingested food is thoroughly mixed with the secretions of the stomach glands to form chyme. This mixing is accomplished by gentle mixing waves, which are peristaltic-like contractions that occur about every 20 seconds and proceed from the body toward the pyloric sphincter to mix the ingested material with the secretions of the stomach. Peristaltic waves occur less frequently, are significantly more powerful than mixing waves, and force the chyme near the periphery of the stomach toward the pyloric sphincter. The more solid material near the center of the stomach is pushed superiorly toward the cardiac region for further digestion. Roughly 80% of the contractions are mixing waves, and 20% are peristaltic waves.

1. Mixing waves initiated in the body of the stomach progress toward the pyloric region (*pink arrows directed inward*).
2. The more fluid part of the chyme is pushed toward the pyloric region (*blue arrows*), whereas the more solid center of the chyme squeezes past the peristaltic constriction back toward the body of the stomach (*orange arrow*).
3. Additional mixing waves (*purple arrows*) move in the same direction and in the same way as the earlier waves (**1**) that reach the pyloric region.
4. Again, the more fluid part of the chyme is pushed toward the pyloric region (*blue arrows*), whereas the more solid center of the chyme squeezes past the peristaltic constriction back toward the body of the stomach (*orange arrow*).
5. Some of the most fluid chyme is squeezed through the pyloric opening into the duodenum (*small blue arrows*), whereas most of the chyme is forced back toward the body of the stomach for further mixing (*orange arrows*).



Movements in the Stomach

Stomach Emptying

The amount of time food remains in the stomach depends on a number of factors, including the type and volume of food. Liquids exit the stomach within 11/2 - 21/2 hours after ingestion. After a typical meal, the stomach is usuallyempty within 3-4 hours. The pyloric sphincter usually remains partially closed because of mild tonic contraction.

Each peristaltic contraction is sufficiently strong to force a small amount of chyme through the pyloric opening and into the duodenum. The peristaltic contractions responsible for movement of chyme through the partially closed pyloric opening are called the pyloric pump.