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الفصل الدراسي الثاني

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Lecture One

Nervous System

The **nervous system** is one of the regulating systems. Electrochemical impulses of the nervous system make it possible to maintain homeostasis.

The functions of the nervous system:

1. To detect changes and feel sensations.
2. To initiate appropriate responses to changes.
3. To organize information for immediate use and store it for future use.

Nerve Tissue

Nerve cells are called **neurons** and the **cell body** contains the nucleus. **Dendrites** are processes (extensions) that transmit impulses toward the cell body. The one **axon** of neuron transmits impulses away from the cell body. It is the cell membrane of the dendrites, cell body, and axon that carries the electrical nerve impulse. In PNS, axons and dendrites are "wrapped" in specialized cells called **Schwann cells**, enclosing them in several layers of Schwann cell membrane. These layers are the **myelin sheath**; myelin is phospholipid that electrically insulates neurons from one another. The spaces between adjacent Schwann cells are called nodes of **Ranvier**. These nodes are the parts of the neuron cell membrane that depolarize when an electrical impulse is transmitted. The nuclei and cytoplasm of the Schwann cells are wrapped around the outside of the myelin sheath and are called the **neurolemma**, In the CNS; the myelin sheaths are formed by **oligodendrocytes**, one of the **neuroglia.**

Types of neurons

Neurons may be classified into three groups: **Sensory neurons** (or **afferent neurons**) carry impulses from receptors to the CNS.

Receptors detect external or internal changes and send the information to the CNS in the form of impulses by way of the afferent neurons. **Motor neurons** (or **efferent neurons**) carry impulses from the central nervous system to **effectors**. **Interneuron** is found entirely within the CNS.

Generation of Nerve Impulse:

Excitability

Excitability is that property of the nerve fiber by virtue of which it responds by generating a nerve signal (electrical impulses or the so-called action potentials) when it is stimulated by a suitable stimulus which may be mechanical, thermal, chemical or electrical.

Resting Membrane Potential

A steady potential difference of −70mV (inside negative) is observed in the nerve fiber (figure 1). This is the resting membrane potential (RMP) and indicates the resting state of cell**,** also called state of **polarization.**

Action Potential

The **action potential** may be defined as the brief sequence of changes which occur in the resting membrane potential when stimulated by a threshold stimulus. When the stimulus is subminimal or subthreshold, it does not produce action potential, but does produce some changes in the RMP. The adequate strength of stimulus necessary for producing the action potential in a nerve fiber is known as **threshold**.

Phases of action potential

The action potential basically occurs in two phases: depolarization and repolarization (figure 2). When the nerve is stimulated, the polarized state is altered, i.e. RMP is abolished and the interior of the nerve becomes positive as compared to the exterior. This is called **depolarization phase**. Within no time there occurs reversal to the nearly original potential and this second phase of action potential is called **repolarization phase**. According to **Hodgkin-Huxley theory,** the sequences of events are:

1. **Polarization phase**. Resting membrane potential (−70 mV) is due to distribution of more cations outside the cell membrane and more anions inside the cell membrane, with Na+ ions more abundant outside the cell, and K+ ions and negative ions more abundant inside. Na^+ cannot enter the cell due to the impermeability of the membrane.

2. **Depolarization phase**. When threshold stimulus is applied to the cell membrane, at the point of stimulation the permeability of the membrane for Na^+ ions increases. There occurs a rapid influx of Na^+ ions into the cell. This rapid entry of Na^+ leads to depolarization.

3. **Repolarization phase**. Repolarization occurs due to decrease in further Na^+ influx and K^+ efflux. The net transfer of positive charge out of the cell serves to complete the repolarization. Then the sodium and potassium pumps return Na+ ions outside and K+ ions inside, and the neuron is ready to respond .

Main Characteristics of Nerve Excitability

1. **All or none response**. A single nerve fiber always obeys '**all or none law**', that is:

- When a stimulus of subthreshold intensity is applied to the axon, then no action potential is produced **(none response);**
- A response in the form of spike of action potential is observed when the stimulus is of threshold intensity; and
- There occurs no increase in the magnitude of action potential when the strength of stimulus is more than the threshold level **{all response)**. This all or none relationship observed between the strength of stimulus and the response achieved is known as '**All or None Law**'.

2. **Refractory period**. Refractory period refers to the period following action potential (produced by a threshold stimulus) during which a nerve fiber either does not respond or responds subnormally to a stimulus of threshold intensity or greater than threshold intensity. It is of two types:

A - **Absolute refractory period (ARP)**. It is a short period following action potential during which second stimulus, no matter how strong it may be, cannot evoke any response (another action potential).In other words during absolute refractory period the nerve fiber completely loses its excitability.

B- **Relative refractory period (RRP)**. It is a short period during which the nerve fiber shows response if the strength of stimulus is more than normal.

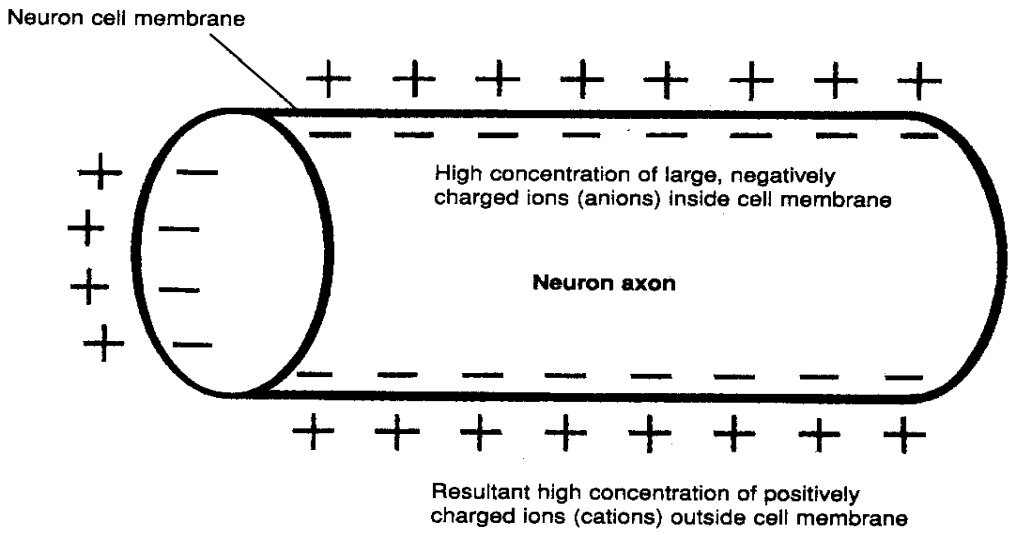

Figure (1): A segment of neuron showing the location of charges

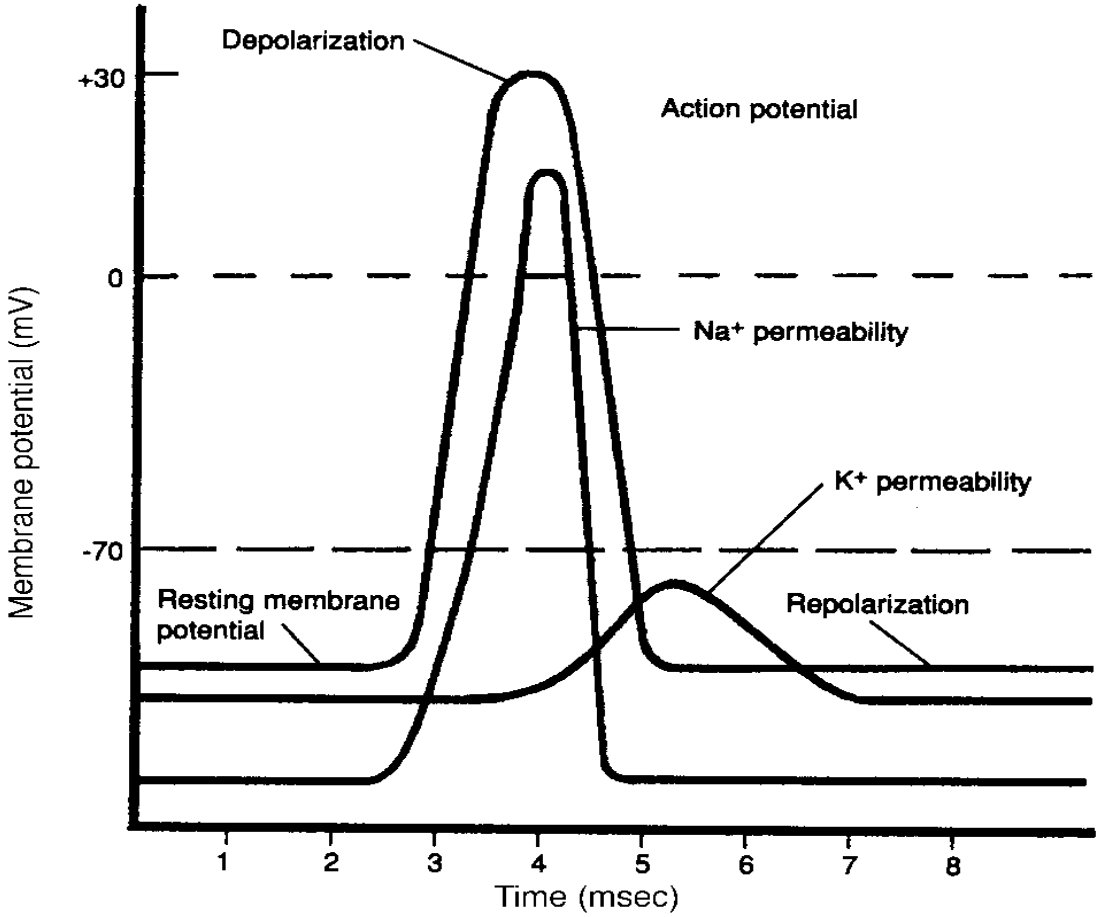

Figure (2): An action potential

Lecture Two

Nervous System

Propagation of action potential in an unmyelinated axon

The steps of propagation of action potential along an unmyelinated axon are summarized:

1-In the resting phase (polarized state) the axonal membrane is outside positive and inside negative.

2-When an unmyelinated axon is stimulated at one site by a threshold stimulus, there occurs action potential at that site, i.e. that site is depolarized. In other words, at that site outside membrane become negative and inside positive (reversal of polarity) but the neighboring areas until now remain in polarized state.

3-The circular current flow depolarizes the neighboring area of the membrane up to firing level and a new action potential is produced which in turn depolarizes the neighboring area ahead. Thus, due to successive depolarization of the neighboring area, the action potential is propagated along the entire length of the axon.

Propagation of action potential in a myelinated axon

The myelinated nerve fibers have a wrapping of myelin sheath with gaps at regular intervals which are devoid of myelin sheath (nodes of Ranvier).The axonal membrane in the naked area (nodes of Ranvier) bears densely packed ion channels. The myelin sheath acts as an insulator and does not allow the current flow. Therefore, in myelinated nerve fibers the **local circuit of current flow** only occurs from one node of Ranvier to the adjacent node . That is, the impulse

(action potential) jumps from one node of Ranvier to next. This is known as **saltatory conduction**. Since the impulse jumps from one node to other, the speed of conduction in myelinated fibers is much rapid (50 to 100 times faster) than the unmyelinated fiber.

Factors affecting conduction velocity

The velocity of conduction in nerve fibers varies from as little as 0.25 m/sec in very small unmyelinated fibers to as high as 100 m/sec in very large myelinated fibers. In general the factors affecting conduction velocity are:

1. Temperature: A decrease in temperature delays conduction i.e. slows down the conduction velocity.

2. Axon diameter: affects the conduction velocity through the resistance offered by the axoplasm to the flow of axoplasmic current. If the diameter of the axon is greater, the axoplasmic resistance is lesser and hence the velocity of conduction is higher.

3. Myelination: increases conduction velocity by increasing the axon diameter, and by the saltatory conduction.

Synapse

Neurons that transmit impulses to other neurons do not actually touch one another. The small gap or space between the axon of one neuron and the dendrites or cell body of the next neuron is called the **synapse**. Within the synaptic knob (terminal end) of the presynaptic axon is a chemical **neurotransmitter** that is released into the synapse by the arrival of an electrical nerve impulse (figure 3).

The neurotransmitter diffuses across the synapse, combines with specific receptor sites on the cell membrane of the postsynaptic neuron, and there generates an electrical impulse that is, in turn, carried by this neuron's axon to the next synapse, and so forth. A chemical **inactivator** at the cell body or dendrite of the

postsynaptic neuron quickly inactivates the neurotransmitter. This prevents unwanted, continuous impulses, unless a new impulse from the first neuron releases more neurotransmitter. Many synapses are termed **excitatory**, because the neurotransmitter causes the postsynaptic neuron to depolarize (become more negative outside as Na+ ions enter the cell) and transmit an electrical impulse to another neuron, muscle cell, or gland. Some synapses, however, are **inhibitory**, meaning that the neurotransmitter causes the postsynaptic neuron to hyperpolarize(become even more positive outside as K+ ions leave the cell or Cl^- ions enter the cell) and therefore **not** transmit an electrical impulse.

Such inhibitory synapses are important, for example, for slowing the heart rate, and for balancing the excitatory impulses transmitted to skeletal muscles. With respect to the skeletal muscles, this inhibition prevents excessive contraction and is important for coordination. An example of a neurotransmitter is **acetylcholine**, which is found at neuromuscular junctions, in the CNS, and in much of the peripheral nervous system. Acetylcholine usually makes a postsynaptic membrane more permeable to Na+ ions, which brings about depolarization of the postsynaptic neuron. **Cholinesterase** is the inactivator of acetylcholine.

Spinal Cord Reflexes

A **reflex** is an involuntary response to a stimulus, that is, an automatic action stimulated by a specific change of some kind. **Spinal cord reflexes** are those that do not depend directly on the brain, although the brain may inhibit or enhance them.

Reflex Arc

A reflex arc is the pathway that nerve impulses travel when a reflex is elicited, and there are five essential parts:

1. **Receptors**—detect a change (the stimulus) and generate impulses.

2. **Sensory neurons**—transmit impulses from receptors to the CNS.

3. **Central nervous system**—contains one or more synapses (interneurons may be part of the pathway).

4. **Motor neurons**—transmit impulses from the CNS to the effector.

5. **Effector**—performs its characteristic action.

Patellar Reflex or Knee- Jerk

In this reflex, a tap on the patellar tendon just below the kneecap causes extension of the lower leg. This is a **stretch reflex**, which means that a muscle that is stretched will automatically contract. In the quadriceps femoris muscle are stretch receptors that detect the stretching produced by striking the patellar tendon. These receptors generate impulses that are carried along sensory neurons in the femoral nerve to the spinal cord. In the spinal cord, the sensory neurons synapse with motor neurons (this is a two-neuron reflex). The motor neurons in the femoral nerve carry impulses back to the quadriceps femoris, the effector, which contracts and extends the lower leg. The patellar reflex is one of many used clinically to determine whether the nervous system is functioning properly. If the patellar reflex were absent in a patient, the problem could be in the thigh muscle, the femoral nerve, or the spinal cord. If the reflex is normal, however, that means that all parts of the reflex arc are intact. Since these are spinal cord reflexes, the brain is not directly involved.

The Autonomic Nervous System

The **autonomic nervous system** (**ANS**) is actually part of the peripheral nervous system in that it consists of motor portions of some cranial and spinal nerves. The ANS has two divisions: **sympathetic** and **parasympathetic**. Often, they function in opposition to each other.

Sympathetic Division

The sympathetic division brings about widespread responses in many organs. The sympathetic division is dominant in stressful situations, which include anger, fear, or anxiety, as well as exercise. For our prehistoric ancestors, stressful situations often involved the need for intense physical activity—the "fight or flight response. The heart rate increases, vasodilation in skeletal muscles supplies them with more oxygen, the bronchioles dilate to take in more air and the liver changes glycogen to glucose to supply energy. At the same time digestive secretions decrease and peristalsis slows; these are not important in a stress situation. Vasoconstriction in the skin and viscera shunts blood to more vital organs such as the heart, muscles, and brain.

Parasympathetic Division

The parasympathetic division dominates in relaxed (non-stress) situation to promote normal functioning of several organ systems.

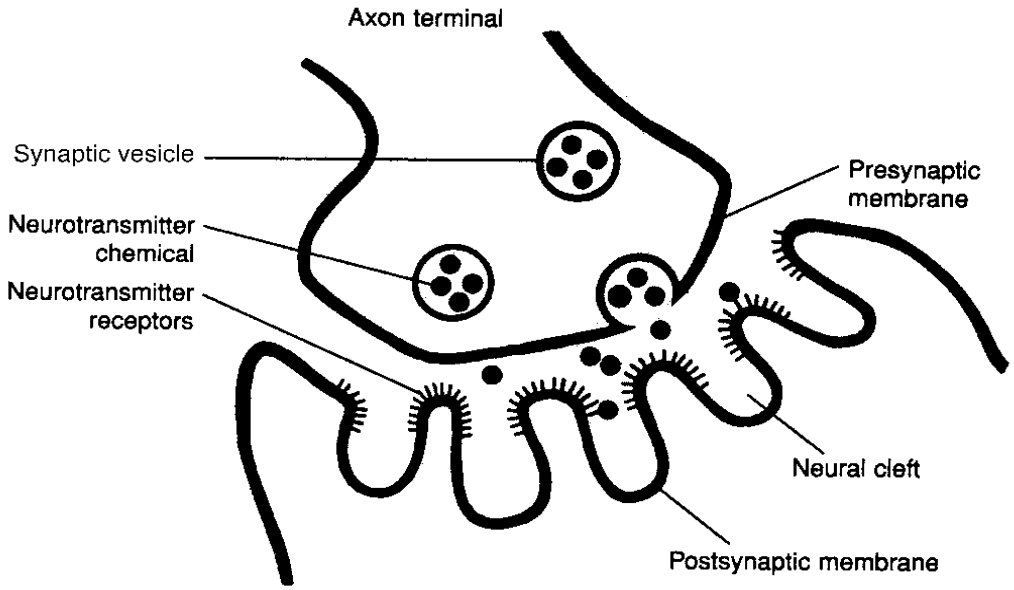

Figure (3): Synaptic transmission

Lecture Three

Digestive System

The **digestive system**, it is also referred to as the **gastrointestinal (GI) system**, includes the tubular **gastrointestinal (GI) tract** plus the **accessory digestive organs.** The GI tract which is approximately 9 m long; it includes the mouth, pharynx, esophagus, stomach, small intestine, and large intestine. The accessory digestive organs which are not part of the tract but secrete substances into it via connecting ducts; they include the salivary glands, liver, gallbladder, and pancreas.

Functions of the gastrointestinal system

The overall function of the GI system is to process ingested foods into molecular forms that are then transferred, along with salts and water to the body's internal environment, where they can be distributed to cells by the circulatory system.

The functions of the GI system can be described in terms of the following four processes:-

1. Digestion: This refers to the breakdown of food molecules into their smaller subunits, which can be absorbed. During digestion, two main processes occur at the same time:

a. Mechanical digestion: Larger pieces of food get broken down into smaller pieces while being prepared for chemical digestion. Mechanical digestion starts in the mouth and continues into the stomach.

b. Chemical digestion: Several different enzymes break down macromolecules into smaller molecules that can be absorbed. Chemical digestion starts in the mouth and continues into the intestines.

2. Secretion: This includes both exocrine and endocrine secretions.

a. Exocrine secretions: Water, hydrochloric acid, bicarbonate, and many digestive enzymes are secreted into the lumen of the GI tract.

b. Endocrine secretions: The stomach and small intestine secrete a number of hormones that help to regulate the digestive system.

3. Absorption: This refers to the passage of digested end products from the lumen of the GI tract across a layer of epithelial cells into the blood or lymph.

4. Motility: This refers to the movement of food through the digestive tract through the processes of:

a. Ingestion: Taking food into the mouth.

b. Mastication: Chewing the food and mixing it with saliva.

c. Deglutition: Swallowing the food.

d. Peristalsis: Rhythmic, wavelike contractions that move food through the GI tract.

Phases of digestion:

Oral cavity and esophagus

The GI tract begins with the **mouth,** and digestion starts there with chewing, which breaks up large pieces of food into smaller particles that can be swallowed. **Saliva** was secreted by three pairs of **salivary glands;** they are parotid glands, submandibular glands and sublingual glands. Saliva, which contains mucus, moistens and lubricates the food particles before swallowing. It also contains the enzyme **amylase,** which partially digests polysaccharides.

The next segments of the GI tract, the **pharynx** and **esophagus,** contribute nothing to digestion but provide the pathway by which ingested materials reach the stomach. The muscles in the walls of these segments control swallowing.

Stomach

The **stomach** is a saclike organ, located between the esophagus and the small intestine; it is the most distensible part of the GI tract. The stomach is divided into four sections:-

1- Cardiac region is where the contents of the esophagus empty into the stomach.

2- Fundus is formed by the upper curvature of the organ.

3- Body is the main central region.

4- Pylorus is the lower region that facilitates emptying the contents into the small intestine.

There are two sphincters keep the contents of the stomach: **cardiac or esophageal sphincter** dividing the tract above and **pyloric sphincter** dividing the stomach from the small intestine.

The functions of the stomach are to store food, to initiate the digestion of proteins, to kill bacteria with the strong acidity of gastric juice, and to move the food into the small intestine as a pasty material called **chyme,** which contains molecular fragments of proteins and polysaccharides, droplets of fat, and salt, water, and various other small molecules ingested in the food.

The glands lining the stomach wall are called **gastric glands**; these glands contain several types of cells that secrete different products:-

1. Goblet cells secrete mucus.

2. Parietal cells secrete hydrochloric acid (HCl).

3. Chief cells secrete pepsinogen, an inactive form of the protein-digesting enzyme pepsin.

Small intestine

The small intestine is divided into three segments: An initial short segment, the **duodenum**, is followed by the **jejunum** and then by the longest segment, the **ileum**. Normally, most of the chyme entering from the stomach is digested and absorbed in the first quarter of the small intestine, in the duodenum and jejunum.

Digestion's final stages and most absorption occur in the small intestine. Here molecules of intact or partially digested carbohydrates, fats, and proteins are broken down by hydrolytic enzymes into monosaccharides, fatty acids, and amino acids. Some of these enzymes are on the luminal surface of the intestinal lining cells, while others are secreted by the pancreas and enter the intestinal lumen.

Digestive enzymes

Reaction	Enzymes	Produced by	Site of Occurrence
Starch + H_20 →maltose	Salivary amylase	Salivary gland	Mouth
	Pancreatic amylase	Pancreas	Small intestine
Maltose + H_20→ glucose	Maltase	Intestinal cells	Small intestine
Protein + H_20 → peptides	Pepsin	Gastric glands	Stomach
	Trypsin	Pancreas	Small intestine
Peptides+ H_20 → amino acids	Peptidase	Intestinal cells	Small intestine
Fats+ H_20 → glycerol + fatty acids	Lipase	Pancreas	Small intestine

The mucosa of the small intestine contains many folds that are covered with tiny fingerlike projections called **villi**. In turn, the villi are covered with microscopic projections called **microvilli**. These structures create a vast surface area through which nutrients can be absorbed. The products of digestion are absorbed across the epithelial cells and enter the blood and/or lymph.

Each villus has a network of capillaries and fine lymphatic vessels called **lacteals** close to its surface. The epithelial cells of the villi transport nutrients from the lumen of the intestine into these capillaries (amino acids and carbohydrates) and lacteals (lipids). The food that remains undigested and unabsorbed passes into the large intestine.

Large intestine

The large intestine is divided into the **cecum**, **colon**, **rectum**, and **anal canal**. The cecum is a blind pouch containing **appendix** (open only at one end) at the beginning of the large intestine.

The large intestine has little or no digestive function, but it does absorb water and electrolytes. Bacteria residing in the intestine, referred to as the **intestinal microflora,** ferment undigested nutrients, make gas, and produce vitamin K and folic acid which are absorbed in the large intestine. Waste materials pass through the ascending colon, transverse colon, descending colon, sigmoid colon, rectum, and anal canal. Then, the feces is excreted through the anus, the external opening of the anal canal.

Pancreas, Liver, and Gallbladder

Pancreas

The pancreas is an elongated gland located behind the stomach. It has both endocrine and exocrine functions. The exocrine portion of the pancreas secretes digestive enzymes and a fluid rich in bicarbonate ions. The high acidity of the chyme coming from the stomach would inactivate the pancreatic enzymes in the small intestine if the acid were not neutralized by the bicarbonate ions.

Liver

The liver is located under the diaphragm on the right side of the upper abdomen; it makes a kind of bed for the gallbladder. The liver plays a major role in metabolism and has a number of functions. It also produces and excretes bile, which is necessary for adequate digestion and absorption of fats.

Gallbladder

The gallbladder is a pear shaped organ that stores about 50 ml of bile until the body needs it for digestion. Bile is stored between meals in the gallbladder. At mealtime, it is squeezed out of the gallbladder, through the bile ducts, and into the intestine to mix with the fat in food.

Neural and endocrine regulation of the digestive system

Neural and endocrine control mechanisms modify the activity of the digestive system.

Neural regulation

The GI tract has its own local nervous system, known as the **enteric nervous system,** in the form of two nerve networks, the **myenteric plexus,** lies between longitudinal and circular muscles layers and the **Meissner's or submucosa plexus,** lies in the submucosa .In addition, nerve fibers from both the sympathetic and parasympathetic branches of the autonomic nervous system enter the intestinal tract and synapse with neurons in both plexuses. Parasympathetic nerves stimulate motility and secretions of the GI tract. The effects of the sympathetic nerves reduce peristalsis and secretory activity and stimulate the contraction of sphincter muscles along the GI tract

It should be noted that not all neural reflexes are indicated by signals within the tract. The sight or smell of food and the emotional state of an individual can

have significant effects on the GI tract, effects that are mediated by the central nervous system via autonomic neurons.

Hormonal regulation

The major hormones that control the functions of the GI system are produced and released by endocrine cells in the mucosa of the stomach and small intestine. One surface of each endocrine cell is exposed to the lumen of the GI tract. At this surface, various chemical substances in the chyme stimulate the cell to release its hormones from the opposite side of the cell into the blood. The main hormones that control digestion and their effects are summarized in the following table:

Gastrointestinal Hormones

Hormone	**Secreted by**	**Stimuli for hormone release**	**Effects**
Gastrin	Stomach	Amino acids, peptides in stomach	-Stimulates parietal cells to secrete HCl. -Stimulates chief cells to secrete pepsinogen.
Secretin	Small intestine	Acid in small intestine	-Stimulates secretion of bicarbonate by pancreas.
Cholecystokinin (CCK)	Small intestine	Amino acids, fatty acids in small intestine	-Stimulates contraction of gallbladder. -Stimulates secretion of pancreatic enzymes. -Inhibits gastric motility and secretion.
Glucose-dependent insulinotropic peptide (GIP)	Small intestine	Glucose, fat in small intestine	-Stimulates secretion of insulin from pancreatic islets. -Inhibits gastric motility and secretion.

Lecture Four

The Circulatory System

The circulatory system consists of a muscular chambered **heart**, a network of closed branching **blood vessels** and **blood**, the fluid which is circulated. Together, the heart and blood vessels comprise the **cardiovascular system**. Humans have a **closed** circulatory system; this means that the blood is always contained in tubes and vessels.

The circulatory system has the following three main functions:

1. It transports gases, nutrients, waste materials, and chemical substances from one part of the body to the other.

2. It regulates internal temperature by altering the blood flow through the skin.

3. It protects against blood loss from injury and against disease-causing microbes or toxic substances.

The heart

The heart is a muscular cone-shaped organ about the size of a closed fist; it is located in the center of the thorax between the lungs, slightly tilted to the left**.** The heart wall is composed of three layers of tissue: the **epicardium**, the **myocardium**, and the **endocardium**. The heart has four chambers, two relatively small upper chambers called **atria** and two larger lower chambers called **ventricles**. The heart can be thought of as two pumps sitting side by side; vertically dividing the two sides of the heart is a wall, known as the **septum.** The septum prevents the mixing of oxygenated (left side) and deoxygenated (right side) blood.

The blood pumped by the right ventricle enters the pulmonary artery, whereas the left ventricle pumps blood into the aorta. The deoxygenated blood pumped into the pulmonary artery is passed on to the lungs from where the oxygenated blood is

carried by the pulmonary veins into the left atrium. This pathway constitutes the **pulmonary circulation**. The oxygenated blood entering the aorta is carried by a network of arteries, arterioles and capillaries to the tissues from where the deoxygenated blood is collected by a system of venules, veins and vena cava and emptied into the right atrium. This is the **systemic circulation.** The heart itself is supplied by blood vessels that are in the heart muscle; the movement of blood through the heart tissues is called **cardiac circulation** (figure 1).

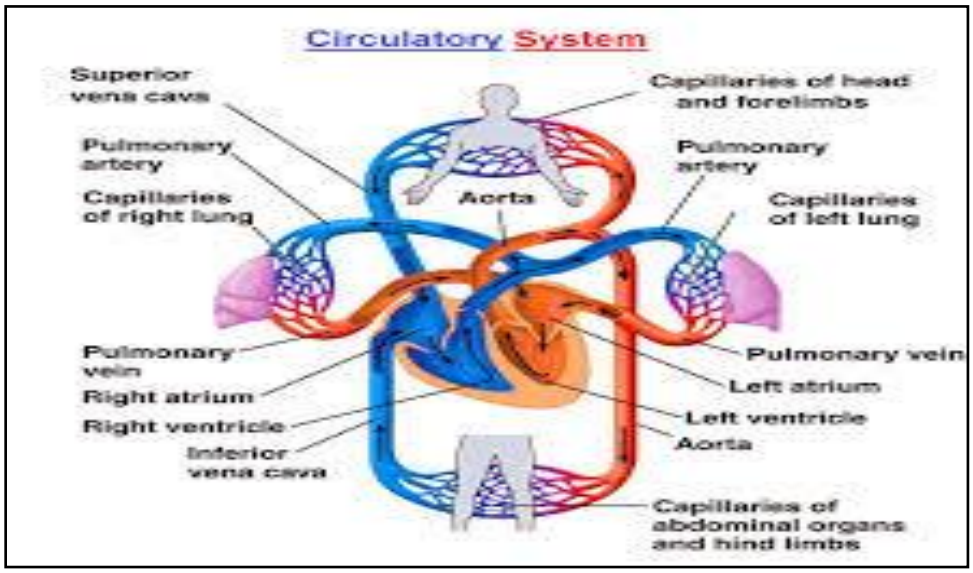

Figure (1)The circulatory system

Heart valves

The heart has four valves inside it. The atria and ventricles are separated from each other by two valves called **atrioventricular valves**. The atrioventricular valve on the right side is called the **tricuspid valve** because it is made up of three flaps. The atrioventricular valve on the left side is called the **bicuspid valve (or mitral valve)** because it has only two flaps.

The aorta and pulmonary trunk possess **aortic** and **pulmonary semilunar valves,** respectively. They so called because of their half-moon shape. The valves in the heart allow the flow of blood only in one direction, and prevent any backward flow (figure 2).

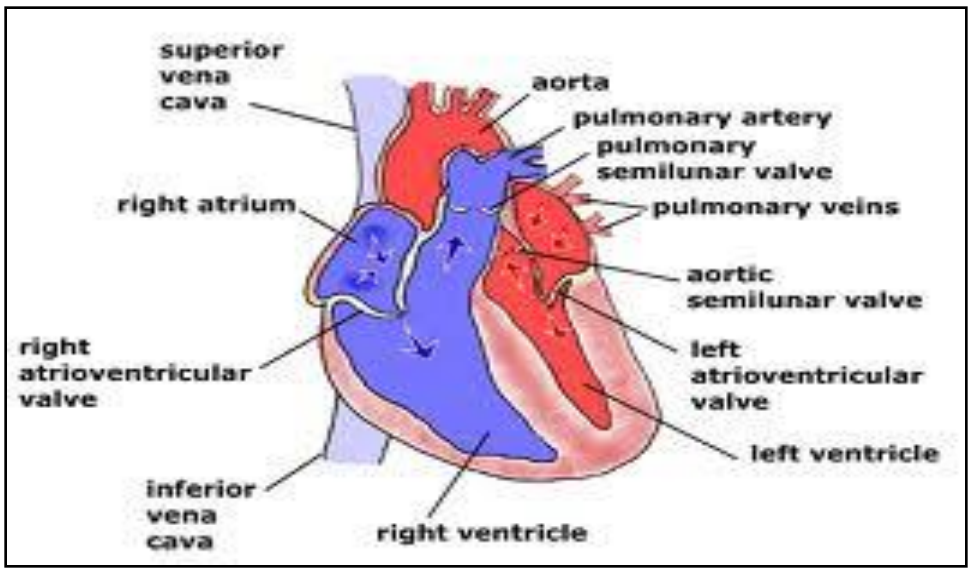

Figure (2)The heart valves

Cardiac cycle

The **cardiac cycle** is the sequence of events in one heartbeat. It is the simultaneous contraction of both atria, followed a fraction of a second later by the simultaneous contraction of both ventricles. A heartbeat has two phases:

Phase 1: Systole is the term for contraction. This occurs when the ventricles contract, closing the atrioventricular valves and opening the semilunar valves to pump blood into the two major vessels leaving the heart.

Phase 2: Diastole is the term for relaxation. This occurs when the ventricles relax, allowing the back pressure of the blood to close the semilunar valves and opening the atrioventricular valves.

During each cardiac cycle two prominent sounds are produced which can be easily heard through a stethoscope. The **first heart sound (lub)** is associated with the closure of the tricuspid and bicuspid valves whereas the **second heart sound (dub)** is associated with the closure of the semilunar valves. These sounds are of clinical diagnostic significance. If any of the valves do not close properly, an extra sound called a **heart murmur** may be heard.

Cardiac output and Stroke volume

The amount of blood pumped by the heart is often referred to as **cardiac output** and is measured in ml/min. Cardiac output is an indicator of the level of oxygen delivered to the body. Two factors contribute to cardiac output: **heart rate** and **stroke volume**. Heart rate is the number of heart beats per minute. Stroke volume is the amount of blood forced out of the heart with each heartbeat.

Cardiac output = heart rate × stroke volume.

The average person has a **stroke volume** of about **70 ml** and a **resting heart rate** of about **70 beats per minute**. This means that the cardiac output for a typical adult at rest is 70 × 70= **4900 ml/minute**.

Contraction of the heart

Within the heart and in the wall of the right atrium, a specialized muscle tissue, called the **sinoatrial (SA) node**, stimulates the muscle cells to contract and relax rhythmically. The SA node is referred to as the **pacemaker**, because it sets the pace for cardiac activity. The SA node generates an electrical signal that spreads over the two atria and makes them contract simultaneously. As the atria contract, the signal reaches another node, called the **atrioventricular (AV) node** which transmits the electrical signal through a bundle of specialized fibers called the **bundle of His** which relay the signal through two branches of bundles that divide into fast-conducting **Purkinje fibers**. The Purkinje fibers initiate the almost simultaneous contraction of all cells of the right and left ventricles. A wave of contraction is initiated by the SA node, which forces blood from the atria into the ventricles. A subsequent wave of contraction begins at the apex of the heart causing the ventricles to forcibly expel blood into the pulmonary artery and the aorta (figure 3) .

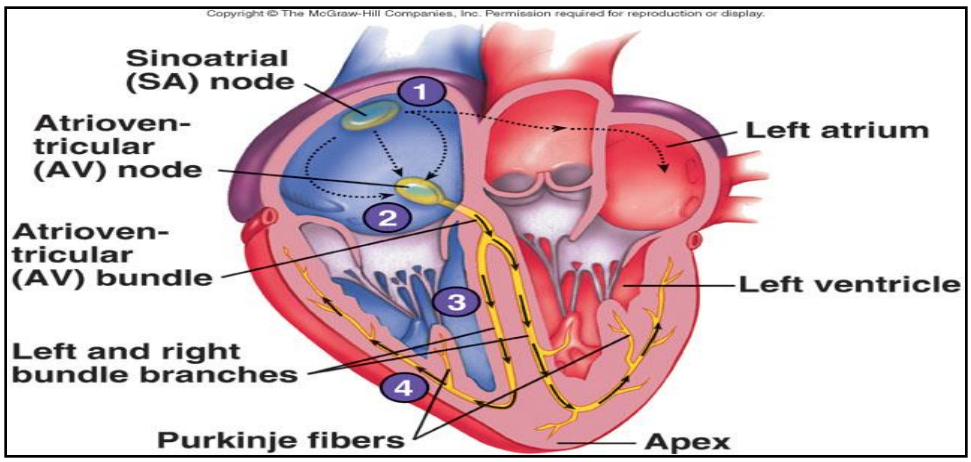

Figure (3)The Conduction system of the heart

The electrocardiogram (ECG)

The electrical pulses that cause the heart to beat create small voltage changes that can be measured by electrodes placed on the skin of the chest. These voltage measurements produce an **electrocardiogram (ECG)** that physicians use to diagnose the health of the heart. ECG is a graphical representation of the electrical activity of the heart during a cardiac cycle. To obtain a standard ECG, a patient is connected to the machine (**electrocardiograph**) with three electrical leads (one to each wrist and to the left ankle) that monitor the heart activity.

Each peak in the ECG is identified with a letter from P to T that corresponds to a specific electrical activity of the heart (figure 4).

The P wave: It represents the **depolarization of the atria**, which leads to the contraction of the atria.

The QRS complex: It represents the **depolarization of the ventricles**, which initiates the ventricular contraction. The contraction starts shortly after Q and marks the beginning of the systole.

The T wave: It represents the return of the ventricles from excited to normal state (**repolarization**). The end of the T-wave marks the end of systole **.**

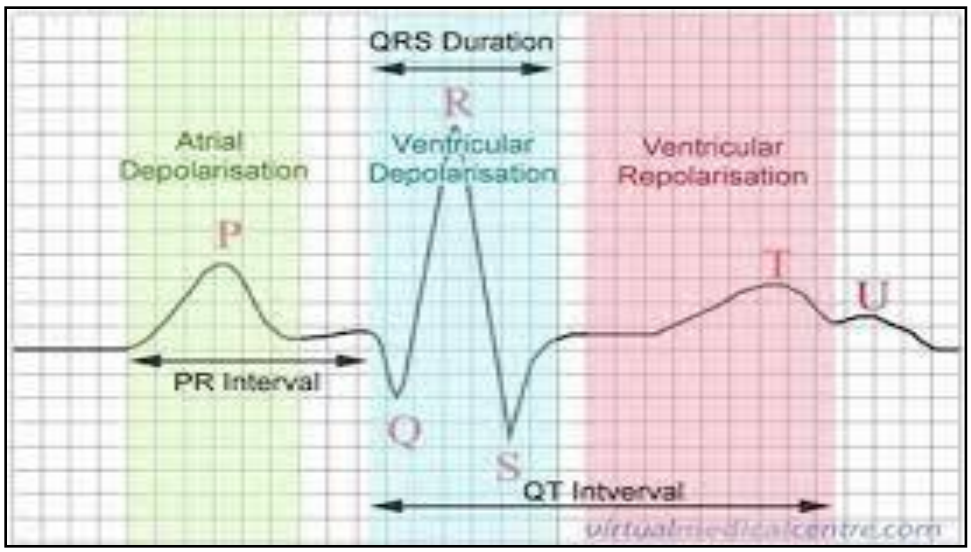

Figure (4)Electrocardiogram

Regulation of cardiac activity

Normal activities of the heart are regulated intrinsically, i.e., auto regulated by specialized muscles (nodal tissue), hence the heart is called **myogenic**. A special neural center in the medulla oblongata can moderate the cardiac function through autonomic nervous system (ANS). Neural signals through the sympathetic nerves (part of ANS) can increase the rate of heart beat, the strength of ventricular contraction and thereby the cardiac output. On the other hand, parasympathetic neural signals (another component of ANS) decrease the rate of heart beat, speed of conduction of action potential and thereby the cardiac output. Adrenal medullar hormones can also increase the cardiac output.

Lecture Five

Respiratory System

The **respiratory system** or **respiratory tract** is the path of air from the nose to the lungs. The organs of the respiratory system ensure that oxygen enters the body and carbon dioxide leaves the body. As air moves along the respiratory tract, it is cleansed, warmed, and moistened. Anatomically, the respiratory tract is divided into two sections:

Upper respiratory tract

Upper respiratory tract includes the organs located outside of the chest cavity (i.e. **nose**, **nasal cavity**, **pharynx**, and **larynx**). Its primary function is to receive the air from the external environment and filter, warm, and humidify it before it reaches the lungs where gas exchange will occur.

Lower respiratory tract

Lower respiratory tract includes the organs located entirely within the chest cavity (i.e. **trachea**, **bronchi**, **bronchioles**, and **alveoli**).

Respiration physiology

The primary function of the respiratory system is to supply the body with oxygen and remove carbon dioxide. In addition to this main process, the respiratory system serves for regulation of blood pH, defense against microbes, and control of body temperature.

The organs of the respiratory system can be divided functionally into the **conducting zone** and the **respiratory zone**. The conducting zone is the airway from the nose or mouth down to the bronchioles; it is responsible for transporting air and any foreign particles. The respiratory zone includes the respiratory

bronchioles down to the alveoli, where gas exchange takes place through a diffusion process. There are four processes of respiration as following:-

1. Breathing or **Ventilation:** It is the exchange of air between the external environment and the alveoli. There are two phases of ventilation; **inspiration (inhalation)** and **expiration (exhalation)**. Air moves into the lungs from the nose or mouth during inspiration and then moves out of the lungs during expiration. During each phase the body changes the lung dimensions to produce a flow of air either in or out of the lungs depending on the pressure in the alveoli. All pressures in the respiratory system are relative to atmospheric pressure (760 mmHg at sea level). Air moves from an area of high pressure to low pressure. The body changes the pressure in the alveoli by changing the volume of the lungs; as volume increases pressure decreases and as volume decreases pressure increases.

2. External respiration: It is the exchange of gases (oxygen and carbon dioxide) between the air in the alveoli and the blood within the pulmonary capillaries.

3. Internal respiration: It is the exchange of gases (oxygen and carbon dioxide) between the blood and tissue fluids.

4. Cellular respiration: It is also called aerobic respiration. It is the process of moving energy from one chemical (glucose) into another (ATP), since all cells use ATP for all metabolic reactions. It is in the mitochondria of the cells where oxygen is actually consumed and carbon dioxide produced.

Inspiration and Expiration:

Inspiration

Inspiration is the active phase of ventilation because it is the phase in which the diaphragm and the external intercostal muscles contract. In its relaxed state, the diaphragm is dome-shaped; during deep inspiration, it contracts and lowers. Also, the external intercostal muscles contract, and the rib cage moves upward and

outward. Following contraction of the diaphragm and the external intercostal muscles, the volume of the thoracic cavity will be larger than it was before. As the thoracic volume increases, the lungs expand. Now the air pressure within the alveoli decreases, creating a partial vacuum. Because alveolar pressure is now less than atmospheric pressure, air naturally flows from outside the body into the respiratory passages and into the alveoli.

Expiration

Expiration is the passive phase of breathing, and no effort is required to bring it about. During expiration, the elastic properties of the thoracic wall and lungs cause them to recoil. In addition, the lungs recoil because the surface tension of the fluid lining the alveoli tends to draw them closed. The diaphragm and external intercostal muscles are usually relaxed when expiration occurs. Contraction of the internal intercostal muscles can force the rib cage to move down and inward. Also, during expiration, the abdominal organs press up against the diaphragm and the rib cage moves downward and inward. The increased pressure in the thoracic cavity helps expel air.

Gas exchange

Respiration includes the exchange of gases in the lungs and the exchange of gases in the tissues. Gases exert pressure, and the amount of pressure each gas exerts is called its **partial pressure**. The exchange of O_2 and CO_2 occurs through **diffusion** which is the net movement of gas molecules from a region that has a higher partial pressure to another region that has a lower partial pressure (figure 1).

External respiration

External respiration refers to the exchange of gases between air in the alveoli and blood in the pulmonary capillaries. In external respiration, gases diffuse in either direction across the walls of the alveoli; O_2 diffuses from the air into the

blood and CO_2 diffuses out of the blood into the air. Most of the CO_2 is carried to the lungs in plasma as bicarbonate ions (HCO_3^-). When blood enters the pulmonary capillaries HCO_3^- and H^+ are converted to carbonic acid (H_2CO_3) and then back into CO_2 and H_2O.The enzyme **carbonic anhydrase,** present in red blood cells, speeds the breakdown of H_2CO_3.

The pressure pattern for O_2 during external respiration is the reverse of that for CO_2. Blood in the pulmonary capillaries is low in O_2, and alveolar air contains a higher partial pressure of O_2. Therefore, O_2 diffuses into plasma and then into red blood cells in the lungs. Hemoglobin takes up this O_2 and becomes **oxyhemoglobin (HbO_2)**.

De-oxygenated blood coming from the pulmonary arteries has PO_2 of 40 mmHg and PCO_2 of 45 mmHg. Oxygenated blood leaving the lungs via the pulmonary veins has PO_2 of 100 mmHg and PCO_2 of 40 mmHg.

Internal respiration

Internal respiration refers to the exchange of gases between the blood in the systemic capillaries and the tissue fluid. Oxygen diffuses out of the blood into the tissues because the PO_2 of tissue fluid is lower than that of blood. Carbon dioxide diffuses into the blood from the tissues because the PCO_2 of tissue fluid is higher than that of blood. After CO_2 diffuses into the blood, it enters the red blood cells, where a small amount is taken up by hemoglobin, forming **carbaminohemoglobin ($HbCO_2$)**.

Most of the CO_2 combines with H_20 forming H_2CO_3, which dissociates to H^+ and HCO_3^-. HCO_3^- diffuses out of red blood cells and is carried in the plasma. The globin portion of hemoglobin combines with excess H^+ produced by the overall reaction, and Hb becomes **reduced hemoglobin (HHb).**

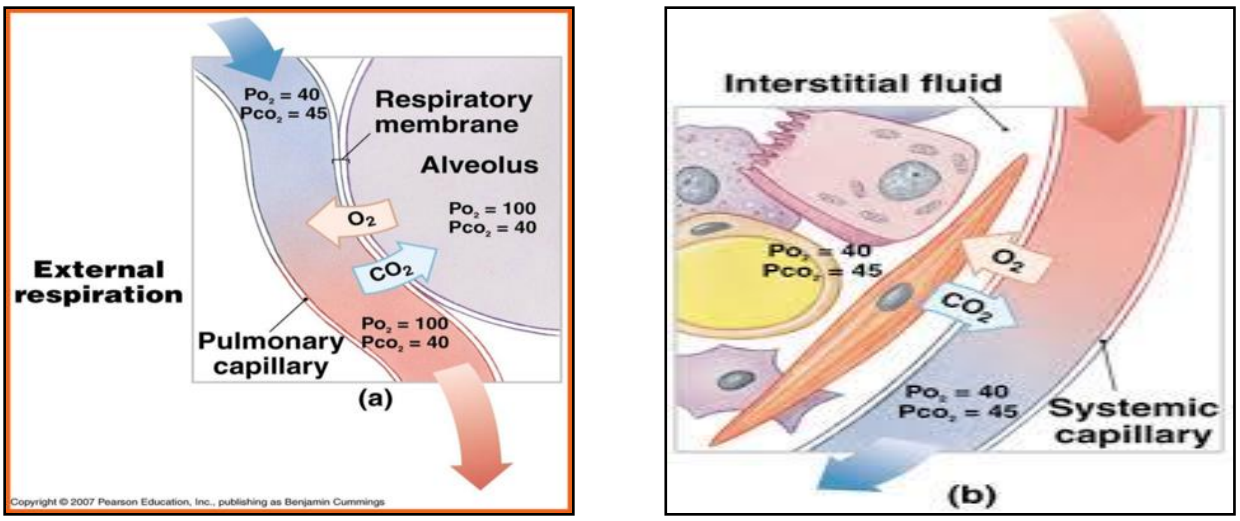

Figure (1) Gas exchange, (a) External respiration, (b) Internal respiration

Regulation of respiration

Normal adults have a breathing rate of 12-20 respirations per minute. The rhythm of ventilation is controlled by a **respiratory center** located in the **medulla oblongata** of the brain. During inspiration, the respiratory center stimulates the diaphragm to contract via the **phrenic nerve** and stimulates the external intercostal muscles to contract via the **intercostal nerves**. Expiration occurs due to a lack of stimulation from the respiratory center to the diaphragm and intercostal muscles. Although the respiratory center automatically controls the rate and depth of breathing, its activity can also be influenced by nervous input and chemical input.

Nervous input: Following forced inspiration, stretch receptors in the alveolar walls initiate inhibitory nerve impulses that travel from the inflated lungs to the respiratory center. This stops the respiratory center from sending out nerve impulses.

Chemical input: The respiratory center is directly sensitive to the levels of H^+. However, when CO_2 enters the blood, it reacts with H_2O and releases H^+. In this way, CO_2 participates in regulating the breathing rate. When H^+ rises in the blood; the respiratory center increases the rate and depth of breathing. The center is not

affected directly by low O_2 levels. However, chemoreceptors in the **carotid bodies,** located in the carotid arteries, and in the **aortic bodies,** located in the aorta, are sensitive to the level of O_2 in the blood. When the concentration of O_2 decreases, these bodies communicate with the respiratory center, and the rate and depth of breathing increase.

Lung volumes and capacities

Several terms have been developed to describe the various physiological volumes and capacities of the lung. Normally the lung volumes are measured with a **spirometer**, while the lung capacity is inferred from the measurements.

Lung volumes and capacities

Volume or Capacity	Definition	Typical value
Tidal volume (TV)	The volume of air that is inspired and exhaled during normal breathing at rest.	500 ml
Inspiratory reserve volume (IRV)	The maximum volume that can be inhaled above the tidal volume.	3000 ml
Expiratory reserve volume (ERV)	The maximum volume of air that can be expired after the expiration of a tidal volume.	1100 ml
Residual volume (RV)	The volume of air in the lungs after maximal expiration.	1200 ml
Functional residual capacity (FRC)	The volume of air left in the lungs that can be exhaled after normal expiration.	2300 ml
Inspiratory capacity (IC)	The volume of maximum inhalation.	3500 ml
Vital capacity (VC)	The maximal volume of air that can be expelled following maximal inspiration.	4600 ml
Total lung capacity (TLC)	The volume of gas in the lungs following maximal inspiration.	5800 ml

Lecture Six

Urinary System

Urinary System is a group of organs in the body concerned with filtering out excess fluid and other substances from the bloodstream. The substances are filtered out from the body in the form of **urine**. Urine is a transparent yellow fluid containing unwanted wastes mostly excess water, salts, and nitrogen compounds (In general 95% water and 5% solutes). Excretion is the process of eliminating, from an organism, waste products of metabolism and other materials that are of no use. The kidneys are the most important excretory organ; they also accomplish several other functions:

1- Regulation of plasma ionic composition such as sodium, potassium, calcium, magnesium, chloride, bicarbonate, and phosphates

2- Regulation of plasma volume by controlling how much water a person excretes. The plasma volume has a direct effect on the total blood volume, which has a direct effect on blood pressure. Salts such as NaCI can cause osmosis, the diffusion of water into the blood.

3- Regulation of plasma hydrogen ion concentration (pH) with the lungs (regulated the acid- base balance) because they control the amount of bicarbonate excreted or held onto. The kidneys help maintain the blood pH mainly by excreting hydrogen ions and reabsorbing bicarbonate ions as needed.

4- Removal of metabolic waste products and foreign substances from the plasma like nitrogenous waste(**urea**, **ammonia**, **creatinine** and **uric acid**) **urea** comes from combines that ammonia with carbon dioxide by the liver .The **creatinine** comes from the metabolic breakdown of creatine phospate (a high-energy phosphate in muscles). **Uric acid** comes from the breakdown of nucleotides. Uric

acid is insoluble and too much uric acid in the blood will build up and form crystals that can collect in the joints and cause gout.

5- Secretion of hormones like **Renin**, it is needed to stimulate the secretion of aldosterone by the adrenal cortex which promotes the kidneys to reabsorb the (Na^+) ions. The kidneys also secrete **erythropoietin** when the blood doesn't have the capacity to carry oxygen; erythropoietin stimulates red blood cell production. Vitamin D from the skin is also activated with help from the kidneys. Calcium (Ca^+) absorption from the digestive tract is promoted by vitamin D.

Formation of Urine:-

The formation of urine involves three major processes: The first is glomerular filtration, which takes place in the renal corpuscles. The second and third are tubular reabsorption and tubular secretion, which take place in the renal tubules (figure 1).

Glomerular Filtration:

Filtration is the process in which blood pressure forces plasma and dissolved material out of capillaries. In **glomerular filtration**, blood pressure forces plasma, dissolved substances, and small proteins out of the glomeruli and into Bowman's capsules, this fluid is no longer plasma but is called **renal filtrate**. The blood pressure in the glomeruli, compared with that in other capillaries, is relatively high, "up to four times", about 60 mmHg (because the diameter of the afferent arteriole going to the glomerulus is 25% larger than normal). The pressure in Bowman's capsule is very low, and its inner, podocyte layer is very permeable, so that approximately 20% to 25% of the blood that enters glomeruli becomes renal filtrate in Bowman's capsules.

The blood cells and larger proteins are too large to be forced out of the glomeruli, so they remain in the blood. Waste products are dissolved in blood plasma, so they pass into the renal filtrate. Useful materials such as nutrients and

minerals are also dissolved in plasma and are also present in renal filtrate. Filtration is not selective with respect to usefulness; it is selective only with respect to size. Therefore, renal filtrate is very much like blood plasma, except that there is far less protein and no blood cells are present.

The **glomerular filtration rate** (GFR) is the amount of renal filtrate formed by the kidneys in 1 minute, and averages 100 to 125 ml per minute (remove about 19% of blood plasma). GFR may be altered if the rate of blood flows through the kidney changes. If blood flow increases, the GFR increases, and more filtrate is formed. If blood flow decreases (as may happen following a severe hemorrhage), the GFR decreases, less filtrate is formed, and urinary output decreases.

Tubular Reabsorption:

Tubular reabsorption takes place from the renal tubules into the peritubular capillaries (the blood pressure in the peritubular capillaries is15 mmHg). In a 24-hour period, the kidneys form 150 to 180 liters of filtrate, and normal urinary output in that time is 1 to 2 liters. Therefore, it becomes apparent that most of the renal filtrate does not become urine. Approximately 99% of the filtrate is reabsorbed back into the blood in the peritubular capillaries. Only about 1% of the filtrate will enter the renal pelvis as urine.

Most reabsorption and secretion (about 65%) take place in the proximal convoluted tubules whose cells have **microvilli** that greatly increase their surface area. Water, Na^+, Cl^-, K^+, glucose, amino acid are reabsorbed in proximal convoluted tubules whale other does not reabsorb like inulin, creatinine . About 20% of filtered Na^+ and Cl^-, 15% of filtered water and cations such as K^+, Ca^{2+} and Mg^{2+} are reabsorbed in the loop of Henle. The distal convoluted tubules and collecting tubules are also important sites for the reabsorption, approximately 7% of the filtered NaCl and about 8-17% of water is reabsorbed. Sodium chloride

reabsorbed into the system increases the osmolarity of blood in comparison to the glomerular filtrate. This reabsorption process allows water (H_2O) to pass from the glomerular filtrate back into the circulatory system. Glucose and various amino acids also are reabsorbed (towards the end of the proximal convoluted tubules) into the circulatory system, these nutrients have carrier molecules that claim the glomerular molecule and release it back into the circulatory system. If all of the carrier molecules are used up, excess glucose or amino acids are set free into the urine.

Reabsorption of Water and Salt:

Direct control of water excretion in the kidneys is exercised by the **anti-diuretic hormone (ADH)**, released by the posterior lobe of the pituitary gland. ADH causes the insertion of water channels into the membranes of cells lining the collecting ducts, allowing water reabsorption to occur. Without ADH, little water is reabsorbed in the collecting ducts and dilute urine is excreted. There are several factors that influence the secretion of ADH. The first of these happen when the blood plasma gets too concentrated, when this occurs, special receptors in the hypothalamus release ADH. When blood pressure falls, stretch receptors in the aorta and carotid arteries stimulate ADH secretion to increase volume of the blood.

Aldosterone is secreted by the adrenal cortex in response to a high blood potassium level, to a low blood sodium level, or to a decrease in blood pressure. Aldosterone promotes the excretion of potassium ions and the reabsorption of sodium ions, when aldosterone stimulates the reabsorption of Na^+ ions, water follows from the filtrate back to the blood. This helps maintain normal blood volume and blood pressure. The release of Aldosterone is initiated by the secretion of renin the enzyme that converts angiotensinogen (a large plasma protein produced by the liver) into **Angiotensin I** and eventually into **Angiotensin II** which stimulates the adrenal cortex to produce aldosterone.

The antagonist to aldosterone is **atrial natriuretic peptide** (ANP), which is secreted by the atria of the heart when the atrial walls are stretched by high blood pressure or greater blood volume. ANP inhibits the secretion of renin by the juxtaglomerular apparatus and the secretion of the aldosterone by the adrenal cortex. This promotes the excretion of sodium. When sodium is excreted so is water. This causes blood pressure and volume to decrease.

Tubular Secretion:

Some substances are removed from blood through the peritubular capillary network into the distal convoluted tubule or collecting duct and K^+ and H^+ are secreted in these segments .This mechanism also changes the composition of urine. In **tubular secretion**, substances are actively secreted from the blood in the peritubular capillaries into the filtrate in the renal tubules. Waste products, such as ammonia and some creatinine, and the metabolic products of medications may be secreted into the filtrate to be eliminated in urine. Hydrogen ions (H^+) may be secreted by the tubule cells to help maintain the normal pH of blood.

Diseases of the Kidney:-

1- Diabetic nephropathy; Is a progressive kidney disease caused by angiopathy of capillaries in the kidney glomeruli. It is characterized by nodular glomerulosclerosis. It is due to longstanding diabetes mellitus.

In medicine **hematuria** (or "haematuria") is the presence of blood in the urine. It is a sign of a large number of diseases of the kidneys and the urinary tract, ranging from trivial to lethal.

2- Kidney stones: Also known as nephrolithiases, urolithiases or renal calculi, are solid accretions (crystals) of dissolved minerals in urine found inside the kidneys or ureters. They vary in size from as small as a grain of sand to as large as a golf ball. Kidney stones typically leave the body in the urine stream; if they grow relatively large before passing (on the order of millimeters), obstruction of a ureter

and distention with urine can cause severe pain most commonly felt in the flank, lower abdomen and groin. Kidney stones are unrelated to gallstones.

3- Pyelonephritis: When an infection of the renal pelvis and calices, called pyelitis, spreads to involve the rest of the kidney as well, the result is pyelonephritis. It usually results from the spread of fecal bacterium Escherichia coli from the anal region superiorly through the urinary tract. In severe cases, the kidney swells and scars, abscesses form, and the renal pelvis fill with pus. Left untreated, the infected kidney may be severely damaged, but administration of antibiotics usually achieves a total cure.

4- Urinary tract infections (UTI's): The second most common type of bacterial infections is UTI's. In the hospital indwelling catheters and straight catheterizing predispose the opportunity for urinary tract infections. In females there are three stages in life that predispose urinary tract infections that is menarche, manipulation between intercourse, and menopause.

5- Glomerulonephritis: Inflammation of the glomerular can be caused by immunologic abnormalities, drugs or toxins, vascular disorders, and systemic diseases. Glomerulonephritis can be acute, chronic or progressive.

Two major changes in the urine are distinctive of glomerulonephritis: hematuria and proteinuria with albumin as the major protein. There is also a decrease in urine as there is a decrease in GFR (glomerular filtration rate).

6- Renal Failure: Uremia is a syndrome of renal failure and includes elevated blood urea and creatinine levels. Acute renal failure can be reversed if diagnosed early. Acute renal failure can be caused by severe hypotension or severe glomerular disease.

Diabetes Insipidus:

This is caused by the deficiency of or decrease of ADH. The person with (DI) has the inability to concentrate their urine in water restriction, in turn they will void up 3 to 20 liters/day. There are two forms of (DI), neurogenic, and nephrogenic. In nephrogenic (DI) the kidneys do not respond to ADH. Usually the nephrogenic (DI) is characterized by the impairment of the urine concentrating capability of the kidney along with concentration of water.

The cause may be a genetic trait, electrolyte disorder, or side effect of drugs. In the neurogenic (DI), it is usually caused by head injury near the hypophysisal tract.

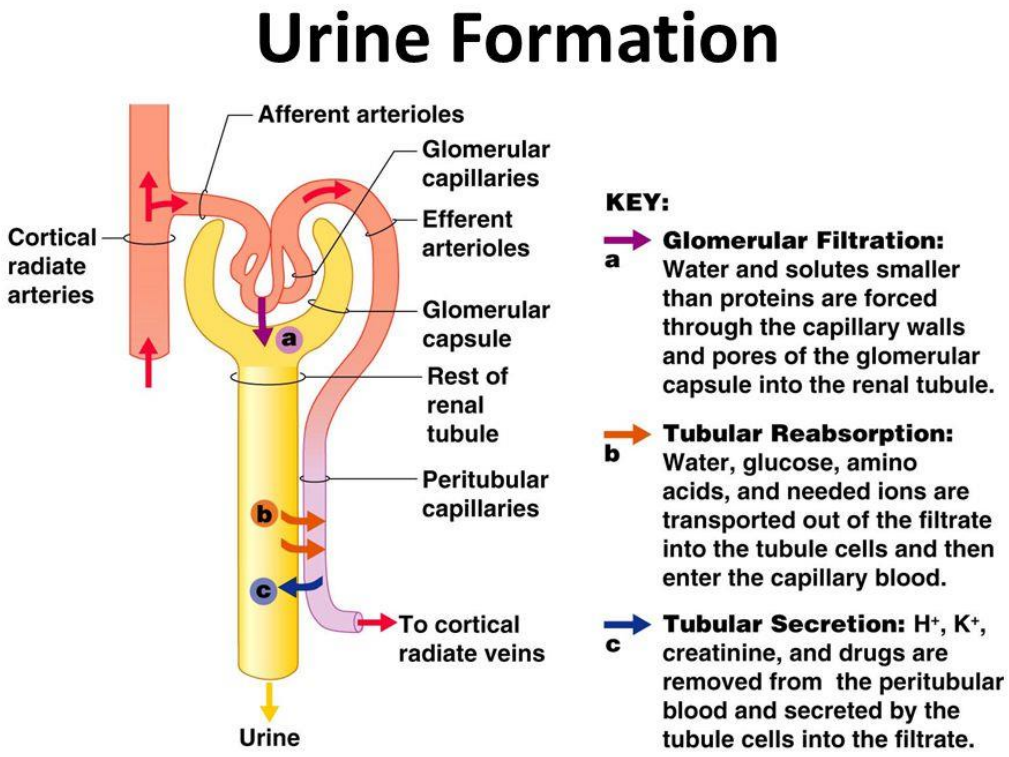

Figure (1): Formation of urine

Lecture Seven

Muscle Physiology

Muscle tissue is composed of specialized cells (**fibers**) that respond to stimulation from the nervous system by undergoing internal changes that cause them to shorten. As muscle tissue shortens, it exerts physical forces on other tissues and organs to produce movement; these movements include voluntary motion of body parts, blood circulation, respiratory activities, propulsion of materials along the digestive tract and waste elimination.

The three histological types of muscle in the body are **skeletal** muscle, **cardiac** muscle, and **smooth** muscle. They vary in their appearance, location, physiology, internal organization, and means of control by the nervous system. Regular transverse bands along the length of the fibers are present in **striated** muscle and absent in **smooth** muscle. Functionally, muscle either is under the control of the will (**voluntary** muscle) or is not (**involuntary** muscle) **.**

Thin and thick filaments:

The bundles of myofilaments are classified as thin myofilaments (usually simply called **thin filaments**) and thick myofilaments (usually simply called **thick filaments**) . **Thin filaments** are only about 5-6 nanometers in diameter. They are composed primarily of two strands of the protein **actin** that are twisted around each other to form a helical shape. In each helical strand of actin, many small, spherical molecules connected to each other form a long filament resembling a string of beads. Each spherical molecule has a binding site for **myosin**, the protein that makes up the thick filaments. Tow regulatory proteins, **tropomyosin** and **troponin**, are part of thin filaments. The tropomyosin molecule resembles a shorter, thinner, twisted filament that covers small sections of the actin strands, while the troponin has two functions: (1) attaching to actin to anchor the troponin

in place, and (2) attaching to tropomyosin to hold it in place over the surface of the actin.

In contrast, **thick filaments** are about twice as large as thin filaments and have a diameter of about 11 nanometers. Thick filaments are assembled from bundles of the protein **myosin**. Each myosin molecule in a thick filament consists of two strands: each strand has a free, globular head and an attached, elongated tail. The myosin molecules are oriented on either end of the thick filaments that the long tails point toward the center of the filament and the heads point toward the edges of the filament and project outward toward the surrounding thin filament. Myosin heads are also referred to as **crossbridges** because during a contraction they bind thick filaments to thin filaments, thus forming a "bridge" between them.

Organization of sarcomere:

A **sarcomere** is the functional contractile unit of skeletal muscle fiber. A sarcomere is defined as the distance from one **Z disc** to the next adjacent **Z disc**. Myofibrils contain multiple **Z disc**; thus, there are numerous sarcomeres in each myofibril. Each sarcomere shortens as the muscle fiber contracts. An individual sarcomere is shown in figure 10.6. Notice that thick filaments are positioned at the center of the sarcomere. A cross section through the lateral parts of the **A band** reveals the relative sizes, arrangements, and organization of thick and thin filaments. In cross section, each thin filament is sandwiched by three thick filaments that form a triangle at its periphery, and similarly each thick filament when viewed in cross section is surrounding by six thin filaments.

Contraction of skeletal muscle fibers:

A contracting muscle fiber typically shortens in length and exerts tension on the portion of the skeleton where it is attached. The thick and thin protein filaments in sarcomeres interact to cause muscle contraction. The mechanism for contraction is explained by the sliding filament theory.

The sliding filament theory:

According to the **sliding filament theory**, when a muscle contracts, thick and thin filaments slide past each other, and the sarcomere shortens.

The following changes occur within a sarcomere during contraction:

1- The width of the **A band** remains constant, but the H zone disappears.

2- The **Z discs** in one sarcomere move closer together.

3- The sarcomere narrows.

4- The **I bands** narrows.

Thick and thin filaments maintain their same length, whether the muscle is relaxed or contracted. However, during muscle contraction, the relative position between the thick and thin filaments changed markedly. Muscle contraction begins when a nerve impulse stimulates an impulse in a muscle fiber. Each muscle fiber is controlled by one motor neuron. The motor neuron transmits the effect of a nerve impulse to the muscle fiber at a **neuromuscular junction**, the point where a motor neuron meets a skeletal muscle fiber . The neuromuscular junction has the following components:

1- The **synaptic knob** of the neuron is an expanded tip of an axon. A nerve impulse travels through the axon to the synaptic knob.

2- The synaptic knob cytoplasm houses numerous **synaptic vesicles** (small membrane sacs) filled with molecules of the neurotransmitter **acetylcholine** (**ACh**).

3- The **motor end plate** is a specialized region of sarcolemma. It has folds and indentations to increase the membrane surface area covered by the synaptic knob.

4- The **synaptic cleft** is a narrow space separating the synaptic knob and the motor end plate.

5- **ACh receptors** in the motor end plate act like doors that normally are closed. **ACh** is the only "key" to open these receptor doors.

6- The enzyme **acetylcholinesterase (AChE)** resides in the synaptic cleft and breaks down molecules of **ACh**.

Physiology of muscle contraction:

The arrival of a nerve impulse at the synaptic knob causes synaptic vesicles to release **ACh** into the synaptic cleft. **ACh** attaches to receptors in the motor end plate. This causes the receptors to open, allowing sodium (Na+) ions to enter the muscle fiber. This ion movement changes the voltage (potential) across the sarcolemma, and a muscle impulse is initiated. The muscle impulse travels along the sarcolemma and into the muscle fiber by the T-tubules. The muscle impulse continues to spread throughout the muscle fiber as long as **ACh** keeps the receptors open. Usually **ACh** is quickly broken down and removed from the receptor by acetylcholinesterase.

Interaction between the T-tubules and terminal cisternae:

Recall that T-tubules distribute the muscle impulse through the inside of the muscle fiber, and they are sandwiched by terminal cisternae, which are reservoirs storing the calcium ions required for muscle contraction. Spread of a muscle impulse along the T-tubule membrane causes calcium ions to leak out of the terminal cisternae into the sarcoplasm of the muscle fiber. These calcium ions diffuse throughout the sarcoplasm and attach to the **troponin** in the thin filaments.

Interaction between thick and thin filaments:

As the calcium ion concentration rises in the sarcoplasm, some calcium ions bind to one troponin molecules subunit, causing the troponin to change conformation. Recall that troponin molecules are attached to tropomyosin. When the fiber is at rest, the tropomyosin molecules block active sites for myosin on the actin. Thus, the thick filaments are unable to attach to thin filaments. So as troponin changes shape, the tropomyosin is moved away from the active sites on actin molecules. Contraction of muscle fiber requires that the myosin heads in the thick filament bind to active site on actin molecules within the thin filaments .

The mechanism of sliding:

After the myosin heads bind to thin filaments, myofilament sliding begins. As crossbridges form, the myosin heads pivot toward the center of the sarcomere. This action pulls the thin filaments toward the sarcomere center, causing the Z discs to move closer together as the sarcomere shortens. When the myosin head completes pivoting, the crossbridge detaches and returns to its original cocked position, ready to repeat the cycle of "attach, pivot, detach, and return". Energy to drive this myosin movement is provided in the form of ATP. Myosin head attachment and pivoting do not require energy, but ATP is needed in order for the myosin head crossbridge to detach from actin. Energy is released to power the detachment when ATP binds to the myosin head and is broken down into ADP and P (phosphate). The return of the fiber to its resting length is completely passive and results from the pull of antagonistic muscles and from elastic forces in the contracting muscle fibers.

Lecture Eight

Thermal Regulation

On the basis of body temperature animals are classified as warm blooded (**homeothermic**) animals which are capable of maintaining a relatively constant body temperature in spite of great variations of external temperature or cold blooded (**poikilothermic**) animals in which the body temperature varies with that of the environment. Poikilotherms include invertebrates and aquatic animals like fishes and amphibians.

Some animals have a high rate of thermal conductance and low rate of heat production. Such animals acquire heat from the environment and regulate their body temperature quite independent of the heat produced in the body; these animals are known as **ectothermic**. In contrast to this, a few animals produce sufficient heat due to their own oxidative metabolism and maintain body temperature at a constant level. Such animals are called **endothermic** which include homeotherms like birds and mammals. Another category of animals which do not maintain constant body temperature, but during activity they show endothermic regulation, these are called **heterothermic** animals, they are also called facultative endotherms since they are capable of regulating physiological temperature at certain time only.

The habitats of animals can be divided into **terrestrial**, **aquatic** and **aerial**. Animals living in terrestrial environment have an acute problem of temperature because of the radiant heat of the sun. Also air has a low specific heat and so it gains or loses heat rapidly. Animals living in aquatic habitats do not face acute thermal problems because water has a high specific heat and it gains or loses heat slowly, thus making little changes in temperature. Aerial animals like birds have a higher limit of thermal tolerance (35C º-42C º) due to higher rate of metabolism.

Heat Production

Cell respiration, the process that releases energy from food to produce ATP, also produces heat as one of its energy products. Although cell respiration takes place constantly, many factors influence the rate of this process:

1. The hormone **thyroxin** (and T3), produced by the thyroid gland, increases the rate of cell respiration and heat production. The secretion of thyroxin is regulated by the body's rate of energy production, the metabolic rate itself. When the metabolic rate decreases, the thyroid gland is stimulated to secrete more thyroxin. As thyroxin increases the rate of cell respiration, a negative feedback mechanism inhibits further secretion until metabolic rate decreases again.

2. In stress situations, **epinephrine** and **norepinephrine** are secreted by the adrenal medulla, and the **sympathetic** nervous system becomes more active. Epinephrine increases the rate of cell respiration, especially in organs such as the heart, skeletal muscles, and liver. Sympathetic stimulation also increases the activity of these organs. The increased production of ATP to meet the demands of the stress situation also means that more heat will be produced.

3. Organs that are normally active (producing ATP) are significant sources of heat when the body is at rest. The skeletal muscles, for example, are usually in a state of slight contraction called muscle tone. Because even slight contraction requires ATP, the muscles are also producing heat. This amounts to about 25% of the total body heat at rest and much more during exercise, when more ATP is produced.

The liver is another organ that is continually active, producing ATP to supply energy for its many functions. As a result, the liver produces as much as 20% of the total body heat at rest. The heat produced by these active organs is dispersed throughout the body by the blood. As the relatively cooler blood flows through organs such as the muscles and liver, the heat they produce is transferred to the blood, warming it.

4. The intake of food also increases heat production, because the metabolic activity of the digestive tract is increased. Heat is generated as the digestive organs produce ATP for peristalsis and for the synthesis of digestive enzymes.

5. Changes in body temperature also have an effect on metabolic rate and heat production. This becomes clinically important when a person has a **fever**, an abnormally high body temperature.

Heat Loss through the Skin

Because the skin covers the body, most body heat is lost from the skin to the environment. When the environment is cooler than body temperature (as it usually is), heat loss is unavoidable.

The amount of heat that is lost is determined by blood flow through the skin and by the activity of sweat glands. Blood flow through the skin influences the amount of heat lost by the processes of radiation, conduction, and convection. **Radiation** means that heat from the body is transferred to cooler objects not touching the skin. **Conduction** is the loss of heat to cooler air or objects, such as clothing, that touch the skin.

Convection means that air currents move the warmer air away from the skin surface and facilitate the loss of heat; this is why a fan makes us feel cooler on hot days. The temperature of the skin and the subsequent loss of heat are determined by blood flow through the skin. The arterioles in the dermis may constrict or dilate to decrease or increase blood flow. In a cold environment, **vasoconstriction** decreases blood flow through the dermis and thereby decreases heat loss. In a warm environment, **vasodilation** in the dermis increases blood flow to the body surface and loss of heat to the environment.

The other mechanism by which heat is lost from the skin is sweating. The **sweat glands** secrete sweat (water) onto the skin surface and excess body heat evaporates the sweat. Sweating is most efficient when the humidity of the

surrounding air is low. Humidity is the percentage of the maximum amount of water vapor the atmosphere can contain. A humidity reading of 90% means that the air is already 90% saturated with water vapor and can hold little more. In such a situation, sweat does not readily evaporate, but instead remains on the skin even as more sweat is secreted. If the humidity is 40%, however, the air can hold a great deal more water vapor, and sweat evaporates quickly from the skin surface, removing excess body heat. In air that is completely dry, a person may tolerate a temperature of 75C º for nearly 1 hour.

Although sweating is a very effective mechanism of heat loss, it does have a disadvantage in that it requires the loss of water in order to also lose heat. Water loss during sweating may rapidly lead to dehydration, and the water lost must be replaced by drinking fluids. Small amounts of heat are also lost in what is called "insensible water loss." Because the skin is not like a plastic bag, but is somewhat permeable to water, a small amount of water diffuses through the skin and is evaporated by body heat. Compared to sweating, however, insensible water loss is a minor source of heat loss.

Heat Loss through the Respiratory Tract

Heat is lost from the respiratory tract as the warmth of the respiratory mucosa evaporates some water from the living epithelial surface. The water vapor formed is exhaled, and a small amount of heat is lost.

Animals such as dogs that do not have numerous sweat glands often pant in warm weather. Panting is the rapid movement of air into and out of the upper respiratory passages, where the warm surfaces evaporate large amounts of water. In this way the animal may lose large amounts of heat.

Heat Loss through the Urinary and Digestive Tracts

When excreted, urine and feces are at body temperature, and their elimination results in a very small amount of heat loss.

Regulation of Body Temperature

The **hypothalamus** is responsible for the regulation of body temperature and is considered the “thermostat" of the body. As the thermostat, the hypothalamus maintains the “setting” of body temperature by balancing heat production and heat loss to keep the body at the set temperature. To do this, the hypothalamus must receive information about the temperature within the body and about the environmental temperature. Specialized neurons of the hypothalamus detect changes in the temperature of the blood that flows through the brain. The temperature receptors in the skin provide information about the external temperature changes to which the body is exposed. The hypothalamus then integrates this sensory information and promotes the necessary responses to maintain body temperature within the normal range.

Mechanisms to Increase Heat Loss

In a warm environment or during exercise, the body temperature tends to rise, and greater heat loss is needed. This is accomplished by vasodilation in the dermis and an increase in sweating. Vasodilation brings more warm blood close to the body surface, and heat is lost to the environment. However, if the environmental temperature is close to or higher than body temperature, this mechanism becomes ineffective. The second mechanism is increased sweating, in which excess body heat evaporates the sweat on the skin surface. As mentioned previously, sweating becomes inefficient when the atmospheric humidity is high. On hot days, heat production may also be decreased by a decrease in muscle tone. This is why we may feel very sluggish on hot days; our muscles are even slightly less contracted than usual and are slower to respond.

Mechanisms to Conserve Heat

In a cold environment, heat loss from the body is unavoidable but may be reduced to some extent. Vasoconstriction in the dermis shunts blood away from the body surface, so that more heat is kept in the core of the body. Sweating decreases, and will stop completely if the temperature of the hypothalamus falls below about 37C º. If these mechanisms are not sufficient to prevent the body temperature from dropping, more heat maybe produced by increasing muscle tone.

When this greater muscle tone becomes noticeable and rhythmic, it is called shivering and may increase heat production by as much as five times the normal. People also have behavioral responses to cold, and these too are important to prevent heat loss.

Low temperature effects

The protoplasm can exist in living state between 0C º and 45C º and freezes a few degrees below zero. Freezing causes:

1- Formation the ice crystals in the cell and disturbs the cell organization.

2- Metabolism is greatly lowered and as such the rate of oxygen consumption is also very low because the diffusion of O2 and CO2 through the ice is very low.

3- The enzymes become inactive.

Lecture Nine

The Lymphatic System

Water and plasma are forced from the capillaries into intracellular spaces; this interstitial fluid transports materials between the cells. Most of this fluid is collected in the capillaries of a secondary system which is called the **lymphatic system.** The lymphatic system consists of a fluid (lymph), lymphatic vessels that transport the lymph, and lymphatic organs(figure 1and 2). The lymphatic system has three basic functions:

1- Removal of excess fluids from body tissues and its return to the bloodstream.

2- Absorption of fatty acids and subsequent transport to the blood.

3- Formation of white blood cells, and initiation of immunity through the formation of antibodies.

Lymphatic vessels and ducts

The lymphatic vessels are similar in structure to the cardiovascular veins, meaning they also have valves. They are dependent upon the contraction of skeletal muscle, respiratory movements and valves that do not allow backward flow. The vessels merge before entering one of two ducts:-

Thoracic duct: This duct serves the abdomen, lower extremities and the left side of the upper body.

Right lymphatic duct: This duct serves all of the right side of the upper body and thoracic area.

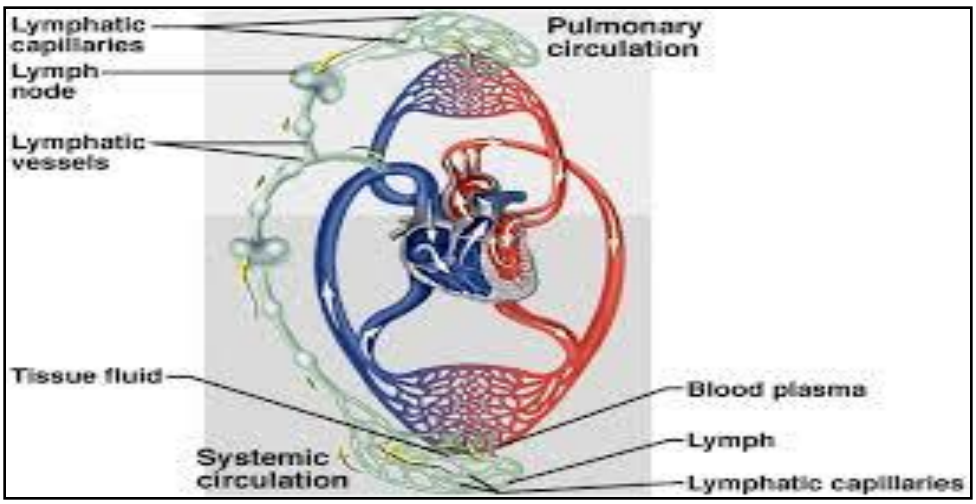

Figure (1).The lymphatic system

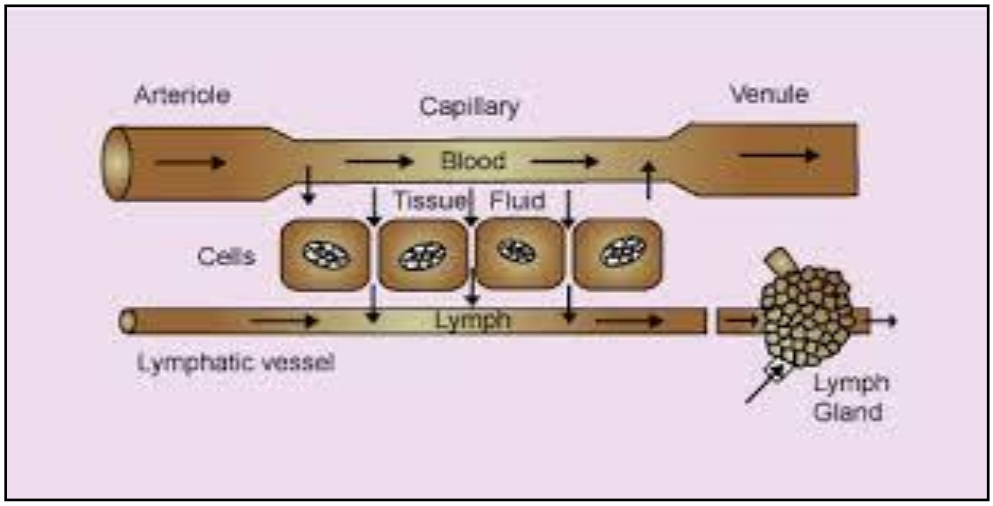

Figure (2).Components of the lymphatic system

Lymphatic organs

Lymphatic organs are subdivided into primary and secondary lymphatic organs. The **primary lymphatic organs** are the **red bone marrow** and the **thymus**. They are the site of production and maturation of lymphocytes, the type of white blood cell that carries out the most important work of the immune system. The **secondary lymphatic organs** include the **lymph nodes, spleen**, **tonsils**, **Peyer's patches**, and the **appendix**. They also play an important role in the

immune system as they are places where lymphocytes find and bind with antigens(figure 3).

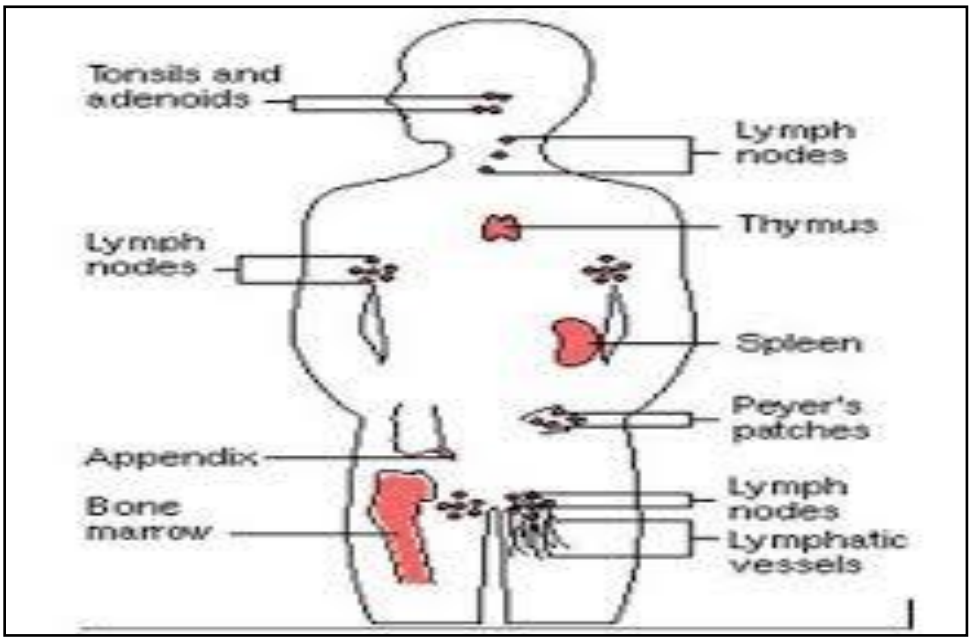

Figure (3).The lymphatic organs

Red bone marrow

Red bone marrow, the soft, spongy, nutrient rich tissue in the cavities of certain long bones, is the organ that is the site of blood cell production. It is also the site of maturation of **B lymphocytes**.

Thymus gland

The thymus gland is a soft organ with two lobes that is located in the upper thoracic cavity posterior to the sternum. It is divided into an outer cortex and an inner medulla. It is an organ that is more active in children, and shrinks as we get older. **T lymphocytes** mature in the thymus. Also, the thymus gland produces a hormone, **thymosin** which thought to aid in the maturation of T lymphocytes.

Lymph nodes

The lymph nodes are small oval shaped structures located along the lymphatic vessels. They act as filters, with an internal connective tissue filled with lymphocytes that collect and destroy bacteria and viruses. They concentrated in the neck, armpit, groin, and abdominal cavity.

The spleen

The spleen is the largest of the lymphatic organs and lies in the left part of the abdominal cavity between the stomach and the diaphragm. It is divided into two partial compartments known as **white pulp** and **red pulp**. The white pulp contains lymphocytes and the red pulp contains venous sinuses. When blood enters the spleen and flows through the sinuses for filtration, lymphocytes react to pathogens; macrophages engulf debris and remove old, worn out red blood cells.

Tonsils

The tonsils are a group of small rounded organs in the pharynx. They are filled with lymphocytes, macrophages, and macrophage-like cells. Their lymphocytes respond to microbes that arrive by way of ingested food as well as inspired air.

Peyer's patches

Peyer's patches are lymphoid tissues found in the wall of the small intestine, although they're more concentrated in the ileum.

Appendix

Appendix extends from the inferior end of the large intestine's cecum. The submucosa of the appendix contains many masses of lymphoid tissue. The presence of lymphoid tissue suggests that the appendix may play a role in the immune system.

Lecture Ten

Endocrine System

The endocrine system is a network of glands that produce and secrete hormones, chemical substances produced in the body that regulate the activity of cells or organs. These hormones regulate the body's growth, metabolism (the physical and chemical processes of the body), and sexual development and function. The hormones are released into the bloodstream and may affect one or several organs throughout the body.

The Hormones

Hormones are chemical messengers that are secreted directly into the blood, which carries them to organs and tissues of the body to exert their functions. Hormones may reach all parts of the body, but only certain types of cells, target cells, are equipped to respond.

All hormones act on cells by way of their ‘receptors’. Each hormone has its own receptor to which it binds, matching rather like a lock and key. This is why hormones circulating throughout the body in the blood may leave capillaries to enter the extracellular fluid of many tissues, but act only on those cells which possess the appropriate receptor. There are many types of hormones that act on different aspects of bodily functions and processes. Some of these include:

- Development and growth
- Metabolism of food items
- Sexual function and reproductive growth and health
- Cognitive function and mood
- Maintenance of body temperature and thirst.

The endocrine system is regulated by feedback in much the same way that a thermostat regulates the temperature in a room. For the hormones that are regulated by the pituitary gland, a signal is sent from the hypothalamus to the pituitary gland in the form of a "releasing hormone," which stimulates the pituitary to secrete a "stimulating hormone" into the circulation. The stimulating hormone then signals the target gland to secrete its hormone. As the level of this hormone rises in the circulation, the hypothalamus and the pituitary gland shut down secretion of the releasing hormone and the stimulating hormone, which in turn slows the secretion by the target gland. This system results in stable blood concentrations of the hormones that are regulated by the pituitary gland.

Types of Hormones

There are three types of hormones that can be grouped by their chemical structure: Steroids, Peptides and Amines.

1- Steroid hormones that are secreted by the gonads, adrenal cortex, and placenta. Two common steroid hormones are progesterone and testosterone.
2- Peptide hormones include oxytocin, luteinizing hormone, a thyrotropin releasing hormone.
3- Amine hormones include epinephrine, norepinephrine, T3 (triiodothyroxin), and T4 (tetraiodothyroxin).

Hypothalamus

Hypothalamus is located above the pituitary gland near the base of the brain. One of the most important functions is to link the nervous system to the endocrine system via the pituitary gland. The hypothalamus is responsible for regulating certain metabolic processes and other activities of the autonomic nervous system.

It synthesizes and secretes certain neurohormones, called releasing hormones or hypothalamic hormones, and these in turn stimulate or inhibit the secretion of hormones from the pituitary gland. The hypothalamus controls body temperature, hunger, important aspects of parenting and maternal attachment behaviors, thirst, fatigue, sleep, circadian rhythms, and is important in certain social behaviors, such as sexual and aggressive behaviors.

Pituitary Gland

The pituitary gland is located at the base of the brain. It is composed of two parts, the anterior and posterior pituitary glands. The pituitary controls the hormonal secretions of numerous endocrine glands.

Hormones of the Anterior Pituitary

1. **Growth Hormone (GH): It** stimulates growth, cell reproduction, and cell regeneration in humans and other animals. It is thus important in human development. GH also stimulates production of Insulin-like growth factor 1 (IGF-1) and increases the concentration of glucose and free fatty acids.
2. **Prolactin (PRL)**: It stimulates the mammary glands to produce milk (lactation).
3. **Thyroid-stimulating hormone (TSH):** It stimulates the thyroid gland to produce thyroxine (T_4), and then triiodothyronine (T_3) which stimulates the metabolism of almost every tissue in the body.
4. **Adrenocorticotropic hormone** (**ACTH):** It stimulates secretion of glucocorticoid steroid hormones from adrenal cortex cells
5. **Gonadotropic hormones:** They regulate hormonal activity of the gonads:

I. Follicle-stimulating hormone (FSH) which stimulates follicle development in ovaries and sperm development in testes. It regulates the development, growth, pubertal maturation, and reproductive processes of the body.
II. Luteinizing hormone (LH) which triggers ovulation, causes ruptured follicle to become the corpus luteum and stimulates testosterone production in males.

Release of these hormones is controlled by releasing and inhibiting hormones produced by the hypothalamus.

Hormones of the Posterior Pituitary

1. **Oxytocin**: It stimulates contractions of the uterus during labor and causes milk ejection.

2. **Antidiuretic hormone (ADH):** It causes the kidneys to reabsorb solute-free water and return it to the circulation from the tubules of the nephron. It constricts arterioles, which increases peripheral vascular resistance and raises arterial blood pressure (vasopressin).

Thyroid gland

Thyroid gland consists of two lobes located on either side of the trachea or windpipe in the lower part of the neck. The lobes are conical and have upper and lower poles. Microscopically, it consists of many follicles, their shape depends on the stimulating by thyrotrophin (thyroid stimulating hormone, TSH).

Thyroid gland secretes two types of hormones:

1. The follicular cells which produce thyroid hormones (non-steroid hormones); Triiodothyronine (T3) and Thyroxine (T4) that regulate

metabolism, increases protein synthesis, promote glycolysis, gluconeogenesis and glucose uptake.

2. Calcitonin: plays a role in calcium homeostasis.

Secretion of the two thyroid hormones is regulated by thyroid-stimulating hormone (TSH), which is secreted from the anterior pituitary gland. TSH is regulated by thyrotropin-releasing hormone (TRH), which is produced by the hypothalamus.

Parathyroid glands

Parathyroid glands include four small ovoid glands smaller than the pea which lie on the posterior surface of the thyroid gland. They are two pairs superior and inferior. They released parathyroid hormone (PTH) which maintains the level of calcium and phosphorus in the blood.

The Adrenal glands

They are two small flattened yellowish bodies situated on the upper of each kidney. The outer part of the gland is the cortex (yellowish) and the inner part of the gland is the Medulla (dark).

The adrenal medulla situated directly on the top each kidney and stimulated by the sympathetic nervous system to secretes the catecholamines which function to produce a rapid response throughout the body in stress situations. These include epinephrine (adrenaline 80%) and norepinephrine (noradrenaline 20%) which help maintain blood pressure and stimulate smooth muscles. Adrenaline elicits a fight or flight response, increase blood pressure, increase respiration, increase metabolic rate, increase glycogenolysis and constriction of blood vessels in many parts of the body.

Adrenal Cortex secretes over 30 different steroid hormones (corticosteroids) which included three main types:

1. Mineralocorticoids: such as Aldosterone which maintains electrolyte balance and blood pressure.

2. Glucocorticoids: Cortisol and cortisone which functions include the regulation of metabolism of proteins, fats and sugars as well as influence on the immune system

3. Gonadocorticoids (Androgens) that are converted to fully functional sex hormones (testosterone, estrogen, progesterone) in the gonads and other target organs. The production of steroid hormones is called steroidogenesis.

Pancreas

Pancreas is located slightly behind the stomach. The pancreas is a mixed or heterocrine gland, i.e., it has both an endocrine and a digestive exocrine function. 99% of the pancreas is exocrine and 1% is endocrine. As an endocrine gland, it functions mostly to regulate blood sugar levels, secreting the hormones insulin, glucagon, somatostatin and pancreatic polypeptide. Cells within the pancreas help to maintain blood glucose levels (homeostasis). When blood glucose levels are low, alpha cells secrete glucagon, which increases blood glucose levels. When blood glucose levels are high beta cells secrete insulin to decrease glucose in blood. Delta cells in the islet also secrete somatostatin which decreases the release of insulin and glucagon.

Insulin acts to decrease blood glucose levels by facilitating uptake by cells (particularly skeletal muscle). Glucagon acts to increase glucose levels by

promoting the creation of glucose and the breakdown of glycogen to glucose in the liver. It also decreases the uptake of glucose in fat and muscle. Glucagon release is stimulated by low blood glucose or insulin levels, and during exercise.

Pineal Gland

Pineal gland is a small endocrine gland in the brain of most vertebrates. It is a small reddish –gray structure (about the size of a pea) situated in the midline of the brain immediately behind the third ventricle. The pineal gland produces melatonin, a serotonin- derived hormone which modulates sleep patterns in both circadian and seasonal cycles. Melatonin production is stimulated by darkness and inhibited by light.

Gonads

A gonad or sex gland or reproductive gland is a mixed gland that produces the gametes and sex hormones of an organism. The sex hormones include the androgens, estrogens, and progestogens which secreted from ovaries in female and testes in male. Sex hormones principally exert their effects to produce sexual differentiation and reproduction. These hormones play an essential role in reproduction and sexual development, puberty, cholesterol regulation, high growth, distribution of body fat, and inflammatory response.