Biyani Girls College

Session - (2017-2018)

Set B

B.Sc. (Part II) Zoology

Second Paper (Animal Physiology and Biochemistry)

Time allowed : Three Hour **Maximum Marks : 33**

Question No. 1 in Part I is compulsory. Attempt FOUR questions from Part II, selecting at least ONE question from each Section.

All questions carry equal marks.

PART -I

1. **Answer the following questions in two or three lines (maximum 25 words) :- (1x9)**

(i) What is excretion?

Ans. Excretion is the process by which an organism gets rid of the waste products of metabolism in its cells.

(ii) What is action potential?

Ans. Action potentials are caused when different ions cross the neuron membrane. The change in electrical potential associated with the passage of an impulse along the membrane of a muscle cell or nerve cell.

(iii) What is the respiratory pigment explain with example?

Ans. A coloured compound that is capable of reversibly binding with oxygen at high oxygen concentrations and releasing it at low oxygen concentrations. The most common respiratory pigments are hemoglobin, haemocyanin, haemerythrin and chlorocruorin

(iv) By which food component are the nitrogenous excretory products obtained? Name the various nitrogenous excretory substances.

Ans. Protein and amino acid are the substances that nitrogenous product obtain. Ammonia, urea, uric acid, and creatinine are examples

(v) What do we call the junction of two continuous neurons? How many types of junctions are found?

Ans. Synapse is a junction of two neuron. There are two types of synaptic junction which are electrical transmission and chemical transmission.

(vi) What is muscle? Differentiate the type of muscles.

Ans. A bundle of fibrous tissue in a human or animal body that has the ability to contract, producing movement in or maintaining the position of parts of the body. In the muscular system, muscle tissue is categorized into three distinct types: skeletal, cardiac, and smooth

(vii)Write down the names of non-neural hormones of insects.

Ans. Ecdyosone and Juvenile harmone

(viii) What are Scleroproteins? Write down the types of scleroproteins.

Ans. Any of a class of fibrous animal proteins insoluble in water such as keratin, collagen, or elastin.

(ix)What is the roll of pancreatic harmones?

Ans. Pancreatic hormones are responsible for storage of fat and glucose, as glycogen, after meal**.**

PART II

SECTION A

2. Defines the Active and passive Transport? Describe in detail the mechanism of Active Transport. (1x6)

Ans. Active Transport: Active transport is the movement of molecules or ions against a concentration gradient (from an area of lower to higher concentration), which does not ordinarily occur, so enzymes and energy (ATP) are required.

Passive Transport: - Passive transport is the movement of molecules or ions from an area of higher to lower concentration. There are multiple forms of passive transport: simple diffusion, facilitated diffusion, filtration, and osmosis. Passive transport occurs because of the entropy of the system, so additional energy isn't required for it to occur. Active transport requires energy, which is obtained mainly by breakdown of high energy compounds like **adenosine triphosphate** (ATP).

CARRIER PROTEINS PATHWAY OF ACTIVE TRANSPORT

Carrier proteins pathway involved in active transport are of two types:

1. Uniport
2. Symport
3. antiport.

1. *UNIPORT:* Carrier protein that carries only one substance in a single direction is called uniport. It is also known as **uniport pump.**

2. *SYMPORT or ANTIPORT*

Symport or antiport is the carrier protein that transports two substances at a time. Carrier protein that transports two different substances in the same direction is called **symport** or **symport pump.** Carrier protein that transports two different substances in opposite directions is called **antiport** or **antiport pump.**

MECHANISM OF ACTIVE TRANSPORT

ATP hydrolysis is used to transport molecules against theelectrochemical gradient (from low to high ionic concentration of the molecules). When a substance to be transported across the cell membrane comes near the cell, it combines with the carrier protein of the cell membrane and forms substance-protein complex. This complex moves towards the inner surface of the cell membrane, induce a conformational (shape) change that drives the substances to transport against the electrochemical gradient.

Then, the substance is released into the interstitial fluid (ICF) from the carrier proteins. The same carrier proteins move back to the outer surface of the cell membrane (i.e. restore back to its original conformation) to transport another molecule of the substance**.**

SUBSTANCE TRANSPORTED BY ACTIVE TRANSPORT

Substances, which are transported actively, are in ionic form and non-ionic form. Substances in ionic form are **sodium, potassium, calcium, hydrogen, chloride and iodide.** Substances in non-ionic form are **glucose, amino acids and urea.**

TYPES OF ACTIVE TRANSPORT

Active transport is of two major types:

1. Primary active transport
2. Secondary active transport.

However, there is also occurrence tertiary active transport.

PRIMARY ACTIVE TRANSPORT

Primary active transport, (also called direct active transport), directly uses metabolic energy to transport molecules across a membrane. This energy in form adenosine triphosphate (ATP) is hydrolyse to adenosine diphosphate (ADP) and liberating a high-energy phosphate bond of energy. This is carried out by the carrier protein ATPase, when activated by binding to a molecule.

Among the substances that are transported by primary active transport are sodium, potassium, calcium, hydrogen, chloride, and a few other ions**.**

EXAMPLES OF PRIMARY ACTIVE TRANSPORT

In the transport of ion, there are

- primary active transport of sodium/potassium (Na+/K+)
- primary active transport of calcium (Ca+)
- Primary active transport of hydrogen (H+)

PRIMARY ACTIVE TRANSPORT OF SODIUM AND POTASSIUM (sodium-potassium pump)

Sodium and potassium ions are transported across the cell membrane by means of a common carrier protein called sodium-potassium (Na+-K+) pump. It is also called Na+-K+ ATPase pump or Na+-K+ ATPase. This pump transports sodium from inside to outside the cell and potassium from outside to

inside the cell. This pump is present in all the cells of the body. Na+-K+ pump is responsible for the distribution of sodium and potassium ions across the cell membrane and the development of resting membrane potential.

Structure of Na+ - K+ Pump

Carrier protein that constitutes Na+-K+ pump is made up of two protein subunit molecules, an α-subunit with a molecular weight of 100,000 and a β-subunit with a molecular weight of 55,000. Transport of Na+ and K+ occurs only by α-subunit. The β-subunit is a glycoprotein the function of which is not clear. α-subunit of the Na+-K+ pump has got six sites:

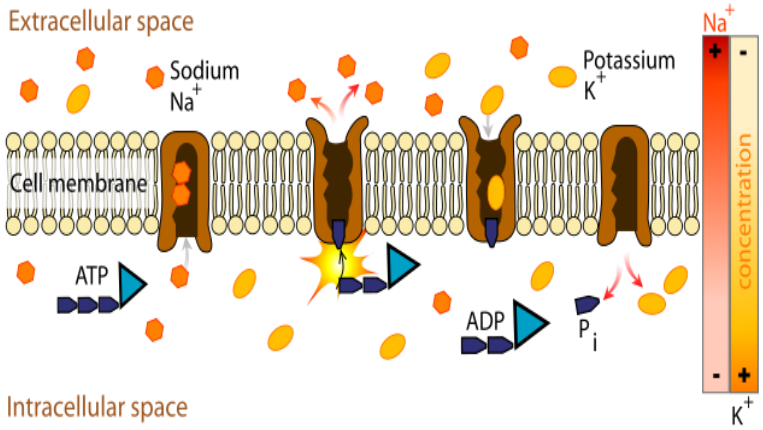
i. Three receptor sites for sodium ions on the inner (towards cytoplasm) surface of the protein molecule

ii. Two receptor sites for potassium ions on the outer (towards ECF) surface of the protein molecule

iii. One site for enzyme adenosine triphosphatase (ATPase), which is near the sites for sodium.

MECHANISM OF ACTION OF NA+-K+ PUMP

Three sodium ions from the cell get attached to the receptor sites of sodium ions on the inner surface of the carrier protein. Two potassium ions outside the cell bind to the receptor sites of potassium ions located on the outer surface of the carrier protein. (see fig. 1 above)



Diagrammatic illustration of Na+/K+ movement across the membrane.

Binding of sodium and potassium ions to carrier protein activates the enzyme ATPase. ATPase causes breakdown of ATP into adenosine diphosphate (ADP) with the release of one high energy phosphate.

However, the energy liberated causes some sort of conformational change in the molecule of the carrier protein. Because of this, the outer surface of the molecule (with potassium ions) now faces the inner side of the cell. And, the inner surface of the protein molecule (with sodium ions) faces the outer side of the cell.

Dissociation and release of the ions take place so that the sodium ions are released outside the cell (ECF) and the potassium ions are released inside the cell (ICF). Exact mechanisms involved in the dissociation and release of ions are not yet known.

Electrogenic activity of Na+-K+ pump

Na+-K+ pump moves three sodium ions outside the cell and two potassium ions inside cell. Thus, when the pump works once, there is a net loss of one positively charged ion from the cell. Continuous activity of the sodium-potassium pumps causes reduction in the number of positively charged ions inside the cell leading to increase in the negativity inside the cell. This is called the electrogenic activity of Na+-K+ pump.

Importance of the Na+-K+ Pump

1. For Controlling Cell Volume.

One of the most important functions of the Na+-K+ pump is to control the volume of each cell. Without function of this pump, most cells of the body would swell until they burst. The mechanism for controlling the volume is as follows:

Inside the cell are large numbers of proteins and other organic molecules that cannot escape from the cell. Most of these are negatively charged and therefore attract large numbers of potassium, sodium, and other positive ions as well. All these molecules and ions then cause osmosis of water to the interior of the cell. Unless this is checked, the cell will swell indefinitely until it bursts. The normal mechanism for preventing this is the Na+K+ pump.

Note again that this device pumps three Na+ ions to the outside of the cell for every two K+ ions pumped to the interior. Also, the membrane is far less permeable to sodium ions than to potassium ions, so that once the sodium ions are on the outside, they have a strong tendency to stay there.

Thus, this represents a net loss of ions out of the cell, which initiates osmosis of water out of the cell as well.

If a cell begins to swell for any reason, this automatically activates the Na+-K+ pump, moving still more ions to the exterior and carrying water with them. Therefore, the Na+-K+ pump performs a continual surveillance role in maintaining normal cell volume.

2. Generation of heat in cell

Thyroid hormone stimulates cells to produce more Na_-K_ pumps. As these pumps consume ATP, they release heat, compensating for the body heat we lose to the cold air around us.

PRIMARY ACTIVE TRANSPORT OF CALCIUM IONS

Calcium is actively transported from inside to outside the cell by calcium pump. Calcium pump is operated by a separate carrier protein. Energy is obtained from ATP by the catalytic activity of ATPase. Calcium pumps are also present in some organelles of the cell such as sarcoplasmic reticulum in the muscle and the mitochondria of all the cells. These pumps move calcium into the organelles.

PRIMARY ACTIVE TRANSPORT OF HYDROGEN IONS

Hydrogen ion is actively transported across the cell membrane by the carrier protein called hydrogen pump. It also obtains energy from ATP by the activity of ATPase. The hydrogen pumps that are present in two important organs have some functional significance.

1**. *Stomach:*** Hydrogen pumps in parietal cells of the gastric glands are involved in the formation of hydrochloric acid.

2. *Kidney:* Hydrogen pumps in epithelial cells of distal convoluted tubules and collecting ducts are involved in the secretion of hydrogen ions from blood into urine .

SECONDARY ACTIVE TRANSPORT

In secondary active transport, also known as *coupled transport* or *co-transport*, energy is used to transport molecules across a membrane; however, in contrast to primary active transport, there is no direct coupling of ATP; instead, the electrochemical potential difference created by pumping ions out of the cell is used. Thus, it involves the transport of sodium coupled with transport of another substance.

When sodium is transported by a carrier protein, another substance is also transported by the same protein simultaneously, either in the same direction (of sodium movement) or in the opposite direction.

Secondary active transport mechanism is of two types:

1. Co transport
2. Counter transport.

Mechanism of sodium co-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.*

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**.**

Sodium co-transport of glucose

One sodium ion and one glucose molecule from the extracellular fluid (ECF) bind with the respective receptor sites of carrier protein of the cell membrane. Now, the carrier protein is activated. It causes conformational changes in the carrier protein, so that sodium and glucose are released into the cell (Fig. 3).

Sodium co-transport of glucose occurs during absorption of glucose from the intestine and reabsorption of glucose from the renal tubule.

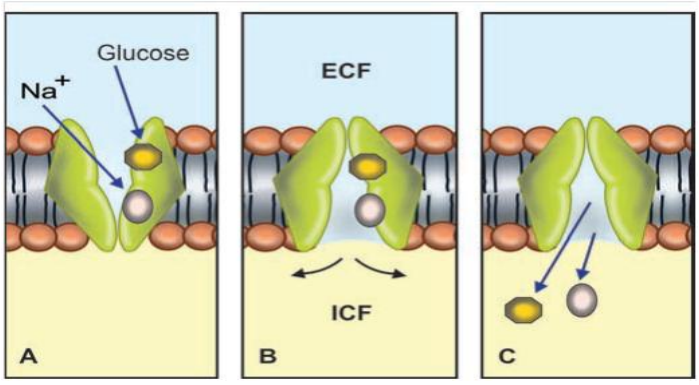


Fig. 3 showing the sodium-glucose cotransport

Sodium co-transport of amino acids

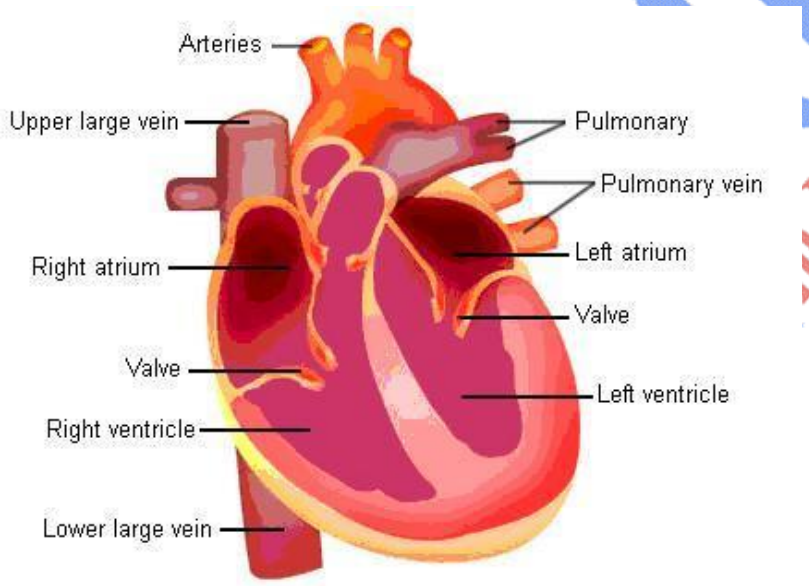
Carrier proteins for the transport of amino acids are different from the carrier proteins for the transport of glucose. For the transport of amino acids, there are five sets of carrier proteins in the cell membrane. Each one carries different amino acids depending upon the molecular weight of the amino acids.

Sodium co-transport of amino acids also occurs during the absorption of amino acids from the intestine and reabsorption from renal tubule.

3. Draw a labeled diagram of Mammalian Heart. Explain the cardiac cycle of the heart.

Ans. Heart Structure

Heart structure and function are closely related, as described below:



1. The Pericardium

This is a fibrous covering that wraps around the heart and holds it in place. This special membrane also contains a fluid which lubricates the heart in the pericardial space or cavity to prevent friction. The pericardium has two layers, consisting of a visceral layer directly coving the heart and a parietal layer, which forms a sac containing the fluid in the pericardial cavity.

2. The Heart Wall

The wall of the heart is made of three layers:

- **The epicardium,** or the outermost layer of the heart, is a thin layer of membrane that lubricates and protects the outside portion of the heart.
- **The myocardium,** or the muscular layer of the heart wall, consists of the muscle tissue. It consists of the majority of the thickness of the heart and is responsible for the pumping action of the heart.
- **The endocardium,** or the innermost layer that lines the inside of your heart, is a smooth lining that keeps blood from sticking to the heart and prevents the formation of potentially harmful blood clots.

3. Chambers of the Heart

The heart has four chambers:

- ŸRight atrium
- ŸLeft atrium

- ŸRight ventricle
- ŸLeft ventricle

Atria are smaller than ventricles and have thin, less muscular walls. They are the receiving chambers of the blood, which is delivered to the heart by the large veins. **Ventricles** are the larger, more muscular pumping chambers that push blood out to the circulation. They are connected to large arteries that carry blood to the circulation.

The right atrium and the right ventricle are smaller than the corresponding chambers on the left. They have less muscle in their walls compared to the left side of the heart. The difference in size is related to their functions. Blood from the right side of the heart goes to the pulmonary circulation while blood from the left chambers is pumped to the rest of the body.

4. Blood Vessels

These are tubes which carry blood to different parts of the body:

- **Arteries** deliver oxygen-rich blood from the heart to the rest of the body. The biggest artery is the aorta, which leaves the heart and gives off smaller branches.
- **Veins** deliver deoxygenated blood back to the heart through theinferior and superior vena cava, which drain into the right atrium.
- **Capillaries** are microscopic vessels that connect arteries to veins.

5. Valves

These are fibrous tissue flaps found between the cardiac chambers and within the veins. They serve as gates that ensure one-way flow and prevent the backflow of blood.

- **Atrioventricular valves** are found between each atrium and ventricle. The valve between the right atrium and ventricle is the tricuspid valve, while that found between the left atrium and ventricle is called the mitral valve.
- **Semilunar valves** are found between the ventricles and the large arteries. There is an aortic valve between the left ventricle and the aorta and a pulmonary valve between the right ventricle and the pulmonary artery.

Cardiac Cycle – Systole and Diastole

The mechanical events occurring during one systole and diastole.

One cardiac cycle = 1 systole + 1 diastole

To study a particular phase of cardiac cycle, one should study what happens to atrium, ventricle, aorta/pulmonary vein, cardiac valves in that phase. Events that occur in left chambers of heart, similar events occur in right chambers of heart.

Events that occur in left chambers of heart, similar events occur in right chambers of heart.

Phases of Cardiac Cycle

Atrial contraction (First Phase)

This is the phase of atrial contraction. 80% of ventricular filling has been done passively even before the onset of atrial contraction and the remaining 20% of ventricular filling is due to atrial contraction. This active filling of ventricles becomes valuable during physical activity.

When pressure in the atrium increases, blood rush into the ventricles through the opened mitral valve. During left atrium contraction, pressure and volume are transferred into left ventricle through opened mitral valve. Remember aortic valve is closed because pressure in aorta is greater than the pressure in left ventricle at this moment.

What is "a" Wave

"a" wave is a pressure wave produced within left atrium due to atrial contraction.

Isovolumetric Contraction (Second Phase)

This is the early phase of ventricular systole. When ventricles contract, there is a progressive increase in intraventricular pressure. When intraventricular pressure increase than atrial pressure, This wil leads to closure of mitral valve. That closure of mitral valve produces first heart sound (S1) and little bulging of mitral valve into atrium causing the slight increase in the atrial pressure, and "c" wave.

Intraventricular pressure progressively increases upto 80mmHg yet it is not competent enough to open the aortic valve. At this moment ventricle is contracting with closed mitral and aortic valves. Meanwhile, intra atrium pressure is gradually increasing due to accumulation of blood returning from lungs into the left atrium. During the same phase, aorta pumps whatever blood it contains into more peripheral part of arterial tree due to its elastic nature.

Isovolumetric Contraction:

This is the stage of ventricular contraction when backward valves are closed yet the forward valves are not opened. Ventricle is contracting as a closed chamber without any change in volume and size of the ventricle. We call it isovolumetric contraction of early part of ventricular systole.

Rapid Ventricular Ejection (Third Phase)

When pressure reaches to 81mmHg, aortic valve opens. Third phase of cardiac cycle has started. Ventricles keep on contracting and there is a progressive increase in intraventricular pressure upto 120mmHg. During this phase, aortic valve opens and blood is ejected rapidly into aorta. Now left ventricle and aorta behave as a single chamber. The pressure changes occurred in the ventricles results in faithfully transmission of pressure to aorta. Meanwhile left atrium is still receiving blood from the lungs and "v" wave is produced due to accumulating blood in the atrium.

Slow Ventricular Ejection (Fourth Phase)

In this phase atrium is still behaving as reservoir of blood and the pressure wave "v" is keep on building. Mitral valve is closed. Ventricles are still contracting but due to ejection of blood intraventricular pressure starts falling. Hence, pressure in aorta also starts falling, but intraventricular pressure is still more than aortic pressure. Aortic valve remains open leading to slow ejection of blood into aorta. Elastic aorta keeps on squeezing the blood and pumps it into peripheral arterial tree.

Isovolumetric Relaxation (Fifth Phase)

In this phase ventricles start relaxing. Intraventricualr pressure falls rapidly. In the beginning, as soon as the ventricular pressure becomes less than pressure in aorta, aortic valve closes. Even though pressure in ventricle is falling, it is still high enough compared to pressure in atrium. So ventricle is relaxing with closed valves and it is known as isovolumetric relaxation. During this phase atrium is still behaving as reservoir of blood.

Rapid Passive Ventricular Filling (Sixth Phase)

When left ventricle start relaxing, pressure in left ventricle start dropping rapidly until it reaches the point where pressure in the ventricle becomes less than the pressure in atrium, leads to opening of mitral valve. Blood which was previously accumulated in atrium will rush into ventricle. This rapid filling is done without atrial contraction.

Slow Passive Ventricular Filling (Seventh Phase)

As atrioventricular valve open, blood coming to atrium directly rushes into the ventricle. Here atrium is not acting as reservoir.

Definition of Heart sounds (S1, S2, S3, S4)

S1 Heart Sound

In the beginning of ventricular systole, mitral and tricuspid valves closure produce a sound. This is called first heart sound.

S2 Heart Sound

Closure of aortic and pulmonary valve at the end of ventricular systole, produce a sound. This is called second heart sound.

S3 Heart Sound

In some young person; in the last moments of rapid passive ventricular filling phase, heart may produce a sound. This is called third heart sound.

S4 Heart Sound

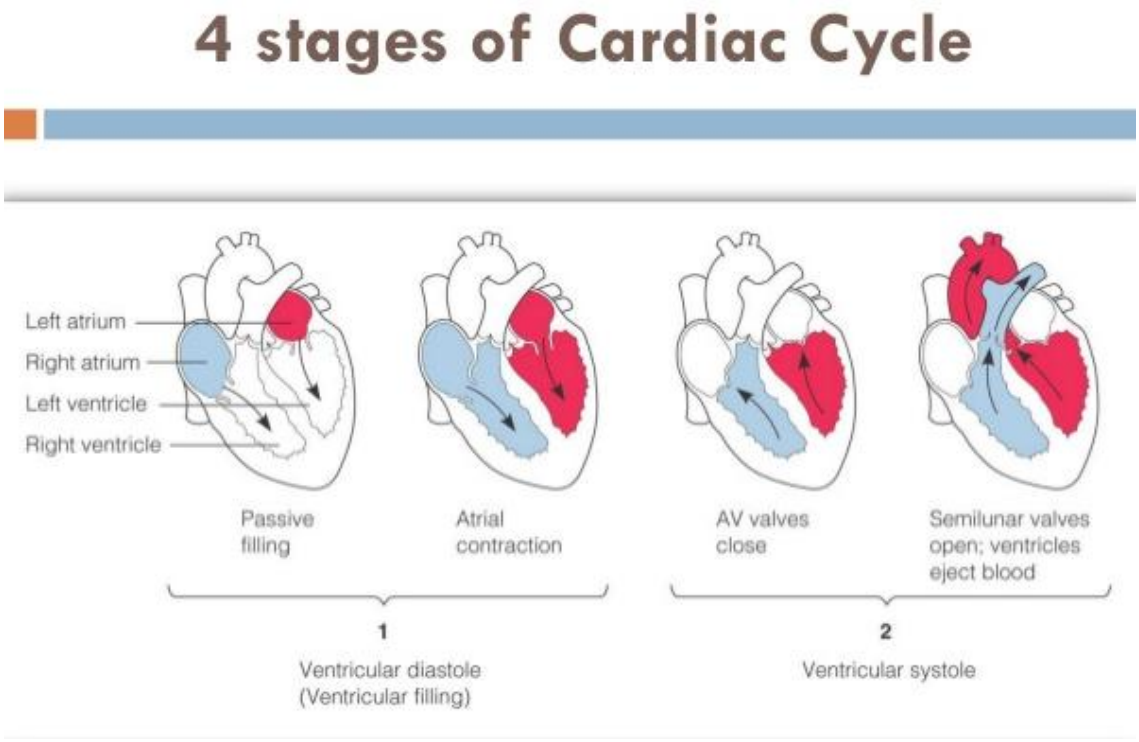
In some young person; in the last moments of rapid passive ventricular filling phase, heart may produce a sound. This is called third heart sound.

Graphical Representation of Cardiac Cycle

To express cardiac cycle on a graph, pressure is taken along y-axis and time shown by x-axis.

The first phase starts with atrial contraction, atrial pressure rise and mitral valve become open. So the pressure transfers to the ventricle. There is equal rise in ventricular pressure graph. Aortic pressure graph still shows 80 mm Hg.

In the next phase ventricles start contracting. As soon as ventricle pressure becomes higher than the atrial pressure, mitral valve closes. Ventricle keep on contracting with closed mitral and aortic valves. There is a production of “c” wave in atrial pressure graph. Graph representing the ventricular pressure keeps on rising but it doesn’t go beyond the aortic pressure graph. The next phase is rapid ventricular ejection. When ventricular pressure becomes higher then aortic pressure, aortic valve opens. Pressure in ventricle is transmitted equally to the aorta. There is equal rise in graph of ventricle and aortic pressures. Both pressure graphs reach to 120mm Hg. Atrium is behaving as reservoir of blood and “v” wave is produced in the atrial pressure graph. In the next phase of slow ventricular ejection, ventricle pressure starts descending and aortic valve closes. The graph of ventricular pressure also descends. The graph of aortic pressure descends till 80mmHg then remains constant at this value. Atrium still behaving as reservoir for blood and “v” wave keeps continuing in the same fashion. In the next phase of isovolumetric relaxation, ventricular pressure graph keeps on descending and reaches below the atrial pressure graph. There is no change in aortic pressure graph; and atrial pressure graph keeps on with “v” wave. These graphs maintain the same fashion until next cardiac cycle starts with the contraction of atrium.



4. Write short notes on any two of the following :- (2x3)

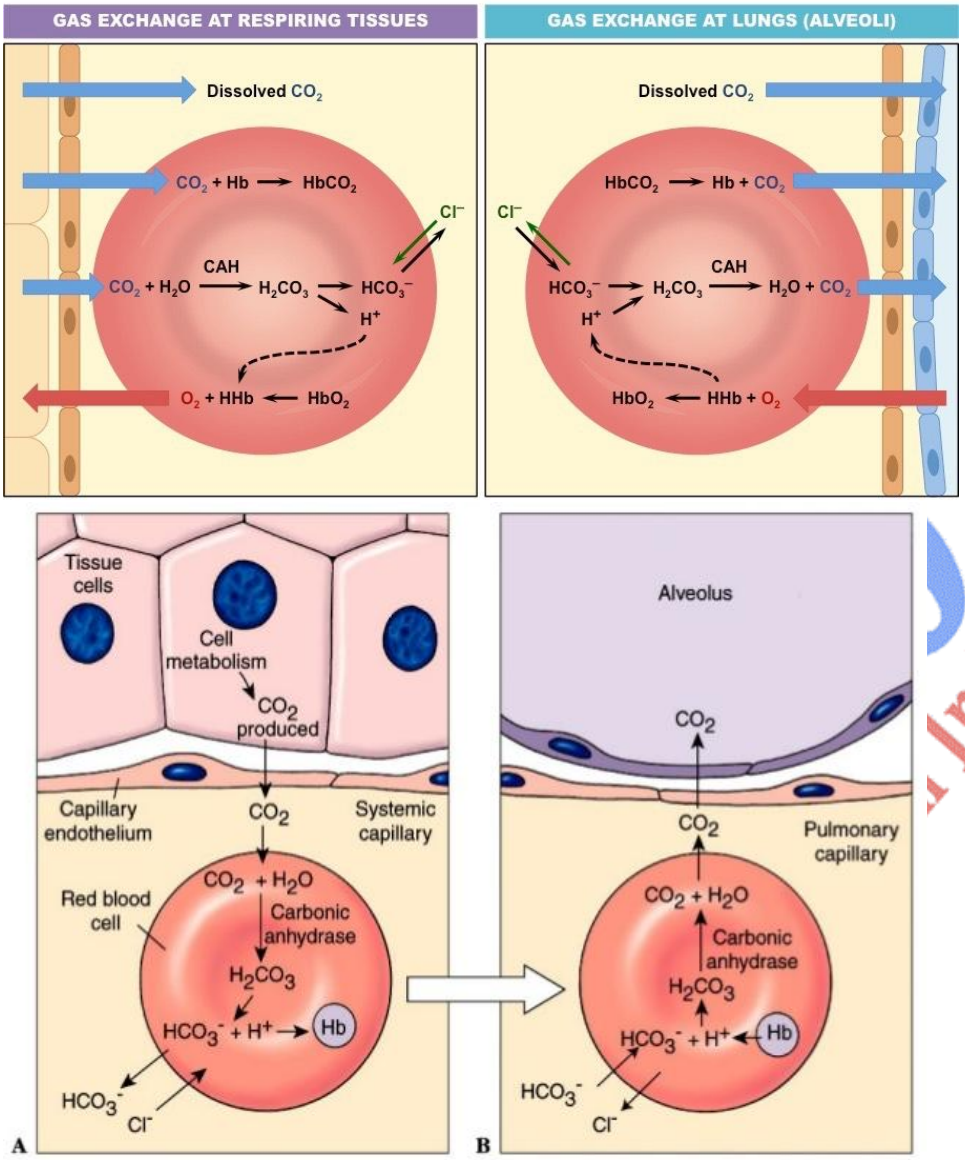
(a) Transport of CO_2 by blood :

Ans: Carbon dioxide is transported between the lungs and the tissues by one of three mechanisms:

- Some is bound to haemoglobin to form $HbCO_2$ (carbon dioxide binds to the globin and so doesn't compete with O_2 binding)
- A very small fraction gets dissolved in water and is carried in solution (~5% – carbon dioxide dissolves poorly in water)
- The majority (~75%) diffuses into the erythrocyte and gets converted into carbonic acid

Transport as Carbonic Acid

- When CO_2 enters the erythrocyte, it combines with water to form carbonic acid (reaction catalysed by carbonic anhydrase)
- The carbonic acid (H_2CO_3) then dissociates to form hydrogen ions (H^+) and bicarbonate (HCO_3^-)
- Bicarbonate is pumped out of the cell in exchange with chloride ions (exchange ensures the erythrocyte remains uncharged)
- The bicarbonate in the blood plasma combines with sodium to form sodium bicarbonate ($NaHCO_3$), which travels to the lungs
- The hydrogen ions within the erythrocyte make the environment less alkaline, causing haemoglobin to release its oxygen
- The haemoglobin absorbs the H^+ ions and acts as a buffer to maintain the intracellular pH
- When the red blood cell reaches the lungs, bicarbonate is pumped back into the cell and the entire process is reversed



(b) Ornithine cycle

Ans. A cyclic enzymatic process consisting of consecutive transformations of the amino acid ornithine and leading to the synthesis of urea. The ornithine cycle is the most important means of assimilation of ammonia (and thus for its neutralization) in many species of animals, as well as in plants and microorganisms.

The reactions of the ornithine cycle have been most thoroughly studied in mammals (H. Krebs and K. Henseleit 1932), in which the reactions take place primarily in the liver. The ornithine cycle consists of three main reactions: the conversion of ornithine into citrulline, the conversion of citrulline into arginine, and the splitting of arginine into urea and ornithine (see Figure 1).

Reactions (I) and (II) require expenditures of energy, which is provided in the form of adenosine triphosphate (ATP).

Reaction (I) proceeds in two steps:

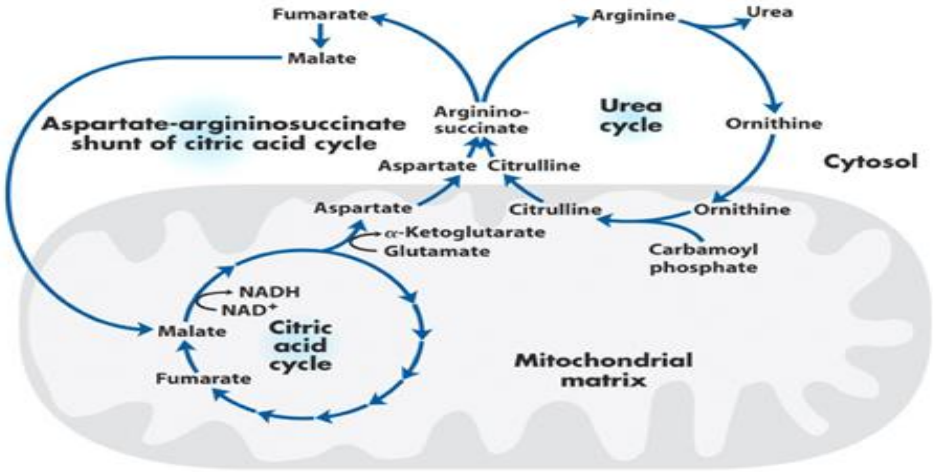
(1) the formation of carbamyl phosphate, which has an energy-rich phosphate bond, from ammonia, carbon dioxide, and two molecules of ATP (the reaction is activated by *N*-acetylglutamic acid; ammonia is apparently supplied to the liver in the form of glutamine, which is split by liver glutaminase into NH3 and glutamic acid); and

(2) the formation of citrulline in the reaction of carbamyl phosphate with ornithine (the reaction proceeds using the energy of the carbamyl phosphate bond).

Reaction (II) also has two stages:

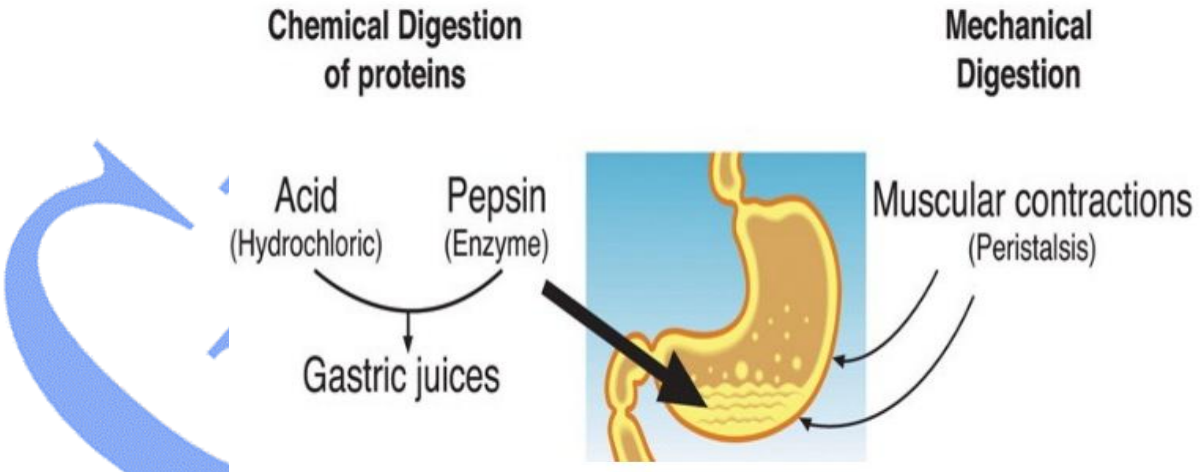
(1) the reaction of citrulline with aspartic acid to form arginosuccinic acid (the reaction proceeds with the participation of ATP, with the liberation of adenylic acid [adenosine monophosphate, or AMP] and pyrophosphate, H4P2O7); and

(2) the splitting of arginosuccinic acid to yield arginine and fumaric acid. In reaction (III), arginine is hydrolyzed to urea and ornithine, which reenters the cycle.



(c) Digestion in stomach

Ans.



(d) Blood clotting

Ans.

SECTION-B

5. Explain the fine structure of neuron? Describe the conduction of nerve impulse with suitable diagrams. (1x6)

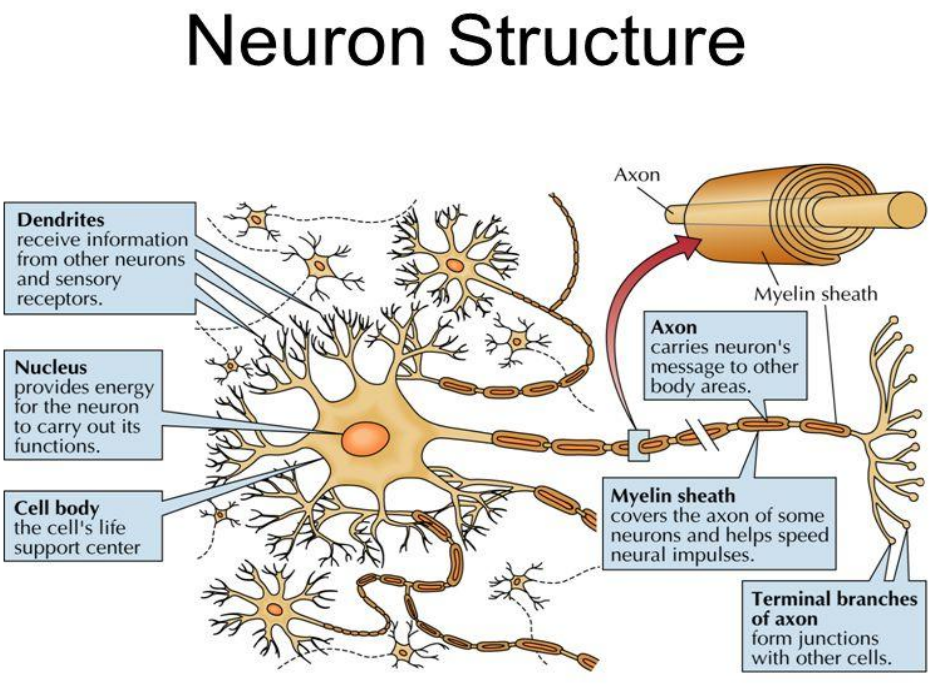
Ans. A neuron is primarily a cell. Therefore, like any other cell it has a cell body wrapped inside a cell membrane. It has a nucleus that contains the chromosomes which constitute the genetic information. It has other standard cellular components, the organelles like mitochondria, golgi bodies, nissil bodies, endoplasmic reticulum and so on. But what distinguishes a neuron from most other cells is the rich and

elaborate wiring that seems to emerge from the cell body, also called soma (fig. 1.1.1.1). Neurons vary greatly in terms of the number of these wiry structures that stick out of the cell body. While a neuron like the bipolar cell, found in the retina of the eye, has only two wires sticking out of the soma, there are neurons like the purkinje cell in the cerebellum, which have about one or two lakh wires per cell. In fact, even at a first glance, this wiring seems to be something odd about a neuron. One would not be totally off track if one surmised that it is these wires that make neuron a special cell, and, by extension, the brain a special organ. Hence broadly, depending on the Dendrite, we can classify the Neuron as

Unipolar cell: 1 wire sticking out of the soma.

- 2)Bipolar cell: 2 wires sticking out of the soma.
- 3)Multipolar cell: Many wires sticking out of the soma.
- 4)Pseudounipolar

Neuron On a closer look, one can distinguish two distinct portions in the wiring system: one portion has shorter, more densely distributed wiring, known as the dendrites; the other portion, consisting typically of a single long wire, known as an axon, branches out into smaller axon terminals at the far end. Neurons use these dendrites and axons to receive and transmit signals to each other. Signals from other neurons are received by the dendrites, while signals to other neurons are transmitted by axon and its terminals. Thus a neuron can be regarded as an input-output system with dendrites as the inputs and the axon terminals as its outputs. Signals from one neuron to another are transmitted across a small gap – between the axon terminal of one neuron and the dendrite of another neuron – known as the synapse

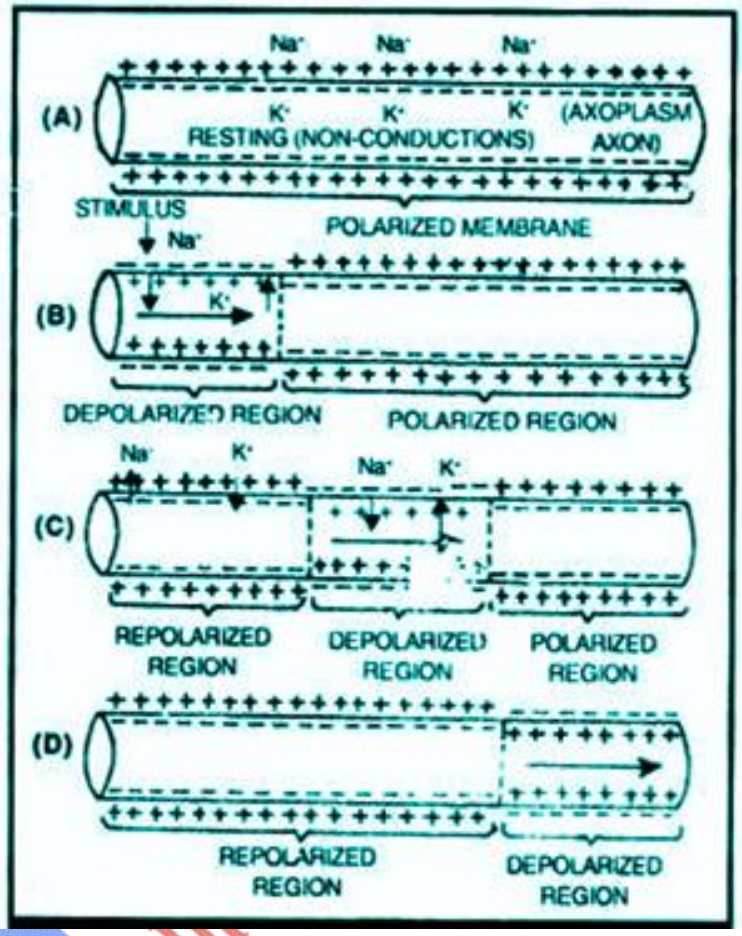


A nerve impulse is the electric signals that pass along the dendrites to generate a nerve impulse or an action potential. An action potential is the movement of ions in and out of the cell. It specifically involves sodium and potassium ions. They are moved in and out of the cell through sodium and potassium channels and sodium-potassium pump.

Conduction of nerve impulse occurs due to the presence of active and electronic potentials along the conductors. Transmission of signals internally between the cells is achieved through a synapse. Nerve conductors comprise of relatively higher membrane resistance and low axial resistance. The electrical synapse has its application in escape reflexes, heart and in the retina of vertebrates. They are mainly used whenever there is a requirement of fast response and timing being crucial. The ionic currents pass through the two cell membrane when the action potential reaches the stage of such synapse.

Mechanism of Transmission of Nerve Impulse

The axon or nerve fibers are in the form of a cylinder wherein the interior of the axon is filled with axoplasm and the exterior is covered with axolemma. The nerve fibers are immersed in ECF. The solution is in ionic form that is present in axoplasm and extracellular fluid or ECF.



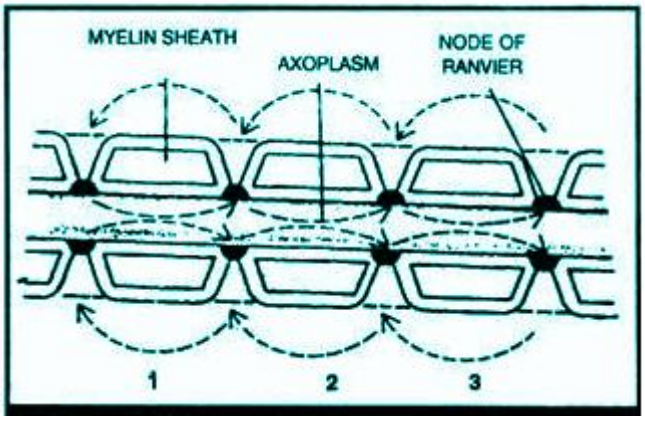
Mechanism of Transmission of Nerve Impulse

Outside the axon, the negatively charged chloride ions are neutralized in the presence of positively charged sodium ions. Negatively charged protein molecules are neutralized in the presence of potassium ions within the axoplasm. The membrane of a neuron -ve inside and +ve outside. Resting potential would be the difference in charge. The difference in charge might vary from seventy to ninety millivolts, as a result, the membrane would be polarized. Sodium potassium metallic pump operates to keep resting potential in equilibrium.

The pump is placed on the axon membrane. Now the potassium ions are pumped from ECF to axoplasm and sodium ions are placed from axoplasm to ECF. The concentration level of sodium ions would be between twenty-eight to thirty times more inside the neuron membrane and the concentration level of sodium ions would be fourteen times more in outside the neuron membrane.

The sodium-potassium pump stops operating when a stimulus is applied to a membrane of a nerve fiber. The stimulus could be either electrical, chemical or mechanical. The potassium ions rush outside the membrane and sodium ions rush inside the membrane as a result negative charges are present outside and positive charges are present inside.

The nerve fibers are either depolarized or they are said to be in action potential. The action potential traveling along the membrane would be the nerve impulse. It is around + 30 mV. The sodium-potassium pump starts to operate once the action potential is completed. As a result, the axon membrane will obtain a resting potential by repolarization.



Now the process takes place in a reverse order. It is a reversal of the process that has taken place during an action potential. Here, potassium ions will be rushed inside and sodium ions will be rushed outside. Impulse would not be transmitted through the nerve fiber during the refractory period.

In a case of white fibers, saltatory propagation takes place. That is impulse jumps from node to node and it increases with increase in speed of nerve impulse. It is around twenty times faster compared to that of the non-medullated nerve fibers. The transmission of nerve impulse would rely upon the diameter of the fiber. For instance, the nerve impulse of a mammal is one twenty meters per second whereas nerve impulse of a Frog is 30 meters per second.

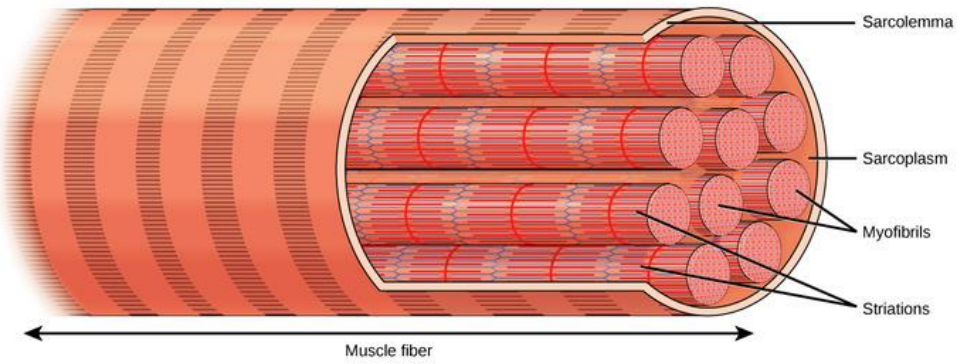
6. Explain the fine structure of myofibril. Describe in detail the molecular theory of muscle contraction.

Ans. Myocyte: Skeletal muscle cell Structure

Myocytes can be incredibly large, with diameters of up to 100 micrometers and lengths of up to 30 centimeters. The sarcoplasm is rich with glycogen and myoglobin, which store the glucose and oxygen required for energy generation, and is almost completely filled with myofibrils, the long fibers composed of myofilaments that facilitate muscle contraction.

The sarcolemma of myocytes contains numerous invaginations (pits) called transverse tubules which are usually perpendicular to the length of the myocyte. Transverse tubules play an important role in supplying the myocyte with Ca^{+} ions, which are key for muscle contraction.

Each myocyte contains multiple nuclei due to their derivation from multiple myoblasts, progenitor cells that give rise to myocytes. These myoblasts asre located to the periphery of the myocyte and flattened so as not to impact myocyte contraction.



Myocyte: Skeletal muscle cell

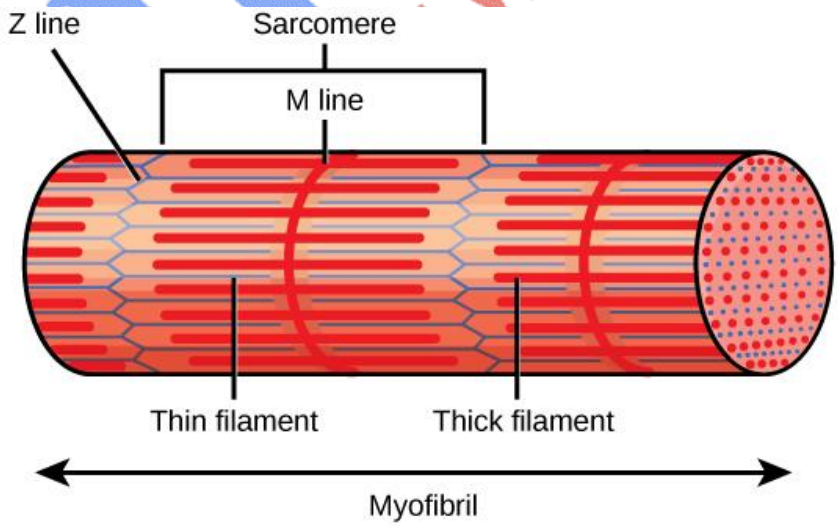
A skeletal muscle cell is surrounded by a plasma membrane called the sarcolemma with a cytoplasm called the sarcoplasm. A muscle fiber is composed of many myofibrils, packaged into orderly units.

Myofibril Structure

Each myocyte can contain many thousands of myofibrils. Myofibrils run parallel to the myocyte and typically run for its entire length, attaching to the sarcolemma at either end. Each myofibril is surrounded by the sarcoplasmic reticulum, which is closely associated with the transverse tubules. The sarcoplasmic reticulum acts as a sink of Ca^{+} ions, which are released upon signalling from the transverse tubules.

Sarcomeres

Myofibrils are composed of long myofilaments of actin, myosin, and other associated proteins. These proteins are organized into regions termed sarcomeres, the functional contractile region of the myocyte. Within the sarcomere actin and myosin, myofilaments are interlaced with each other and slide over each other via the sliding filament model of contraction. The regular organization of these sarcomeres gives skeletal and cardiac muscle their distinctive striated appearance.



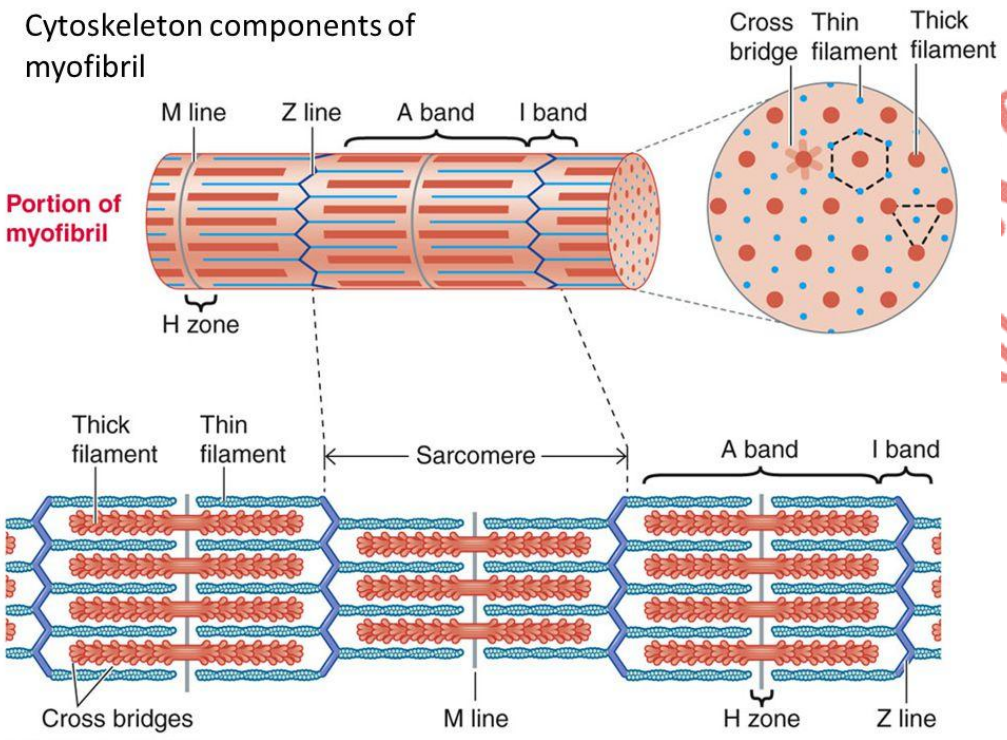
Sarcomere

The sarcomere is the functional contractile region of the myocyte, and defines the region of interaction between a set of thick and thin filaments.

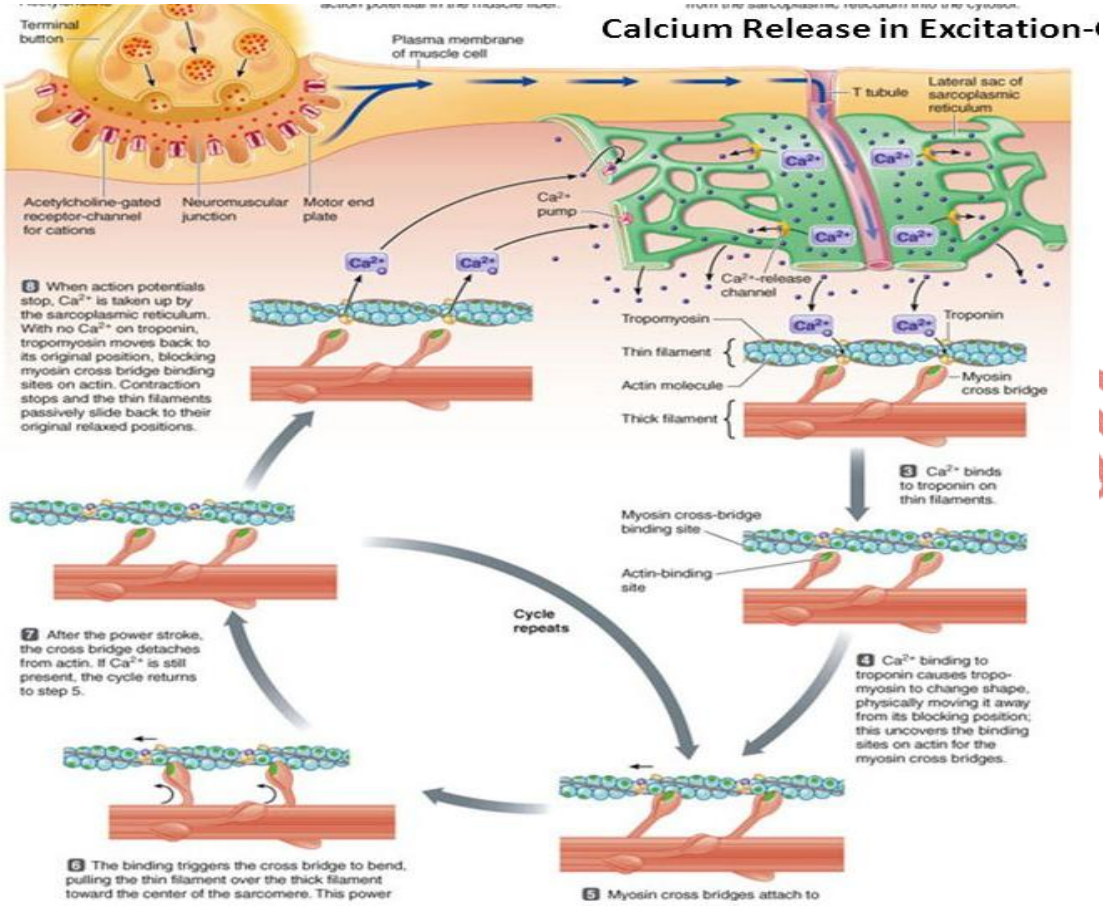
This diagram of a microfibril includes the terms sarcomere, Z-line, M-line, thin filament, and thick filament.

Myofilaments (Thick and Thin Filaments)

Myofibrils are composed of smaller structures called myofilaments. There are two main types of myofilaments: thick filaments and thin filaments. Thick filaments are composed primarily of myosin proteins, the tails of which bind together leaving the heads exposed to the interlaced thin filaments. Thin filaments are composed of actin, tropomyosin, and troponin. The molecular model of contraction which describes the interaction between actin and myosin myofilaments is called the cross-bridge cycle.



molecular theory of muscle contraction:-



7. Write short notes on any two of the following :- (2x3)

(a) Adrenal gland

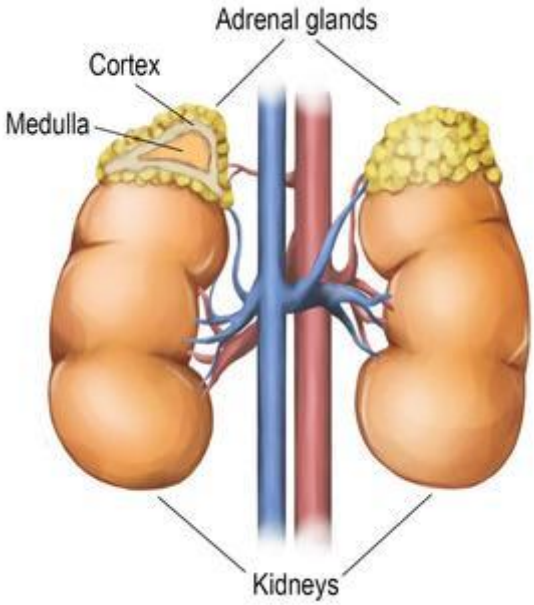
Ans. Human Adrenal Glands:

Here is a simple summary of information about the **adrenal glands**. Information on this page is likely to be appropriate for first-level courses such as AS and A-Level Human Biology, ITEC Anatomy and Physiology, and other courses in Health Sciences.

The location(s) of the Adrenal Glands:

The human body normally* includes two adrenal glands.

They are located immediately anterior to the kidneys, and are encased in a connective tissue capsule that is usually partially buried in an island of fat. The adrenal glands lie beneath the peritoneum (that is, they are "**retroperitoneal**").



The Structure of the Adrenal Glands:

The most obvious aspect of the structure of the adrenal glands is their partitioning into two distinctive components: the paler medulla (centre), and the darker cortex (surround). Both of these tissues contain many blood vessels, hence they may be described as "richly vascularized".

Adrenal Medulla

The medulla consists of many large columnar cells called "**chromaffin cells**". These synthesize and secrete **catecholamines**.

There are also some ganglion cells. Blood from throughout the adrenal gland collects into large medullary veins to exit the gland.

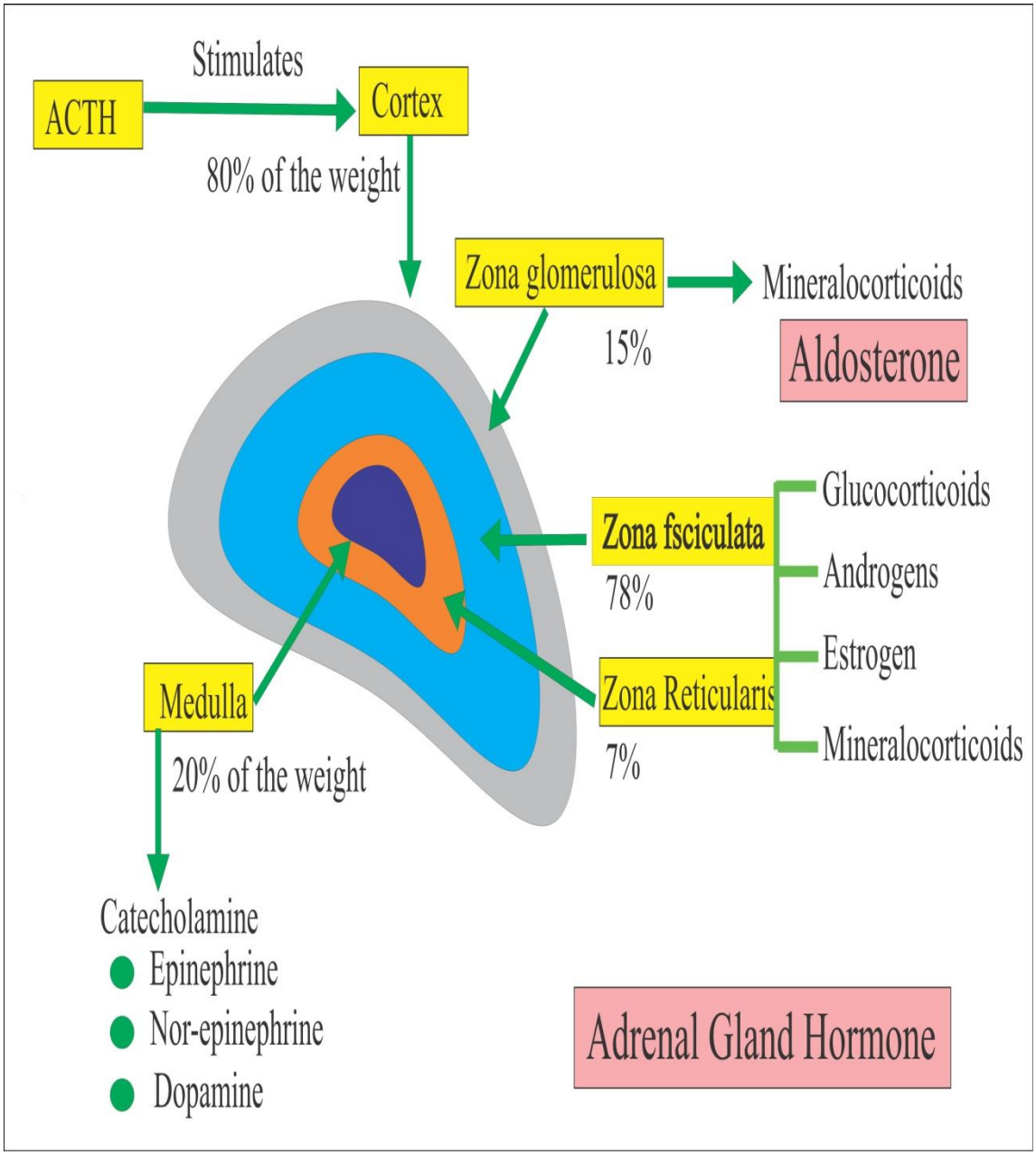
Adrenal Cortex

The adrenal cortex consists of three concentric zones of steroid-synthesizing cells called the:

- glomerulosa
- fasiculata, and
- reticularis.

Although the boundaries between these zones are indistinct, each of these zones has a characteristic arrangement of cells.

Simple Diagram representing the Adrenal Medulla (centre) and the Adrenal Cortex (surround):



Hormones secreted by the Adrenal Glands:

Adrenal Medulla	**Adrenalin**	Prepares the body for "fright, fight or flight" and has many effects: Action of heart increased. Rate and depth of breathing increased. Metabolic rate increased. Force of muscular contraction improves. Onset of muscular fatigue delayed. Blood supply to the bladder and intestines reduced, their muscular walls relax, the sphincters contract.
	Noradrenalin	Similar effects to adrenalin: Constriction of small blood vessels leading to increase in blood pressure. Increased blood flow through the coronary arteries and slowing of heart

		rate. Increase in rate and depth of breathing. Relaxation of the smooth muscle in the intestinal walls.
Adrenal Cortex	**Corticosteroids**	**Glucocorticoids** (e.g. cortisol, cortisone, corticosterone) Utilization of carbohydrate, fat and protein by the body. • Normal response to stress. Anti-inflammatory effects. **Hypersecretion of cortisol results in Cushings Syndrome.**
		Mineralocorticoids (e.g. aldosterone) Regulation of salt and water balance. **Hypersecretion of Alderosterone decreases the potassium in the body (affecting nerve impulse transmission and leading to muscular paralysis).**

(b) Hormonal control on male and female reproduction

Ans. The human male and female reproductive cycles are controlled by the interaction of hormones from the hypothalamus and anterior pituitary with hormones from reproductive tissues and organs. In both sexes, the hypothalamus monitors and causes the release of hormones from the pituitary gland. When the reproductive hormone is required, the hypothalamus sends a gonadotropin-releasing hormone (GnRH) to the anterior pituitary. This causes the release of follicle stimulating hormone (FSH) and luteinizing hormone (LH) from the anterior pituitary into the blood. Note that the body must reach puberty in order for the adrenals to release the hormones that must be present for GnRH to be produced. Although FSH and LH are named after their functions in female reproduction, they are produced in both sexes and play important roles in controlling reproduction. Other hormones have specific functions in the male and female reproductive systems

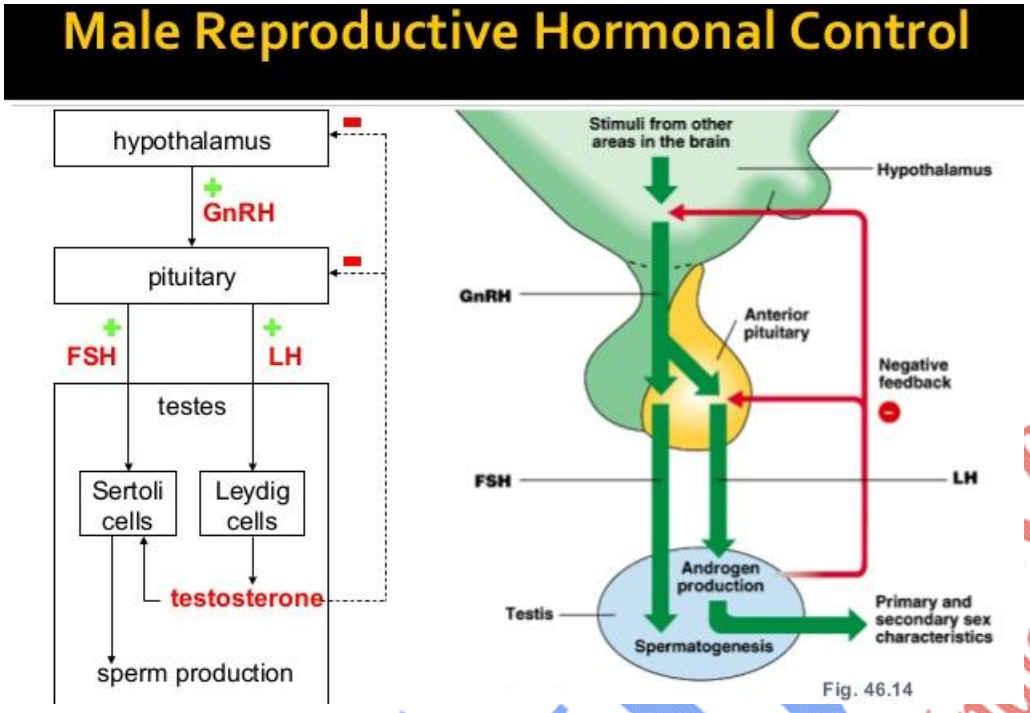


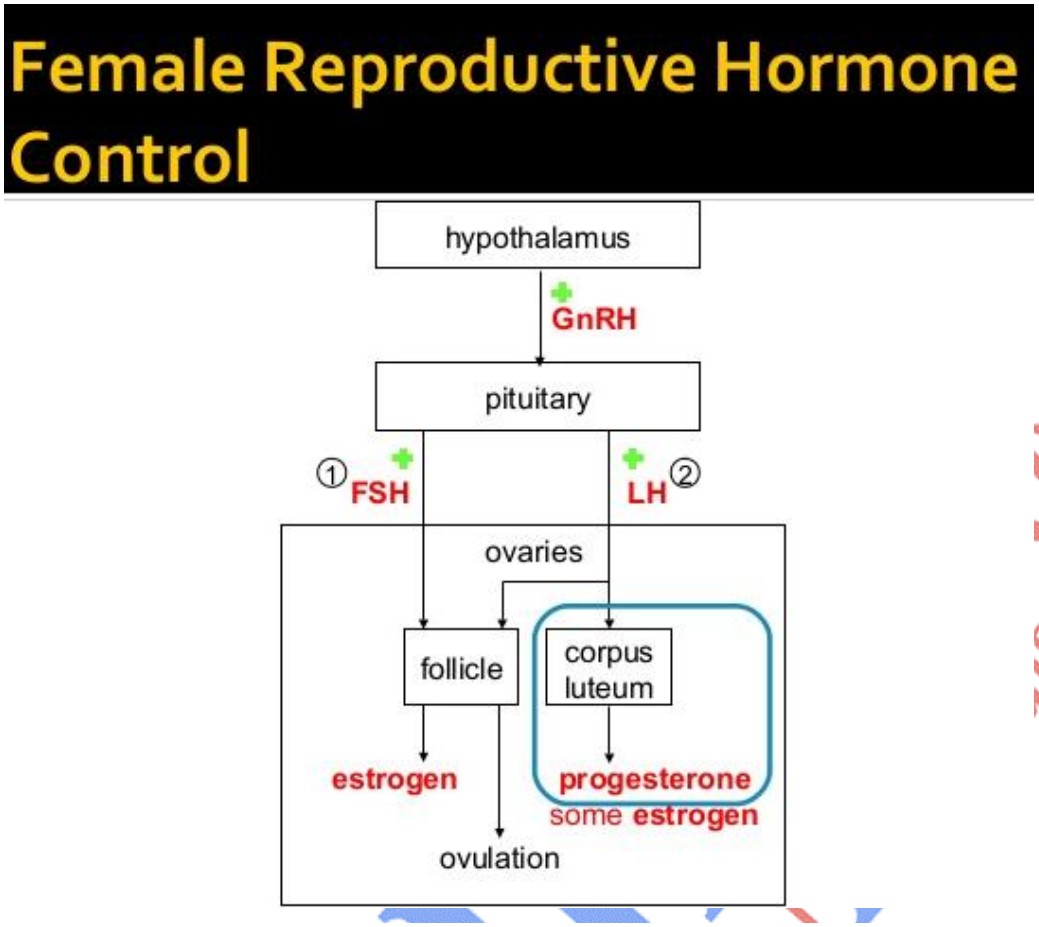
Fig. 46.14

At the onset of puberty, the hypothalamus causes the release of FSH and LH into the male system for the first time. FSH enters the testes and stimulates the **Sertoli cells** to begin facilitating spermatogenesis using negative feedback,

LH also enters the testes and stimulates the **interstitial cells of Leydig** to make and release testosterone into the testes and the blood.

Testosterone, the hormone responsible for the secondary sexual characteristics that develop in the male during adolescence, stimulates spermatogenesis. These secondary sex characteristics include a deepening of the voice, the growth of facial, axillary, and pubic hair, and the beginnings of the sex drive.

A negative feedback system occurs in the male with rising levels of testosterone acting on the hypothalamus and anterior pituitary to inhibit the release of GnRH, FSH, and LH. The Sertoli cells produce the hormone **inhibin**, which is released into the blood when the sperm count is too high. This inhibits the release of GnRH and FSH, which will cause spermatogenesis to slow down. If the sperm count reaches 20 million/ml, the Sertoli cells cease the release of inhibin, and the sperm count increases.



Gonadotropin-releasing hormone (GnRH) is produced by a part of the brain called the *hypothalamus*. When it circulates in the blood, it causes the release of two important hormones (see below, and Figure 4.1) from the *pituitarygland* in another specialised part of the brain.

Gonadotropin is pronounced 'gonn add oh troh pinn'. Hypothalamus is pronounced 'hy poh thah lah mooss'. Pituitary is pronounced 'pitt yoo itt ary'.

Follicle-stimulating hormone (FSH) is produced by the pituitary gland during the first half of the menstrual cycle. It stimulates development of the maturing ovarian follicle and controls ovum production in the female, and sperm production in the male.

Leutenizing hormone (LH) is also produced by the pituitary gland in the brain. It stimulates the ovaries to produce oestrogen and progesterone. It triggers **ovulation** (the release of a mature ovum from the ovary), and it promotes the development of the corpus luteum.

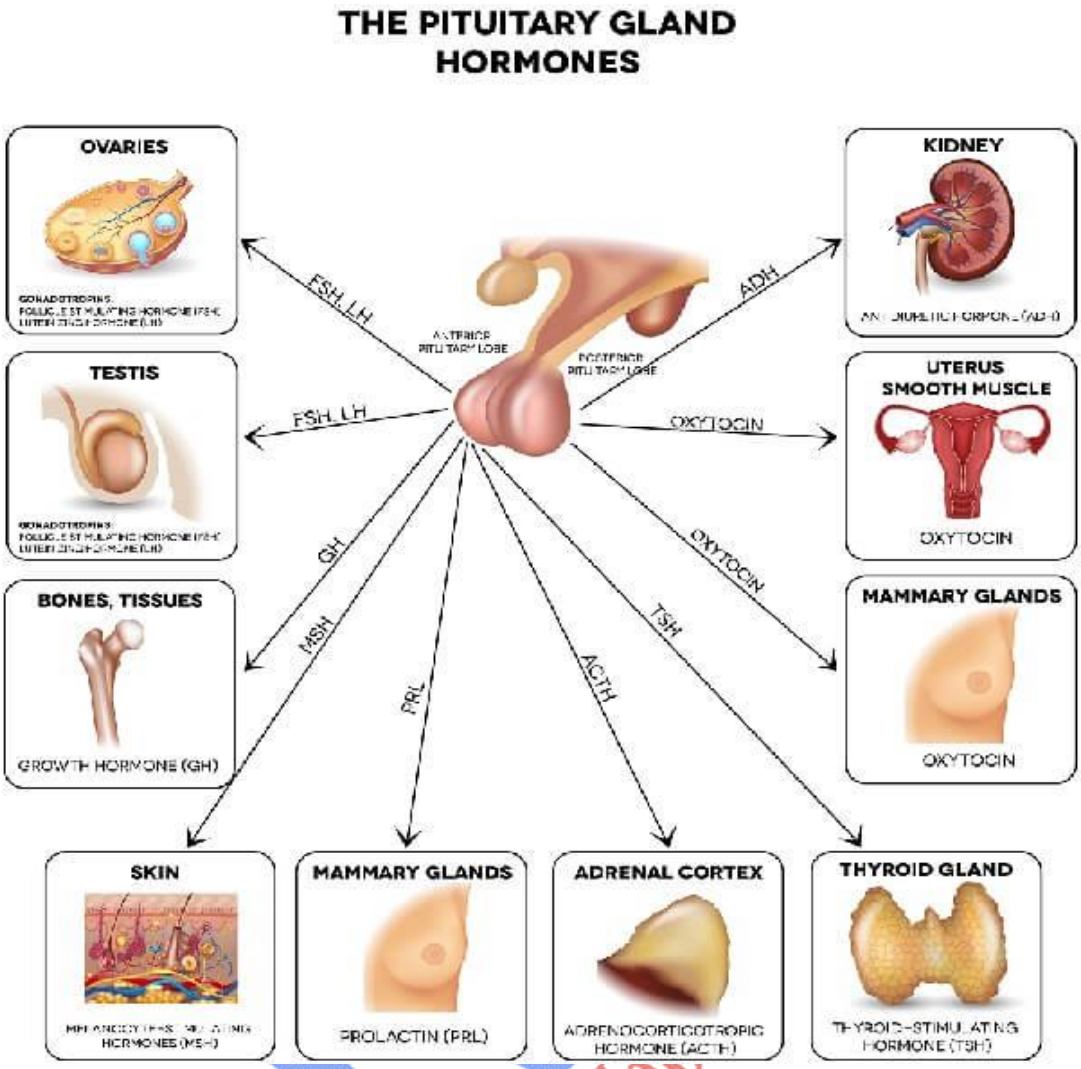
- What is the **corpus luteum**? (Think back to Study Session 3.)
    - The name means 'yellow body', and after ovulation it develops in the ovary from the enlarged ovarian follicle that released the ovum.

Oestrogen is a female reproductive hormone, produced primarily by the ovaries in the non-pregnant woman. It promotes the maturation and release of an ovum in every menstrual cycle. It is also produced by the placenta during pregnancy.

Progesterone is produced by the corpus luteum in the ovary; its function is to prepare the **endometrium** (lining of the uterus) for the reception and development of the fertilised ovum. It also suppresses the production of oestrogen after ovulation has occurred.

(c) Hypothalamic control of pituitary function

Ans.



The neuroendocrine system has been considered in two parts, that part dealing with the posterior pituitary, or neurohypophysis; and that part dealing with the anterior pituitary, or adenohypophysis. However, it is increasingly clear that the immune system also has such an important effect on neuroendocrine regulation that it must now also be considered as a special "diffuse" neuroendocrine component.

The Posterior Pituitary: The posterior pituitary is often termed the neurohypophysis because the hormones of this part of the pituitary are released directly from the axonal endings of their source neurons into the circulation

It is along this tract that the hormones oxytocin and vasopressin (also called antidiuretic hormone or ADH) are cleaved from their prohormones and prepared for release in vesicles along with their co-peptides neurophysin I (oxytocin) and neurophysin II (vasopressin).

Oxytocin. Oxytocin has no diurnal rhythm but is released in three reflexes following the influence of several different types of stimuli.

- In the milk let-down reflex the tactile stimuli applied to the breast by the suckling infant are transmitted to the hypothalamus by the spinohypothalamic tract directly to the preoptic and paraventricular nuclei to excite the magnacellular neurons and so provoke the release of hormone into the circulation. Oxytocin travels through the bloodstream acts on the mammary glands to cause milk release so that about 13 seconds later milk enters the ducts of the gland

- During parturition oxytocin induces powerful contractions of the uterine myometrium

Vasopressin. Vasopressin, also known as arginine vasopressin (AVP), acts on V2 receptors on the contraluminal surface of the distal tubular epithelium primarily in the collecting duct of the kidney to increase permeability and allow reabsorption of water and electrolytes into the circulation . Vasopressin has a diurnal peak late at night and early in the morning and a trough in the mid-afternoon. Sensors for plasma osmolality control the evoked secretion of vasopressin by magnacellular neurons in the paraventricular and supraoptic nuclei of the hypothalamus. The magnacellular neurons have intrinsic osmoreceptors in their plasma membrane and also receive afferent inputs from osmo-sensitive neurons in the organum vasculosum of the lamina terminalis. Sensors in the subfornical organ for angiotensin II also stimulate the release of vasopressin. Angiotensin II in the blood is elevated following the release of renin from the kidney in response to a decrease in blood pressure. Finally, the carotid and aortic arch bodies that signal the hypothalamus via the vagus and glossopharyngeal nerves via relay in the solitary nucleus also detect a decrease in blood oxygen or pressure and promote the release of vasopressin.

The Anterior Pituitary: The Anterior Pituitary is an endocrine gland controlled by the hypothalamus in several fundamentally different fashions than is the posterior pituitary. None of the six major hormones released by the adenohypophysis are of hypothalamic origin, rather all are synthesized in cells embryonically derived from Rathke's pouch in the anterior pituitary itself and released directly into the blood stream.

Growth hormone (GH) is secreted from somatotrophs, which comprise about half of the cells in the anterior pituitary (Figure 2.6). GH release is characteristically pulsatile being very low most of the day except following meals, exercise, during slow wave sleep, and at other individualized intervals. GH is necessary for normal linear growth and greatly influences intermediary metabolism by way of its induction of somatomedians (insulin-like growth factors, IGF) from target tissues most notably including the liver, chondrocytes, kidney, muscle, pituitary and the gastrointestinal tract. The hypothalamic regulation of GH secretion is illustrative of the mechanisms that govern all hormones of the anterior pituitary.

Prolactin. Prolactin is necessary for lactation and is secreted by pituitary lactotrophs, which constitute 15 to 20 percent of the cells in the normal pituitary. Control of prolactin secretion by the hypothalamus is unique to that of the other anterior pituitary hormones in that under normal circumstances it is restrained and not elicited. Dopamine released from the arcuate and paraventricular nuclei acts on D2 receptors to increase adenyl cyclase in lactotrophs and inhibit prolactin release. Increases in plasma prolactin induces increased levels of dopamine in the arcuate and paraventricular nuclei and so establishes short-loop feedback.

Luteinizing hormone and follicle-stimulating hormone control the gonads in men and women. These hormones are secreted by the gonadotrophs, which comprise about 10 percent of the adenohypophysis. Luteinizing hormone-releasing hormone (LHRH) is the hypothalamic factor that controls release of the gonadotrophs and primarily is released itself from the arcuate nucleus. Feedback regulation of LHRH is provided by low levels of estrogen in females and by testosterone in males.

Thyroid-stimulating hormone (TSH) is secreted by about 5 percent of the cells in the pituitary called thyrotrophs and regulates thyroid function. Thyrotropin-releasing hormone (TRH) is found in the highest concentrations in the medial division of the paraventricular nucleus. The thyroid hormones thyroxine (T4) and triiodothyronine (T3) inhibit TSH production and release at the level of

the pituitary (direct long loop) and inhibit the release of TRH at the level of the hypothalamus (indirect long loop).

Adrenocorticotropin (ACTH) controls glucocorticoid function of the adrenal cortex. ACTH is produced by the corticotrophs that comprise the remaining 15 percent of pituitary cells as part of the larger pro-opiomelanocortin gene product from which γ-melanocyte stimulating hormone and ß-endorphin are also derived. ACTH is released in pulses with an overall circadian rhythm peak at around 4 AM and a trough in the early evening. Corticotropin releasing-factor (CRH) is the primary but not the only hypothalamic factor that regulates ACTH release. CRH is primarily found in the paraventricular nucleus. The release of both ACTH and CRH are inhibited by the hormone cortisol secreted from the adrenal, and the release of both are strongly stimulated by stress.

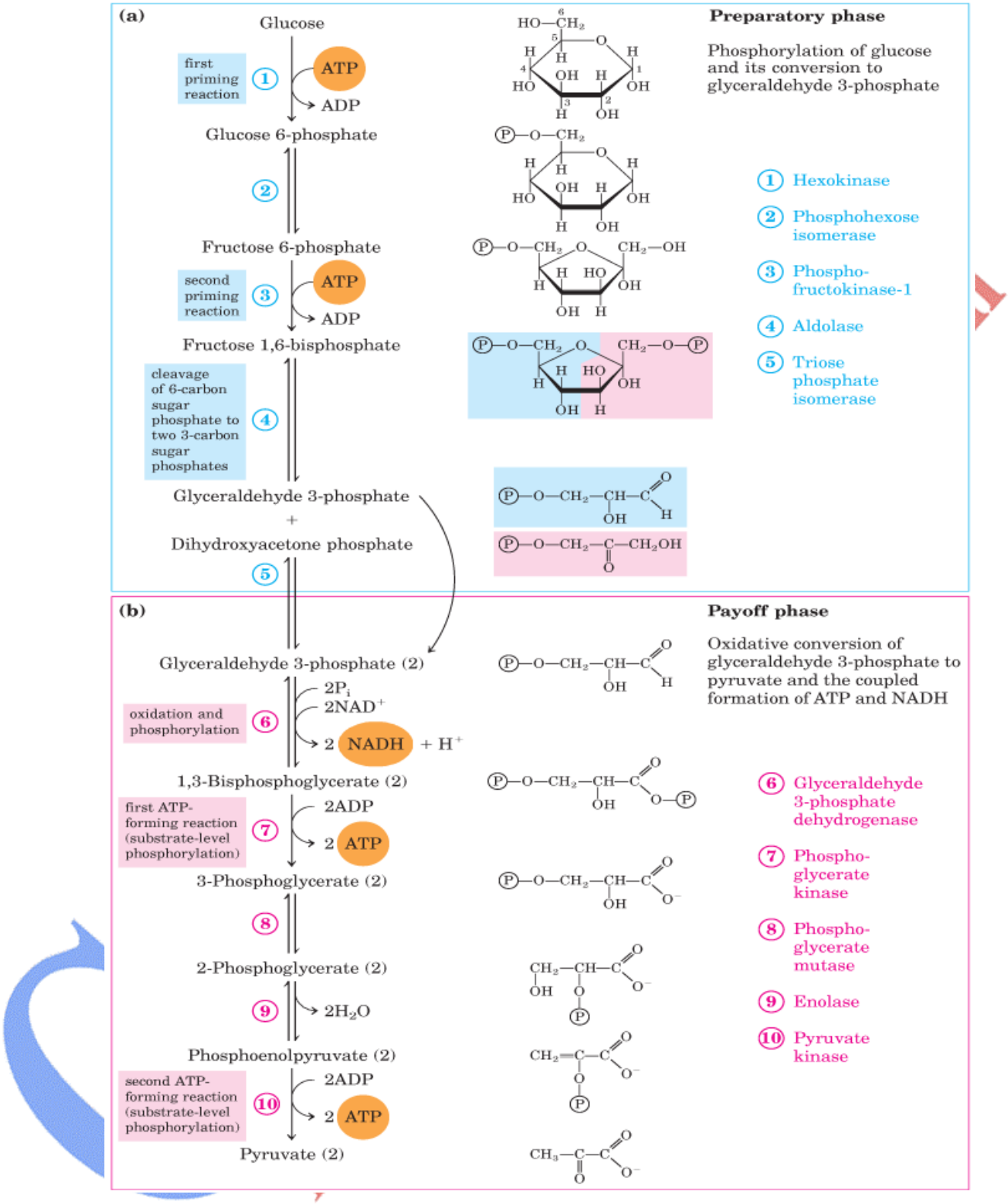
SECTION-C

8. What do you mean by carbohydrate catabolism? Explain the glycolysis and its control. (1x6)

Ans. Carbohydrate catabolism is the breakdown of **carbohydrates** to yield an energy rich compound called ATP. The production of ATP is achieved through the oxidation of glucose molecules. In oxidation, the electrons are stripped from a glucose molecule to reduce NAD+ and FAD.

Glycolysis:- Glycolysis literally means "splitting sugars" and is the process of releasing energy within sugars. In glycolysis, glucose (a six carbon sugar) is split into two molecules of the three-carbon sugar pyruvate. This multi-step process yields two molecules of ATP (free energy containing molecule), two molecules of pyruvate, and two "high energy" electron carrying molecules of NADH. Glycolysis can occur with or without oxygen.

In the presence of oxygen, glycolysis is the first stage of cellular respiration. In the abscence of oxygen, glycolysis allows cells to make small amounts of ATP through the process of fermentation. Glycolysis takes place in the cytosol of the cell's cytoplasm. However, the next stage of cellular respiration known as the citric acid cycle, occurs in the matrix of cell mitochondria. Glycolysis in two major stages. The first involves the phosphorylation of the glucose ring in preparation for an eventual breakdown into two 3-carbon molecules. In the second stage, the two 3-carbon molecules are converted into pyruvate.



Below are the 10 steps of glycolysis:

Step 1

The enzyme hexokinase phosphorylates (adds a phosphate group to) glucose in the cell's cytoplasm. In the process, a phosphate group from ATP is transferred to glucose producing glucose 6-phosphate.

Glucose ($C_6H_{12}O_6$) + hexokinase + ATP → ADP + Glucose 6-phosphate ($C_6H_{13}O_9P$)

Step 2

The enzyme phosphoglucoisomerase converts glucose 6-phosphate into its isomerfructose 6-phosphate. Isomers have the same molecular formula, but the atoms of each molecule are arranged differently.

Glucose 6-phosphate ($C_6H_{13}O_9P$) + Phosphoglucoisomerase → Fructose 6-phosphate ($C_6H_{13}O_9P$)

Step 3

The enzyme phosphofructokinase uses another ATP molecule to transfer a phosphate group to fructose 6-phosphate to form fructose 1, 6-bisphosphate.

Fructose 6-phosphate ($C_6H_{13}O_9P$) + phosphofructokinase + ATP → ADP + Fructose 1, 6-bisphosphate ($C_6H_{14}O_{12}P_2$)

Step 4

The enzyme aldolase splits fructose 1, 6-bisphosphate into two sugars that are isomers of each other. These two sugars are dihydroxyacetone phosphate and glyceraldehyde phosphate.

Fructose 1, 6-bisphosphate ($C_6H_{14}O_{12}P_2$) + aldolase → Dihydroxyacetone phosphate ($C_3H_7O_6P$) + Glyceraldehyde phosphate ($C_3H_7O_6P$)

Step 5

The enzyme triose phosphate isomerase rapidly inter-converts the molecules dihydroxyacetone phosphate and glyceraldehyde 3-phosphate. Glyceraldehyde 3-phosphate is removed as soon as it is formed to be used in the next step of glycolysis.

Dihydroxyacetone phosphate ($C_3H_7O_6P$) → Glyceraldehyde 3-phosphate ($C_3H_7O_6P$)

Net result for steps 4 and 5: Fructose 1, 6-bisphosphate ($C_6H_{14}O_{12}P_2$) ↔ 2 molecules of glyceraldehyde 3-phosphate ($C_3H_7O_6P$)

Step 6

The enzyme triose phosphate dehydrogenase serves two functions in this step. First the enzyme transfers a hydrogen (H^-) from glyceraldehyde phosphate to the oxidizing agent nicotinamide adenine dinucleotide (NAD^+) to form NADH. Next triose phosphate dehydrogenase adds a phosphate (P) from the cytosol to the oxidized glyceraldehyde phosphate to form 1, 3-bisphosphoglycerate. This occurs for both molecules of glyceraldehyde 3-phosphate produced in step 5.

A. Triose phosphate dehydrogenase + 2 H^- + 2 NAD^+ → 2 NADH + 2 H^+

B. Triose phosphate dehydrogenase + 2 P + 2 glyceraldehyde 3-phosphate ($C_3H_7O_6P$) → 2 molecules of 1,3-bisphosphoglycerate ($C_3H_8O_{10}P_2$)

Step 7

The enzyme phosphoglycerokinase transfers a P from 1,3-bisphosphoglycerate to a molecule of ADP to form ATP. This happens for each molecule of 1,3-bisphosphoglycerate. The process yields two 3-phosphoglycerate molecules and two ATP molecules.

2 molecules of 1,3-bisphoshoglycerate ($C_3H_8O_{10}P_2$) + phosphoglycerokinase + 2 ADP → 2 molecules of 3-phosphoglycerate ($C_3H_7O_7P$) + 2 ATP

Step 8

The enzyme phosphoglyceromutase relocates the P from 3-phosphoglycerate from the third carbon to the second carbon to form 2-phosphoglycerate.

2 molecules of 3-Phosphoglycerate ($C_3H_7O_7P$) + phosphoglyceromutase → 2 molecules of 2-Phosphoglycerate ($C_3H_7O_7P$)

Step 9

The enzyme enolase removes a molecule of water from 2-phosphoglycerate to form phosphoenolpyruvate (PEP). This happens for each molecule of 2-phosphoglycerate.

2 molecules of 2-Phosphoglycerate ($C_3H_7O_7P$) + enolase → 2 molecules of phosphoenolpyruvate (PEP) ($C_3H_5O_6P$)

Step 10

The enzyme pyruvate kinase transfers a P from PEP to ADP to form pyruvate and ATP. This happens for each molecule of phosphoenolpyruvate. This reaction yields 2 molecules of pyruvate and 2 ATP molecules.

2 molecules of phosphoenolpyruvate ($C_3H_5O_6P$) + pyruvate kinase + 2 ADP → 2 molecules of pyruvate ($C_3H_3O_3^-$) + 2 ATP

Summary

In summary, a single glucose molecule in glycolysis produces a total of 2 molecules of pyruvate, 2 molecules of ATP, 2 molecules of NADH and 2 molecules of water.

Although 2 ATP molecules are used in steps 1-3, 2 ATP molecules are generated in step 7 and 2 more in step 10. This gives a total of 4 ATP molecules produced. If you subtract the 2 ATP molecules used in steps 1-3 from the 4 generated at the end of step 10, you end up with a net total of 2 ATP molecules produced.

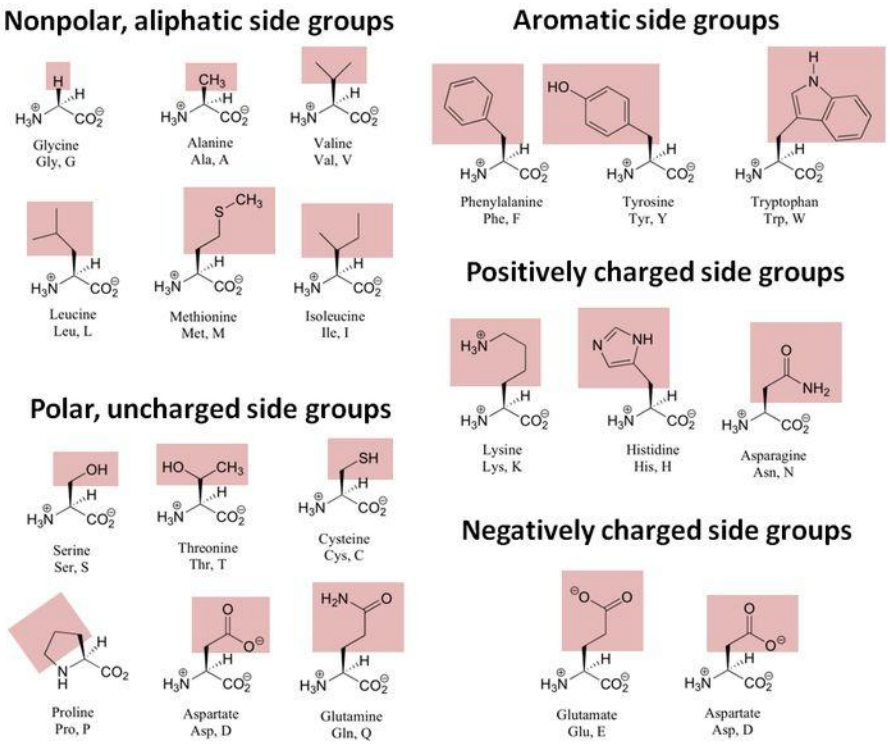
9. What are Amino acids? Explain in detail the oxidation of Amino acids.

Ans. Amino acids are organic compounds that combine to form proteins. Amino acids and proteins are the building blocks of life.

When proteins are digested or broken down, amino acids are left. The human body uses amino acids to make proteins to help the body:

- Break down food
- Grow
- Repair body tissue
- Perform many other body functions

Amino acids can also be used as a source of energy by the body.



Amino acids are classified into three groups:

- Essential amino acids
- Nonessential amino acids
- Conditional amino acids

Essential amino acids

- Essential amino acids cannot be made by the body. As a result, they must come from food.
- The 9 essential amino acids are: histidine, isoleucine, leucine, lysine, methionine, phenylalanine, threonine, tryptophan, and valine.

Nonessential amino acids

- "Nonessential" means that our bodies produce an amino acid, even if we do not get it from the food we eat.
- Nonessential amino acids include: alanine, asparagine, aspartic acid, and glutamic acid.

Conditional amino acids

- Conditional amino acids are usually not essential, except in times of illness and stress.
- Conditional amino acids include: arginine, cysteine, glutamine, tyrosine, glycine, ornithine, proline, and serine.

You do not need to eat essential and nonessential amino acids at every meal, but getting a balance of them over the whole day is important. A diet based on a single plant item will not be adequate but we no longer worry about pairing proteins (such as beans with rice) at a single meal. Instead we look at the adequacy of the diet overall throughout the day.

Amino Acid Oxidation and the Production of Urea

Amino acids, derived largely from protein in the diet or from degradation of intracellular proteins, are the final class of biomolecules whose oxidation makes a significant contribution to the generation of metabolic energy. The fraction of metabolic energy derived from amino acids varies greatly with the type of organism and with the metabolic situation in which an organism finds itself. Carnivores,

immediately following a meal, may obtain up to 90% of their energy requirements from amino acid oxidation. Herbivores may obtain only a small fraction of their energy needs from this source. Most microorganisms can scavenge amino acids from their environment if they are available; these can be oxidized as fuel when required by metabolic conditions. Photosynthetic plants, on the other hand, rarely, if ever, oxidize amino acids to provide energy. Instead, they convert CO_2 and H_2O into the carbohydrate that is used almost exclusively as an energy source. The amounts of amino acids in plant tissues are carefully regulated to just meet the requirements for biosynthesis of proteins, nucleic acids, and a few other molecules needed to support growth. Amino acid catabolism does occur in plants, but it is generally concerned with the production of metabolites for other biosynthetic pathways.

In animals, amino acids can undergo oxidative degradation in three different metabolic circumstances. (1) During the normal synthesis and degradation of cellular proteins (protein turnover. some of the amino acids released during protein breakdown will undergo oxidative degradation if they are not needed for new protein synthesis. (2) When a diet is rich in protein, and amino acids are ingested in excess of the body's needs for protein synthesis, the surplus may be catabolized; amino acids cannot be stored. (3) During starvation or in diabetes mellitus, when carbohydrates are either unavailable or not properly utilized, body proteins are called upon as fuel. Under these different circumstances, amino acids lose their amino groups, and the a-keto acids so formed may undergo oxidation to CO_2 and H_2O. In addition, and often equally important, the carbon skeletons of the amino acids provide three- and four-carbon units that can be converted to glucose, which in turn can fuel the functions of the brain, muscle, and other tissues.

Amino acid degradative pathways are quite similar in most organisms. The focus of this chapter is on vertebrates, because amino acid catabolism has received the most attention in these organisms. As is the case for sugar and fatty acid catabolic pathways, the processes of amino acid degradation converge on the central catabolic pathways for carbon metabolism. The carbon skeletons of the amino acids generally find their way to the citric acid cycle, and from there they are either oxidized to produce chemical energy or funneled into gluconeogenesis. In some cases the reaction pathways closely parallel steps in the catabolism of fatty acids.

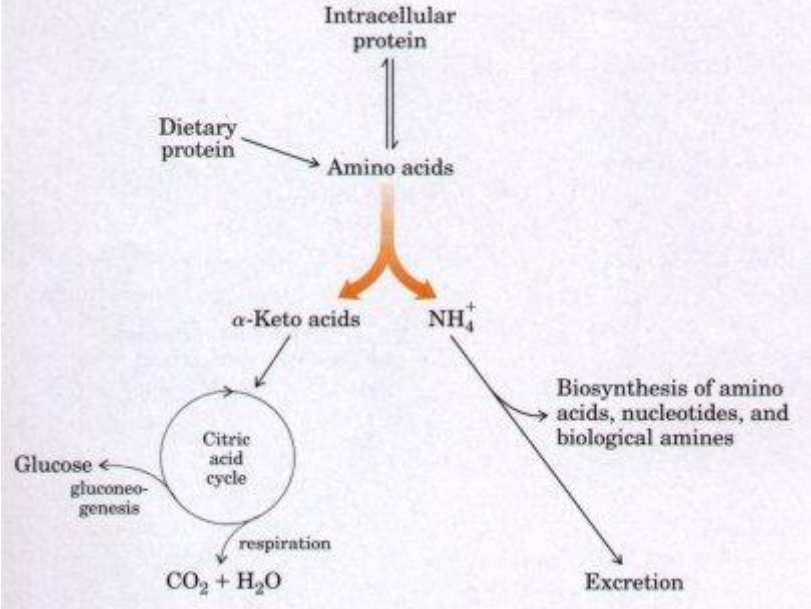
However, one major factor distinguishes amino acid degradation from the catabolic processes described to this point: every amino acid contains an amino group. Every degradative pathway therefore passes through a key step in which the a-amino group is separated from the carbon skeleton and shunted into the specialized pathways for amino group metabolism. This biochemical fork in the road is the point around which this chapter is organized. We deal first with amino group metabolism and nitrogen excretion, then with the fate of the carbon skeletons derived from the amino acids.

Metabolic Fates of Amino Groups

Nitrogen ranks fourth, behind carbon, hydrogen, and oxygen, in its contribution to the mass of living cells. Atmospheric nitrogen, N_2, is abundant but is too inert for use in most biochemical processes. Because only a few microorganisms can convert N_2 to biologically useful forms such as NH_3, amino groups are used with great economy in biological systems.

An overview of the catabolism of ammonia and amino groups in vertebrates is provided in Figure 17-2 (p. 508). Amino acids derived from dietary proteins are the source of most amino groups. Most of the amino acids are metabolized in the liver. Some of the ammonia that is generated is recycled and used in a variety of biosynthetic processes; the excess is either excreted directly or converted to uric acid or urea for excretion, depending on the organism. Excess ammonia generated in other (extrahepatic) tissues is transported to the liver (in the form of amino groups, as described below) for

conversion to the appropriate excreted form. With these reactions we encounter the coenzyme pyridoxal phosphate, the functional form of vitamin B_6 and a coenzyme of major importance in nitrogen metabolism



10. Write short notes on any two of the following :- (2x3)

(a) Biosynthesis of triglycerides

Ans. Most of the fatty acids synthesized or ingested by an organism have one of two fates: incorporation into triacylglycerols for the storage of metabolic energy or incorporation into the phospholipid components of membranes. The partitioning between these alternative fates depends on the requirements of the organism. During rapid growth, the synthesis of new membranes requires membrane phospholipid synthesis; organisms that have a plentiful supply of food but are not actively growing shunt most of their fatty acids into storage fats. The pathways to storage fats and several classes of membrane phospholipids begin at the same point: the formation of fatty acyl esters of glycerol. First we discuss the route to triacylglycerols and its regulation.

Triacylglycerols and Glycerophospholipids Are Synthesized from Common Precursors

Animals can synthesize and store large quantities of triacylglycerols, to be used later as fuel (see Box 16-1). In humans only a few hundred grams of glycogen can be stored in the liver and muscles, barely enough to supply the body's energy needs for 12 hours. In contrast, the total amount of stored triacylglycerol in a 70 kg man of average build is about 15 kg, enough to supply his basal energy needs for as long as 12 weeks (see Table 22-5). Whenever carbohydrate is ingested in excess of the capacity to store glycogen, it is converted into triacylglycerols and stored in adipose tissue. Plants also manufacture triacylglycerols as an energy-rich fuel, stored especially in fruits, nuts, and seeds.

Triacylglycerols and glycerophospholipids such as phosphatidylethanolamine share two precursors (fatty acyl-CoAs and glycerol-3-phosphate) and several enzymatic steps in their biosynthesis in animal tissues. Glycerol-3-phosphate can be formed in two ways (Fig. 20-18). It can arise from dihydroxyacetone phosphate generated during glycolysis by the action of the cytosolic NAD-linked **glycerol-3phosphate dehydrogenase**, and in liver and kidney it is also formed from glycerol

by the action of **glycerol kinase**. The other precursors of triacylglycerols are fatty acyl-CoAs, formed from fatty acids by **acylCoA synthetases** (Fig. 20-18), the same enzymes responsible for the activation of fatty acids for β oxidation (Chapter 16).

The first stage in the biosynthesis of triacylglycerols is the acylation of the two free hydroxyl groups of glycerol-3-phosphate by two molecules of fatty acyl-CoA to yield **diacylglycerol-3-phosphate**, more commonly called **phosphatidate** (Fig. 20-18). Phosphatidate occurs in only trace amounts in cells, but is a central intermediate in lipid biosynthesis; it can be converted either to a triacylglycerol or to a glycerophospholipid. In the pathway to triacylglycerols, phosphatidate is hydrolyzed by **phosphatidate phosphatase** to form a 1,2-diacylglycerol (Fig. 20-19). Diacylglycerols are then converted into triacylglycerols by transesterification with a third fatty acyl-CoA.

Triacylglycerol Biosynthesis in Animals Is Regulated by Hormones

In humans, the amount of body fat stays relatively constant over long periods, although there may be minor short-term changes as the caloric intake fluctuates. However, if carbohydrate, fat, or protein is consumed in amounts exceeding energy needs, the excess is stored in the form of triacylglycerols. The fat stored in this way can be drawn upon for energy and enables the body to withstand periods of fasting.

The biosynthesis and degradation of triacylglycerols are regulated reciprocally, with the favored path depending upon the metabolic resources and requirements of the moment. The rate of triacylglycerol biosynthesis is profoundly altered by the action of several hormones. Insulin, for example, promotes the conversion of carbohydrate into triacylglycerols (Fig. 20-20). People with severe diabetes mellitus, due to failure of insulin secretion or action, not only are unable to use glucose properly but also fail to synthesize fatty acids from carbohydrates or amino acids. They show increased rates of fat oxidation and ketone body formation (Chapter 16). As a consequence they lose weight. Triacylglycerol metabolism is also influenced by glucagon (Chapter 22), and by pituitary growth hormone and adrenal cortical hormones.

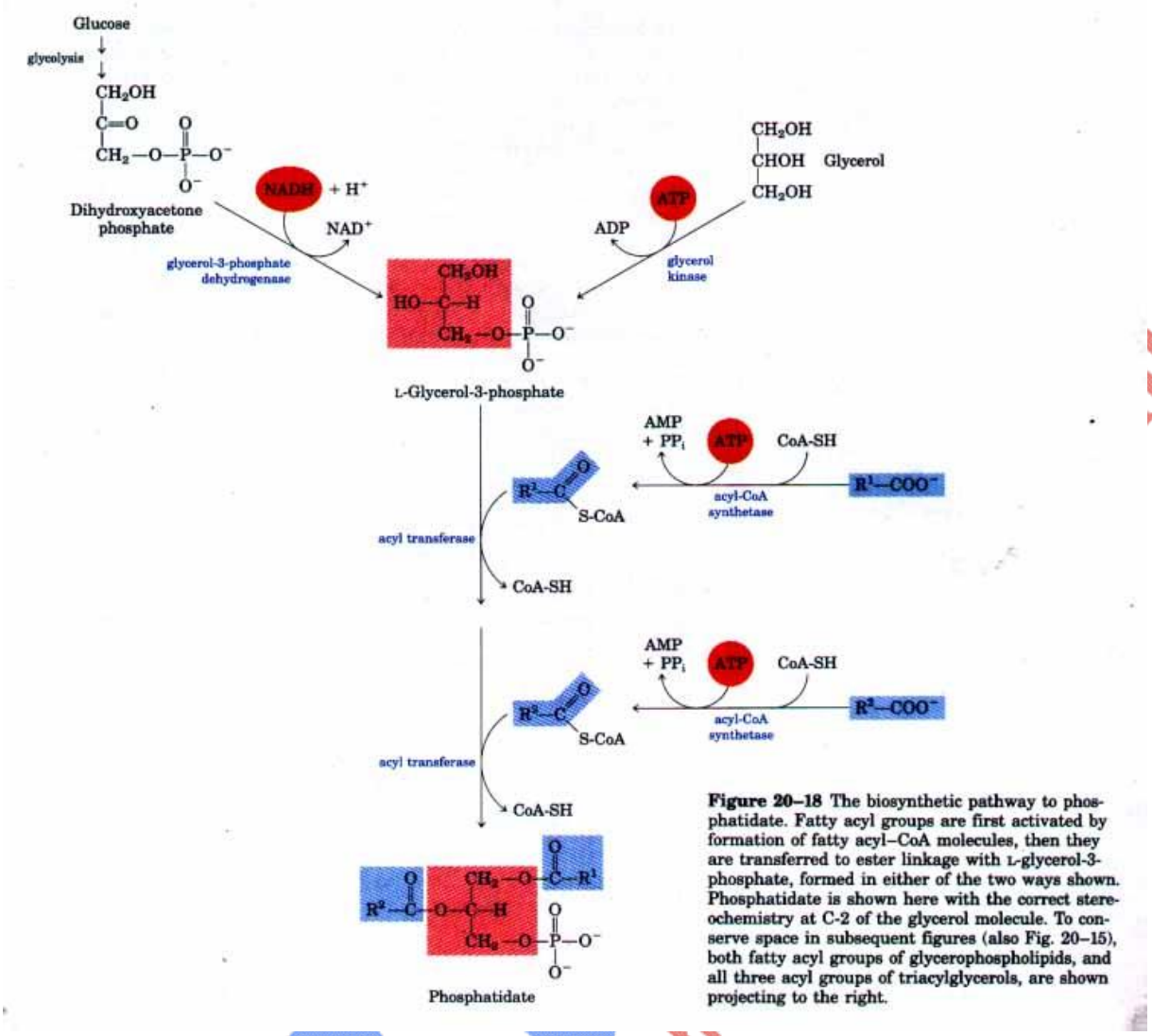


Figure 20–18 The biosynthetic pathway to phosphatidate. Fatty acyl groups are first activated by formation of fatty acyl–CoA molecules, then they are transferred to ester linkage with L-glycerol-3-phosphate, formed in either of the two ways shown. Phosphatidate is shown here with the correct stereochemistry at C-2 of the glycerol molecule. To conserve space in subsequent figures (also Fig. 20–15), both fatty acyl groups of glycerophospholipids, and all three acyl groups of triacylglycerols, are shown projecting to the right.

(b) Mineral metabolism

Ans. Mineral Metabolism:

Living beings have organic and inorganic types of chemical constituents. The organic constituents i.e. proteins, carbohydrates, fats etc. are made up of C, H, O and N. The inorganic constituents described as ‘minerals’ comprise of the elements present in the body other than C, H, O and N. Although they constitute a relatively small amount of the total body tissues, they are essential for many vital processes.

There are 31 elements present in the body.

They are divided into two classes:

(1) Essential elements and

(2) Non-essential elements.

Essential elements:

Those which are essential to maintain the normal living state of a tissue.

They are again divided into two sub groups:

Macro elements:

They are required to be present in the diet, more than 1 mg.

Ex. Ca, P, Mg, Na, K, CI and S.

Micro elements:

They are 8 in number and utilized in trace quantities (in microgram or Nano-gram). Hence they are called trace elements. These are Fe, Cu, Zn, Co, Mo, F, I and Mn.

Non-essential elements:

They are 8 in number. They are present in tissues but their functions if any are not clearly defined. They include Al, B, Se, Cr, Br, As, Ti and Pb. Four additional elements, Ni, Tin, Vanadium and Silicon have been suggested as essential trace elements in nutrition but their implications for human nutrition are unknown.

The mineral elements present in the body are supplied in the diet. In poor diets consumed by a large majority of people, calcium and iron deficiency occur commonly. Iodine deficiency occurs in people living in certain hilly tracts, where the soil and water are deficient in iodine. In tropical countries, addition of sodium chloride in the diet is of great importance, because of the loss of NaCl in sweat. The deficiencies of other minerals do not occur normally in average diets.

i. Sodium, potassium and chlorine are involved mainly in the maintenance of acid-base balance and osmotic control of water metabolism.

ii. Calcium, phosphorus and magnesium are constituents of bone and teeth.

iii. Phosphorus is the constituent of body cells of the tissues, such as muscle, liver etc.

iv. Sulphur is present in cysteine, methionine, thiamine, biotin, lipoic acid and coenzyme A.

Calcium:

Source:

Milk (0.2 gm./100 ml) and cheese are important dietary sources. Other sources-are egg yolk, lentils, nuts, cabbage, cauliflower and asparagus, etc.

Requirement:

(1) Men and women after 18 years of age require 800 mg/day.

(2) During lactation and in pregnancy of 2^{nd} and 3^{rd} term 1.2 gm./day is required.

(3) Infants under 1 year require-360-540 mg/day.

(4) Children of 1-18 years need 800-1200 mg/day.

Absorption:

Calcium is taken in the diet as calcium phosphate, carbonate, tartarate and oxalate. Calcium is absorbed actively in the upper small intestine. The active process is regulated by 1,25 dihyrocholecalciferol, a metabolite of vitamin D which is produced in the kidney in response to low plasma Ca^{++} concentrations. Absorption of calcium by the intestine is never complete. Ca is absorbed by an active transport process occurring mainly in the upper small intestine.

Calcium absorption is influenced by the following factors:

1. Vitamin D promotes absorption of Ca.

2. Acidic pH favous calcium absorption because Ca salts (phosphate and carbonates) are quite soluble in acid solution arid are relatively insoluble in alkaline solutions. Hence an increase in acidophilic flora, e.g. lactobacilli is recommended to lower pH which favours the absorption of Calcium.

3. Organic acids, lactose and basic amino acids in the diet favour calcium absorption.

4. Higher levels of proteins in the diet help to increase the absorption of calcium. On a high protein diet, about 15% of the dietary calcium is absorbed, compared with 5% absorption on a low protein diet. Certain calcium salts are much more soluble in aqueous solution of amino acids than in water and thus absorption of calcium is increased in presence of amino acids.

5. If calcium: phosphorus ratio is much high, $Ca_3(PO_4)_2$ will be formed and absorption of calcium is reduced. The optimal ratio for both elements is about 1:1 (1:2 to 2:1) and with ratios outside these limits, absorption is decreased. This is because of formation of insoluble calcium phosphate.

6. When fat absorption is impaired much free fatty acids are formed due to hydrolysis. These fatty acids react with free calcium to form insoluble calcium soap and then Ca is lost in faeces.

7. Absorption of calcium is inhibited by a number of dietary factors that cause formation of insoluble calcium salts, i.e. phytate (cereal grain), oxalate, phosphate and iron, etc.

8. High concentration of Mg in the diet decreases absorption of Ca.

9. Presence of excess fibre in the diet interferes with the absorption of Ca.

10. Percentage of calcium absorption decreases as its intake increases.

11. Parathyroid hormone increases the intestinal absorption of calcium.

12. Adrenal glucocorticoids diminish intestinal transport of Ca.

13. After the age of 55 to 60 there is gradual diminution of intestinal transport of calcium. During menopause many women develop negative calcium-phosphorus balance leading to a type of osteoporosis. This is usually accompanied by pain and fractures. The negative balance of calcium and phosphorous are markedly improved by administration of estrogen or by androgens such as testosterone. A combination of estrogen and androgen is more effective.

14. Kidney threshold regulates the blood calcium level. In a normal adult any extra calcium absorbed from the intestine is readily excreted in the urine. In hypocalcaemia kidney threshold also becomes abnormal.

15. Excess of iron also dis-favours absorption of calcium and phosphorus, as ferric phosphate is highly insoluble. The net result is an upset in the Ca:P ratio.

16. Oxalate in certain foods precipitate calcium in the intestine as insoluble calcium oxalate. The phytic acids of food form insoluble salt with calcium and reduce calcium absorption.

17. Vitamin D increases calcium and phosphorus absorption from the intestine. Vitamin D promotes synthesis of specific calcium binding protein which participates in the active transport of calcium across the small intestinal mucosa. Lack of vitamin D, excess of phytates, low Ca/P ratio in diet, increased pH of upper intestine and malabsorption syndromes influence the amount of calcium absorption adversely.

Biological role:

Calcium is involved in the following biological processes:

1. Constituent of bones and teeth:

Calcium along with phosphate constitutes the mineral part of the skeleton and teeth where it is present to the extent of 99% of the total calcium present in the body. It is primarily in the form of crystals of hydroxyapatite, while some is in combination with phosphate (calcium phosphate) in the form of amorphous crystals.

2. Neuromuscular functions:

This involves excitability of nerve function, neural transmission, and contractility of cardiac and skeletal muscle. Normal concentration of calcium ions is required for the normal excitability of heart muscle.

3. Blood coagulation:

It plays a vital role in blood clotting process since it activates the enzymic conversion of prothrombin into thrombin and production of thromboplastin. The removal of calcium from the blood can prevent blood coagulation and because of this reason EDTA, oxalates, citrates are used as anticoagulant because these ions can precipitate calcium into the respective insoluble salts.

4. Membrane function:

It controls the permeability of all membranes and is often bound by lecithine in the membrane, i.e. it decreases the permeability and balances the opposite action of sodium and potassium capillary permeability. This involves transfer of inorganic ions across cell membranes and release of neurotransmitters at synaptic junction.

5. Selected enzymatic reactions:

Calcium acts as activator for number of en2ymes like ATPase, succinic dehydrogenase, lipase, etc. It also antagonizes the effect of magnesium on many enzymes. It releases cellular enzymes such as amylase from the parotid and increases the level of activity of intracellular enzymes such as—Isocitric dehydrogenase, phosphorylase and phosphof ructokinase.

6. Regulation of secretion of certain peptide hormones:

Pituitary hormones, parathyroid hormone, calcitonin and vasopressin are regulated through calcium ionic concentration. Calcium along with zinc plays a vital role in release of insulin from pancreas. Calcium homeostasis: Normal blood values are 9.5-10.5 mg/100 ml. 35-45% of this is bound to proteins, mostly to the albumin fraction. In the extracellular fluid nearly all the calcium is in ionized form (55-65%). 0.5 (5-10%) mg is complexed to organic acids, phosphate, citrate, etc., while in renal failure, it may be complexed to other organic ions as well.

The skeleton is in a dynamic state of equilibrium to maintain calcium homeostasis. 4-8 gm. of calcium in bone is rapidly exchangeable with that in plasma and is present on the surface of the bone crystals—labile calcium storage pool. The remaining 99% of bone calcium is more firmly fixed in bone tissue and exchanges at a very slow rate.

Metabolism:

The blood cells contain very little amount of calcium, most of the blood calcium is therefore, in the plasma, where it is present in 3 fractions:

(1) Ionized about 2 mg/100 ml.

(2) Non-diffusible (protein bound) above 3.5 mg/100 ml.

(3) A small amount as calcium complex of citrate and phosphate.

All these forms of calcium in the serum are in equilibrium with one another. A decrease in ionized calcium in the serum causes tetany. This may be due to an increase in the pH of blood or lack of calcium because of poor absorption from the intestine, decreased dietary intake, increased renal excretion as in nephritis or parathyroid deficiency.

Factors influencing blood calcium level:

1. Parathyroid hormone:

In fasting condition or state there is no absorption from the intestine, the normal plasma Ca concentration is maintained by its rate of excretion and its mobilization from bones through the action of the parathyroid hormone.

2. Vitamin D:

It enhances absorption of Ca from the intestine and thus maintains normal Ca concentration.

3. Plasma proteins:

Half of the blood Ca (non-diffusible) is bound to plasma proteins and thus any decrease in these proteins will be accompanied by a decrease in the total calcium level.

4. Plasma phosphate:

A reciprocal relationship exists between the concentration of Ca and phosphate ions in plasma. The marked increase in serum phosphate causes a fall in serum calcium concentration.

5. Calcitonin:

An increase in the ionized Ca levels in the plasma is the stimulus for the production of calcitonin which then causes a deposition of Ca in bone.

Excretion:

Calcium is excreted in the urine, bile and digestive secretion. About 75% of dietary calcium is absorbed and rest is excreted as fecal calcium. Nearly 10 g of Ca is filtered by the renal glomeruli in 24 hours. But only 200 mg appear in the urine, which is in the ionic state as well as in the complexes with citrate and other organic anions. A very small amount of Ca is excreted into the intestine after absorption. About 15 mg of Ca is excreted in the sweat. Vigorous physical exercise increases the loss of Ca by way of sweat.

Disease state:

Calcium metabolism is highly influenced by parathyroid hormones. In hyperparathyroidism serum calcium rises (12-22 mg/100 ml) (hypercalcaemia), phosphatase activity is increased, urinary calcium is decreased and phosphorus rises in serum. The calcium, phosphorus ratio is important in ossification. In the serum the product of calcium and phosphorus (in mg/100 ml) is normally 50 in children and may be below 30 during rickets.

The following are the diseases related to calcium in the body:

(a) Effects of parathyroid:

1. In hyperparathyroidism, the following changes occur:

(i) Hypercalcemia (12-22 mg/dl).

(ii) Decrease in serum phosphate.

(iii) Diminished renal tubular reabsorption of phosphate.

(iv) Increased phosphatase activity.

(v) Renal urinary Ca and phosphorus found from bone decalcification and dehydration.

(vi) Extra Ca and P are lost from soft tissue and bones by increased bone destroying activity.

2. In hypoparathyroidism, the following changes occur:

(i) The concentration of serum Ca may drop below 7 mg/100 ml.

(ii) Increased serum phosphate and decreased urinary excretion of calcium and phosphorus.

(iii) Normal or occasionally raised serum phosphatase activity.

(iv) Normal acid-base equilibrium.

(v) Probably increased bone density.

(b) Tetany:

Decreased ionized fraction of serum Ca causes tetany.

This may be due to:

1. Increase in the pH of blood.
2. Poor absorption of Ca from the intestine.
3. Decreased dietary intake of Ca.
4. Increased excretion of Ca as in hepatitis.
5. Parathyroid deficiency.
6. Increased retention of phosphorus as in renal tubular disease.

Symptoms:

Muscles lose tone and become flabby.

Affects the face, hands and feet.

(c) Rickets:

This is characterized by faulty calcification of bones in children showing serum phosphate values of 1 to 2 mg/100 ml.

This may be due to:

1. Vitamin D deficiency.
2. A deficiency of Ca and P in the diet or a combination of both.
3. Poor absorption of Ca from the intestine.
4. Parathyroid deficiency.
5. Increased alkaline phosphatase activity.

(d) Osteoporosis:

This disease occurs in adults due to the following causes:

1. Decalcification of bones as a result of Ca deficiency in the diet.
2. Hypoparathyroidism.
3. Low vitamin D content of the body.

Symptoms:

Fractures of the brittle bones occur even after minor accidents.

Pain due to fracture of vertebrae (may radiate round the trunk, to the buttocks or down the legs).

Renal rickets:

It is a hereditary disease. It is called familial hypophosphatemia rickets. Affected persons show severe rickets with hypophosphatemia.

The causes are:

(i) Defective transport of phosphate by the intestine and the renal tubules

(ii) Lowered serum phosphorus and hyperphosphaturia

(iii) Reduced intestinal absorption of calcium and phosphorus. Vitamin D in ordinary doses does not relieve the disease. Hence, it is referred to as vitamin D resistant rickets.

Phosphorus:

Source:

Phosphorus is present in nearly all foods therefore a dietary deficiency is not known to occur in man. Dairy products, cereals, egg yolk, meat, beans and nuts are usually rich sources. The daily average intake is 800-1000 mg and is about twice that of calcium.

Absorption:

Like calcium, phosphorus is also absorbed by upper small intestine and factors influencing the absorption are also similar. The normal range for plasma inorganic phosphorus is 3.0-4.5 mg/dl. In children values are higher (5-6 mg/dl) and remain so up-till puberty.

Distribution:

Phosphorus is distributed more widely than calcium. 15% is found in muscle and other soft tissues and 85% in the inorganic mineral phase of bone. It is an integral part of many macromolecules. Ex. Phospholipids, phosphoproteins and nucleic acids.

Functions:

It has no physiological effects comparable to that of calcium but it has many other functions which are as follows:

1. Formation of bone and teeth.

2. Formation of phospholipids essential to every cell.

3. Formation of nucleic acids and derivatives.

Ex. Adenylic acid and is thus significant in (RNA and DNA) protein synthesis and from genetics point of view.

4. Formation of organic phosphates as intermediate in metabolic processes.

Ex. In glycolysis, Glucose + ATP → G-6-P + ADP.

5. Formation of energy rich phosphate compounds.

Ex. ATP (energy currency of the cell).

6. Both inorganic and organic phosphates can take part in buffering the cell.

Ex, Sodium-potassium-phosphates.

7. Formation of coenzymes.

Ex. TPP, NADP.

8. Formation of phosphoprotein.

Ex. Casein.

Excretion:

Urinary excretion is equivalent to dietary phosphate intake. It varies diurnally, more being excreted at night. The usual daily loss is 600-800 mg, tubular resorption being 85-95%. Renal loss of phosphate can be of significant magnitude to lower serum phosphorus values and enhance osteoid demineralization.

Homeostasis:

There is a greater fluctuation observed in blood phosphate values due to easy shift between extracellular fluid and intracellular compartments. Thus it is quite dependent on dietary phosphorus. Inorganic phosphate affects the net movement of calcium into and out of bone.

Raised phosphate will lead to depression of the solubility of the calcium of bone crystals and thus shift equilibrium towards bone. In this manner it opposes the effect of the parathyroids. Ingestion of heavy dose of phosphate can lower serum calcium and increase excretion of calcium in urine. Lowered phosphorus on the other hand will make parathyroid activity more apparent.

Hormonal factors are not directly linked. However renal phosphate clearance is very vital in homeostasis and seems to be secondarily involved in certain endocrinopathies, e.g. involving parathormone, growth hormone and corticosteroids.

Disease state:

The following are the disease states of phosphorus in the body:

1. In rickets, serum phosphate is as low as 1-2 mg/100 ml (There is a temporary decrease in serum P during absorption of carbohydrates and some fats).

2. Organic P content is low but inorganic content is high in the serum in diabetes.

3. P retention causes acidosis in severe renal diseases. This results in increase of serum P.

4. Serum P levels are increased in hypoparathyroidism and decreased in hyperparathyroidism and celiac disease.

5. In renal rickets, blood P is very low with an increased alkaline phosphatase activity.

6. The deficiency of vitamin D is the cause of low serum P and the defects in the calcification of bones (referred to as vitamin D resistant rickets).

Magnesium:

Source:

Magnesium is present in milk, egg, cabbage, cauliflower etc.

Daily requirement:

Infants—100-150 mg; Children—150-200 mg and Adults—200-300 mg.

Absorption:

A greater part of the daily ingested Mg is not absorbed. A very high intake of fat, phosphate, calcium and alkalies diminish its absorption. Parathyroid hormone increases its absorption.

Distribution:

Whole blood it is 2-4 mg/dl, CSF it is 3 mg/100 ml and muscle it is 2 mg/100 ml.

Functions:

1. 70% of the total magnesium content (21g) of the body is combined with calcium and phosphorus in the complex salts of bone. The remainder is in the soft tissues and body fluids. It is the principal cation of the soft tissue.

2. Magnesium ions act as activators for many of the phosphate group transfer enzymes.

3. It is found in certain enzymes, such as co-carboxylase.

4. It functions as a cofactor for oxidative phosphorylation.

Disease state:

The following are the disease states of magnesium in the body:

1. Magnesium deficiency causes depression, muscular weakness and liability to convulsions. Its deficiency has also been observed in chronic alcoholics with low serum mg and muscular weakness.

2. Low in Kwashiorkor, causing weakness.

Low levels of Mg are reported in uremia, normal and abnormal pregnancy, rickets, growth hormone treatment, hypercalcemia and recovery phase of diabetic coma.

Sodium, Potassium, Chloride:

Substances whose solutions conduct an electric current are called 'electrolytes'. They are about 11 in general. Na, K, Ca and Mg are cations whereas CI, HCO_3, HPO_4, SO_4, organic acids and proteins are anions. Among these sodium, potassium and chloride are important in the distribution and the retention of body water, thus have close relationship among them. Hence these three elements appear as a single question in the university exams.

Source:

The most important source of Na and CI in the diet is common table salt (NaCl). The good source of K are chicken, calf flesh, beef liver, dried apricot, dried peaches, bananas, the juice of orange and pineapple, potatoes etc.

Absorption:

Normally Na, K and CI are completely absorbed from the gastro-intestinal tract. About 95% of sodium which leaves the body is excreted in the urine.

Distribution:

In the tissues both Na and K occur in a relatively large amount as compared to chloride and other inorganic salts as well as protein and organic salts. Sodium is present in extra cellular fluid and in a very low concentration inside the cells whereas potassium is mainly found inside the cells and in a very low concentration in the extracellular fluid.

Functions of sodium and potassium:

These electrolytes maintain normal osmotic pressure in the body and protect the body against excessive loss of fluid.

1. They maintain the acid base balance in the body. Sodium bicarbonate, sodium phosphate, potassium phosphate form the buffer system of extracellular and intracellular fluids.

2. They maintain normal water balance.

3. Na also functions in the preservation of normal excitability of muscle and the permeability of the cells. K inhibits 'muscular contraction' in general.

4. High intracellular potassium concentrations are essential for several important metabolic functions, including protein biosynthesis by ribosomes.

5. Sodium and Potassium chlorides maintain the viscosity of blood. A number of enzymes including glycolytic enzymes, such as pyruvate kinase, require K^+ for maximal activity.

6. Na helps in the formation of the gastric juice. NaCl takes part in the series of reactions as a result of which HC1 is manufactured by the stomach.

7. K of KHb in the red cells helps in carbon dioxide transport.

8. K ions inhibit cardiac contraction and prolong relaxation.

9. K ions exert important effect on the function of nervous system.

Functions of chloride:

1. It provides 2/3rd of the anion of plasma and is the main factor for regulating body reactions.

2. NaCl and KCl are important agents in regulation of osmotic pressure in the body.

3. HCl of gastric juice is ultimately derived from the blood chlorides.

4. Chloride ions are essential for the action of ptyalin and pancreatic amylase.

5. It is essential in acid-base regulation. Chloride plays a role in the body by chloride shift mechanism.

Metabolism:

The metabolism of these elements is influenced by the following factors:

Hormones:

Mainly adrenocortical steroids and some of the sex hormones facilitate the retention of sodium and chloride in the body and excretion of potassium by kidneys in the urine. In adrenocortical deficiency, serum sodium decreases because excretion increases.

Temperature:

When atmospheric temperature is high as in summer, large amounts of sodium and chloride are lost in perspiration (sweating) and this loss may be checked when temperature is low (in winter).

Renal function:

In renal disease, with acidosis, Na and CI ion excretion in urine is increased due to poor tubular reabsorption of sodium whereas that of K ion is decreased leading to hyponatraemia and hypochloraemia but hyperkalaemia.

Average requirement of Na and K in human body is 5-15 and 4 gm. per day, respectively.

Disorders:

Hyponatraemia:

On sodium deficient diet, young ones grow slowly, lack fat deposit, there is muscle and testicular atrophy, lung infection and deficiency of osteoid tissues. There will also be loss of water, which will be evident by rapid weight loss.

Hypokalaemia:

Extreme potassium depletion in circulating blood causes hypokalemia in young one, they grow slowly and both sexes become sterile. The heart rate is slow, muscle weakness, irritability and paralysis are seen. Bone growth is retarded and in becomes excessively fragile and kidney hypertrophy is exhibited.

Hyperkalemia:

Hyperkalemia paralysis occurs due to excessive amount of potassium in blood. The disease is characterized by periodical attacks of weakness or paralysis. The symptoms of hyperkalaemia are chiefly cardiac and central nervous system depression. They are related to the elevated plasma potassium level and not to increase in intracellular potassium levels.

A dietary chlorine deficiency produces no symptom except a subnormal growth rate. Under normal dietary condition human beings are not subject to a deficiency of sodium, potassium or chlorine. However excessive diarrhoea, vomiting or extreme sweating over long period may bring about a NaCl deficiency. Sometimes the metabolism of individual minerals is asked as a separate question in the university exams. Hence each one is described separately in detail, hereunder.

Sodium:

Physiological functions:

1. Major component of extracellular fluids and exists in the body in association with anions chloride, bicarbonate, phosphate and lactate.

2. In association with chloride and bicarbonate it plays a role in acid base equilibrium.

3. Maintains osmotic pressure of the body fluids and thus protects the body against excessive fluid loss.

4. Plays an important role in the absorption of glucose and galactose from small intestine.

5. Maintains normal water balance and distribution.

6. Maintains the normal neuromuscular function.

7. Functions in permeability of cells.

Distribution:

About 1 /3rd of the total sodium content of the body is present in the inorganic portion of the skeleton. Most of the sodium is present in the extracellular fluid.

Plasma — 330 mg/100 ml

Muscles — 60 to 160 mg/100 gm.

Cells — 85 mg/100 gm.

Nerve — 312 mg/100 gm.

Daily requirement:

Adults require 5-15 gms/day. In temperate region, NaCl intake is less. In tropical region, NaCl intake is more. Hypertension patients should not take more than 1 gm. of Na per day.

Absorption:

Normally, Na is completely absorbed from gastro-intestinal tract. Less than 2% is eliminated in feces. In persons suffering from diarrhoea, large amounts are lost in feces.

Excretion:

Urine — 5-35 gm.

Skin — 25-50 mg

Stool — 10-125 mg

Excessive loss of Na by sweating causes heat arrays.

Disease state:

1. Adrenal cortical steroids regulate the metabolism of Na. Insufficiency of adrenal cortical steroids decreases serum Na level with an increase in sodium excretion.

2. In chronic renal disease when acidosis exists, Na depletion occurs due to poor tubular reabsorption of Na as well as to the loss of Na in the buffering acids.

3. In persons not adapted to high environmental temperature large amount of Na is lost in the sweat, developing muscular cramps of extremities, oedema, headache, nausea and diarrhoea.

4. Hyponatremia causes dehydration and reduced blood pressure, decreased blood volume and circulatory failure.

This may be due to:

(a) Prolonged vomiting and diarrhoea resulting in excessive loss of digestive fluid.

(b) Chronic renal disease with acidosis due to poor tubular reabsorption of Na.

(c) Adrenocortical insufficiency.

(d) Loss of weight due to loss of water.

5. In Hypernatremia, serum Na is high.

This occurs in:

(a) Hyperactivity of adrenal cortex as in Cushing's syndrome.

(b) Prolonged treatment with cortisone and ACTH as well as sex hormones, this results in—

(i) Increased retention of water in the body.

(ii) Increase in blood volume,

(iii) Increase in blood pressure.

6. Steroid hormones cause retention of Na and water in pregnancy.

Potassium:

Physiological junctions:

1. Potassium is largely present in intracellular fluid and it is also present in small amounts in the extra cellular fluid because it influences the cardiac muscle activity.

2. It plays an important role in the regulation of acid-base balance in the cell.

3. It maintains osmotic pressure.

4. It functions in water retention.

5. It is essential for protein biosynthesis by ribosomes.

6. The glycolytic enzyme pyruvate kinase requires K^+ for maximal activity.

Sources:

High content of potassium is found in chicken, beef, liver, bananas, orange juice, pineapple, yam, potatoes etc.

Distribution:

Plasma — 20 mg/100 ml

Cells — 440 mg/100 gm.

Muscles — 250-400 mg/100g

Nerves — 530 mg/100g.

Daily requirement:

Normal intake of K^+ in food is about 4 gm. It is so widely distributed that its deficiency is rare except in pathological condition.

Blood potassium:

Normal level of serum K is 14-20 mg/100 ml. Erythrocytes contain large amounts of K which avoids hemolysis. Serum K decreases during increased carbohydrate utilization following glucose or insulin administration. Aldosterone decreases serum K.

Absorption:

Normally, K is practically completely absorbed from gastrointestinal tract and less than 10% of K is eliminated in the feces. In subjects with diarrhea large amounts are lost in feces.

Excretion:

K is normally eliminated almost entirely in urine and a small amount in the feces. Aldosterone exerts an influence on potassium excretion. In normal kidney function; K is very promptly and efficiently removed from the blood.

Disease state:

1. K is not only filtered by the kidney but is also secreted by the renal tubules. Excretion of K is greatly influenced by changes in acid-base balance and also by adrenal cortex. The capacity of kidney to excrete K is very great and therefore hyperkalaemia does not occur even after ingestion of K, if kidney function is impaired K should not be given intravenously unless, circulatory collapse and dehydration are corrected.

2. Hyperkalaemia occurs in patients in the following conditions.

(a) Renal failure

(b) Severe dehydration

(c) Addison's disease due to decreased excretion of K by the kidney

K deficiency occurs in chronic wasting diseases like malnutrition, prolonged negative nitrogen balance, gastrointestinal losses and metabolic alkalosis.

Chlorine:

Physiological functions:

1. As a component of sodium chloride, chloride ion is essential in acid-base balance.

2. As Cl^- it is also essential in water balance and osmotic pressure regulation.

3. It is also important in the production of HCl in the gastric juice.

4. Cl^- ion is an activator of amylase.

Sources:

Mainly as NaCl salt (table salt).

Distribution:

Plasma — 365 mg/100ml

Cells — 190 mg/ 100mg

CSF — 440 mg/100ml

Muscle — 40 mg/100g

Nerve — 171 mg/100g

Daily requirement:

5-20 gms. Excess consumption of NaCl increases blood pressure in hypertensive patients. Causes edema in protein deficiency.

Absorption:

Normally CI is practically completely absorbed from the GI tract.

Excretion:

CI is chiefly eliminated in the urine, also in sweat. Its concentration in sweat is increased in hot climates and decreased by aldosterone.

Diseases state:

1. CI deficit also occurs when losses of Na are excessive in diarrhoea, sweating and certain endocrine disturbances.

2. Loss of CI due to loss of gastric juice by vomiting or pyloric or duodenal obstruction.

3. Hypochloremia alkalosis may develop in Cushing's syndrome or after administration of ACTH or cortisone.

Sulphur:

Sources:

Sulphur is taken mainly as cysteine and methionine present in proteins. Other compounds in the diet contribute small amounts of sulphur.

Absorption:

Inorganic sulphate is absorbed as such from intestine into the portal circulation. Small amount of sulphide may be formed in the bowel by the action of bacteria, but if absorbed into the blood stream, it is rapidly oxidized to sulphate.

Sulphur in blood (serum):

Inorganic — 0.5-1.1 mg/100 ml

Ethereal sulphate — 0.1-1.0 mg/100 ml

Neutral sulphur — 1.7-3.5 mg/100 ml

Physiological functions:

1. Sulphur is present primarily in the cell protein in the form of cysteine and methionine.

2. Cysteine plays important part in the protein structure and enzyme activity.

3. Methionine is the principal methyl group donor in the body. The 'activated' form of methionine, s-adenosyl methionine is the precursor in the synthesis of a large number of methylated compounds which are involved in intermediary metabolism and detoxification mechanism.

4. Sulphur is a constituent of coenzyme A and lipoic acid which are utilized in the synthesis of acetyl-CoA, malonyl CoA, Acyl-CoA and S-acetyl lipoate (involved in fatty acid oxidation and synthesis).

5. It is a component of a number of other organic compounds such as heparin, glutathione, thiamine, pantothenic acid, biotin, ergothionine, taurocholic acids, sulphocyamides, indoxyl sulphate, chondroitin sulphate, insulin, penicillin, anterior pituitary hormones and melanin.

Excretion:

Excreted in urine in 3 forms. Total sulphate excretion may be diminished in renal function impairment and is increased in condition accompanied by excessive tissue breakdown as in high fever and increased metabolism.

Disease state:

Serum sulphate is increased in renal function impairment, pyloric and intestinal obstruction and leukemia.

Marked sulphate retention in advanced glomerulo-nephritis causes the development of acidosis.

Increase in blood indica (indoxyl potassium sulphate) may occur in uremia.

Iron:

Iron is present in all organisms and in all the cells. It does not exist in the free state, instead is always present in organic combination, usually with proteins. It exists in two forms i.e. Fe^{2+} (ferrous) and Fe^{3+} (ferric). It serves as an oxygen and electron carrier and is incorporated into redox enzymes and substances which carry out the function of oxygen transport such as haemoglobin and cytochromes.

Total iron content in normal adult is 4 to 5 grams. 60-70% is present in hemoglobin, 3% in myoglobin and 0.1% in plasma combined with β-globulin transport protein transferrin. Hemoprotein and flavoprotein make up to less than 1% of total iron. Rest is stored as ferritin.

Source:

Rich – Liver, heart, kidney, spleen.

Good – Egg yolk, fish, nuts, dates, beans, spinach, molasses, apples, bananas, etc.

Poor — Milk, wheat flour, polished rice, potatoes etc.

Daily requirement:

Only about 10% of ingested iron is absorbed.

i. Infants – 10-15 mg..

ii. Children – 1-3 years 15 mg.

iii. 4-10 years – 10 mg.

iv. Older children and adults of 11 to 18 years — 18 mg.

v. 19 years and above — 10 mg.

vi. Females between 11 and 50 years of age and during pregnancy or lactation – 18 mg.

vii. After 51 years of age — 10 mg.

viii. In adult women the average loss of iron with blood during menstrual period is 16-32 mg per month or an additional loss of 0.5 to 1.0 mg per day. This amount is easily obtained from diet.

ix. In excessive menstrual blood loss and in chronic iron-deficiency anemia, a supplement of 100 mg of iron per day is sufficient to replenish.

x. During growth, pregnancy and lactation iron demand is more.

xi. In healthy adult male or post menopause women dietary iron requirement is negligible unless any deficiency or loss of iron occurs.

xii. Iron deficiency occurs as a result of malabsorption from gastro-intestinal tract.

xiii. A defect in hemoglobin synthesis in anemia is commonly found in copper deficiency.

Biologically active compounds that contain iron:

1. Haemic compounds:

In these compounds the protoporphyrin is combined with iron to form haem (divalent iron) and haematin.

Ex. Hemoglobin, myoglobin, cytochromes, catalases and peroxidases.

2. Non-haemic compounds:

These include Transferrin (siderophilin) to transport iron, ferritin and haemosiderin which are the stored forms of iron and miscellaneous compounds like enzymes.

Absorption:

Very little (less than 10%) of dietary iron is absorbed. Excretion in the urine is minimal. Infants and children absorb more iron as compared to adults. Iron deficiency in infants is due to dietary deficiency. Iron deficient children absorb approximately twice as much as normal children do. Absorption mainly occurs in the duodenum and the proximal jejunum.

(a) Most of the iron in food occurs in the ferric form (Fe^{3+}), ex. either as ferric hydroxide or as ferric organic compounds. Acidic pH of the gastrointestinal tract favours the absorption whereas alkaline pH decreases it. In an acid medium, these compounds are broken down into free ferric ions or loosely bound organic iron, reducing substances such as —SH groups ex. cysteine and ascorbic acid

which convert ferric iron into the reduced (ferrous) state, in this form iron is more soluble and should therefore be more readily absorbed.

(b) A diet high in phosphate, phytic acid and oxalic acid decreases iron absorption since these substances form the insoluble compounds with iron. Conversely, a diet very low in phosphate markedly increases iron absorption.

(c) The extent of absorption depends on the degree of saturation of the tissue, ex. anemic individuals absorb more than normal individuals.

(d) Iron absorption is enhanced by protein, possibly as a result of the formation of low molecular weight digestive products (peptides, amino acids) which can form soluble iron chelates.

(e) It is also increased in pernicious anaemia and in hypo plastic anaemia.

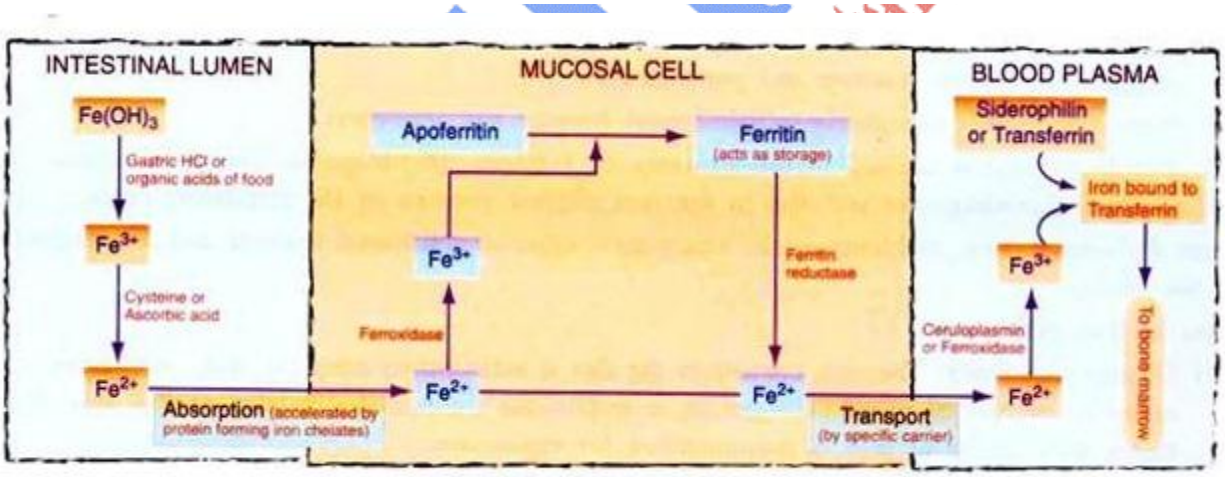
(f) Impaired absorption takes place in patients who have total removal of stomach or a removal of considerable amount of the intestine.

(g) Achlorhydria, administration of alkali, copper deficiency decrease iron absorption.

(h) Alcohol ingestion favours iron absorption.

Mechanism of Iron Absorption:

Ferrous ion on entering the mucosal cells is oxidized to ferric state and then combines with apoferritin forming ferritin which contains 23% of iron by weight. When apoferritin gets saturated with iron no further iron can be taken up by the mucosal cells to store it in the form of ferritin. Heme enters the mucosal cells without being released from the porphyrin ring. Heme is broken down in the mucosa and iron appears in the plasma transferrin.



Mechanism of iron absorption

Transport:

In the plasma, the iron is bound to transferrin which is only partially saturated. Plasma iron is also in exchange with interstitial and intra-cellular compartments. The iron in these compartments is generally referred to as ‘labile iron pool’ and is estimated to be in the order of 80 to 90 mg. Here the iron may stay briefly on the cell membrane before its incorporation into haem or storage compounds. Nearly all the iron released from the mucosal cell enter the portal blood mostly in the ferrous state (Fe^{2+}). In the plasma, Fe^{2+} is oxidized rapidly to the ferric state (Fe^{3+}) and then incorporated into a specific protein.

Storage:

Stores of iron are maintained chiefly in the liver, spleen and bone marrow in the form of ferritin and haemosiderin. Women have lower stores than men and therefore, develop anaemia much more

frequently than men. Iron stores are increased in haemochromatosis, severe haemolytic anaemias, aplastic anaemia and in persons receiving multiple blood transfusions, prolonged oral or parenteral iron therapy.

The normal content of protein bound iron (FBI) in plasma of males is 120-140 jig/100 ml; in females it is 90-120 pg/100ml. However, the total iron binding capacity (TIBC) is about the same in both sexes i.e. 300-360 pg/100 ml.

Excretion:

Physiological excretion of iron is minimal. The normal routes of excretion are urine, bile, faeces, cellular desquamation, and sweat. Daily excretion in an adult male is estimated to be about 1 mg. In women of reproductive age, additional loss through menstruation averages to 1 mg per day.

Abnormal iron metabolism:

Ferritin and hemosiderin, the storage forms of iron act as internal iron reserve to protect against sudden loss of iron by bleeding. Ferritin is present not only in the intestine but also in liver (about 700 mg) spleen and bone marrow. If excess iron is administered parenterally exceeding the capacity of the body to store it as ferritin, it accumulates in the liver as hemosiderin, a form of colloidal iron oxide in association with protein.

Iron metabolism is disturbed mainly by the following causes:

(a) Decreased formation of hemoglobin.

(b) Decrease in circulating hemoglobin.

(c) Abnormalities in the serum iron concentration

(d) Abnormal deposition of iron-combining pigments in the tissues.

Physiological functions:

1. Iron functions mainly in the transport of oxygen to the tissues.

2. Involved in the process of cellular respiration.

3. Essential component of hemoglobin, myoglobin, cytochromes and the respiratory enzyme systems (cytochrome oxidase, catalase and peroxidase).

4. Non-heme iron is completely protein-bound (storage and transport).

5. Non-heme iron is utilized in the structure of xanthine dehydrogenase (xanthine oxidase) and succinate dehydrogenase and also in the iron sulphur proteins of the respiratory chain.

Iron deficiency:

Iron deficiency is the commonest cause of nutritional anaemia and is prevalent all over the world. Causes of iron deficiency:

(1) Dietary deficiency:

The iron content in the diet is sufficient to meet the daily requirements, but excessive amount of phytates in cereals, is responsible for non-absorbability of this iron. Hence higher daily intake of iron is recommended for vegetarians.

(2) Lack of absorption:

This may be seen in malabsorptive syndromes.

(3) Increased demand:

This occurs during rapid growth in infancy and pregnancy.

(4) Poor stores at birth:

These are found in premature birth and twin pregnancy.

(5) Pathological blood loss:

With loss of 1g of haemoglobin 3.4 mg of iron is lost. Hook-worm infestation is the most important factor responsible for blood loss. Other sources of blood loss are bleeding piles, peptic ulcer, hiatus hernia, cancer of gastrointestinal tract, chronic aspirin ingestion, and oesophageal varies.

(6) Iron deficiency anemia:

Iron deficiency anemia is widely prevalent among children, adolescent girls and nursing mothers. The hemoglobin content of the blood during iron deficiency anemia is 5 to 9 g/100 ml.

(a) Women of child bearing age:

The clinical symptoms are breathlessness on exertion, giddiness and pallor of the skin. In severe cases, there may be edema of the ankles.

(b) Weaned infants and young children:

The hemoglobin level is 5 to 9 g/100 ml of blood. The children are dull and inactive and show pallor of the skin. The appetite is poor and growth and development are retarded.

Treatment of iron deficiency anaemia:

Anaemia responds to oral iron therapy. The commonly used preparations are ferrous sulphate, ferrous fumarate and ferrous gluconate. Iron dextran can be administered both intramuscularly and intravenously, iron sorbitex is given intramuscularly, and saccharide iron oxide is given intravenously.

Anemic women should take ferrous sulphate tablet. For a child below 12 months, a mixture of ferrous ammonium citrate sweetened with glycerine and for children of 1 to 5 years ferrous ammonium citrate mixture should be given for curing.

Iron overload:

Hypersiderosis may occur as a primary disorder (Idiopathic haemochromatosis) or secondary with excessive entry of exogenous, iron into the body.

1. Siderosis:

When excessive amounts of iron are released in or introduced into the body beyond the capacity for its utilization, the excess is deposited in various tissues, mainly in the liver. This may occur due to repeated blood transfusions, excessive breakdown of erythrocytes in hemolytic types of anemia and inadequate synthesis of hemoglobin as in pernicious anemia.

2. Nutritional siderosis:

This disorder is found among Bantus in South Africa. Bantus cook their food in large iron pots and consume iron-rich food. The absorption of iron appears to be high, leading to the development of nutritional siderosis. Livers of the Bantus contain large amounts of iron.

Hemochromatosis:

Hemochromatosis is a rare disease in which large amounts of iron are deposited in the tissues, especially the liver, pancreas, spleen and skin producing various disorders. Accumulation of iron in the liver, pancreas and skin produces hepatic cirrhosis, bronze diabetes and bronze-state pigment respectively.

Copper:

Source:

Richest sources:

Liver, kidney, other meats, shell fish, nuts and dried legumes.

Poor sources:

Milk and milk products. The concentration of copper in the fetal liver is 5-10 times higher than that in liver of an adult.

Daily requirements:

Infants and children – 0.05 mg/kg body weight

Adults – 2.5 mg

A nutritional deficiency of copper has never been demonstrated in man, although it has been suspected in case of nephrosis.

Absorption:

About 30% of the normal daily diet of copper is absorbed in the duodenum.

Blood copper:

The normal concentration of copper in serum is 90 µg/100 ml. Both RBC and serum contain copper. 80% of RBC copper is present as superoxide dismutase (erythrocuperin), Plasma copper occurs as firmly bound form and loosely bound forms. The firmly bound copper consists of ceruloplas-min. Loosely bound copper is called 'directly reacting copper' and is bound to serum albumin. The plasma copper levels increase in pregnancy because of their estrogen content. Oral contraceptives have a similar effect.

Physiological functions:

1. It has important role in hemoglobin synthesis.

2. It is required for melanin formation, phospholipids synthesis and collagen synthesis.

3. It has a role in bone formation and in maintenance of the integrity of myelin sheath.

4. It is a constituent of several enzymes such as tyrosinase, cytochrome oxidase, ascorbic acid oxidase, uricase, ferroxidase I (ceruloplasmin), ferroxidase II, superoxide dismutase, amino oxidase and dopamine hydroxylase.

5. Three copper containing proteins namely cerebrocuperin, erythrocuperin and hepatocuperin are present in brain, RBC and liver respectively.

Excretion:

Only 10 to 60 mg of copper is excreted in the urine. 0.5 to 1.3 mg is excreted through bile and 0.1 to 0.3 mg is excreted by intestinal mucosa into the bowel lumen.

Effects of copper deficiency:

1. Although iron absorption is not disturbed but the release of iron into the plasma is prevented due to the decreased synthesis of ceruloplasmin. As a result, hypoferremia occurs which leads to the depressed synthesis of heme developing anemia in severe deficiency of copper.

2. The experimental animals on a copper deficient diet lose weight and die.

3. In copper deficient lambs, low cytochrome oxidase activity results in neonatal ataxia.

4. Copper deficiency produces marked skeletal changes, osteoporosis and spontaneous fractures.

5. Elastin formation is impaired in the deficiency of copper. Because a copper containing enzyme plays an important role in the connective tissue metabolism, especially in the oxidation of lysine into

aldehyde group which is necessary for cross linkage of the polypeptide chains of elastin and collagen.

6. Copper deficiency results in myocardial fibrosis in cows. It is suggested that reduction in cyto-chrome oxidase activity may lead to cardiac hypertrophy.

Disorders of copper metabolism:

Wilson's disease (hepatoreticular degeneration):

Wilson's disease is a rare hereditary disorder of copper metabolism.

The following disorders have been observed in this disease:

(a) The absorption of copper from the intestine is very high (about 50 percent); whereas 2 to 5 percent copper is absorbed in normal subjects.

(b) Ceruloplasmin formation is very less. Hence a greater part of serum copper remains loosely bound to serum protein-notably albumin and therefore, copper can be transported to the tissues, such as brain and liver or to the urine.

(c) Excessive deposition of copper in the liver and the kidney causes hepatic cirrhosis and renal tubular damage respectively. The renal tubular damage results in the increased urinary excretion of amino acids, peptides and glucose.

Iodine:

Source:

Rich sources are sea water, marine vegetation and vegetables as well as fruits grown on the sea board. Plants grown at high altitudes are deficient in iodine because of its low concentration in the water. In such regions, iodide is commonly added to the drinking water or table salt in concentrations of 1:5000 to 1:200000.

Daily requirement:

Adults – 100 to 150 μg

In adolescence and in pregnancy – 200 μg

Distribution:

Normal iodine content of body is 10 to 20 mg. 70 to 80% of this is present in thyroid gland. Muscles contain large amount of iodine. The concentration of iodine in the salivary glands, ovaries, pituitary gland, brain and bile is greater than that in muscle. Iodine in saliva is inorganic iodide, while most of the iodine present in tissue is in the organic form.

Blood Iodine:

Practically all the iodine in the blood is in the plasma. The normal concentration in plasma or serum is 4 to 10 μg/100 ml. 0.06 to 0.08 μg/100 ml is in inorganic form, 4 to 8 μg/100 ml is in the organic form bound to protein, precipitated by protein precipitating agents. 90% of the organic form consists of thyroxine and the remainder tri and di-iodothyronine. About 0.05% of thyroxine is in the free state. RBC contains no organic iodine.

Absorption:

Iodine and iodide are absorbed most readily from the small intestine. Organic iodide compounds (di-iodothyronine and thyroxine) are partly absorbed as such and a part is broken down in the stomach and intestines with the formation of iodides. Absorption also takes place from outer mucus membrane and skin.

Storage:

90% of the iodine of the thyroid gland is in organic combination and stored in the follicular colloid as 'thyroglobulin' a glycoprotein containing thyroxine, di-iodothyronine and smaller amounts of triiodothyronine.

On demand these substances are mobilized and thyroxine as well as triiodothyronine is passed into the systemic circulation. They undergo metabolic degradation in the liver.

Excretion:

1. Inorganic iodine is mostly excreted by the kidney, liver, skin, lungs and intestine and in milk.

2. About 10% of circulating organic iodine is excreted in feces. This is entirely unabsorbed food iodine.

3. 40 to 80 % is usually excreted in the urine, 20 to 70 µg daily in adults, 20 to 35 µg in children. The urinary elimination is largest when the intake is lowest.

4. Urinary iodine is increased by exercise and other metabolic factors.

Physiological functions:

Iodine is required for the formation of thyroxine and triiodothyronine hormones of the thyroid gland. These thyroid hormones are involved in cellular oxidation, growth, reproduction and the activity of the central and autonomic nervous systems. Triiodothyronine is more active than thyroxine in many respects.

Iodine deficiency:

1. In adults the thyroid gland is enlarged producing goiter. If treatment is started very early, the thyroid becomes normal. If treatment is delayed, the enlargement persists.

2. In children, severe iodine deficiency results in the extreme retardation of growth causing cretinism.

Prevention of goiter:

Goiter can be prevented by the regular use of iodized salt or iodine added to the drinking water.

Goitrogenic substances in foods:

Cabbage, cauliflower and radish contain substance like vinyl-2- thiooxazolidone which makes iodide present in the food unavailable by reacting with it. Such substances are called 'goitrogenic' substances.

Selenium:

i. Good dietary sources are kidney cortex, pancreas, pituitary and liver.

ii. It is rapidly absorbed mainly in duodenum.

iii. It is distributed in liver 0.44 µg/gm in skin 0.27 µg/gm and in muscle 0.37 µg/gm.

iv. In the cells it is present as selenocystine nad selenomethionine.

v. Selenium along with Vitamin E plays an important role in tissue respiration.

vi. Selenium is involved in biosynthesis of coenzyme Q (ubiquinone), which is involved in respiratory chain.

vii. Selenium acts as an antioxidant providing protection against peroxidation in tissues and membrane.

viii. It is an essential component of glutathione peroxidase, an enzyme which catalyzes the conversion of reduced glutathione to its oxidized form.

ix. Selenium is excreted in faeces, urine and via exhalation.

x. It causes toxic effect called selenosis

(c) Enzyme

Ans. Thousands of chemical reactions proceed very rapidly at any given instant within all living cells of an organism. Virtually all of these reactions are mediated by remarkable molecular devices called enzymes. That is, the enzymes are central to every biochemical reaction and are called the catalysts of biological systems (biocatalysts).

Characteristics of Enzymes:

All enzymes are proteins, but a functional enzyme has different components and these components are named differently, viz.,

Holoenzyme:

A conjugated protein and functional enzyme.

Apoenzyme:

Polypeptide segment of the enzyme, which is catalytically inactive.

Coenzyme:

The non-protein organic moiety, which can frequently be separated from the apoenzyme.

Prosthetic group:

If a substance is firmly (covalently) attached to the protein part of the enzyme, it is referred to as a prosthetic group. It is the non-protein portion of any conjugated protein. So coenzyme is a specific example of prosthetic group.

Activator:

There are many metalloprotein enzymes in which the metal ion (e.g. Mg^{++}, Mn^{++}, and Zn^{++}) is bonded either to the apoenzyme or to the coenzyme. The metal is usually designated as activator. They form a co-ordination complex between the enzyme and the substrate, and activate the substrate by prompting electronic shifts.

Pro-enzyme or Zymogens:

They are simple protein enzymes, which are secreted, in an inactive form.

Activation:

It is the process in which an inactive protein (pro-enzyme or zymogens) is transformed into an active enzyme.

Note # 10. Nomenclature of Enzymes:

All enzyme names should end in suffixase. Exceptions are some old names, e.g., ptyalin, pepsin, trypsin. Some old names indicate the source but not the action, e.g., papain from Papaya, bromelain from Pineapple of family Bromeliaceous.

In modem system enzyme names are given after:

(i) Substrate acted upon, e.g., sucrase (after sucrose), lipase, proteinase, nuclease, peptidases, maltase

(ii) Chemical reaction, e.g., dehydrogenase, oxidase, carboxylase, decarboxylase, etc.

The second category of names are group names. They are often qualified by the addition of the name of substrate, e.g., succinic dehydrogenase, isocitric dehydrogenase, glutamate-pyruvate transaminase, DNA polymerase.

Thus DNA polymerase catalyses synthesis of DNA segments through polymerisation of deoxyribonucleotides. Similarly glutamate-pyruvate transaminase transfers amino group (—NH_2) from glutamate to pyruvate.

Classification of Enzymes:

In older times enzymes were classified into two broad categories:

(i) Hydrolysing:

Catalysing hydrolysis of larger molecules into smaller ones, e.g., carbohydrates or amylases, proteases, lipases, esterases, phosphorylases, amidases. Digestive enzymes are hydrolysing in nature. They are often grouped into three types— proteolytic, amylolytic and lipolytic,

(ii) Desmolysing:

Catalysing reactions other than hyrolysis, e.g., aldolases, dehydrogenases, oxidases, peroxidases, catalases, carboxylases, etc. The modem system of enzyme classification was introduced by International Union of Biochemistry (IUB) in 1961. It groups enzymes into the following six categories.

a. Oxidoreductases:

They take part in oxidation and reduction reactions or transfer of electrons.

$$\text{S reduced} + \text{S}' \text{ oxidised} \xrightarrow{\text{oxido reductase}} \text{S oxidised} + \text{S}' \text{ reduced}$$

Oxidoreductases are of three types— oxidases, dehydrogenases and reductases, e.g., cytochrome oxidase (oxidises cytochrome), succinate dehydrogenase, nitrate reductase.

$$2AH_2 + O_2 \xrightarrow{\text{oxidase}} 2A + 2H_2O$$

$$AH_2 \xrightarrow{\text{dehydrogenase}} A + 2(H)$$

$$A + 2(H) \xrightarrow{\text{reductase}} AH_2$$

b. Transferases:

They transfer a group from one molecule to another e.g., glutamate- pyruvate transaminase (transfers amino group from glutamate to pyruvate during synthesis of alanine). The chemical group transfer does not occur in the Free State.

$$S - G + S' \xrightarrow{\text{transferase}} S + S' - G$$

$$\underset{\text{(amino acid)}}{\text{Glutamic Acid}} + \underset{\text{(organic acid)}}{\text{Oxaloacetic Acid}} \xrightarrow{\text{transferase}} \underset{\text{(organic acid)}}{\alpha\text{-ketoglutaric Acid}} + \underset{\text{(amino acid}}{\text{Aspartic A}}$$

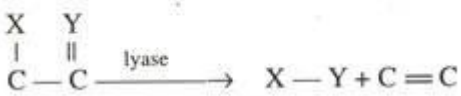
c. Hydrolases:

They catalyse hydrolysis of bonds like ester, ether, peptide, glycosidic, C-C, C halide, P—N, etc. which are formed by dehydration condensation. Hydrolases break up large molecules into smaller ones with the help of hydrogen and hydroxyl groups of water molecules. The phenomenon is called

hydrolysis. Digestive enzymes belong to this group, e.g., amylase (hydrolysis of starch), sucrase, lactase.

d. Lyases:

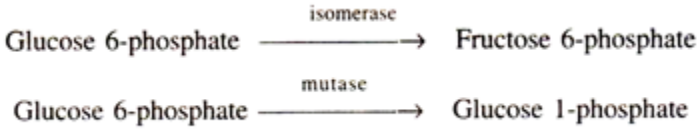
The enzymes cause cleavage, removal of groups without hydrolysis, addition of groups to double bonds or removal of a group producing double bond, e.g., histidine decarboxylase (breaks histidine to histamine and CO_2), aldolase (fructose-1, 6-diphosphate to dihydroxy acetone phosphate and glyceraldehyde phosphate).



Fructose 1, 6-diphosphate – aldolase → Dihydroxy acetone phosphate + Glyceraldehyde phosphate.

e. Isomerases:

The enzymes cause rearrangement of molecular structure to effect isomeric changes. They are of three types, isomerases (aldose to ketose group or vice-versa like glucose 6-phosphate to fructose 6-phosphate), epimerases (change in position of one constituent or carbon group like xylulose phosphate to ribulose phosphate) and mutases (shifting the position of side group like glucose-6-phosphate to glucose-1- phosphate).



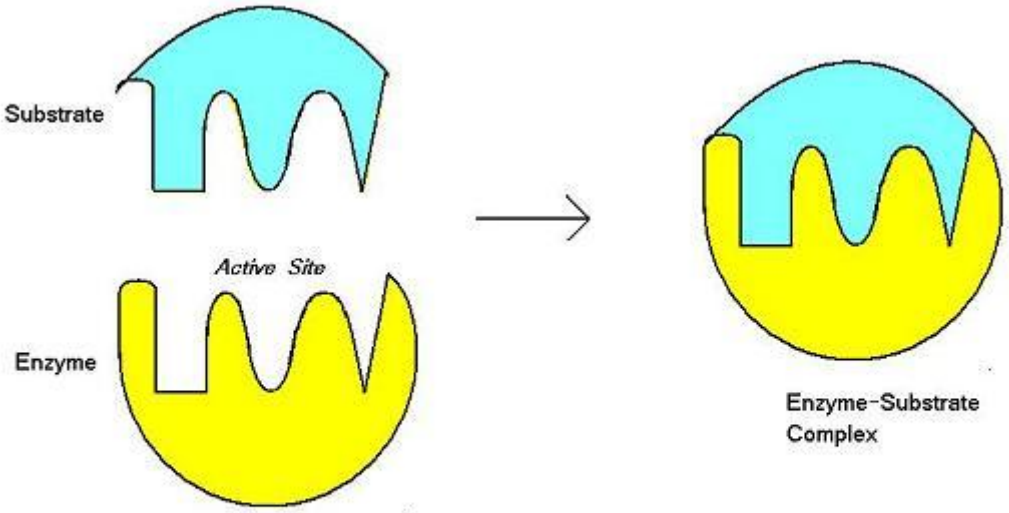
f. Ligases (Synthetizes):

The enzymes catalyse bonding of two chemicals with the help of energy obtained from ATP resulting in formation of such bonds as C-O, C-S, C-N and P-O, e.g., pyruvate carboxylase. It combines pyruvic acid with CO_2 to produce oxaloacetic acid.

- The Activation Energy of a reaction is lowered by putting stress on the bonds within a molecule, or by holding molecules close together. This increases the likelihood of a reaction, and so lowers the energy required to begin it.

The Lock-and-key Hypothesis

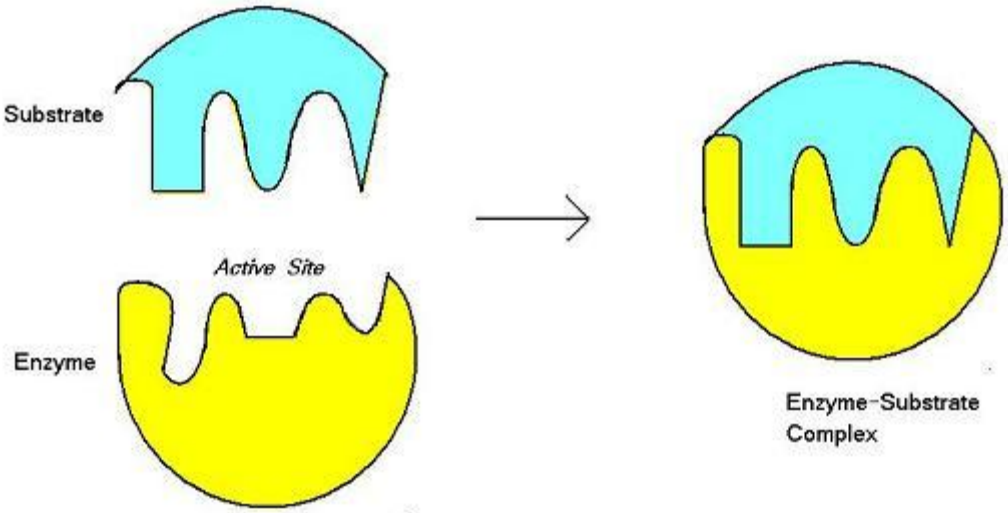
- The Lock-and-key Hypothesis is a model of how Enzymes catalyse Substrate reactions. It states that the shape of the Active Sites of Enzymes are exactly Complementary to the shape of the Substrate.
- When a substrate molecule collides with an enzyme whose Active Site shape is complementary, the substrate will fit into the Active Site and an Enzyme-Substrate Complex will form.
- The enzyme will catalyse the reaction, and the products, together with the enzyme, will form an Enzyme-Product Complex. According to this model, it is possible for an enzyme to catalyse a reverse reaction.



Lock-and-key Model.- The substrate and enzyme active site have complementary shapes

The Induced-Fit Hypothesis

- A more recent model, which is backed up by evidence ,and is widely accepted as describing the way enzymes work, is the Induced-Fit Hypothesis. It states that the shape of Active Sites are not exactly Complementary, but change shape in the presence of a specific substrate to become Complementary.
- When a substrate molecule collides with an enzyme, if its composition is specifically correct, the shape of the enzyme's Active Site will change so that the substrate fits into it and an Enzyme-Substrate Complex can form. The reaction is then catalysed and an Enzyme-Product Complexforms.



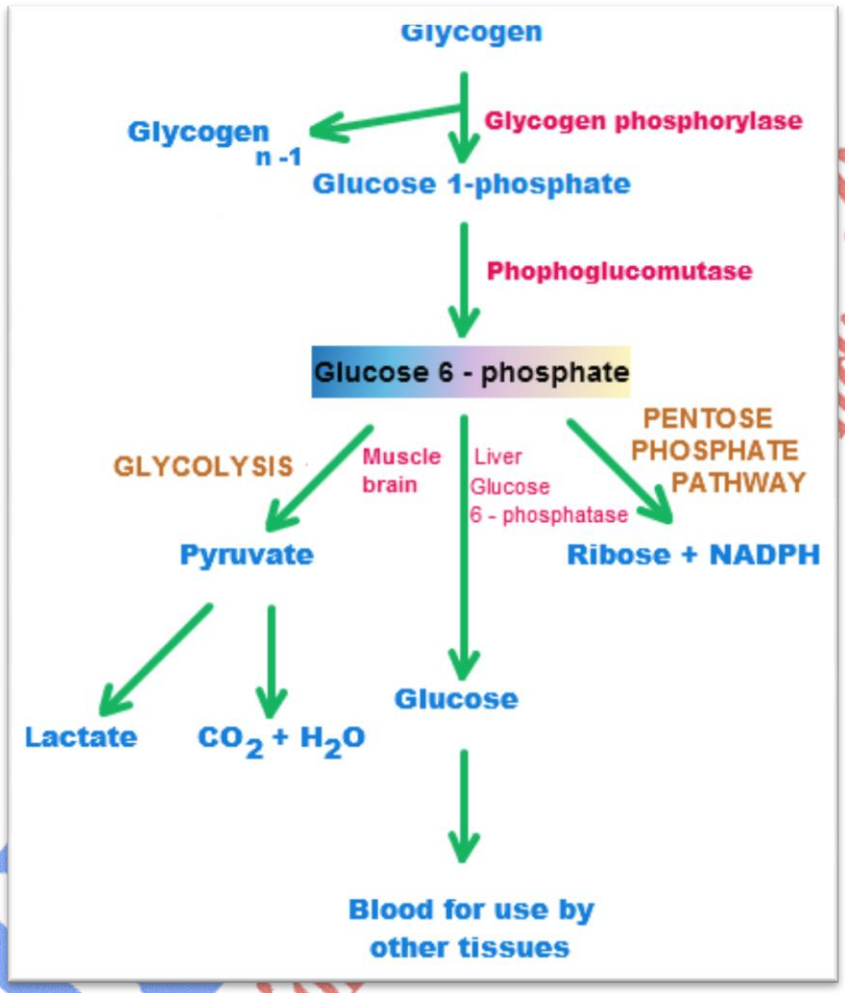
Induced-fit Model. - The enzyme active site forms a complementary shape to the substrate after binding.

(d) Interconversion of glycogen and glucose in liver

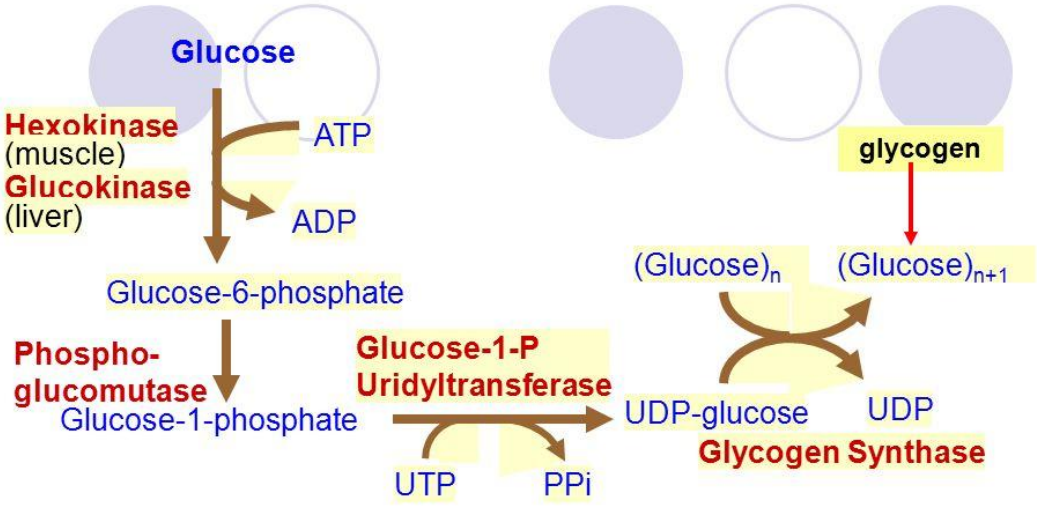
Ans. Glycogenolysis is the biochemical breakdown of glycogen to glucose whereas glycogenesis is the opposite, the formation of glycogen from glucose. Glycogenolysis takes place in the cells of muscle and liver tissues in response to hormonal and neural signals. In particular, glycogenolysis

plays an important role in the adrenaline-induced fight-or-flight response and the regulation of glucose levels in the blood. The reverse process, glycogenesis, the formation of glycogen from glucose, occurs in liver and muscle cells when glucose and ATP are present in relatively high amounts. In the synthesis of glycogen, one ATP is required for every glucose unit incorporated into the polymeric branched structure of glycogen. The glucose (in the form of glucose-6-phosphate) is synthesized directly from glucose or as the end product of gluconeogenesis.

Glycogen to glucose



Glucose to glycogen :-



Pathway of glycogen synthesis (glycogenesis)