Homeostasis and across cell membrane

"Homeostasis" means the maintenance of constant internal environment.

The internal environment in the body is the ECF which contains nutrients, ions and all other substances necessary for the survival of the cells and in this environment the cells live. It includes the blood and interstitial fluid. For the operation of homeostatic mechanism, the body must recognize the deviation of any physiological activity from the normal limits.

Transport through Cell Membrane

Transport mechanism in the body is necessary for the supply of essential substances like nutrients, water, electrolytes, etc. to the tissues and to remove the unwanted substances like waste materials, carbon dioxide, etc. from the tissues.

BASIC MECHANISM OF TRANSPORT

Two basic mechanisms for the transport of substances across the cell membrane are:

1. Passive mechanism
2. Active mechanism

PASSIVE TRANSPORT

The transport of the substances along the concentration gradient or electrical gradient or both (electrochemical gradient) is called passive transport. Here, the substances move from the region of higher concentration to the region of lower concentration. It is also known as diffusion or downhill movement. It does not need energy. Diffusion or passive transport is of two types:

1. Simple diffusion
2. Facilitated diffusion.

SIMPLE DIFFUSION

Simple diffusion is of two types:

1. Simple diffusion through lipid layer
2. Simple diffusion through protein layer

Simple Diffusion through Lipid Layer

Lipid soluble substances like oxygen, carbon dioxide and alcohol are transported by simple diffusion through the lipid layer of the cell membrane.

Simple Diffusion through Protein Layer

There are specific protein channels that extend from cell membrane through which the simple diffusion takes place. Water soluble substances like electrolytes are transported through these channels. These channels are selectively permeable to only one type of ion. Accordingly, the channels are named after the ions diffusing through these channels like sodium channels, potassium channels, etc.

Protein Channels

The protein channels are of two types:

1. Ungated channels which are opened continuously
2. Gated channels which are closed all the time and are opened only when required

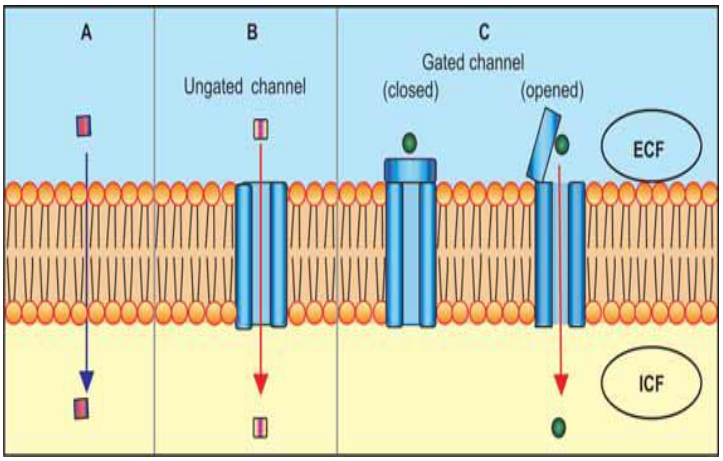
Gated channels

The gated channels are divided into three categories:

i. Voltage gated channels which open by change in the electrical potential.
Examples are the calcium channels present in neuromuscular junction.

ii. Ligand gated channels that open in the presence of hormonal substances (ligand).
Examples are the sodium channels which are opened by acetylcholine in neuromuscular junction.

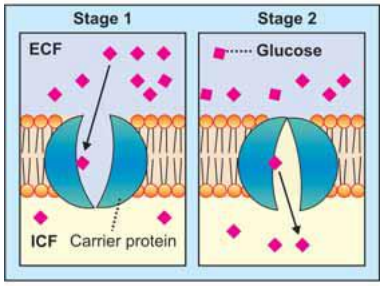
iii. Mechanically gated channels which are opened by some mechanical factors like pressure and force. Examples are the sodium channels in pressure receptors called Pacinian corpuscles.



Hypothetical diagram of simple diffusion through the cell membrane.
A = Diffusion through lipid layer.

B = Diffusion through ungated channel.

C = Diffusion through gated channel



Hypothetical diagram of facilitated diffusion from higher concentration (ECF) to lower concentration (ICF).
Stage 1: Glucose binds with carrier protein. Stage 2: Conformational change occurs in the carrier protein and glucose is released

FACILITATED OR CARRIER MEDIATED DIFFUSION

In this type of diffusion, some carrier proteins help the transport of substances. The water-soluble substances with larger molecules cannot pass through the protein channels by simple diffusion. Such substances are transported with the help of carrier proteins. This type of diffusion is faster than the simple diffusion. Glucose and amino acids are transported by this method.

FACTORS AFFECTING RATE OF DIFFUSION

The rate of diffusion of substances through the cell membrane is directly proportional to the following factors:
1. Permeability of the cell membrane
2. Body temperature
3. Concentration gradient or electrical gradient of the substance across the cell membrane
4. Solubility of the Substance The rate of diffusion of substances through the cell membrane is inversely proportional to the following factors:
1. Thickness of the cell membrane
2. Charge of the ions
3. Size of the molecules.

SPECIAL TYPES OF PASSIVE TRANSPORT

In additions to diffusion there are some special types of passive transport viz.
1. Bulk flow
2. Filtration
3. Osmosis

Bulk Flow

The diffusion of large quantity of substances from a region of high pressure to the region of low pressure is known as bulk flow. Bulk flow is due to the pressure gradient

of the substance across the cell membrane. The best example for this is the exchange of gases across the respiratory membrane in lungs.

Filtration

The movement of water and solutes from an area of high hydrostatic pressure to an area of low hydrostatic pressure is called filtration. The hydrostatic pressure is developed by the weight of the fluid. Filtration process is seen at the arterial end of the capillaries where movement of fluid occurs along with dissolved substances from blood into the interstitial fluid. It also occurs in glomeruli of kidneys.

Osmosis

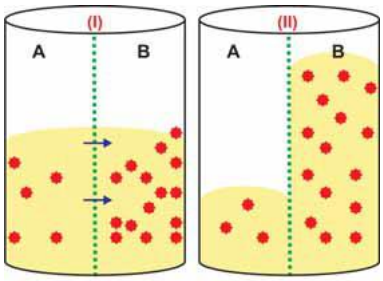
Osmosis is the special type of diffusion. It is the movement of water or any other solvent from an area of lower concentration to an area of higher concentration through a semipermeable membrane Osmosis is of two types:

i. Endosmosis by which water moves into the cell

ii. Exosmosis by which water moves outside the cell.

Osmotic Pressure

The pressure created by the solutes in a fluid is called osmotic pressure. During osmosis, when water or any other solvent moves from the area of lower concentration to the area of higher concentration, the solutes in the area of higher Osmosis.



Red objects = solute. Yellow shade = water. Green dotted line = semipermeable membrane. In (I), concentration of solute is high in the compartment B and low in compartment A. So, water moves from A to B through semipermeable membrane. In (II), entrance of water into B exerts osmotic pressure

Colloidal Osmotic Pressure and Oncotic Pressure

The osmotic pressure exerted by the colloidal substances in the body is called the colloidal osmotic pressure. And, the osmotic pressure exerted by the colloidal substances (proteins) of the plasma is known as oncotic pressure and it is about 25 mm Hg.

ACTIVE TRANSPORT

Movement of substances against the chemical or electrical or electrochemical gradient is called active transport. It is also called uphill transport. Active transport requires energy which is obtained mainly by breakdown of ATP. It also needs a carrier protein.

MECHANISM OF ACTIVE TRANSPORT

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. Now, the substance is released from the carrier proteins. The same carrier protein moves back to the outer surface of the cell membrane to transport another molecule of the substance.

CARRIER PROTEINS

There are two types of carrier proteins:
1. Uniport
2. Symport or antiport

Uniport

The carrier protein that can carry only one substance in a single direction is called uniport. It is also known as uniport pump.

The carrier protein that transports two different substances in the same direction is called symport. The carrier protein that transports two different substances in opposite directions is called antiport.

SUBSTANCES TRANSPORTED BY ACTIVE TRANSPORT

The actively transported substances are in ionic form and nonionic form. The substances in ionic form are sodium, potassium, calcium, hydrogen, chloride and iodide. The substances in nonionic form are glucose, amino acids and urea.

TYPES OF ACTIVE TRANSPORT

The active transport is of two types:
1. Primary active transport
2. Secondary active transport.

PRIMARY ACTIVE TRANSPORT

In primary active transport, the energy is liberated directly from the breakdown of ATP. By this method, the substances like sodium, potassium, calcium, hydrogen and chloride are transported across the cell membrane.

SECONDARY ACTIVE TRANSPORT

The transport of a substance with sodium ions by a common carrier protein is called secondary active transport. It is of two types:

1. Co-transport — transport of the substance in the same direction along with sodium
2. Counter transport — transport of the substance in the opposite direction to that of sodium

SPECIAL CATEGORIES OF ACTIVE TRANSPORT

In addition to primary and secondary active transport systems, some special categories of active transport systems also exist in the body. The special categories of active transport are:

I. Endocytosis
II. Exocytosis
III. Transcytosis.

ENDOCYTOSIS

Endocytosis is the transport mechanism by which the macromolecules enter the cell. The substances with larger molecules are called macromolecules and these cannot pass through the cell membrane either by active or by passive transport mechanism. Such substances are transported into the cell by endocytosis. Endocytosis is of three types:

1. Pinocytosis
2. Phagocytosis
3. Receptor mediated endocytosis.

1. Pinocytosis

It is otherwise called the cell drinking. The macromolecules like bacteria and antigens enter the cells by pinocytosis.

Mechanism of pinocytosis

i. The macromolecules (in the form of droplets of fluid) bind to the outer surface of the cell membrane

ii. Now, the cell membrane evaginates and engulfs the droplets

iv. The engulfed droplets are converted into vesicles and vacuoles, which are called endosomes

v. The endosome travels into the interior of the cell

vi. The primary lysosome in the cytoplasm fuses with the endosome and forms the secondary lysosome
vii. Now, hydrolytic enzymes present in the secondary lysosome are activated resulting in digestion and degradation of the endosomal contents.

2. Phagocytosis

The process by which the particles larger than the macromolecules are engulfed into the cells is called phagocytosis or cell eating. Larger bacteria, larger antigens and other larger foreign bodies are taken inside the cell by means of phagocytosis. Only few cells in the body like neutrophils, monocytes and the tissue macrophages show phagocytosis. Among these cells, the macrophages are the largest phagocytic cells.

Mechanism of phagocytosis

i. When the bacteria or the foreign body enters the body, first the phagocytic cell sends cytoplasmic extension (pseudopodium) around the bacteria or the foreign body
ii. Then, these particles are engulfed and are converted into endosome like vacuole. The vacuole is very large and it is usually called the phagosome
iii. The phagosome travels into the interior of the cell
iv. The primary lysosome fuses with this phagosome and forms secondary lysosome
v. The hydrolytic enzymes present in the secondary lysosome are activated resulting in digestion and degradation of the phagosomal contents

3. Receptor Mediated Endocytosis

Transport of macromolecules which is mediated by a receptor protein is called the receptor mediated endocytosis. The surface of cell membrane has some pits which contain a receptor protein called clathrin. Together with a receptor protein, each pit is called receptor coated pit. The coated pits are involved in the receptor mediated endocytosis.

Mechanism of receptor mediated endocytosis

i. The receptor mediated endocytosis is induced by substances like ligand (hormone) which bind to the receptors in the coated pits and form the ligand receptor complexes
ii. The ligand-receptor complexes get aggregated in the coated pits
iii. Then, the pit is detached from the cell membrane and becomes the coated vesicle. This coated vesicle forms the endosome.
vi. The endosome travels into the interior of the cell. Receptor mediated endocytosis plays an important role in the transport of various types of macromolecules such as hormones, antibodies, lipids, growth factors, toxins, bacteria and viruses.

EXOCYTOSIS

Exocytosis is the process by which the substances are expelled from the cell. In this process, the substances are extruded from the cell without passing through the cell membrane. This is the reverse of endocytosis.

Mechanism of exocytosis

Secretory substances from the cells are released by exocytosis. The secretory substances of the cell are stored in the form of secretory vesicles in the cytoplasm. When required, the vesicles move towards the cell membrane and get fused with it. Later, the contents of the vesicles are released out of the cell.

TRANSCYTOSIS

Transcytosis is a transport mechanism in which an extracellular macromolecule enters through one side of a cell, migrates across cytoplasm of the cell and exits through the other side by means of exocytosis. Examples are movement of proteins and pathogens like HIV from capillary blood into interstitial fluid through endothelial cells of the capillary.

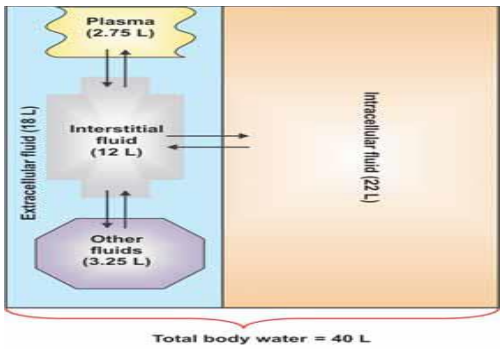
Body Fluids

Body is formed by solids and fluids. The fluid part is more than 2/3 of the whole body. Water forms most of the fluid part of the body. In human beings, the total body water (TBW) varies from 45 to 75% of body weight. In a normal young adult male, body contains 60 to 65% of water and 35 to 40% of solids. In a normal young adult female, the water is 50 to 55% and solids are 45 to 50%. The total quantity of body water in an average human being weighing about 70 kg is about 40 L.

COMPARTMENTS OF BODY FLUIDS — DISTRIBUTION OF BODY FLUIDS

Compartments and distribution of body fluids with the quantity is given in Table 5-1. Water moves between different compartments. TBW (40 L) is distributed into two major fluid compartments:

1. Intracellular fluid (ICF) forming 55% of the total body water (22 L).
2. Extracellular fluid (ECF) forming 45% of the total body water (18 L).



Body fluid compartments and movement of fluid between different compartments.
Other fluids = transcellular fluid, fluid in bones and fluid in connective tissue

COMPOSITION OF BODY FLUIDS

Body fluids contain water and solids. Solids are organic and inorganic substances.

ORGANIC SUBSTANCES

Organic substances present in body fluids are glucose, amino acids and other proteins, fatty acids and other lipids, hormones and enzymes.

INORGANIC SUBSTANCES

The inorganic substances present in body fluids are sodium, potassium, calcium, magnesium, chloride, bicarbonate, phosphate and sulfate.

APPLIED PHYSIOLOGY

DEHYDRATION

Definition

Significant decrease in water content of the body is known as dehydration.

Classification

Basically, dehydration is of three types:

1. Mild dehydration when fluid loss is about 5% of total body fluids.
2. Moderate dehydration when fluid loss is about 10%.
3. Severe dehydration when fluid loss is about 15%.

Causes

1. Severe diarrhea and vomiting
2. Excess water loss through urine
4. Insufficient intake of water
5. Excess sweating
6. Use of laxatives or diuretics.

Signs and Symptoms

Mild and moderate dehydration

1. Dryness of the mouth
2. Excess thirst
3. Decrease in sweating
4. Decrease in urine formation.

Severe dehydration

1. Decrease in blood volume
2. Decrease in cardiac output
3. Cardiac shock.

Very severe dehydration

1. Damage of organs like brain, liver and kidneys

2. Mental depression and confusion
3. Renal failure
4. Coma.

OVERHYDRATION OR WATER INTOXICATION

Definition

Overhydration, hyperhydration, water excess or water intoxication is defined as the condition in which body has too much water.

Causes

Overhydration occurs when more fluid is taken than that can be excreted. It also develops in some conditions such as heart failure, renal disorders and hypersecretion of antidiuretic hormone.

Signs and Symptoms

1. Behavioral changes
2. Drowsiness and inattentiveness
3. Nausea and vomiting
4. Sudden loss of weight followed by weakness and blurred vision
5. Anemia, acidosis, cyanosis, hemorrhage and shock
6. Muscular weakness, cramps and paralysis
7. Severe conditions of overhydration result in:

i. Delirium (extreme mental condition characterized by confused state and illusion)
ii. Seizures (sudden uncontrolled involuntary muscular contractions)
iii. Coma (profound state of unconsciousness in which the person fails to respond to external stimuli and cannot perform voluntary actions).

Edema: Excess Fluid in the Tissues

Edema refers to the presence of excess fluid in the body tissues. In most instances, edema occurs mainly in the extracellular fluid compartment, but it can involve intracellular fluid as well.

Intracellular Edema

Two conditions are especially prone to cause intracellular swelling:
(1) depression of the metabolic systems of the tissues, and
(2) lack of adequate nutrition to the cells. For example, when blood flow to a tissue is decreased, the delivery of oxygen and nutrients is reduced. If the blood flow becomes too low to maintain normal tissue metabolism, the cell membrane ionic pumps become depressed. When this occurs, sodium ions that normally leak into the interior of the cell can no longer be pumped out of the cells, and the excess sodium ions inside the cells cause osmosis of water into the cells. Sometimes this can increase intracellular volume of a tissue area—even of an entire ischemic leg, for example—to two to three times normal. When this occurs, it is usually a prelude to death of the tissue. Intracellular edema can also occur in inflamed tissues. Inflammation usually has a direct effect on the cell membranes to increase their permeability, allowing sodium and other ions to diffuse into the interior of the cell, with subsequent osmosis of water into the cells.

Extracellular Edema

Extracellular fluid edema occurs when there is excess fluid accumulation in the extracellular spaces. There are two general causes of extracellular edema:

(1) abnormal leakage of fluid from the plasma to the interstitial spaces across the capillaries, and

(2) failure of the lymphatics to return fluid from the interstitial back into the blood. The most common clinical cause of interstitial fluid accumulation is excessive capillary fluid filtration.