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Introduction to Human Physiology

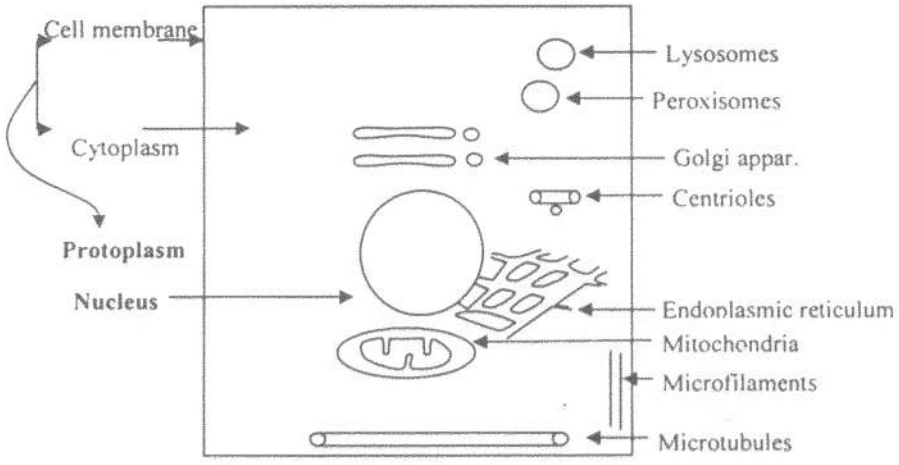
- Human physiology is concerned with the study of normal functions of different parts of human body or is concerned with the specific characteristics and mechanisms of human body that make it a living being.
- **Body composition:** In the average adult male, the body is composed of :-
  1. Water: 60%
  2. Proteins and related substances: 20%
  3. Fat: 15%
  4. Minerals: 5%.
  5. Carbohydrates have little structural function in the cell except as part of glycoprotein molecule but their major role is in nutrition of the cell
- **Organization of the body:**
  - The body is formed of group of systems as nervous system, endocrine system, cardiovascular system, respiratory system, digestive system, urogenital system and musculoskeletal system.
  - Each system is formed of group of organs.
  - Each organ is formed of group of tissues.
  - Each tissue is formed of group of cells.

  Thus, the basic living unit of the body is the cell. The human body contains about 100 trillion cells.

Body ⟶ System ⟶ Organs⟶ Tissues⟶ Cells.

Cell Physiology

The cell is composed of:



1- Cell membrane:- Discussed later.
2- Protoplasm which is composed of:- Discussed in histology.
   a- Cytoplasm that contains cell organelles
      1-Endoplasmic reticulum 2-Golgi apparatus
      3-Mitochondria 4-Lysosomes
      5-Peroxisomes 6-Centerioles
      7-Microtubules 8-Microfilaments.
   b- Nucleus

Cell Membrane

- It is fluid rather than solid matrix. This fluidity makes it more flexible.
- It is semipermeable i.e. allows some substances to pass and prevents others.
- **Structure:-** Composed of lipids (42%), proteins (55%) and carbohydrates (3%):

1- Lipids (lipid bilayer, 42%)

- Continuous over entire surface.
- It provides a barrier that prevents the movement of water soluble substances.
- **Composition:-** Made up of phospholipids (the major lipid in cell membrane) and cholesterol.

A. Phospholipids:

- The major lipid in cell membrane.
- It is 2 molecules in thickness. Each molecule has:
  1. Head:
     - Contains the phosphate radical of phospholipids.
     - Relatively water-soluble (hydrophilic), thus it is exposed to water present inside or outside the cell, i.e., ICF and ECF.
  2. Tail:
     - Contains the free fatty acid radical (FFA).
     - Relatively water insoluble (hydrophobic). Thus, it is present in the water poor interior of the membrane.

B. Cholesterol

- It is dissolved in the phospholipid bilayer.
- Function:
  1. Determine the permeability of the lipid layer to water soluble substances.
  2. Determine the fluidity of the membrane.

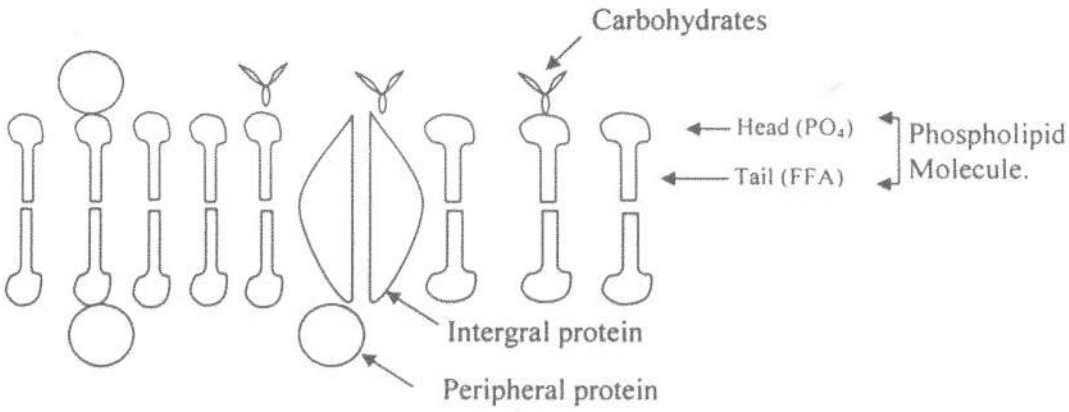
2- Proteins (55%):

They do not form a continuous layer as lipids but they exist as globular masses floating in the lipid bilayer that may be:

a. **Integral proteins**
   - Extend through the whole thickness of the membrane.
   - Functions:- they act as
     1- Ion channels for passage of ions.
     2- Carriers for transport of substances as glucose and amino acids.
     3- Receptors for action of substances as hormones.
     4- Enzymes.

b. **Peripheral proteins**
   - They are attached to cell membrane either from outside or more commonly from inside and not extended through the whole thickness of the membrane.They are often attached to one of the integral proteins.
   - They act mainly as enzymes.

1. **Carbohydrates (Cell glycocalyx, 3%)**
   - Present on the outer surface of cell membrane and in most cells form a loose coat on the entire surface of the cell called glycolcalex.
   - They may be combined with proteins (glycoproteins) or lipids (glycolipids).
   - Functions:
     a. Many of them are negatively charged thus give most cells an overall negative surface charge.
     b. Attach cells to each other.
     c. Act as receptors.
     d. Some enter into immune response.

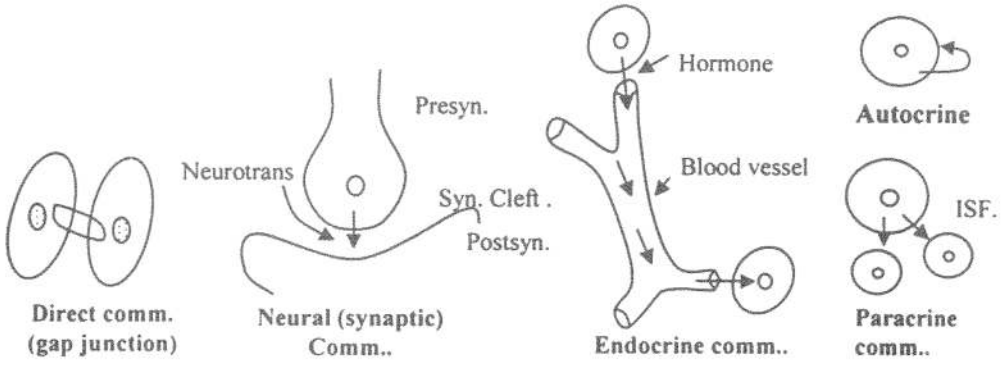


Intercellular communications

Cells communicate with each other by sending signals or chemical messenger to each other. There are 2 types of communication.

1- **Direct (electrical) communication**
   - In which the messenger (mainly depolarization) moves from cell to cell via gap junctions directly without entering to ECF.
   - Gap junctions are channels running across the intercellular space connecting one cell to another. They permit the rapid propagation of action potential from cell to cell.
   - Present in cardiac and smooth ms.

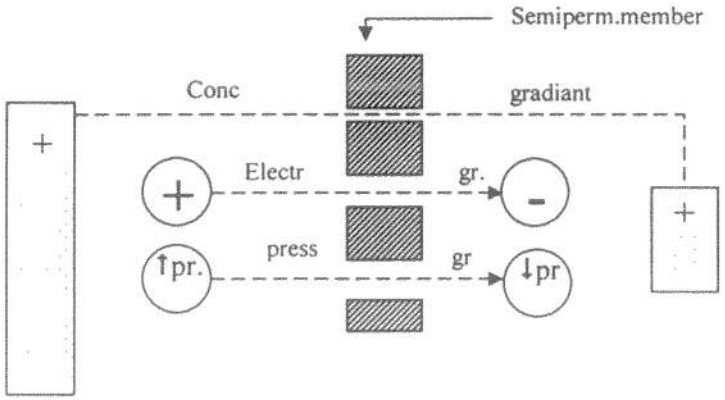
2- **Indirect (chemical) communication**
   - The most common type of communications, in which the cell secrete chemical messenger to ECF to affect other cells by binding to receptor protein on cell membrane, cytoplasm or nucleus. There are 4 types:-
     a. **Neural (synaptic) communication**
        In which chemical messenger (called neurotransmitter) is released from presynaptic neuron passes the synaptic cleft and binds to a receptor on postsynaptic neurone.
     b. **Endocrine communication**
        In which the chemical messenger (called hormone) is secreted to blood and affect **far cells**.
     c. **Paracrine communication**
        In which the chemical messenger (mostly metabolic products as histamine and prostaglandins) is secreted to interstitial fluid and affects **nearby cells**.
     d. **Autocrine communication**
        In which the chemical messenger binds to receptor (affects) on the **same cell** that secrete it.



Membrane transport

A. Passive transport (Diffusion)

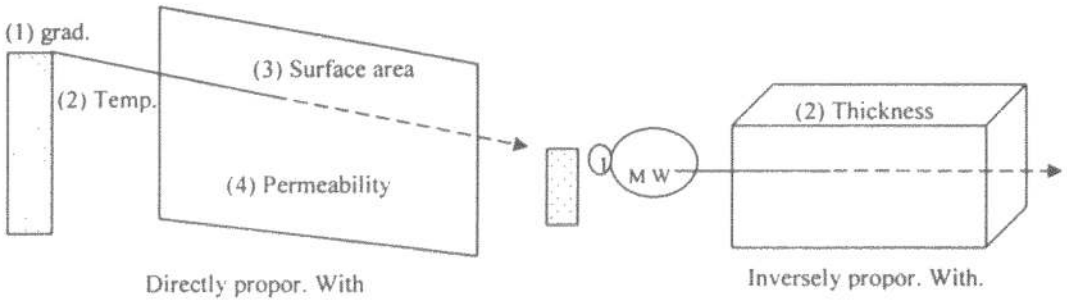
- **Definition**
  - It is transport of a substance across a semipermeable membrane down its electrochemical gradient.
  - Another definition:- It is the process by which a gas or a substance in a solution expands because of the continuous random motion of its particles to fill all of the available volume.
- **Criteria of passive transport**
  1. Occurs down concentration (chemical), electrical or pressure gradient.
  2. Does not need energy.



- **Factors affecting rate of diffusion**

A- Directly proportional with

1- The gradient for diffusion whether chemical, electrical or pressure.
2- Temperature :- increases the random motion of the molecules.
3- Surface area of the membrane available for diffusion.
4- Permeability of the membrane.



B- Inversely proportional with

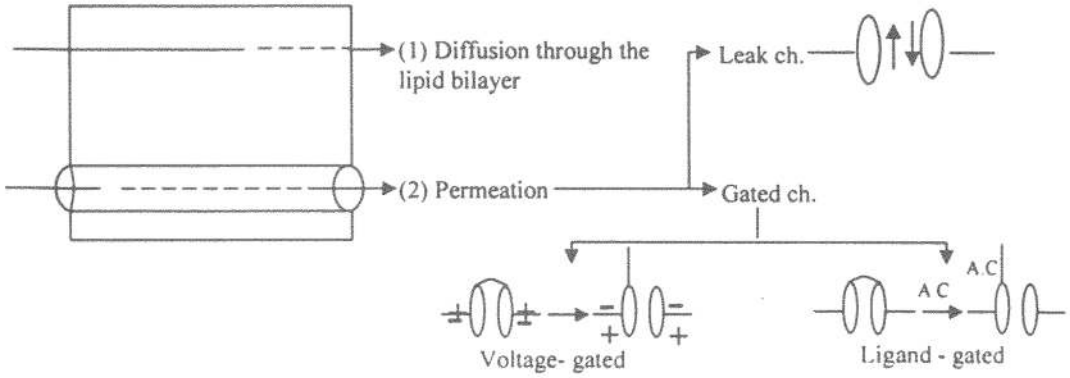
1- Molecular weight (molecular size) of the substance: diffusion rate is inversely proportional with the square root of the molecular size.

2- Thickness of the membrane (the distance across which diffusion takes place).

▪ Types of diffusion

1- Simple diffusion

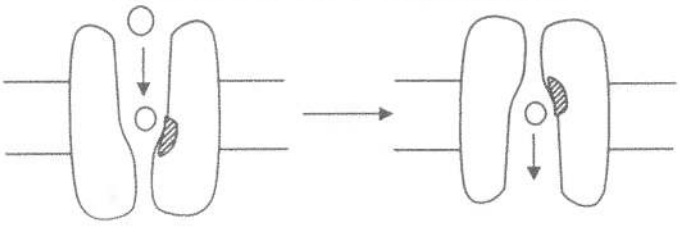
- **Definition:** - Diffusion without a need for carrier.
- **It is concerned with:-** a- Lipid soluble substances.
  b- small water soluble substances, e.g., ions.
- **It occurs through:**
  a. Lipid bilayer
  This is for lipid soluble substances, e.g., O_2, CO_2, fatty acids, glycerol and urea. The diffusion of these substances is directly proportional to their lipid solubility. O_2 is highly lipid soluble so that it enters the cell in large quantities as if the cell membrane did not exist.
  b. Protein channels (permeation)
  This is for small water soluble substance e.g. ions (Na^+, K^+, Cl^- etc).
- **Types of channels in the cell membrane:-**
  1. Leak channels: has no gate (continuously opened), e.g., Na^+-K^+ leak channels.
  2. Gated channels: have gates (open and close) and are of 2 types:
     - Voltage-gated channels: their gates open as a result of change in the electric potential across the cell membrane, e.g., voltage gated Na^+ channel, K^+ channel and Ca^{2+} channel.
     - Ligand-gated channels: their gates open as a result of binding (ligation) of a chemical substance with receptor on the channel protein, e.g., acetylcholine–gated ion channel at motor end plate (neuromuscular junction)

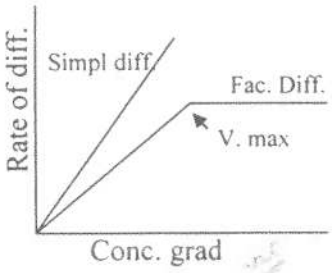


2-Facilitated(carrier mediated) diffusion

- Definition: diffusion that needs carrier protein.

- It is concerned with lipid insoluble large molecules, e.g., glucose and most amino acids.
- Mechanism
  - The carrier protein has a channel large enough to transport the specific molecule, e.g., glucose part way but not all the way through the membrane
  - Binding of the specific molecule, e.g., glucose with a receptor on the carrier protein (a type of integral proteins)→ widening of the inner part of the channel of the carrier protein → facilitation of transport of the molecule across the membrane.





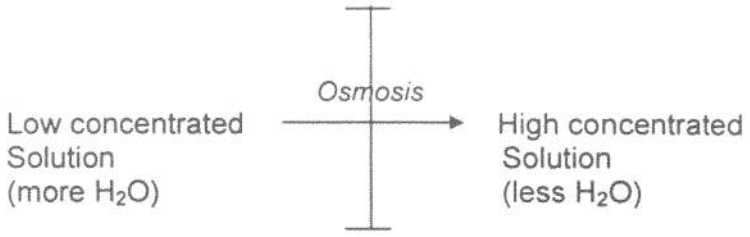
Differences between simple and facilitated diffusion

Simple diffusion	Facilitated diffusion
1. For lipid soluble and small lipid insoluble.	1. For lipid insoluble large molecule.
2. Does not need carrier.	2. Needs carrier.
3. No structural specificity because there is no carrier.	3. High structural specificity:- each carrier is specific for one or very few substances.
4. No competitive inhibition because there is no carrier	4. Competitive inhibition: similar molecules compete with each other for the same carrier and ↓the transport of each other.
5. No saturation, i.e., it ↑ with increasing the concentration gradient without limit (no carrier).	5. Saturation: has a maximum limit (v. max) i.e. it ↑ with increasing the concentration gradient till all the carriers available for this substance become saturated, then it does not increase after that.
6. Less sensitive to temperature changes (no carrier)	6. More sensitive to temperature changes (3 times that of simple diffusion) because binding of the substance with the carrier is through an enzyme.

- **Special types of Passive Transport**

A) Osmosis

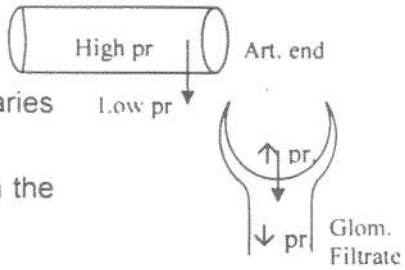
- It is the diffusion of water (the solvent) from area of less concentrated solution (more solvent) to the area of more concentrated solution (less solvent).
- Osmotic pressure is the pressure needed to stop osmosis. Osmotic pressure depends on number rather than the size of particles in a solution



- Diffusion of water (osmosis) takes place through both lipid bilayer and protein channels. This is because water molecules have very small size and high kinetic energy; so that the molecules penetrate the lipid bilayer like bullets before hydrophobic characters of lipid layer stop them.

B) Filtration (Bulk flow):

- Means diffusion of fluid through a membrane that is caused by difference in hydrostatic pressure.
- Examples:
  a. Filtration at arterial end of systemic capillaries to form interstitial fluid.
  b. Filtration through glomerular capillaries in the kidney to form glomerular filtrate.



C) Solvent drag

- Means diffusion of a solute following diffusion of its solvent through the membrane, i.e., the solvent drags the solute after it.
- Example:- Reabsorption of urea after H_2O reabsorption in renal tubules

B- Active transport

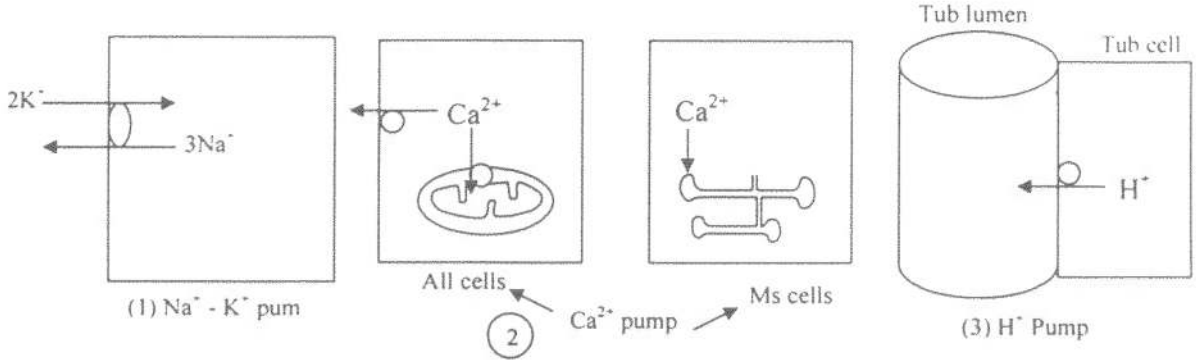
- **Definition:-** Transport of a substance against its electro-chemical gradient.
- **Criteria of active transport:-** two
  1- Occurs against concentration (chemical), electrical or pressure gradient i.e. up hill.
  2- Needs energy.

- **Types of active transport:-**

1-Primary active transport

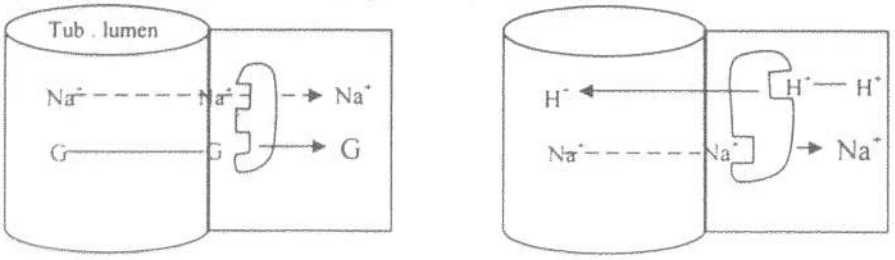
- **Definition:-**Transport of a substance against its electrochemical gradient by a specific carrier and this carrier has ATPpase activity, i.e., hydrolyze ATP and produces energy .
- **Examples:-**
  b. Na^+-K^+ pump: a pump present in all cells of the body that pumps 3 Na^+ to outside the cell coupled with pumping 2 K^+ to the inside of the cell.
  c. Calcium pump:-
    - In all cells, 2 pumps are present
      1. In the cell membrane and pumps Ca^{2+} to outside the cell.
      2. In the mitochondria and pumps Ca^{2+} to the inside of mitochondria.
    - In muscle fibers:- in addition to the previous pumps another pump is present in the sarcoplasmic reticulum that pumps Ca^{2+} to the inside of the sarcoplasmic reticulum.

  Through these pumps, Ca^{2+} is maintained at very low level intracellularly, about 10,000 times less than extracellularly.
  d. H^+ pump:- In the renal tubules (second half of distal tubules and collecting ducts) and pumps H^+ from the cell to the tubular lumen.



2- Secondary active transport

- **Definition:-** Transport of a substance actively (against its electro-chemical gradient) secondary to passive transport of another substance (down its electro chemical gradient).



- **Types:-** two types

a. Co-transport (symport):-

- In which the two substances are transported in the same direction.
- Example:- sodium-glucose and sodium-amino acids co-transport that occurs in epithelial cells of the intestine and renal tubules. In this mechanism, glucose and Na^+ bind to a common carrier and glucose is carried into the cell (against its electrochemical gradient) as Na^+ moves to the inside of the cell (down its electrochemical gradient).

b. Counter transport (Antiport):-

- In which the two substance are transported in opposite directions.
- Example:- sodium-hydrogen counter transport in the renal tubular epithelium. In this mechanism, there is a common carrier for Na^+ and H^+, Na^+ binds to a receptor on the outer surface of the carrier and H^+ binds to a receptor site on the inner surface of the carrier. H^+ is carried outside the cell (against its electrochemical gradient) as Na^+ moves passively to the inside of the cell (down its electrochemical gradient).

3- Endocytosis (cell ingestion)

- **Definition:-** is an active process by which macromolecules, e.g., protein and large particles, e.g., bacteria are transported to the inside of the cell.
- **Types:-** 2 types

a. Pinocytosis (cell drinking)

- Definition:- It is the process by which macromolecules, e.g., proteins are transported to the inside of the cell. It is transported in a vesicle containing ECF, thus the name cell drinking.
- It occurs in most body cells.
- Mechanism:
  1. Attachment of the substance to a specific receptor on the cell membrane. The receptors are concentrated in small pits called coated pits.
  2. The entire pit invaginates inwards by action of contractile elements.
  3. The borders of the invaginated pit close over the attached substance with some ECF and form a vesicle (pinocytic vesicle).
  4. The vesicle separate from the cell membrane and pass to the cytoplasm.

(1) attachment (2) Invagination (3) vesicle formation (4) Separation

b. **Phagocytosis (cell eating)**

- Definition:- It is the process by which large particles e.g. bacteria are transported to the inside of the cell.
- It occurs only in some specific cells of the body (phagocytic cell) e.g.,
  1. Some white blood cells:- mainly neutrophils (microphages) and monocytes (macrophages)
  2. Tissue macrophages.
- Mechanism:- Essentially the same as pinocytosis, but differs in two aspects:-
  1. The phagocytic vesicle contains only particle without ECF and hence the name cell eating.
  2. If the ingested substance is digestable, there will be an additional step in which lysosomes come in contact with the phagocytic vesicles and release its digestive enzymes into the vesicle to digest the ingested substance.

4-Exocytosis (cell excretion)

- Definition:- Is a process by which macromolecules and large particles are transported to the outside of the cell.
- Mechanism:- Reverse to endocytosis.

Donnan Effect
(Gibbs-Donnan Equilibrium)

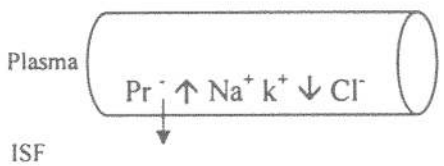
- When there is a non diffusible ion on one side of a semi-permeable membrane, the other diffusible ions redistribute themselves in a predictable way to reach the electrical neutrality on both sides.
- Example:-

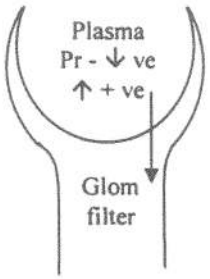
	Side X	Side Y	Side X	Side Y
Diffusible	Cl^- 20	-	Cl^- 8	12
	K^+ 30		K^+ 18	12
Non diffusible	Pr^- 10		Pr^- 10	-
	At start		After equilibrium	

- Donnan and Gibbs showed that in the presence of non-diffusible ion (protein), the other diffusible ions (Cl^- and K^+) distribute themselves so that at equilibrium the concentration ratios are equal (their concentration products on both sides are equal)

  Gibbs-Donnan equation: $\frac{K^+_Y}{K^+_X} = \frac{Cl^-_X}{Cl^-_Y}$ i.e., $K^+_Y X\ Cl^-_y = K^+_X X\ Cl^-_x$

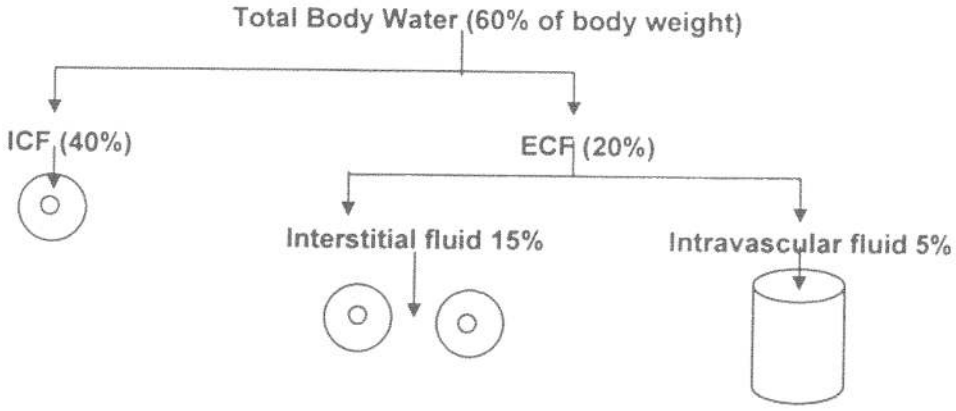
- Effects of Donnan equilibrium:-
  1- Electrical neutrality is preserved on both sides of the membrane.
  2- On the protein containing side there is net increase in the number of osmotically active particles e.g. inside the cell and plasma in systemic and glomerular capillaries.
  3- Also, on protein containing side the number of +ve ions is more and number of -ve ions is less than the other side. Example in the body: the plasma in systemic capillaries and glomerular capillaries contains plasma protein that can not diffuse from plasma to ISF or glomerular filtrate, thus, the plasma contain +ve ions slightly more and –ve ions slightly less than ISF and glomerular filtrate.





Body Water

- Water constitutes about 60% of body weight, i.e. about 42 L in 70Kg adult male.
- **Compartments:** Total Body Water (TBW) is divided into 2 compartments:-
  1- Intracellular fluid (ICF):- present inside the cells and constitute about 40% of body weight, i.e., 2/3 total body water.
  2- Extracellular fluid (ECF):- present outside the cells and constitute about 20% of body weight, i.e., 1/3 total body water. ECF is divided into:-
     a- Interstitial fluid:- present between the cells and constitute about 15% of body weight.
     b- Intravascular fluid (plasma):- present inside blood vessels and constitute about 5% of body weight.



Note:- Interstitial fluid or the ECF as a whole is called the internal environment of the body because it is the environment in which cells are living.

- **Normal variation**
  1- **Variation with age**:-
     1- TBW is more in infants and children (about 75% of body weight)
     2- Reaches adult level at puberty (60% of body weight)
     3- Decrease in old age (about 45% of body weight)

Note: the increase in TBW in children is mainly in ECF i.e. ECF/ICF ratio is more than adults and as ECF is easier to be lost in dehydration thus dehydration develops more rapid and more severe in children than adults.

2- **Variation with sex :-**TBW is less in females than males (about 50% of body weight in adult females) because of high fat content in their bodies (body fat is relatively free of water).

3- **Variation with fat content in body**: TBW is less in obese persons.

❖ Distribution of ions in ICF and ECF (in mEq/L)

	ICF	ECF
Cations (+ve ions)		
Na^+	14	**140**
K^+	**140**	4
Ca^{2+}	0.0001	2.4
Anions(-ve ions)		
Cl^-	4	**104**
HCO^{3-}	10	**28**
Phosphates(PO_4^{3-})	**75**	4
Proteins	**40** (16 gm%)	4 (2 gm%)

Notes:-

1- The 2 components of ECF (ISF and plasma) are nearly similar in ionic composition except for protein which is higher in plasma (17 mEq/L, 7gm%) than ICF (4mEq/L, 2 gm%).

2- Simply, the main cation in ICF is K^+ and in ECF is Na^+, and the main anions in ICF are phosphates and proteins and in ECF are Cl^- and HCO^-_3

❖ Functions (importance) of body water

1- Medium for most biological processes as:-
   A. Digestion in GIT:-
      i. Essential component for all digestive secretions.
      ii. Medium for all secretions to work.
   B. Absorption:- in GIT, renal tubules and venous end of capillaries,
   C. Excretion:- through GIT, kidney and skin (sweat)
   D. Filtration:- in glomeruli of the kidney and arterial end of capillaries

2- Medium for exchange process:-
   a. Exchange of O_2 & CO_2 through alveolar membrane in lungs.
   b. Exchange of nutrients, waste products, and CO_2 through capillary wall.
   c. Exchange of ions and nutrients through cell membrane.

3- Medium for chemical and enzymatic reactions as occur in metabolic processes in the cell.

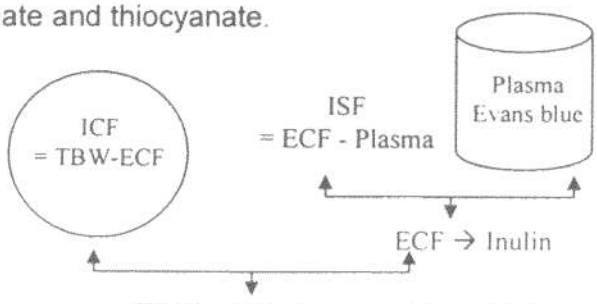
4- Transport medium:- Transport of substances (as nutrients, waste products O_2 and CO_2, hormones, vitamins etc.)to different parts of the body.
5- Regulation of body temperature through heat distribution and evaporation.
6- Essential for homeostatic processes as regulation of pH and osmolarity.
7- Lubricant in:- a-mouth b-joints
c-potential spaces as pleura pericardium and peritoneum
8- Refractive medium in the eye.
9- Mechanical buffer (shock absorber):- Distributes mechanical trauma applied to any part of the body to a large area, so it becomes less harmful.

❖ Measurement of body water compartments

This is done using indicator dilution principle in which a known amount of substance that will stay in only one compartment is injected intravenously. Time is allowed for the substance to distribute uniformly in the compartment then a blood sample is taken and the concentration of the substance in plasma is determined. Then, the volume of water compartment is calculated using the following equation:-

$$\text{Volume of compartment} = \frac{\text{Amount of substance injected}}{\text{Concentration of the substance in plasma}}$$

1- TBW is measured using either:-
   - Antipyrine which is very lipid soluble and can rapidly penetrate cell membrane.
   - Deuterium oxide (heavy water, ^2H_2O) or tritium oxide (isotopically labeled water, ^3H_2O), these forms of water mix with total body water.
2- ECF is measured using substance that distributes in plasma and ISF but do not readily penetrate cell membrane as inulin, sucrose, mannitol thiosulphate and thiocyanate.



3- ICF can not be measured directly. However, it can be calculated as follows: ICF = TBW – ECF.

4- Plasma volume measured using substances that does not readily penetrate capillary membrane but remain in vascular system as Evans blue or albumin labeled with radioactive iodine.

5- ISF can not be measured directly, However, it is calculated as follows: - ISF = ECF – plasma.

Homeostasis

6/6/2015

❖ **Definition**

Homeostasis means keeping the composition of internal environment of the body (interstitial fluid or ECF) constant regarding:

1- Volume (water content).

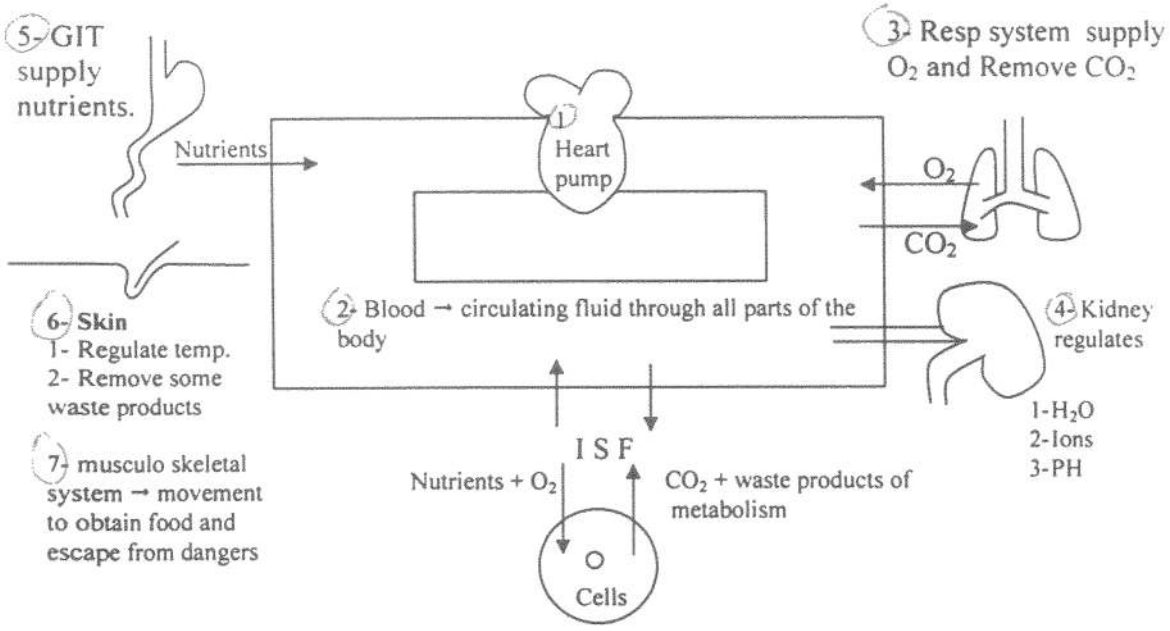
2- Ions (Na^+, K^+, Cl^-, HCO^{3-})

3-temperature

4-pH.

❖ Interstitial fluid or ECF is called the internal environment of the body because it is the environment that surrounds the body cells. Life is possible within narrow limits of change in the chemical or physical properties of internal environment.

❖ Most biological systems in the body work, either directly or indirectly, to maintain homeostasis i.e. to keep the internal environment optimum for cellular function.



❖ The function of these biological systems is regulated by 2 control systems:-

1- Nervous system ⟶ rapid control system.

2- Endocrinal (hormonal) system ⟶ slow control system.

❖ **Feedback control of the homeostatic mechanisms**

- **Definition:** - feedback control means the control of certain function by the resultant effect of this function.
- **Types:**

1. **Negative feedback control**
   - The most common, in which the resultant effect of a function inhibits that function.
   - Negative feedback control leads to stability of internal environment
   - Examples:-

a) Regulation of blood glucose level:-

↑ Blood glucose ⟶ ↑ insulin secretion ⟶ ↑ glucose utilization by tissues ⟶ ↓ blood glucose back to normal.

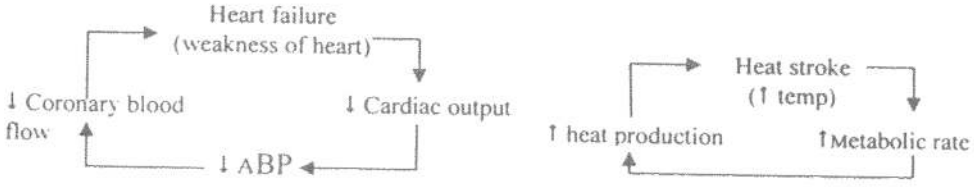
b) Regulation of CO_2 in blood:-

↑ CO_2 in blood ⟶ hyperventilation ⟶ CO_2 wash ⟶ ↓ CO_2 back to normal

c) Regulation of arterial blood pressure (ABP)

↑ ABP ⟶ ↓ heart rate and vasodilatation ⟶ ↓ ABP back to normal

2. **Positive feedback control**:-
   - Less common, in which the resultant effect of a function stimulates that function.
   - It leads to instability of internal environment and often death due to vicious circle (death cycles) e.g.



   - Positive feedback can some times be useful, i.e., operate in the body to complete certain function e.g., process of parturition (labor) : Stretch of uterine cervix → reflex uterine contraction→ descend of baby → more stretch of cervix → more uterine contraction → more descend of baby and so on until labor is complete.