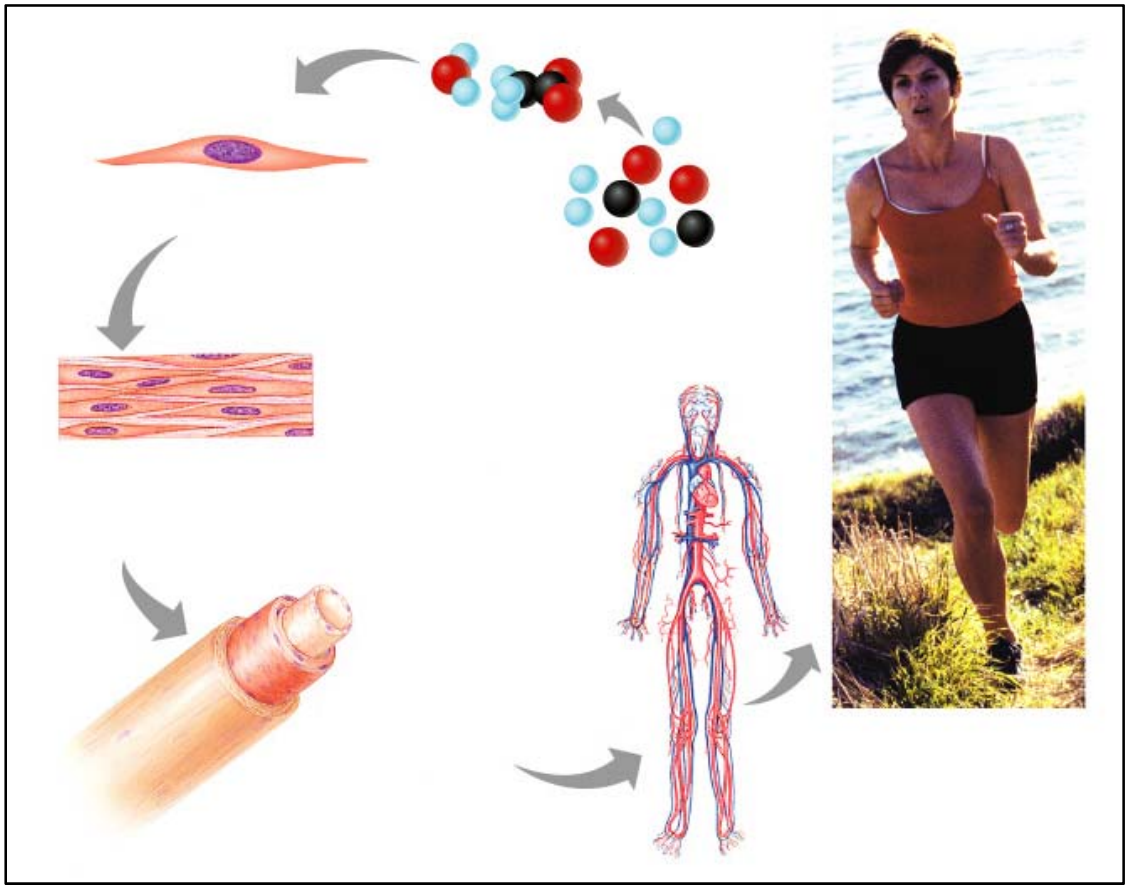
Human Physiology

Introduction to Physiology

- Physiology is one of the cornerstones of medicine.
- Physiology is the study of how the body works, the ways in which cells, organs and the whole body functions, and how these functions are maintained in a changing environment.
- Cellular physiology is the study of the cellular components that primarily determines organ function.
- Systems physiology is the study of the coordinated and networked processes that determine whole body function and adaption to change.

Levels of Structural Organization



Body Fluids

Objectives

At the end of this session, the students should be able to:

- Identify and describe daily intake and output of water and maintenance of water balance.
- List and describe of body fluid compartments as intra-cellular fluid (ICF) Extra-cellular fluid A(ECF), interstitial fluid, trans-cellular fluid and total body water.
- Describe the composition of each fluid compartment, in terms of volume and ions and represent them in graphic forms.
- Physiology factor influencing body fluid: age, sex, adipose tissue, etc. Pathological factors: Dehydration, fluid infusion.

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Serum

3.9 - 5.8	mmol / L	[*]	Fasting Blood Sugar	4.5	
			Urea and Electrolytes		
2.5 - 6.4	mmol / L	[*]	Urea	3.1	
53 - 106	umol/L	[*]	Creatinine	62	
135 - 145	mmol/L	[*]	Sodium	141.0	
3.5 - 5.1	mmol/L	[*]	Potassium	4.4	
98 - 107	mmol/L	[*]	Chloride	102.0	
22 - 32	mmol/L	[*]	Bicarbonate	26.0	
			Liver Function test profile		
3 - 17	umol/L	[*]	Total Bilirubin	5	
0 - 5	umol/L	[*]	Direct Bilirubin	2	
60 - 80	g/L	[*]	Total Protein	72.2	
30 - 50	g/L	[*]	Albumin	43.0	
50 - 136	U/L	[*]	Alkaline Phosphatase	83.0	
20 - 65	U/L	[*]	Alanine Aminotransferase	23.0	
10 - 31	U/L	[*]	Aspartate Aminotransferase	12.0	
5 - 55	U/L	[*]	Gamma Glutamyl Transferase	17.0	
20 - 40	g/L	[*]	Globulins	29.2	
2 - 17	umol/L	[*]	Indirect Bilirubin	3	
			Lipid profile		
0.4 - 1.48	mmol / L	[*]	Triglycerides	0.49	
3.2 - 5.2	mmol / L	[ ]>	Cholesterol	6.40	H
0.93 - 1.94	mmol / L	[*]	HDL-Cholesterol	1.72	
1.63 - 3.63	mmol / L	[ ]>	LDL - Cholesterol	4.46	H

PLS. NOTE THE NEW NORMAL RANGES

RECOMMENDED LEVEL FOR TOTAL SERUM CHOLESTEROL < 5.2 mmol/L

.....
CONSULTANT ON DUTY

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EDTA Whole Blood

	Full Blood Count			
[*]	WBC	7.1	4 - 11	x10.e9/L
[*]	RBC	4.78	4.2 - 5.5	x10.e12/L
[*]	HGB	145	120 - 160	g/L
[*]	HCT	42.1	37 - 47	%
[*]	MCV	88.0	80 - 94	fl
[*]	MCH	30.3	27 - 32	pg
[*]	MCHC	345	320 - 360	g/L
[*]	RDW	13.3	11.5 - 14.5	%
[*]	PLT	222	140 - 450	x10.e9/L
[*]	MPV	8.8	7.2 - 11.1	fl
	Differential			
[*]	%NEUT	60.5	40 - 75	%
[*]	%LYMP	31.3	20 - 45	%
[*]	%MONO	4.6	3 - 9	%
[*]	%EOS	3.1	0 - 6	%
[*]	%BASO	0.5	0 - 1	%
[*]	#NEUT	4.3	2 - 7.5	x10.e9/L
[*]	#LYMP	2.2	1 - 5	x10.e9/L
[*]	#MONO	0.3	0.2 - 0.8	x10.e9/L
[*]	#EOS	0.2	0.0 - 0.8	x10.e9/L

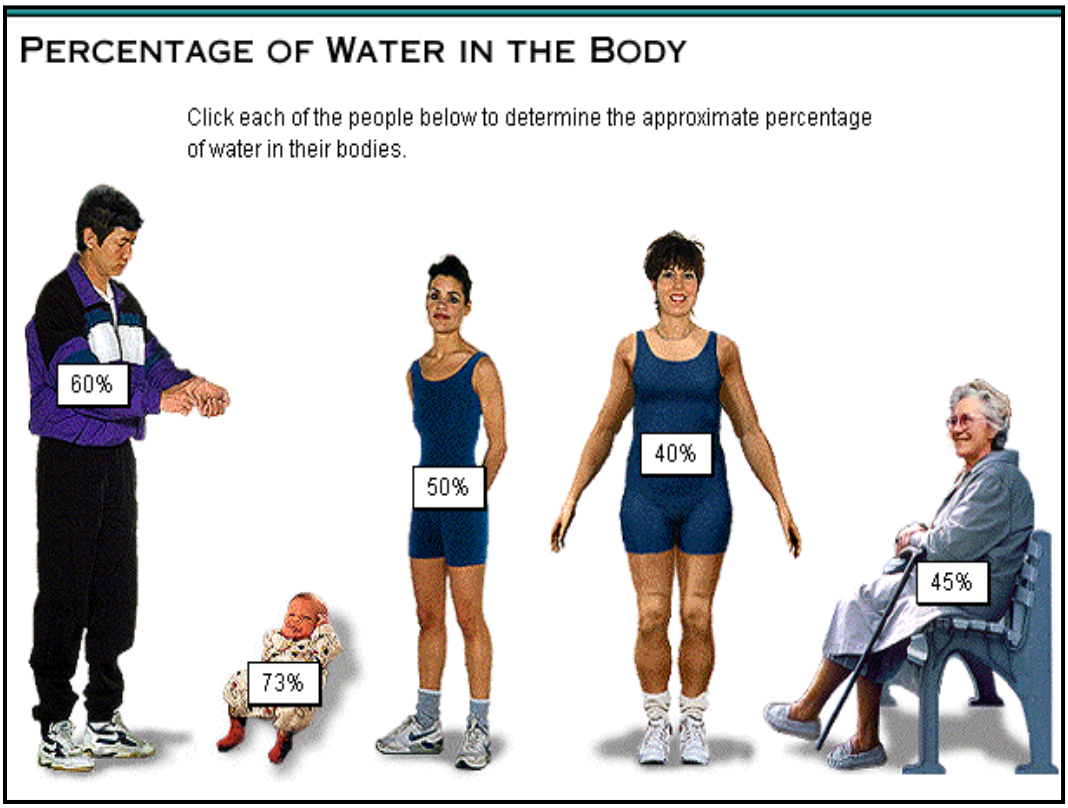
Morophology
Flag Comments
Flag Comment 1
ANISO .....
MICRO .....
MACRO .....
POIKILO .....
HYPO .....
Polychromasia .....
LSHIFT .....

EQUEST COMMENTS:

- Human body contains 50-70% water.
- E.g.:
- 70 kg man has 42 L of water.
- Kg of water = L of water.

Factors affecting

Infant: 73%
Male adult: 60%
Female adult: 40-50%
Obesity ↓
Old age ↓ 45%



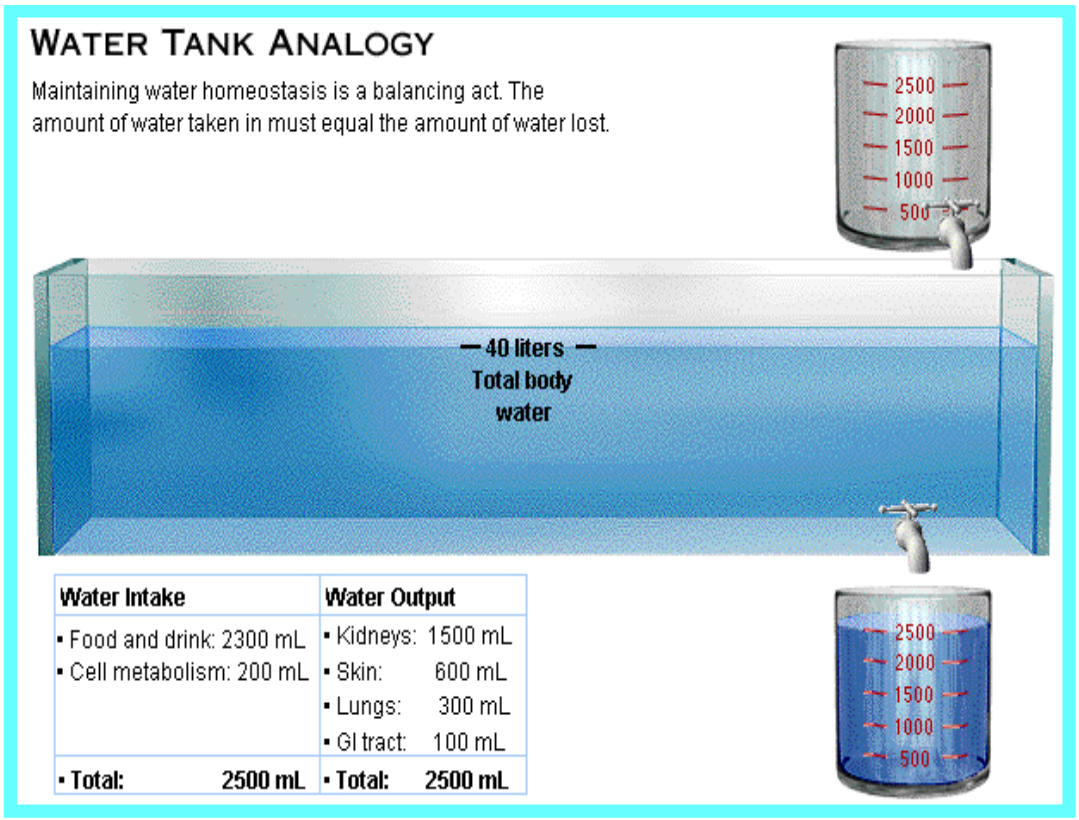
Body Water Content

- Infants have low body fat, low bone mass, and are 73% or more water
- Healthy males are about 60% water; healthy females are around 50%
- This difference reflects females':
    - Higher body fat
    - Smaller amount of skeletal muscle
- In old age, only about 45% of body weight is water
- Total water content declines throughout life.

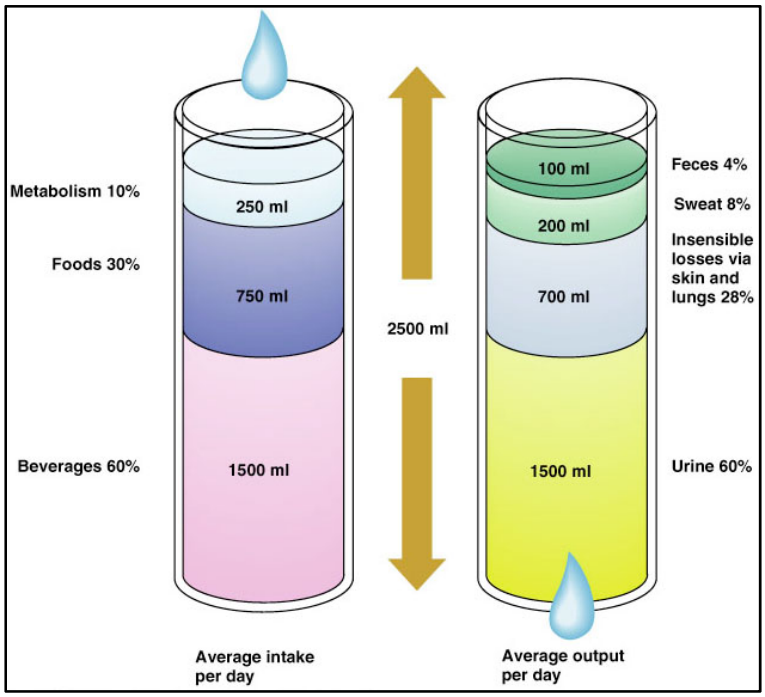
Daily Intake of Water

TABLE 20–1 DAILY INTAKE AND OUTPUT OF WATER
(in ml/day)

	Normal	Prolonged, Heavy Exercise
Intake		
Fluids ingested	2100	?
From metabolism	200	200
Total intake	2300	?
Output		
Insensible—Skin	350	350
Insensible—Lungs	350	650
Sweat	100	5000
Feces	100	100
Urine	1400	500
Total output	2300	6600



Water Intake and Output



Regulation of Water Intake

Climate
Habits
Level of physical activity.

- The hypothalamic thirst center is stimulated:
  - By a decline in plasma volume of 10%–15%
  - By increases in plasma osmolality of 1–2%
  - In steady state water intake= water loss

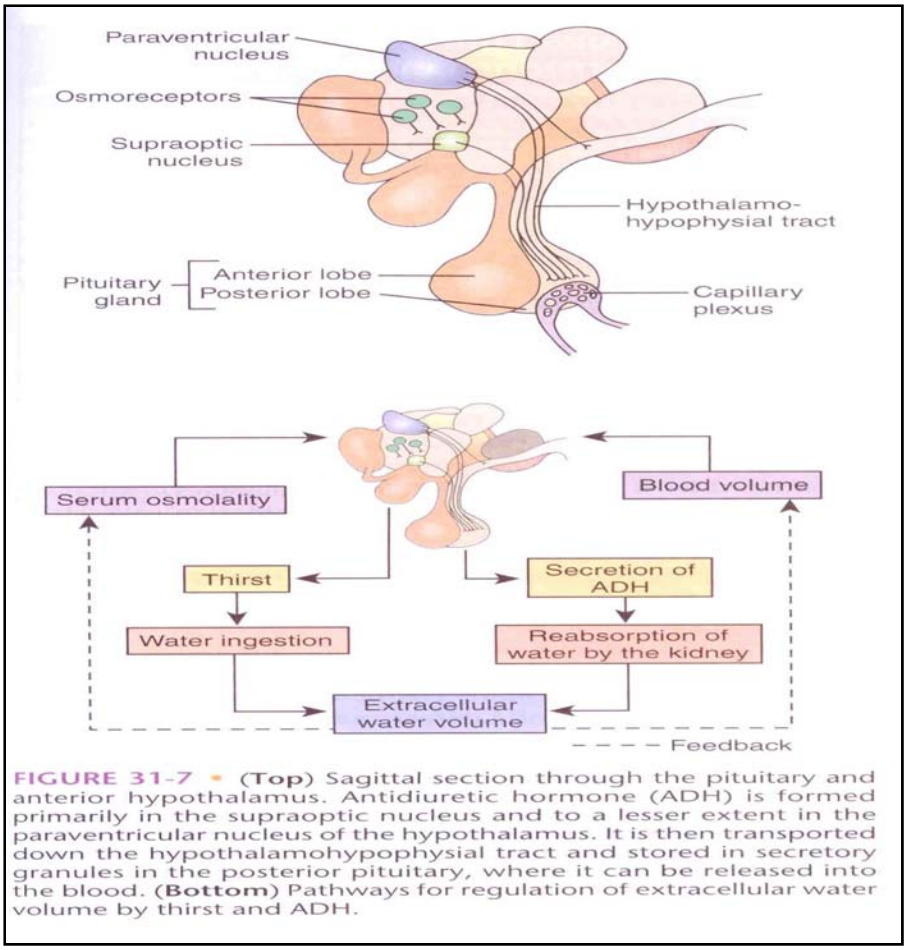


FIGURE 31-7 • (**Top**) Sagittal section through the pituitary and anterior hypothalamus. Antidiuretic hormone (ADH) is formed primarily in the supraoptic nucleus and to a lesser extent in the paraventricular nucleus of the hypothalamus. It is then transported down the hypothalamohypophysial tract and stored in secretory granules in the posterior pituitary, where it can be released into the blood. (**Bottom**) Pathways for regulation of extracellular water volume by thirst and ADH.

Factors that Affect the TBW

Physiological factors

- Age
- Sex
- Body fat
- Climate
- Physical activity

Pathological factors

Vomiting

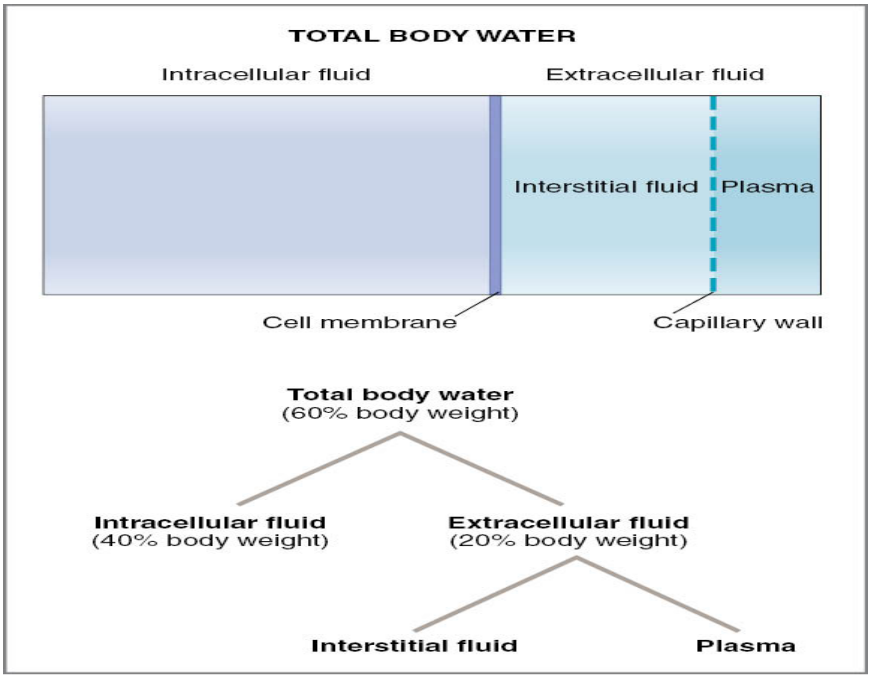
Diarrhea

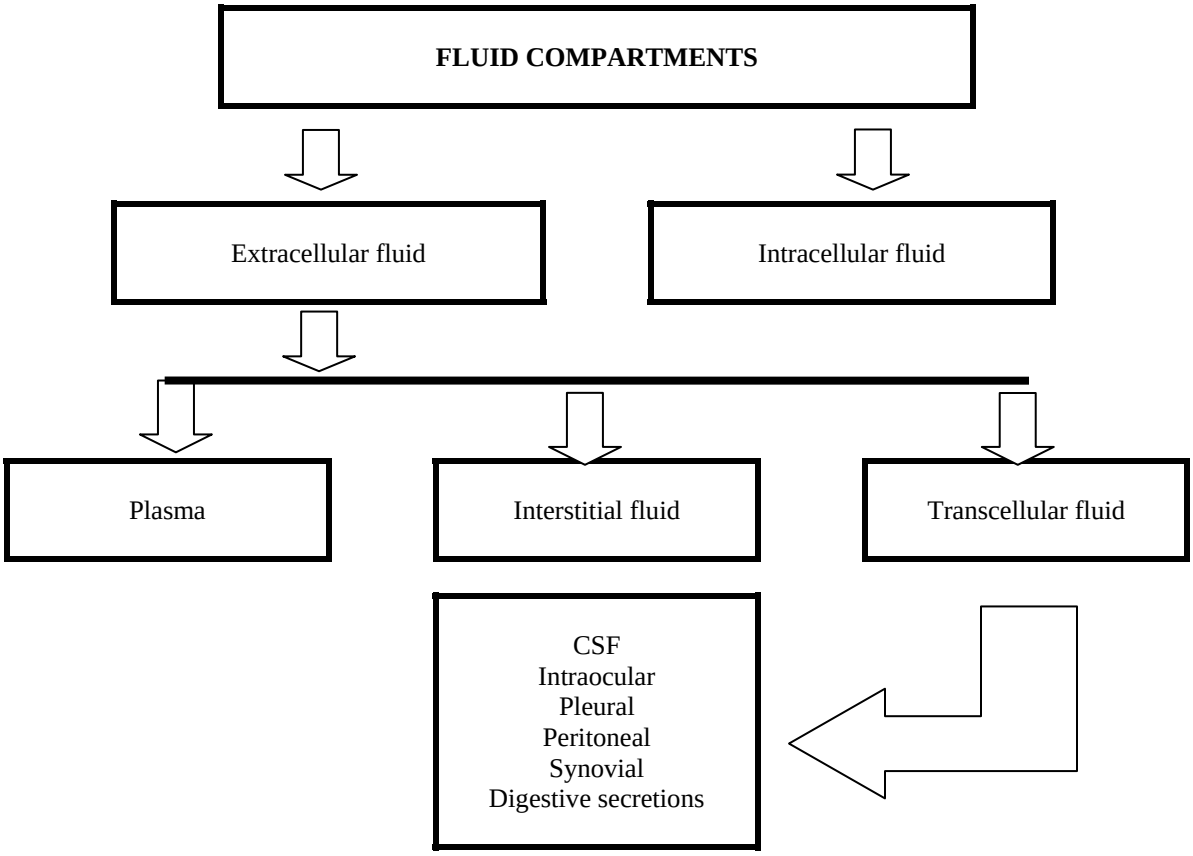
Diseases with excessive loss of water (DM, excessive sweating,….

Blood loss

Fluid Compartments

- Water occupies two main fluid compartments:
- Intracellular fluid (ICF)
- Extracellular fluid (ECF)
    - Plasma
    - Interstitial fluid (IF)





Intracellular fluids (ICF)

- Inside the cell.
- 2/3 of TBW.
- High concentration of protein.

Extracellular fluids (ECF)

- Out side the cell.
- 1/3 of TBW.
- Plasma:
- Fluid circulating in the blood vessels.
- 1/4 of ECF
- Interstitial fluid:
- Fluid bathing the cell.
- Ultra filtration of plasma.
- 3/4 of ECF

Plasma and interstitial fluid are almost having the same composition except for high protein concentration in plasma

Transcellular fluid compartment

- small amount
- CSF, GIT fluid, biliary fluid, synovial fluid, intrapelural fluid, intraperitoneal fluid, intrapericardial fluid and intraoccular fluid.

e.g.

- TBW = 42L.
- ECF = 14L.
- ICF = 28L.
- Plasma = 3,5 L.
- Interstitial = 10,5 L.

Composition of body fluid

- Water is the universal solvent
- Solutes are broadly classified into:
    - Electrolytes – inorganic salts, all acids and bases, and some proteins
    - Nonelectrolytes – examples include glucose, lipids, creatinine, and urea
    - Amount = in moles, osmoles.

Concentration

- Molarity = moles/liter M/L.
- Osmolarity = osmoles/liter osm/L.
- Osmolality = osmoles/kg Osm/kg.

In biological solution

- Millimoles per liter (mM/L)
- Milliosmoles per (mOsm/L)
- 1mM=1/1000 M
- 1mOsm=1/1000 Osm

Constituents of ECF and ICF

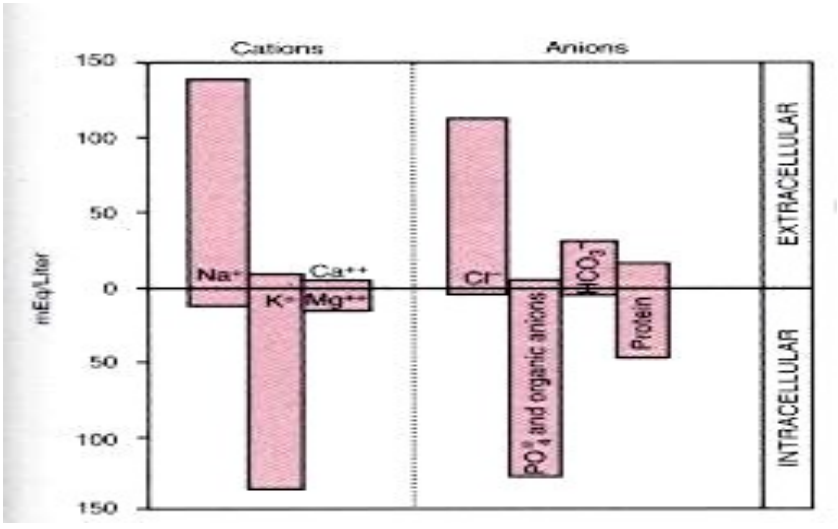
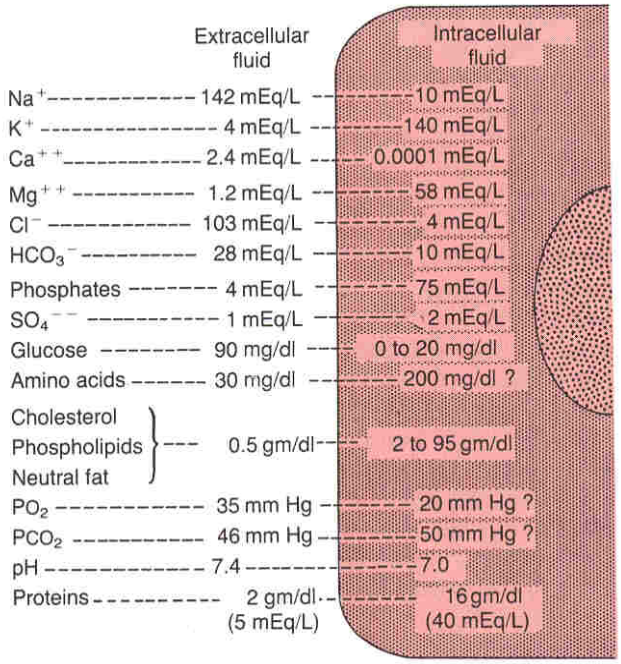


TABLE 20–2 OSMOLAR SUBSTANCES IN EXTRACELLULAR AND INTRACELLULAR FLUIDS

	Plasma (mOsm/liter of H_2O)	Interstitial	Intracellular
Na^+	142	139	14
K^+	4.2	4.0	140
Ca^{++}	1.3	1.2	0
Mg^{++}	0.8	0.7	20
Cl^-	108	108	4
HCO_3^-	24	28.3	10
HPO_4^{--}, $H_2PO_4^-$	2	2	11
SO_4^{--}	0.5	0.5	1
Phosphocreatine			45
Carnosine			14
Amino acids	2	2	8
Creatine	0.2	0.2	9
Lactate	1.2	1.2	1.5
Adenosine triphosphate			5
Hexose monophosphate			3.7
Glucose	5.6	5.6	
Protein	1.2	0.2	4
Urea	4	4	4
Others	4.8	3.9	10
Total mOsm/liter	301.8	300.8	301.2
Corrected osmolar activity (mOsm/liter)	282.0	281.0	281.0
Total osmotic pressure at 37° C (mm Hg)	5443	5423	5423

Extracellular and intracellular fluids

- Each fluid compartment of the body has a distinctive pattern of electrolytes
- Extracellular fluids are similar (except for the high protein content of plasma)
    - Sodium is the chief cation
    - Chloride is the major anion
- Intracellular fluids have low sodium and chloride
    - Potassium is the chief cation
    - Phosphate is the chief anion
    - Each compartment must have almost the same concentration of positive charge (cations) as of negative charge (anion).
      (Electroneutrality)



- Hypokalemia: decrease in K concentration in the ECF. 1-2 mEq/L
- Hyperkalemia: increase in K 60-100% a above normal.
- Hypernatremia: increase in Na concentration in ECF.
- Hyponatremia: decrease in Na concentration in the ECF.

Regulation of fluid exchange

- Intracellular
  cell member
- Extracellular - highly permeable to water
  - relatively impermeable to small ions.
  i.e. only water is moving.
- (osmotic effect of electrolytes Na,K,cl)

Osmotic equilibrium is maintained between intracellular and extracellular fluids:

- Small changes in concentration of solutes in the extracellular fluid can cause tremendous change in cell volume.
- Intracellular osmolarity = extracellular osmolarity .
- ≈ 300 mosm/L

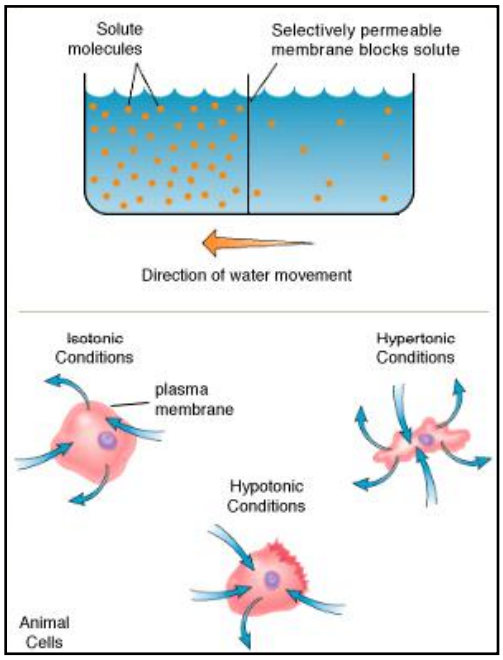
Mechanisms of movement

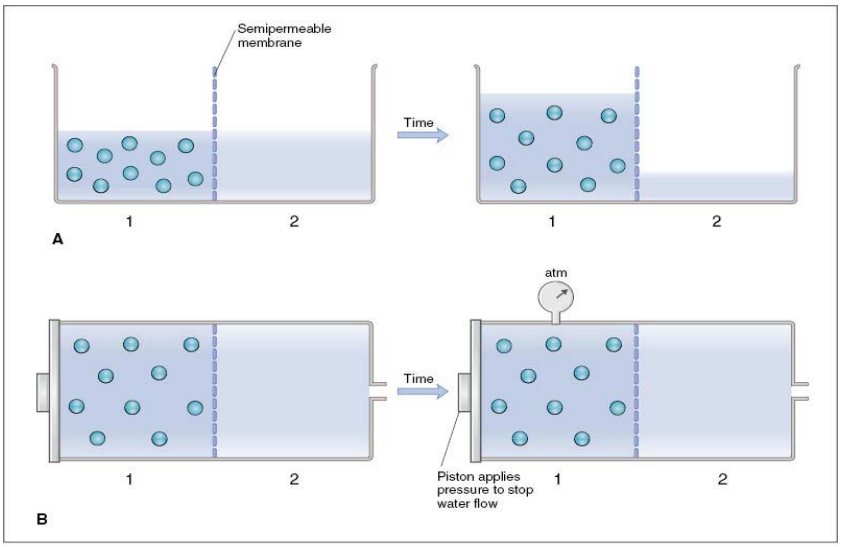
3 general mechanisms:

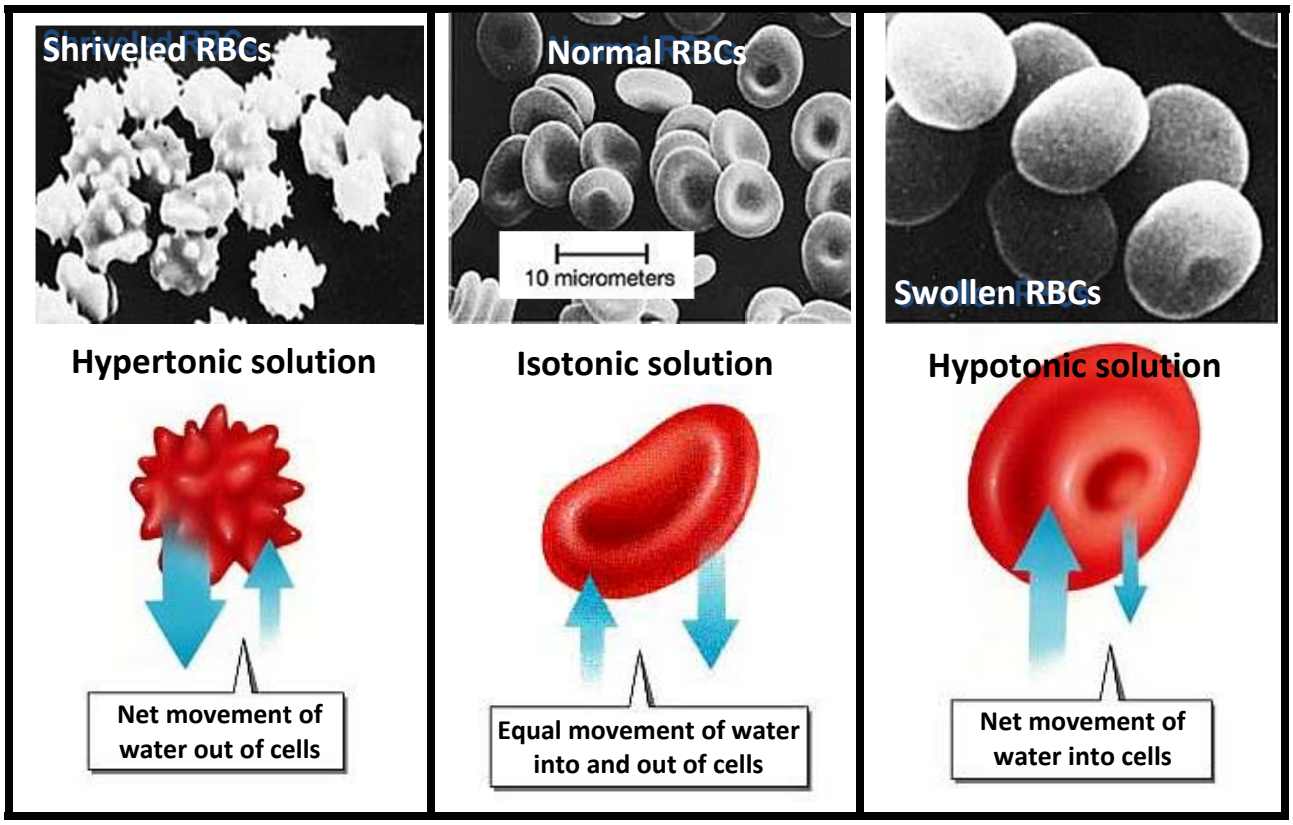
1. simple diffusion (passive)
2. Facilitated transport (passive)
3. Active transport

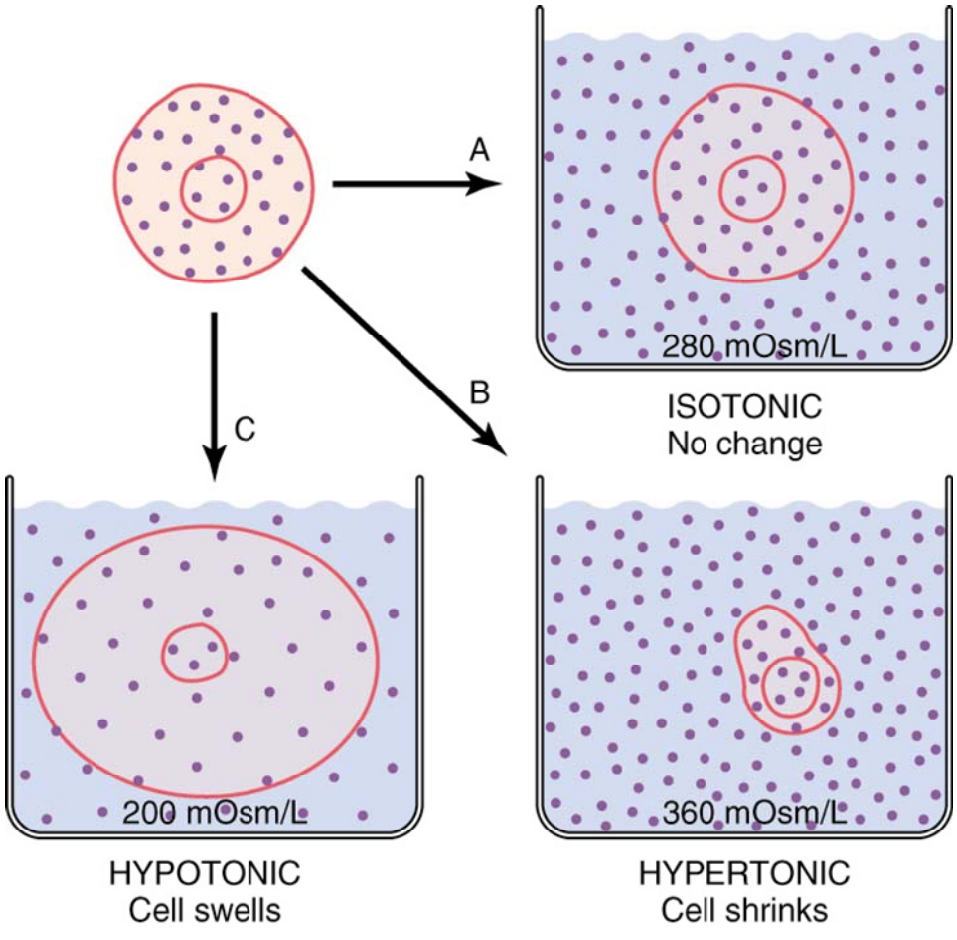
Osmosis

- net diffusion of water from a region of high water concentration to region of low water concentration.






Shriveled RBCs
Normal RBCs
10 micrometers
Swollen RBCs
Hypertonic solution
Isotonic solution
Hypotonic solution
Net movement of water out of cells
Equal movement of water into and out of cells
Net movement of water into cells


A
B
C
280 mOsm/L
ISOTONIC
No change
200 mOsm/L
HYPOTONIC
Cell swells
360 mOsm/L
HYPERTONIC
Cell shrinks

- If environment is:
  - Hypertonic:
    - MORE SOLUTES outside cell
    - MORE WATER IN CELL
    - over time, cell loses water
  - Isotonic:
    - same
    - No change in cell volume
  - Hypotonic:
    - LESS SOLUTES outside cell
    - LESS WATER IN CELL, more solutes in cell.
    - over time, cell gains water

❖ Isotonic solution :
- (no swells or shrink)
- 0.9% solution of sodium chloride or 5% glucose .
- same in and out .

❖ Hypotonic solution :
- (swelling) 0.9%
- in is higher than out .

❖ Hypertonic solution :
- (shrink) 0.9%
- out is higher than in

Glucose and other solutions administered for nutritive purposes

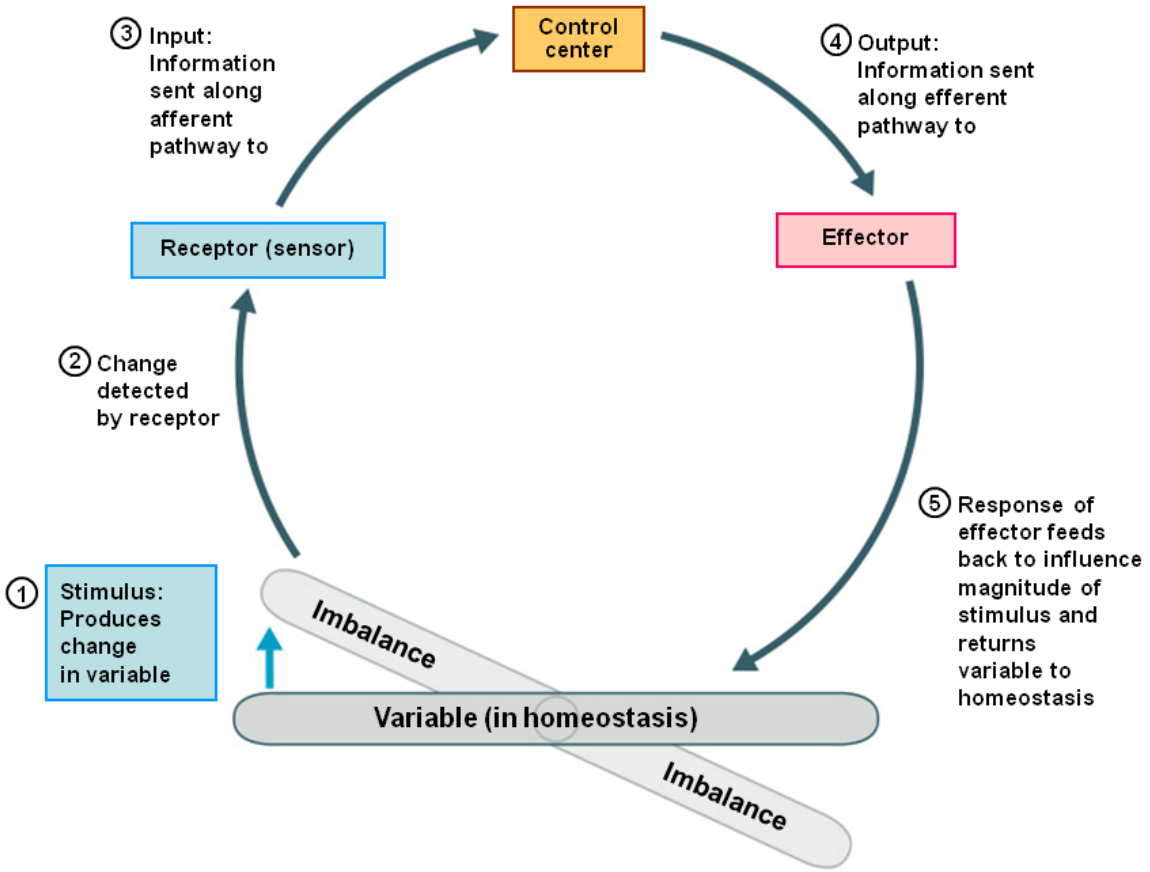
- People who cannot take adequate amount of food.
- Slowly.
- Prepared in isotonic solution.
- Water is excreted.

Homeostasis

- At the end of this session, the students should be able to:
- Understand the concept and importance of homeostasis.
- Review how body fluids are compartmentalized.
- Understand how the steady state is monitored.
- Review the compensatory responses to any change in the steady state.
- Review the disturbances of volumes of ECF and ICF.
- Homeostasis is the ability to maintain a relatively stable internal environment in an ever-changing outside world
- The internal environment of the body (ECF)is in a dynamic state of equilibrium
- All different body systems operate in harmony to provide homeostasis

Homeostatic control mechanism

- The variable produces a change in the body
- The three interdependent components of control mechanisms are:
  - Receptor – monitors the environments and responds to changes (stimuli)
  - Control center – determines the set point at which the variable is maintained
  - Effector – provides the means to respond to the stimulus

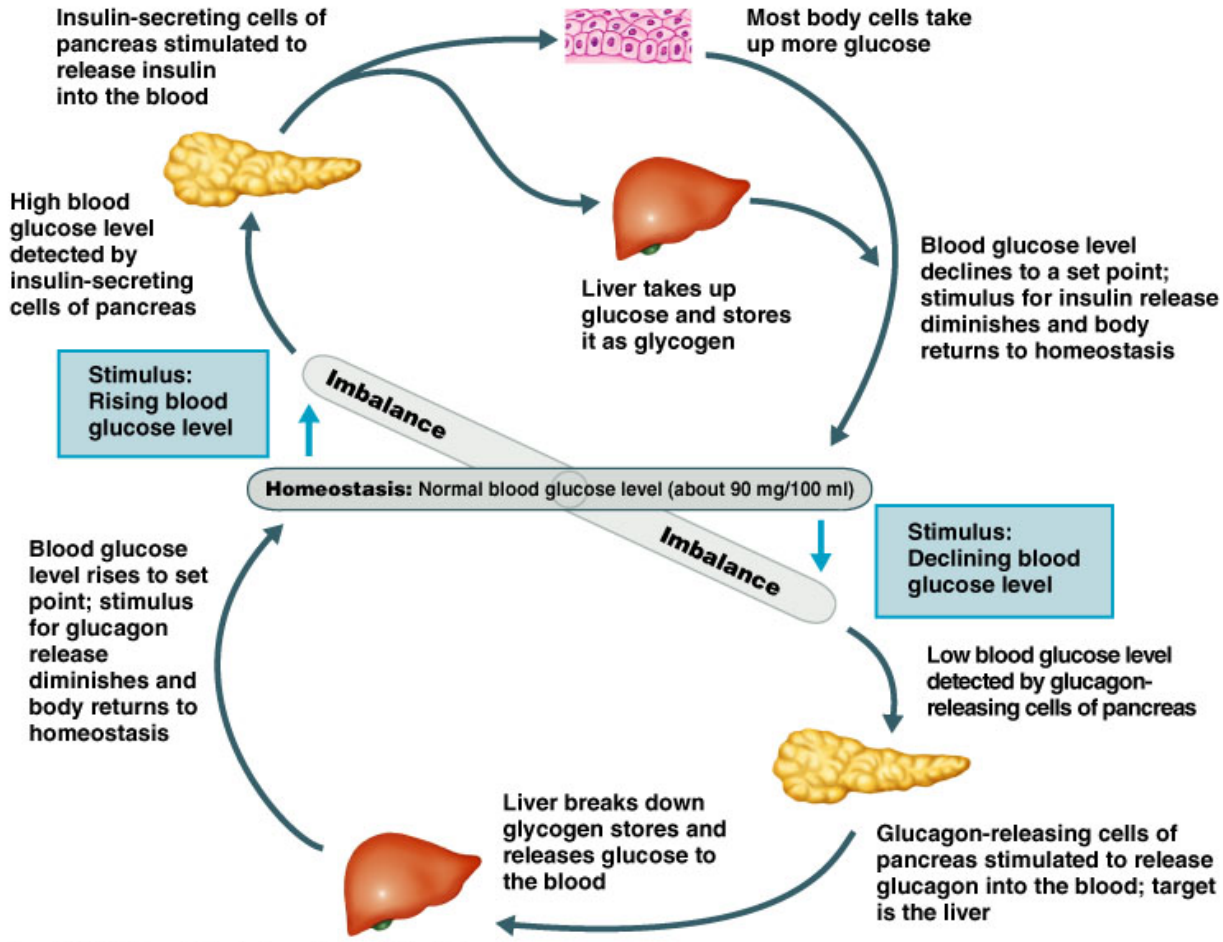


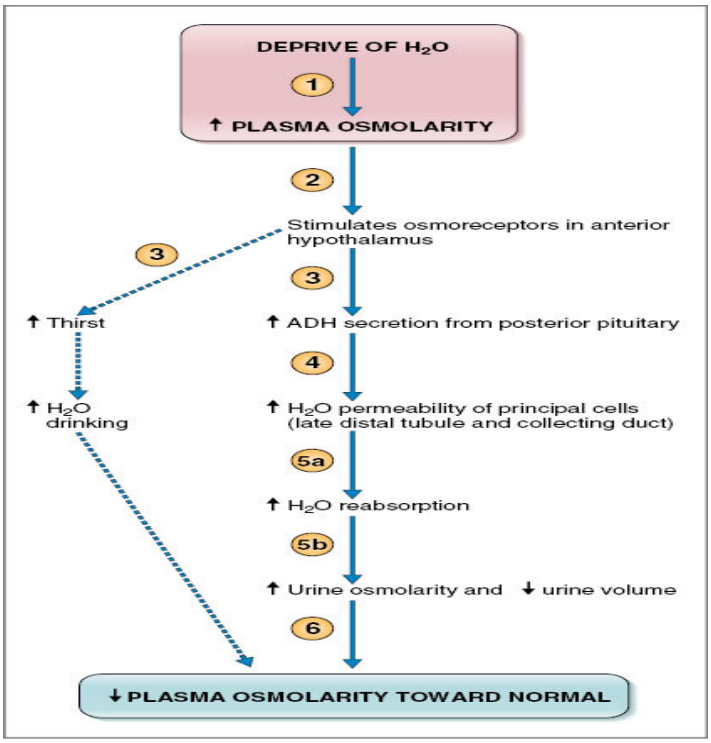
Regulation of body functions

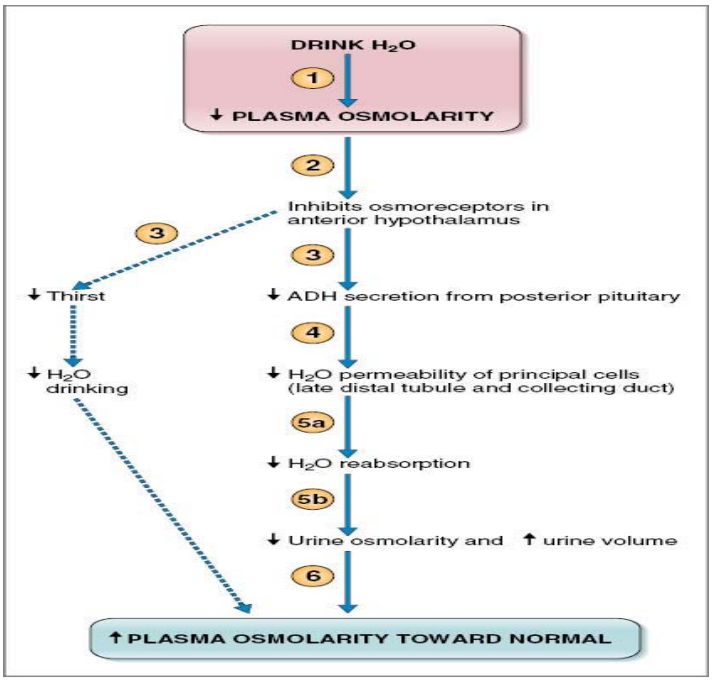
1. Nervous system
   - sensory input.
   - central nervous system.
   - motor output.

2. Hormonal system of regulation.
   - Endocrine gland.
   - Pancreas, thyroid
     e.g. : insulin control glucose level.

Feedback





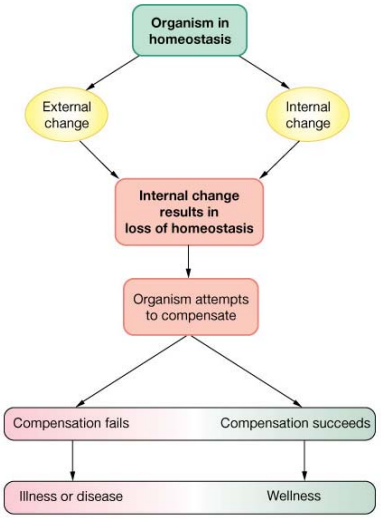


Homeostatic imbalance

- Disturbance of homeostasis or the body's normal equilibrium

Homeostasis and control

- Successful compensation
    - Homeostasis reestablished
- Failure to compensate
    - Pathophysiology
        - Illness
        - Death



Volumes and Osmolarities of ECF and ICF In Abnormal States

- Some factors can cause the change:
  - dehydration.
  - intravenous infusion.
  - abnormal sweating.
  - etc..

- Changes in volume :
  1. Volume expansion.
  2. Volume contraction.

Volume contraction (decrease in the ECF volume) :

1. Diarrhea.
    - osmolarity of fluid lost ≈ osmolarity of ECF (loss of isosmotic fluid).
    - volume in ECF.
    - arterial pressure.

2. Water deprivation :
    - Water and NaCl.
    - Osmolarity and volume will change.
    - Hyposmotic fluid (small NaCl large water)
    - ↑ Osmolarity in both ECF and ICF.
    - ↓Volume in both ECF and ICF.

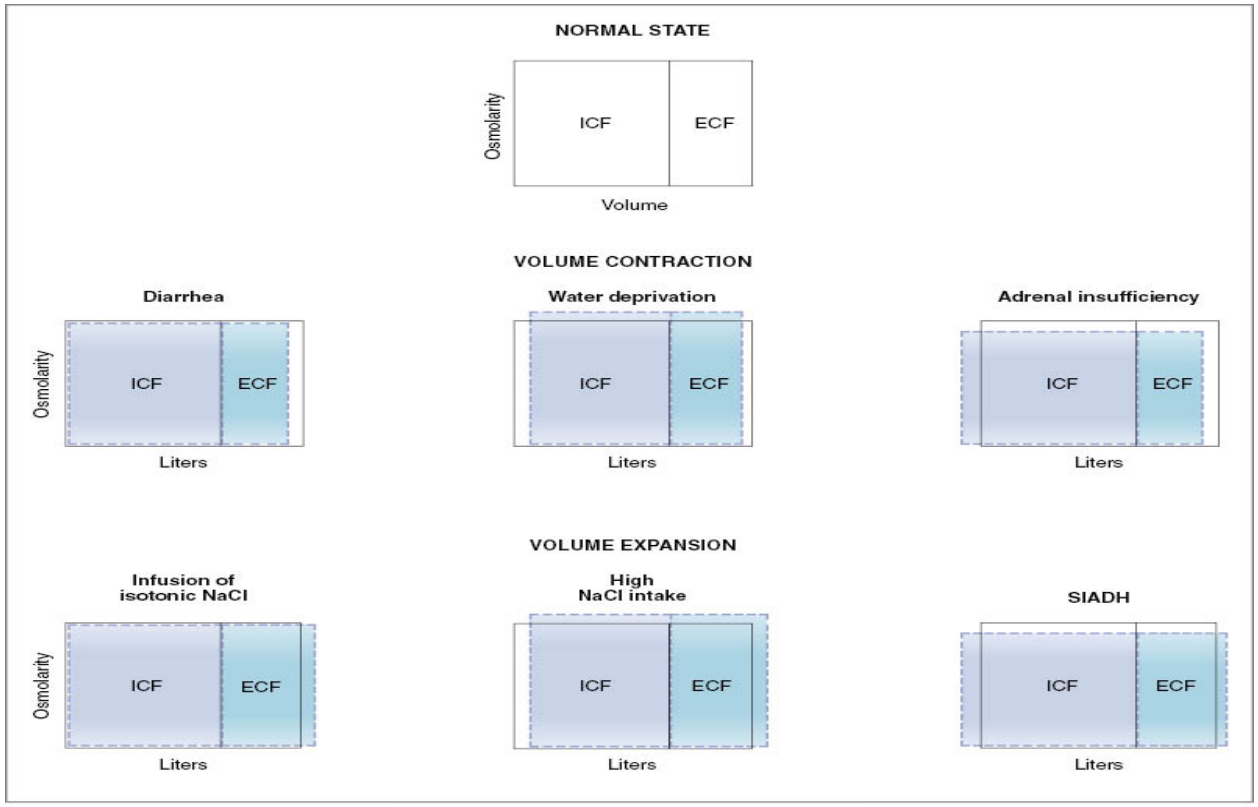
3. Adrenal insufficiency:
    - Aldosterone deficiency.
    - ↓ Na in the ECF.
    - ↓ osmolarity in both.
    - ↓ in ECF volume.
    - ↑ in ICF volume.

Volume expansion

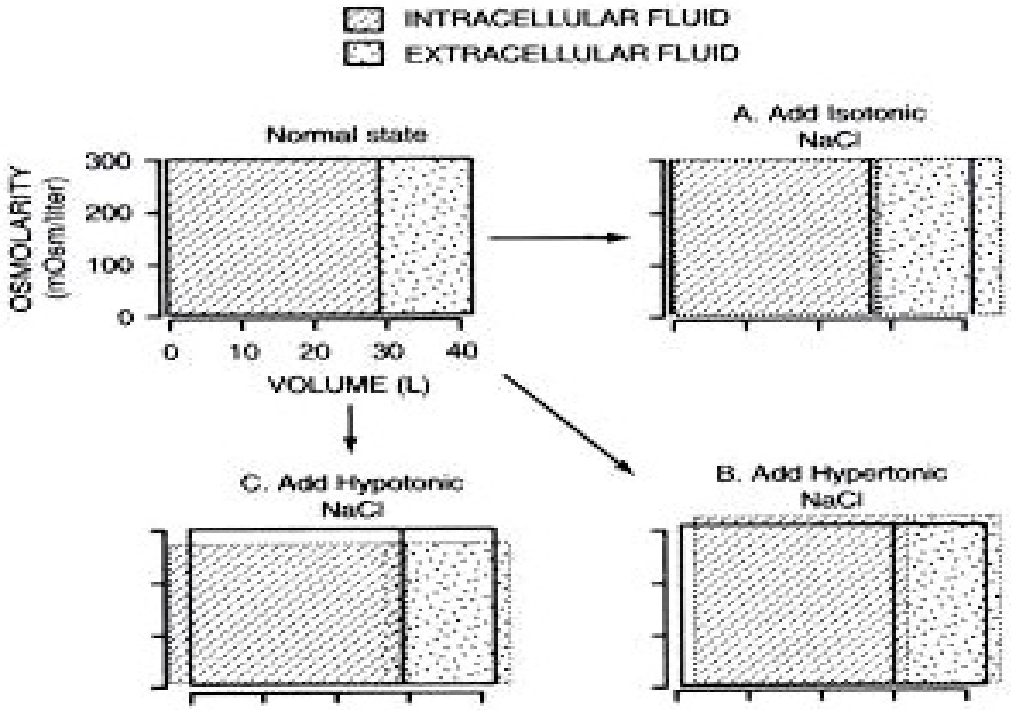
1. Infusion of isotonic NaCl.
   - ↑ ECF volume.
   - No change in osmolarity.
   - Isomotic expansion.

2. High NaCl intake.
   - ↑ eating salt.
   - ↑ osmolarity in both.
   - ↓ volume of ICF.
   - ↑ volume of ECF.
   - hyperosmotic volume expansion.

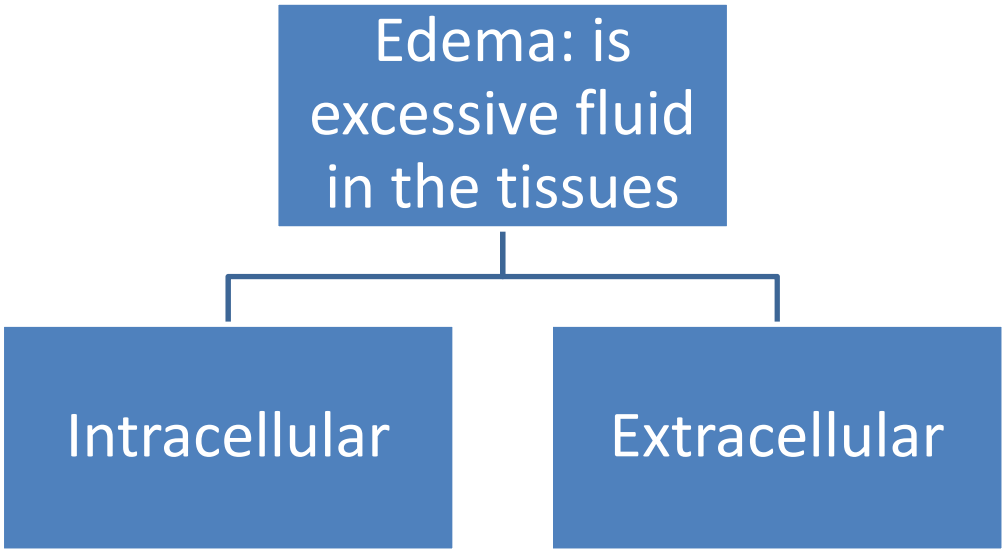
3. Syndrome of inappropriate antidiurtic hormone (SIADH):
   - ↑ volume
   - ↓ osmolarity



Effect of adding saline solution to the ECF

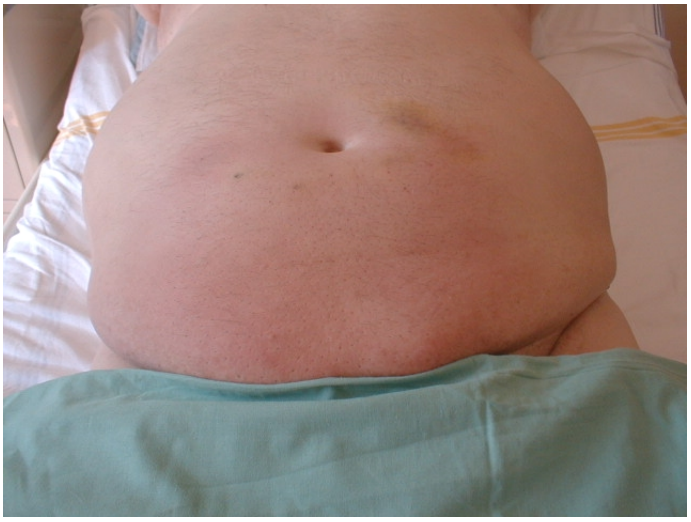


Edema

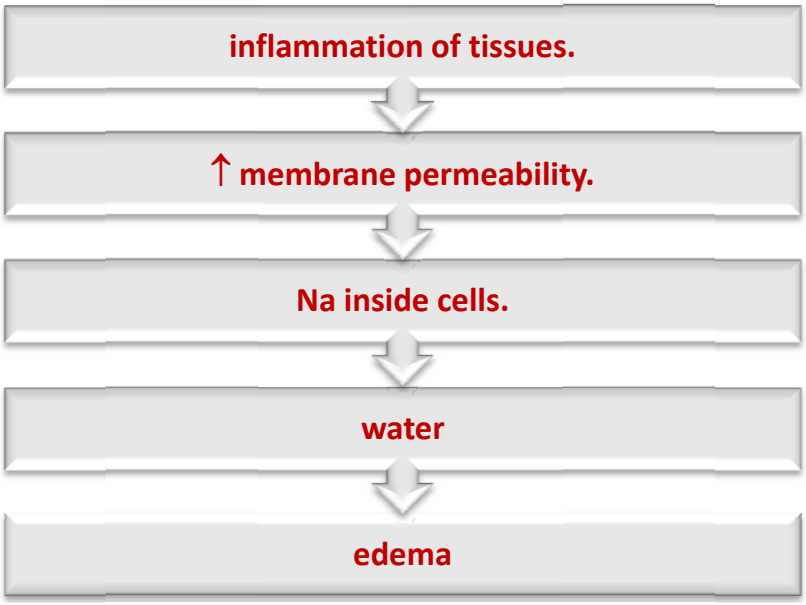


Edema occurs mainly in the extracellular fluid compartment

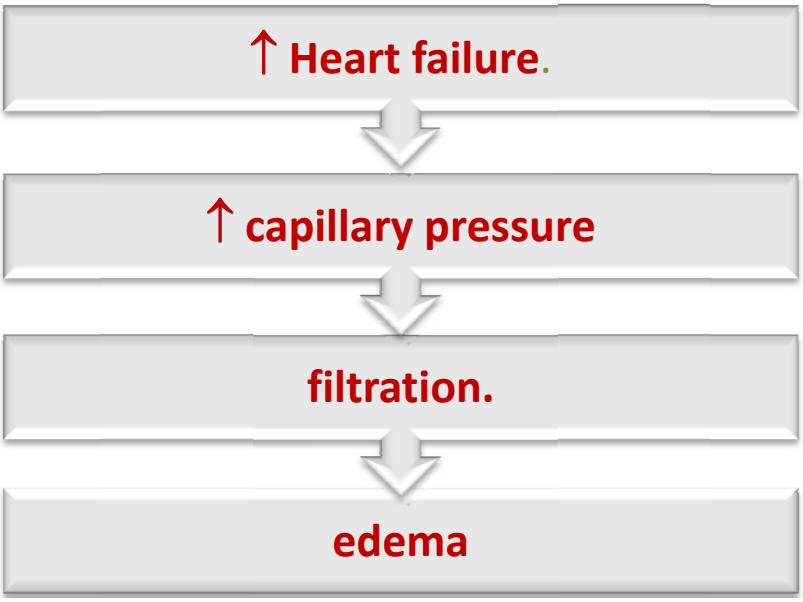

Edema (swelling) of
the ankles and feet



Intracellular edema



Extracellular edema: ***common clinical cause is excessive capillary fluid filtration.***



Cell membrane structure and transport across cell membrane

At the end of this session, the students should be able to:

- Describe the fluid mosaic model of membrane structure and function.
- Define permeability and list factors influencing permeability.
- Identify and describe carried-mediated transport processes: Primary active transport, secondary active transport, facilitates diffusion.

Cell membrane

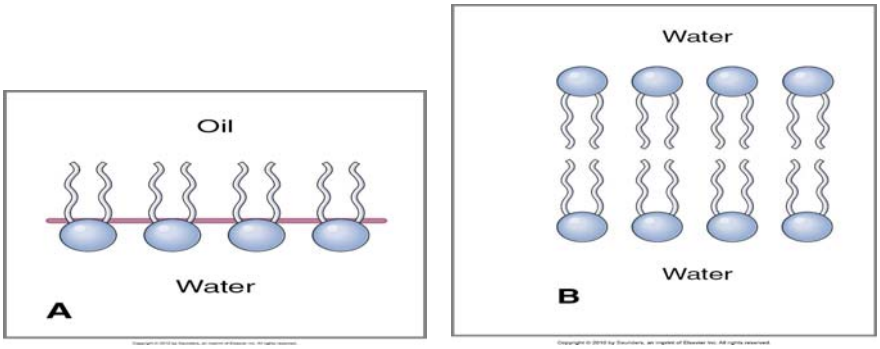
- It covers the cell.
- It is a fluid and not solid.
- It is 10 nanometer thick.
- It is also referred to as the plasma membrane.

Composition

protein 55%
phospholipids 25%
cholesterol 13% } lipid
glycolipid 4%
carbohydrates 3%

The Cell Membrane Phospholipids Consist of:

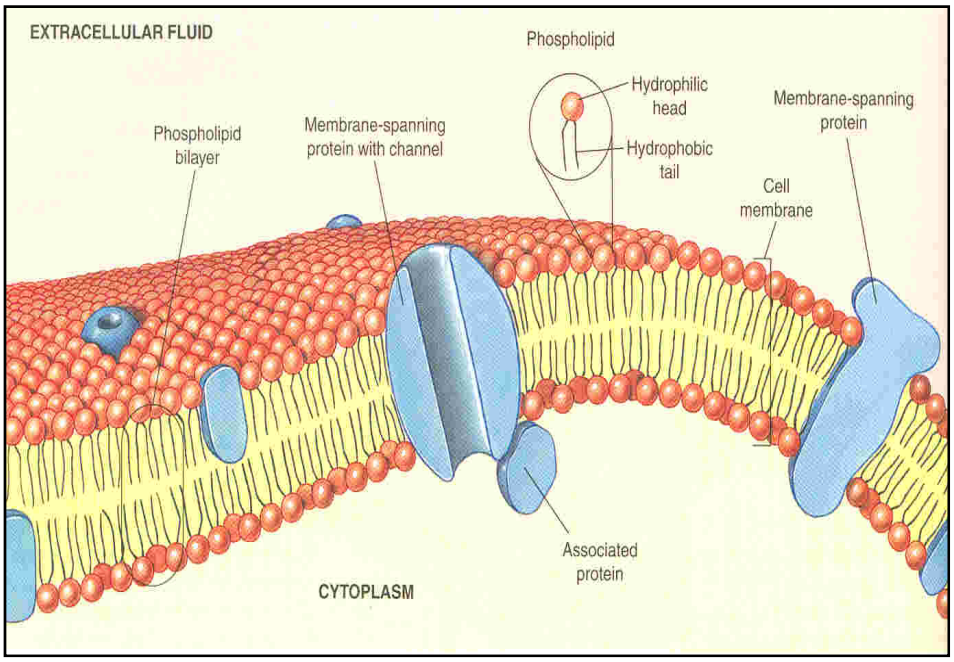
1. Glycerol head (hydrophilic).
2. Two fatty acid ''tails'' (hydrophobic).

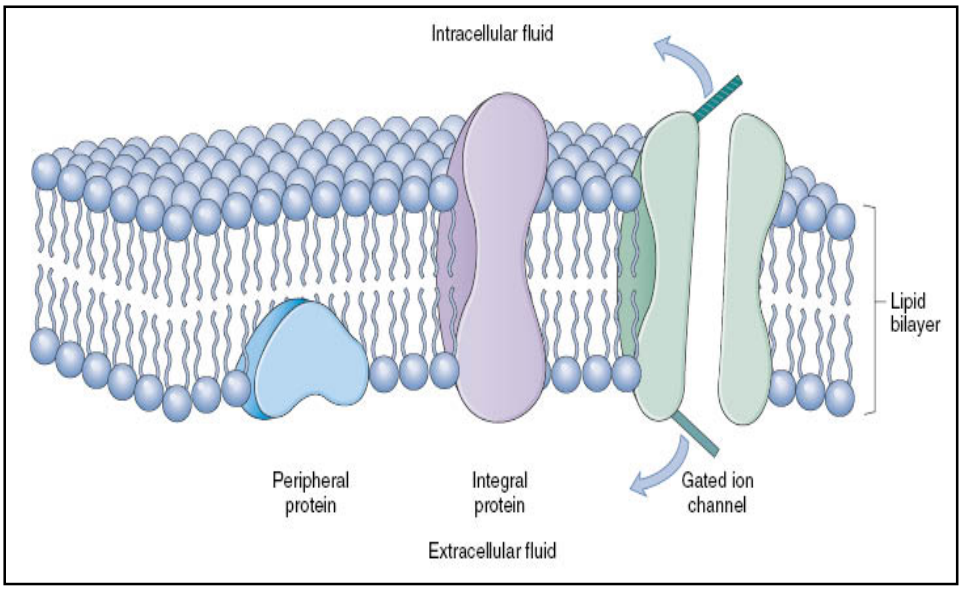


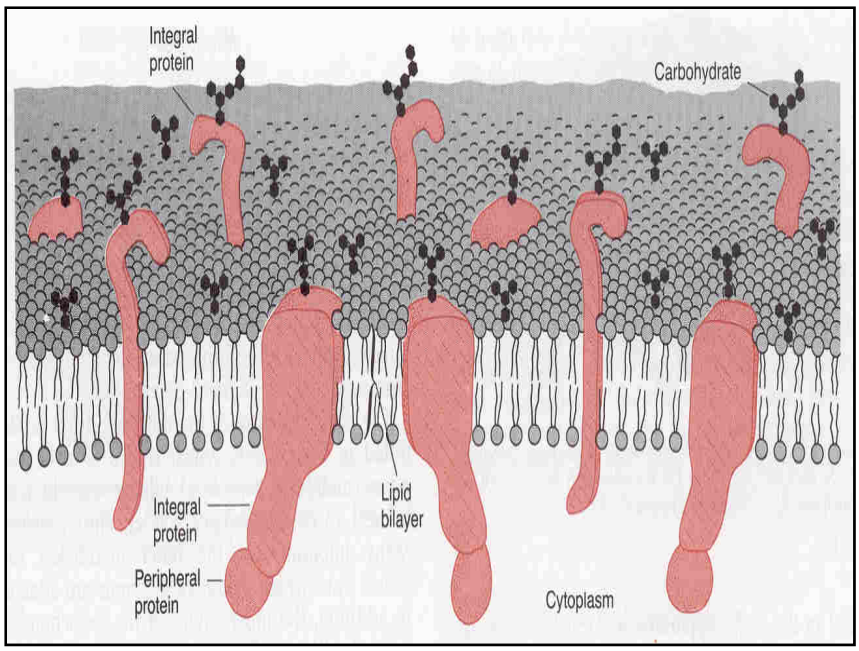
- Heads (hydrophilic) facing ICF and ECF and tails (hydrophobic) face each other in the interior of the bilayer.
- Amphipathic.

The cell membrane proteins

1. Integral proteins span the membrane . Proteins provide structural channels or pores.
2. Peripheral proteins (carrier proteins)
   - Present in one side
   - Hormone receptors
   - Cell surface antigens







The cell membrane carbohydrates

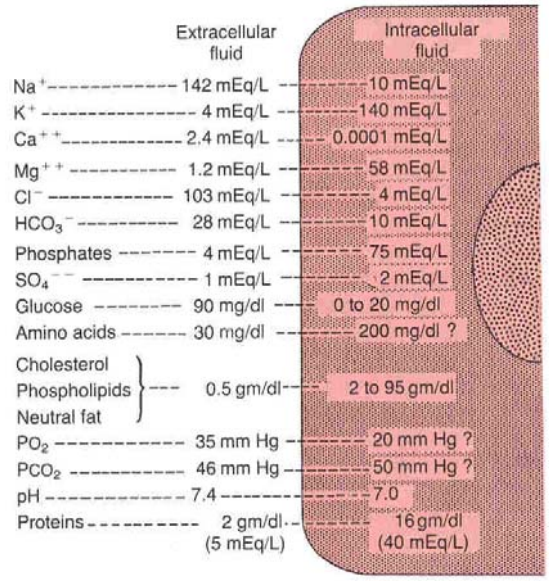
- Glycoproteins (most of it).
- Glycolipids (1/10)
- Proteoglycans (mainly carbohydrate substance bound together by protein)
- ''glyco'' part is in the surface forming.
- Glycocalyx.(loose coat of carbohydrates.

Function of carbohydrates

- Attaches cell to each others.
- Act as receptors substances (help ligand to recognize its receptor).
- Some enter in to immune reactions.
- Give most of cells overall –ve surface.

Transport through the cell membrane

- Cell membrane is selectively permeable.
- Through the proteins.
- water –soluble substances e.g. ions, glucose ..
- Directly through the bilayer.
- Fat – soluble substance (O_2, CO_2, OH..



Types of membrane transport

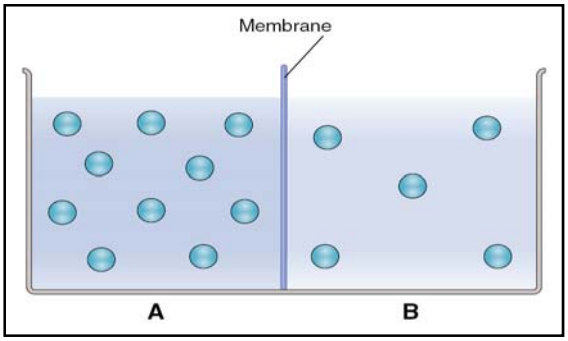
1- **Diffusion**
   - simple diffusion.
   - facilitated diffusion.
2- **Active transport.**
   - primary active transport.
   - secondary active transport.
3- **Osmosis.**

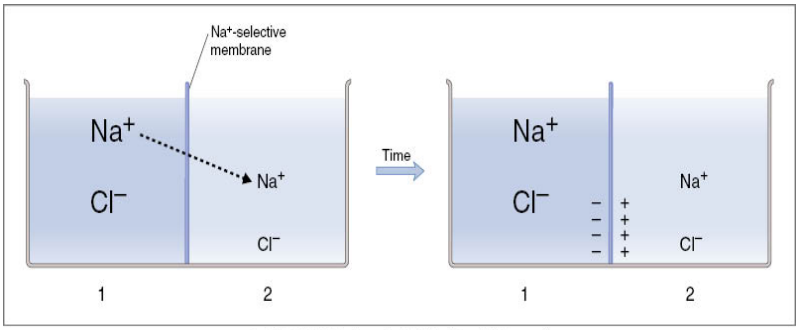
Diffusion

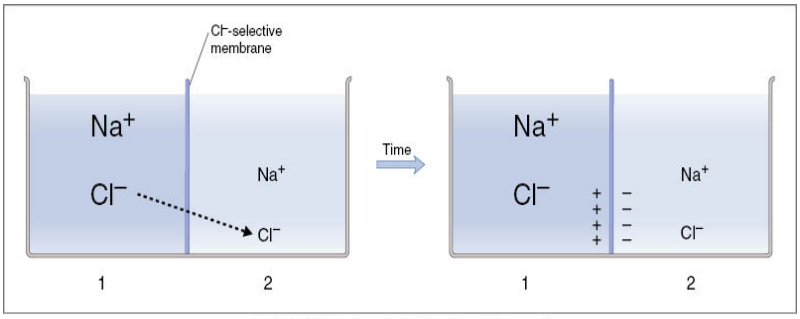
- Random movement of substance either through the membrane directly or in combination with carrier protein <u>down</u> an electrochemical gradient.
  1- Simple diffusion.
  2- facilitated diffusion.

Simple diffusion

- Non carrier mediated transport down an electrochemical gradient.
- Diffusion of non electrolytes (uncharged) from high concentration to low concentration.
- Diffusion of electrolytes (charged) depend on both chemical as well as electrical potential difference.







Rate of simple diffusion depends on:

1- Amount of substance available.
2- The number of opening in the cell membrane for the substance.
   selective gating system
3- Chemical concentration difference.
   net diffusion= P x A (Co-Ci)
4- Electrical potential difference.
   EPD=± 61 log C1/C2
5- Molecular size of the substance.
6- Lipid solubility.
7- Temperature.

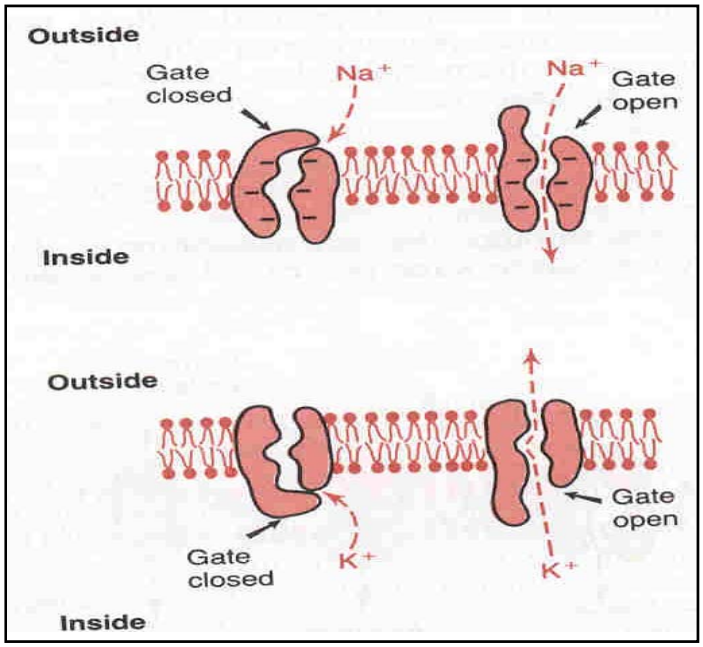
Facilitated diffusion

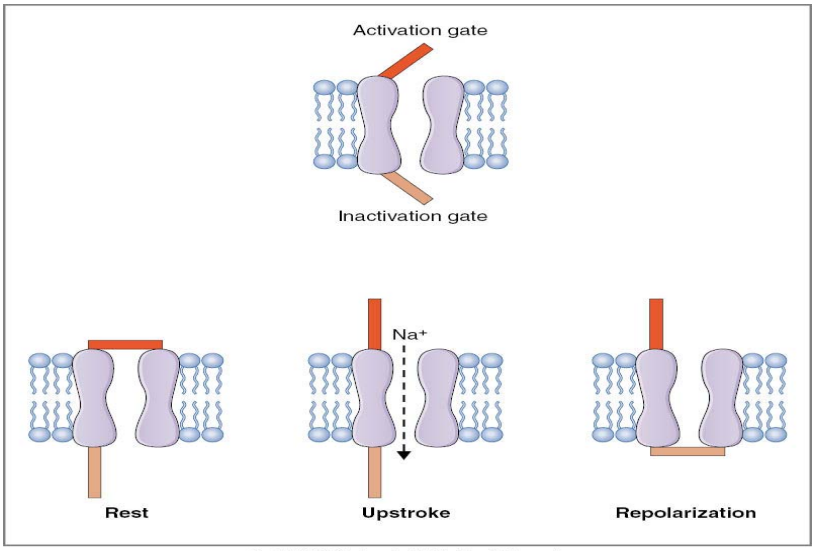
- <u>Carrier mediated</u> transport down an electrochemical gradient.

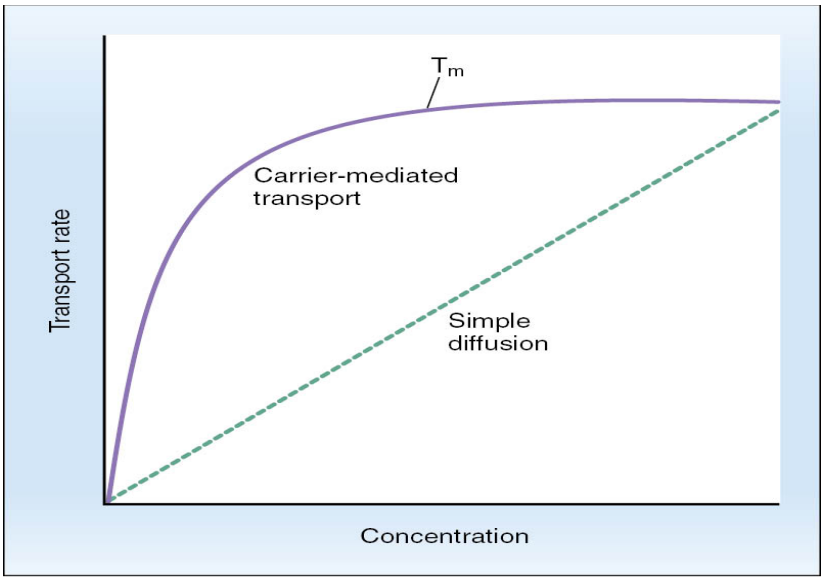
Features Of Carrier Mediated Transport

1- saturation:
   ↑ concentration → ↑ binding of protein
   If all protein is occupied we achieve full saturation.
2- Stereo specificity:
   The binding site recognize a specific substance D-glucose but not L-glucose
3- Competition:
   Chemically similar substance can compete for the same binding site.
   D- galactose D-glucose.

Substance → binding site → substance protein complex → conformational changes release of substance







- Glucose, most of amino acids.

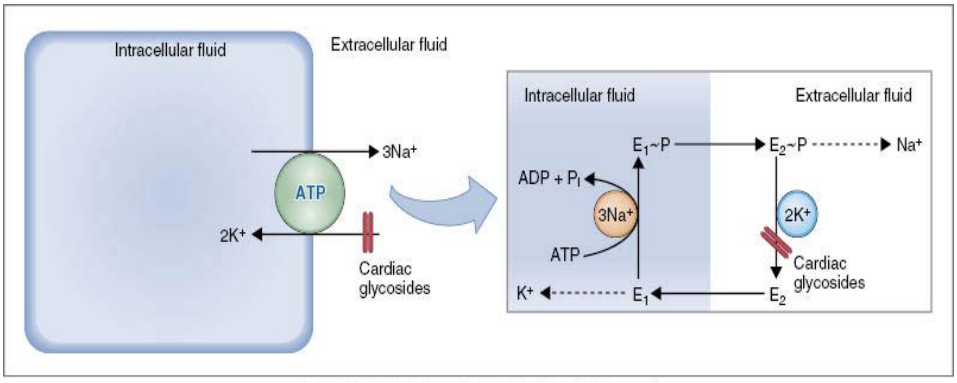
Active transport

- Transport (<u>uphill</u>) → against electrochemical gradient.
- Required energy →direct.
  → indirect.
- Required carrier – protein.

1- Primary active transport

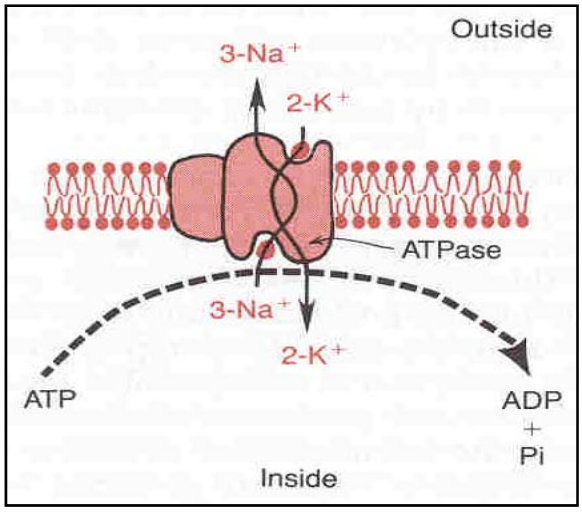
- Energy is supplied directly from ATP.
  ATP ADP +P+ energy.

A. **Sodium-Potassium pump (Na-K pump).**
   - its present in all cell membranes.
   - Na in → out.
   - K out → in.



Characteristic of the pump:

1. Carrier protein is formed from α and β subunits.
2. Binding site for Na inside the cell.
3. Binding site for K outside the cell.
4. It has ATPase activity.
5. 3 Na out.
6. 2 K in.



Function

1. Maintaining Na and K concentration difference .
2. It's the basis of nerve signal transmition .
3. Maintaining –Ve potential inside the cell.

- digitals

B. **primary active transport of calcium (Ca^{2+} ATPase).**

- sarcoplasmic reticulum (SR).
- mitochondria.
- in some cell membranes.

Function:

Maintaining a low Ca^{2+} concentration inside the cell.

C. **primary active transport of hydrogen ions H+-K ATPase.**

- stomach.
- kidneys.
- pump to the lumen.
- H+-K ATPase inhibitors (treat ulcer disease). (omeprazol)

2- Secondary active transport

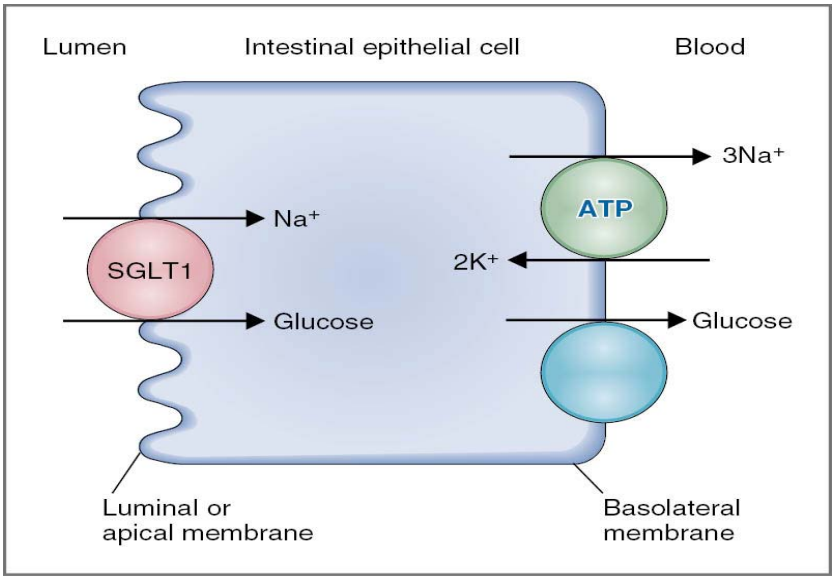
Co- transport and counter transport:

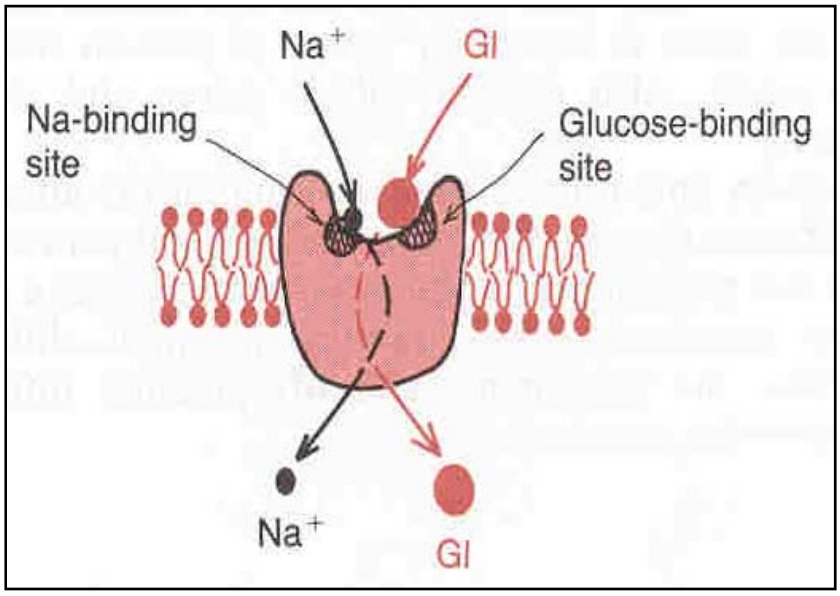
is transport of one or more solutes against an electrochemical gradient , coupled to the transport of another solute down an electrochemical gradient .

- ''downhill'' solute is Na.
- Energy is supplied indirectly form primary transport.

Co transport:

- All solutes move in the same direction
  '' inside cell''.
  e.g.
  - Na - glucose Co transport.
  - Na – amino acid Co transport.
  - in the intestinal tract kidney.





Counter transport:

- Na is moving to the interior causing other substance to move out.
- Ca^{2}+ - Na+ exchange.
  (present in many cell membranes)
- Na –H+ exchange in the kidney.