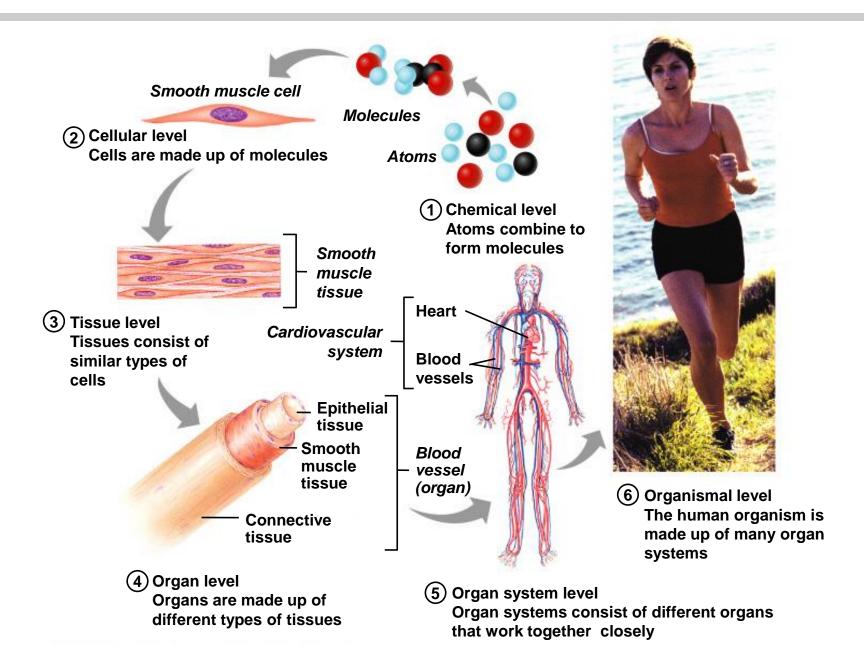
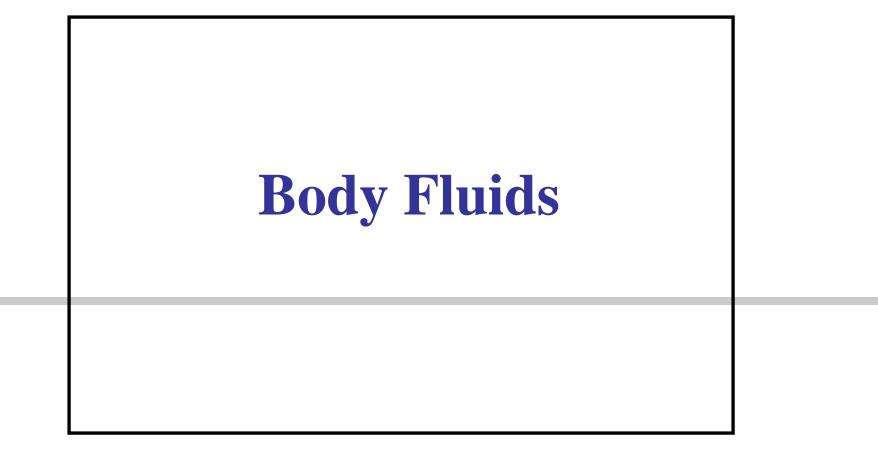
# HUMAN PHYSIOLOGY

# **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**





# 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 intracellular 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.
- Identify and describe Physiology factor influencing body fluid: age, sex, adipose tissue, etc. Pathological factors: Dehydration, fluid infusion.









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Xref: Req No.:R111 Printed:19/0	33779 Date ( 6/1432(22/05/	Coll.:15/06/32(18/05/11) Date Recd.:1 /11)09:03 Time Recd.:1	5/06/32(18/05/ <b>11</b> ) 1:53
Serum			
3.9 - 5.8	mmol / L	[* ] Fasting Blood Sugar Urea and Electrolytes	4.5
2.5 - 6.4	mmol / L	[* ] Urea	
53 - 106		[* ] Creatinine	3.1
135 - 145		[*] Sodium	62
3.5 - 5.1		[*] Potassium	141.0
98 - 107		[ * ] Chloride	4.4
22 - 32	mmol/L	[ * ] Bicarbonate	102.0
		Liver Function test profile	26.0
3 - 17	umol/L	[* ] Total Bilirubin	5
0 - 5	umol/L	[*] Direct Bilirubin	2
60 - 80	g/L		72.2
30 - 50	g/L	<pre>[ * ] Direct Bilirubin [ * ] Total Protein [ * ] Albumin [ * ] Alkaline Phosphatase [* ] Alanine Aminotransferase [* ] Aspartate Aminotransferase</pre>	43.0
50 - 136		* ] 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
100 K (200 K) (200 K)			
0.4 - 1.48		[* ] Triglycerides	0.49
3.2 - 5.2		[ ]> 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
			4.40 H

PLS. NOTE THE NEW NORMAL RANGES

RECOMMENDED LEVEL FOR TOTAL SERUM CHOLESTEROL < 5.2 mmol/L

CONSULTANT ON DUTY

KING KHALID HOSP. PO BOX 7805 RIYADH	  ===================================	MATOLOGY UNIT	
	Pat.N  Name:  Hospital:KING KHALID UNIVERS  Location: (MED) Medical Depa  Doctor:UNKNOWN *	ITY HOSPITA DOB:	Page No.:1 Sex:F 22 Sep 86
Xref: Req No.:H11075127   Printed:19/06/1432(2	Date Coll.:15/06/32(18/05/11) 22/05/11)09:04	Date Recd.:15/06 Time Recd.:12:41	/32(18/05/11)
EDTA Whole Blood Full Blood Co	ount		
<pre>[ * ] RBC [ * ] HGB [ * ] HCT [ * ] MCV [ * ] MCH [ * ] RDW [ * ] PLT [ * ] PLT [ * ] MPV [ * ] %NEUT [ * ] %LYMP [ * ] %EOS [ * ] %BASO [ * ] %B</pre>		$\begin{array}{r} 4 & - & 11 \\ 4.2 & - & 5.5 \\ 120 & - & 160 \\ 37 & - & 47 \\ 80 & - & 94 \\ 27 & - & 32 \\ 320 & - & 360 \\ 11.5 & - & 14.5 \\ 140 & - & 450 \\ 7.2 & - & 11.1 \\ 40 & - & 75 \\ 20 & - & 45 \\ 3 & - & 9 \\ 0 & - & 6 \\ 0 & - & 1 \\ 2 & - & 7.5 \\ 1 & - & 5 \\ 0.2 & - & 0.8 \\ 0.0 & - & 0.8 \end{array}$	<pre>x10.e9/L x10.e12/L g/L % fl pg g/L % x10.e9/L fl % % % % x10.e9/L x10.e9/L x10.e9/L x10.e9/L x10.e9/L x10.e9/L</pre>

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: 70%

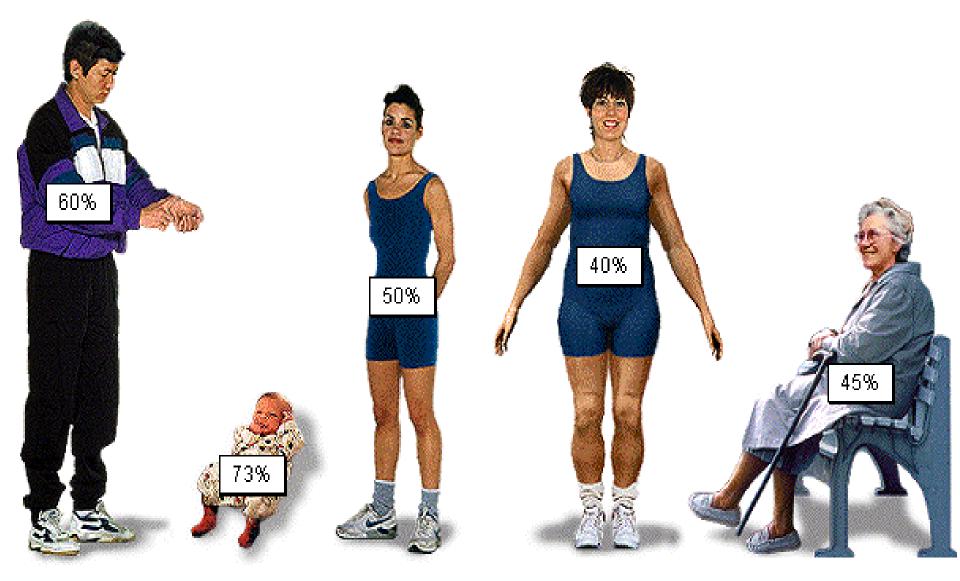
### Male adult: 60%

## Female adult: 40-50%

Obesity Old age 45%

#### PERCENTAGE OF WATER IN THE BODY

Click each of the people below to determine the approximate percentage of water in their bodies.



# **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.

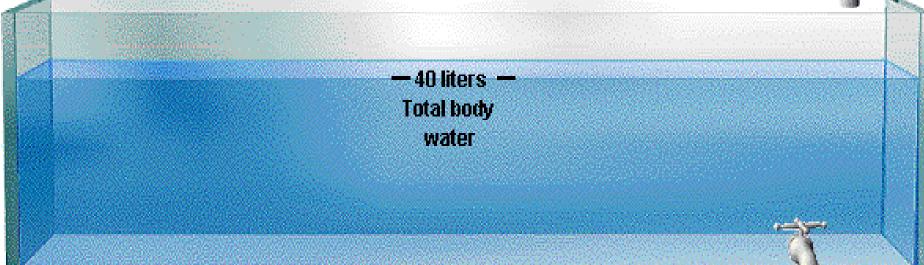
## **Daily intake of water**

TABLE 20-1 DAILY INTAKE AND OUTPUT OF WATER (in mi/day)			
	Normal	Prolonged, Hoovy Exercise	
Intake			
Fluids ingested	2100	2	
From metabolism	200	200	
Total intake	2300	?	
Output	-0-12/12/		
Insensible-Skin	350	350	
Insensible-Lungs	350	650	
Sweat	100	5000	
Feces	100	100	
Urine	1400	500	
Total output	2300	6600	

#### WATER TANK ANALOGY

Maintaining water homeostasis is a balancing act. The amount of water taken in must equal the amount of water lost.

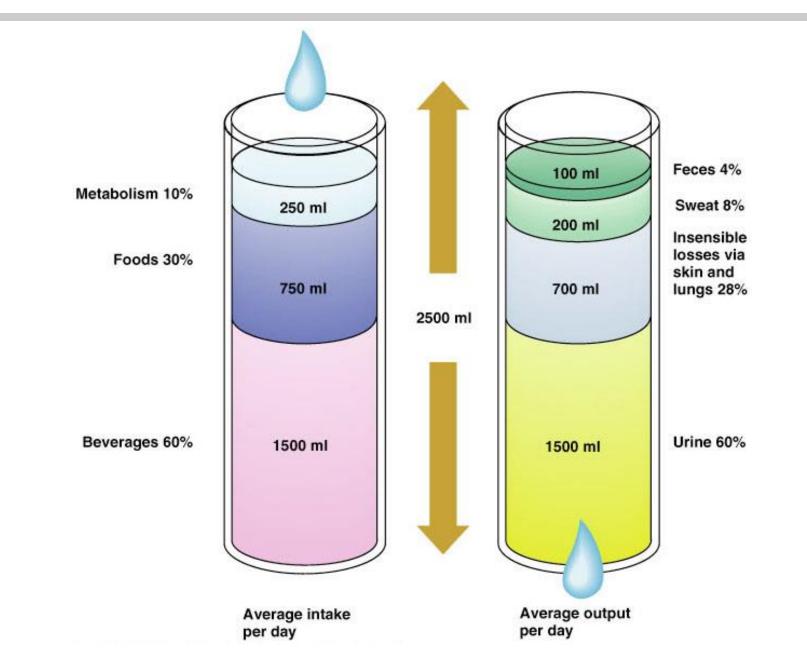




Water Intake		Water Output	
• Food and dri	ink: 2300 mL	<ul> <li>Kidneys:</li> </ul>	1500 mL
• Cell metabo	lism: 200 mL	• Skin:	600 mL
		• Lungs:	300 mL
		• GI tract:	100 mL
• Total:	2500 mL	• Total:	2500 mL



## Water Intake and Output



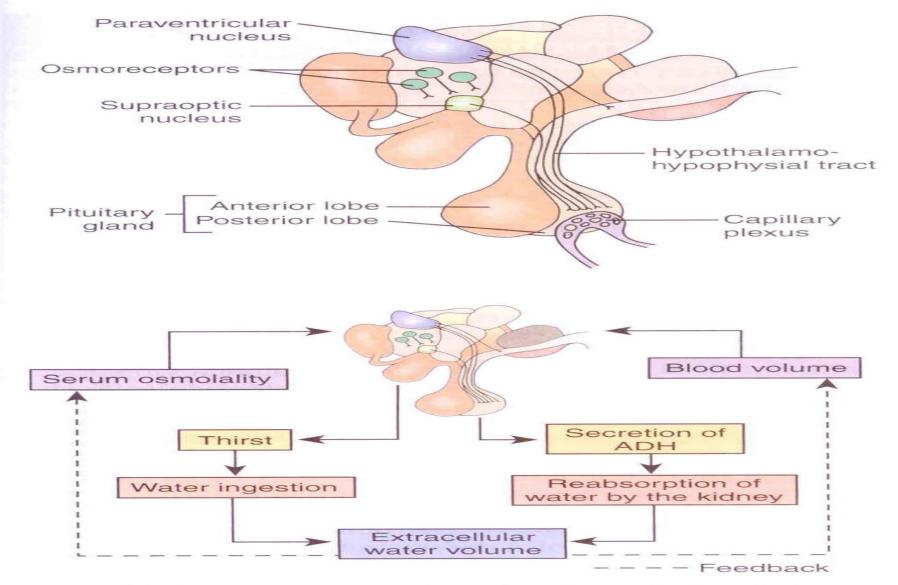
# Climate

# 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)

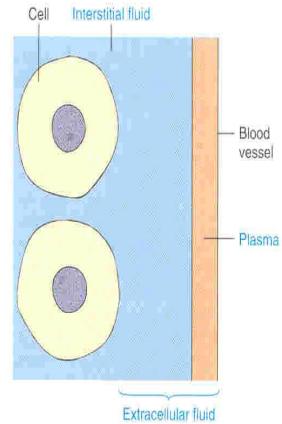


FIGURE 1-2

# **Fluid Compartments**

Total body water volum 40 L, 60% body weight		
	Extracellular fluid volume = 15 L, 20% body weight	
Intracellular fluid volume = 25 L, 40% body weight	Interstitial fluid volume = 12 L, 80% of ECF	Plasma volume = 3 L, 20% of ECF

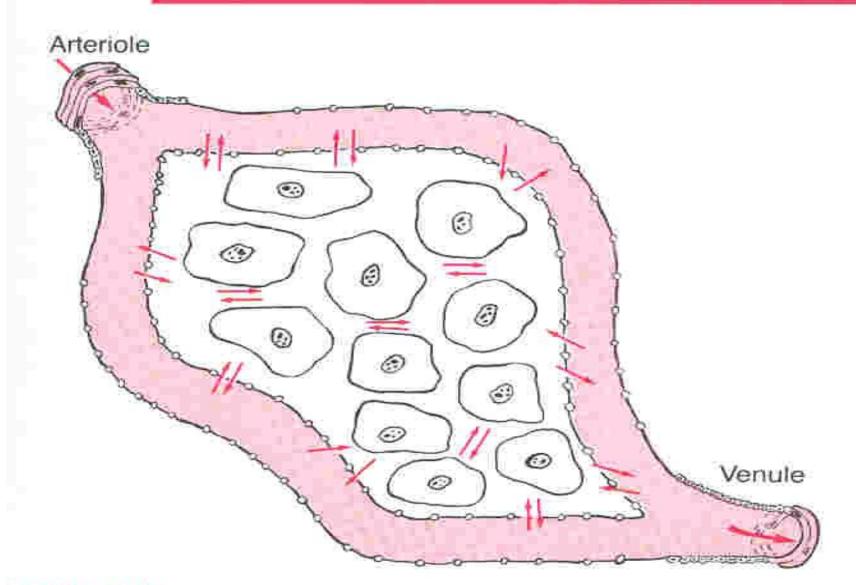
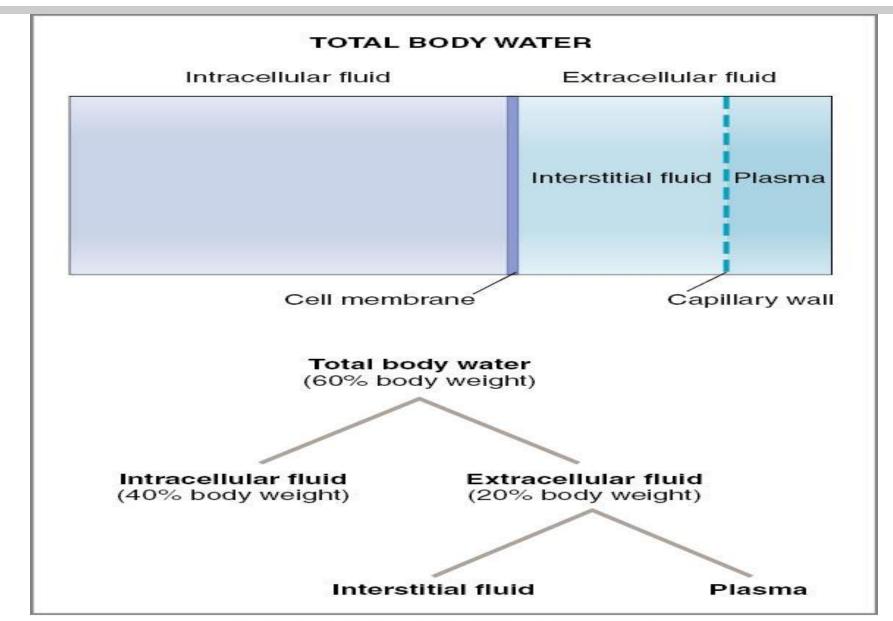
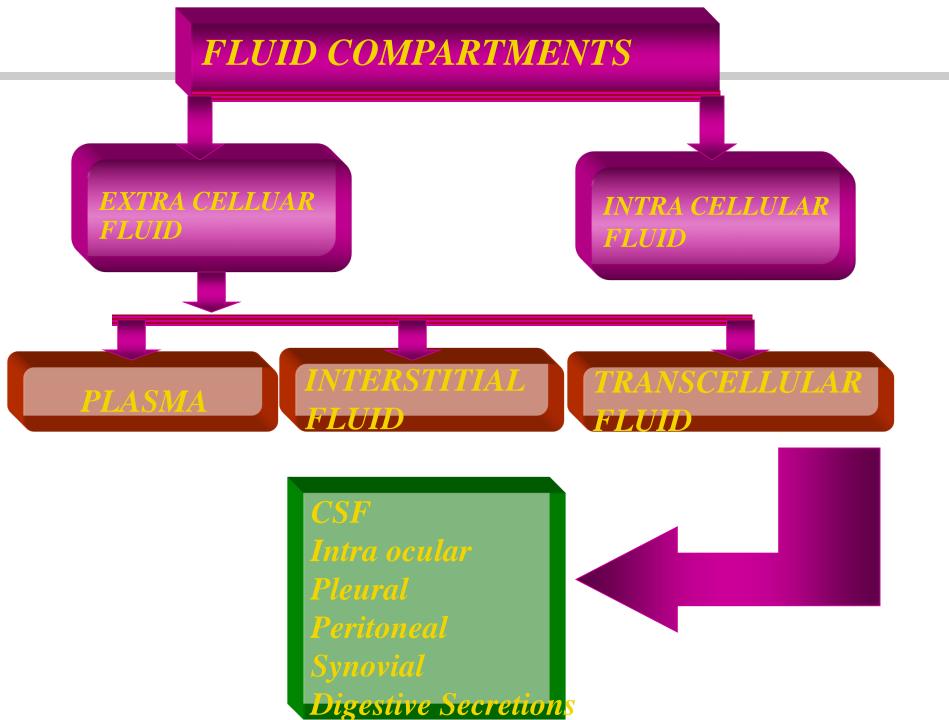


Figure 1.7 Diffusion of fluids through the conillary walls and



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# **Intracellular fluid (ICF)**

• Inside the cell.

- **2/3 of TBW.**
- High concentration of protein.

# **Extracellular fluid (ECF)**

# Out side the cell. 1/3 of TBW.

# 1- Plasma:

# Fluid circulating in the blood vessels. 1/4 of ECF

# 2- 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

# **Trancecellular fluid compartment:**

• small amount.

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

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

# **Composition of Body Fluids**

• 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.

# **1- Molarity = moles/liter M/L.**

# 2- Osmolarity = osmoles/liter osm/L.

# **3-Osmolality** = osmoles/kg Osm/kg.

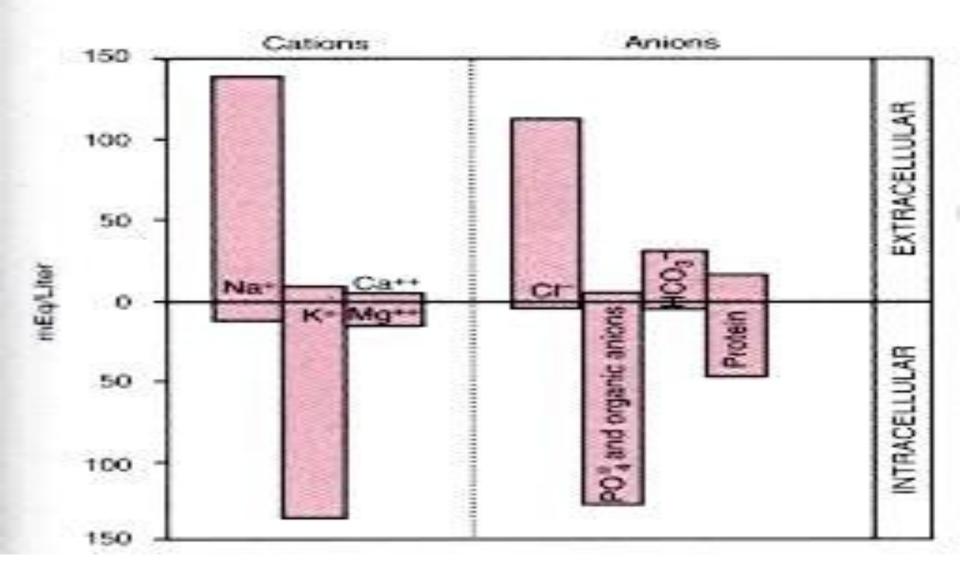
# In biological solutions:

- 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 (m0sm/liter of K <sub>1</sub> D)	Interstitial	Intracellular
Na*	142	139	14
K-	4.2	4.0	140
Ca**	1.3	1.2	0
Mg* CI	0.8	0.7	20
CI-	108	108	4
HCO,	24	28.3	10
HPO, -, H_PO,-	2	2	11
504	0.5	0.5	1
Phosphocreatine			45
Carnosine			14
Amino acids	2	2	8
Creatine	0.2	0.2	8 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

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PLS. NOTE THE NEW NORMAL RANGES

RECOMMENDED LEVEL FOR TOTAL SERUM CHOLESTEROL < 5.2 mmol/L

CONSULTANT ON DUTY

KING KHALID HOSP. PO BOX 7805 RIYADH	HEMATOLOGY UNIT		
	Pat.N  Name:  Hospital:KING KHALID UNIVERS  Location: (MED) Medical Depa  Doctor:UNKNOWN *	ITY HOSPITA DOB:	Page No.:1 Sex:F 22 Sep 86
Xref: Req No.:H11075127   Printed:19/06/1432(2	Date Coll.:15/06/32(18/05/11) 22/05/11)09:04	Date Recd.:15/06 Time Recd.:12:41	/32(18/05/11)
EDTA Whole Blood Full Blood Co	ount		
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EQUEST COMMENTS:

### **Extracellular and Intracellular Fluids**

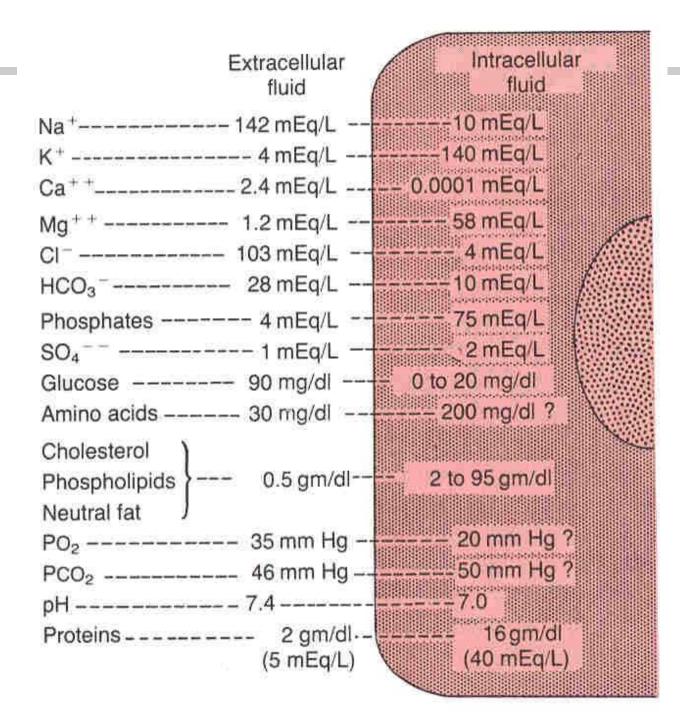
• Each fluid compartment of the body has a distinctive pattern of electrolytes

- 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

•

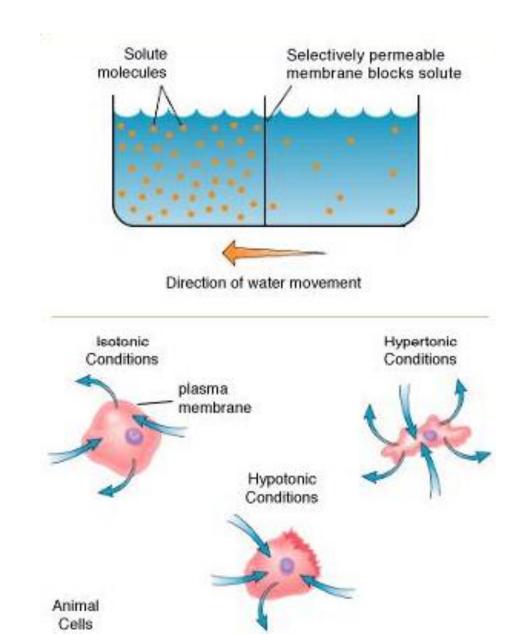
#### **Mechanisms for Movement**

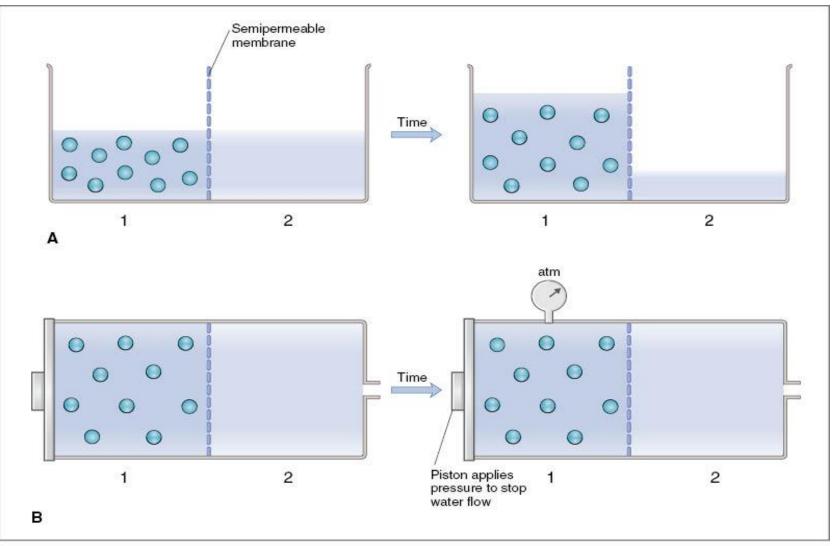
- 3 General mechanisms:
- 1. Simple diffusion (passive)
- 2. Facilitated transport (passive)
- 3. Active transport



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

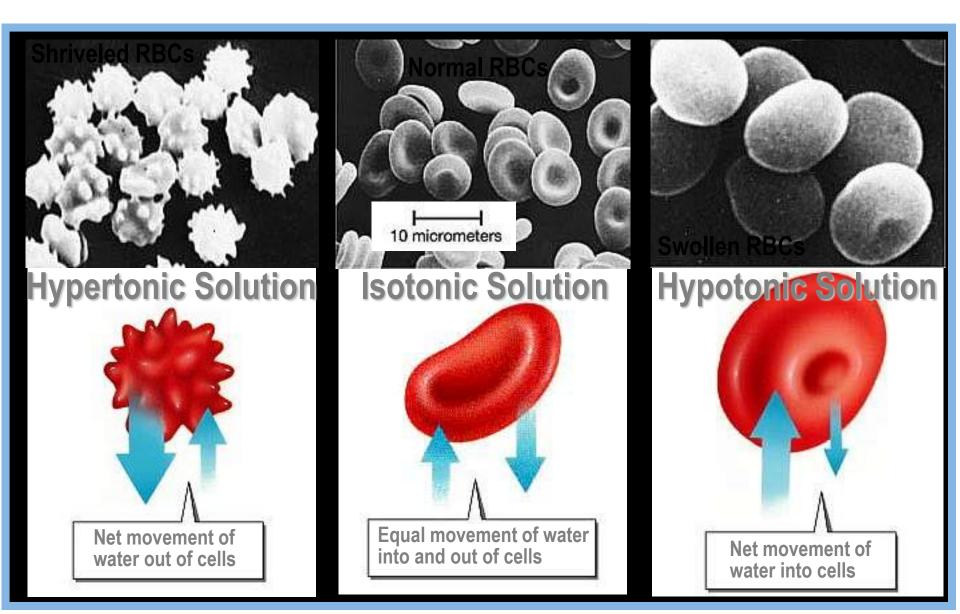
#### Osmosis

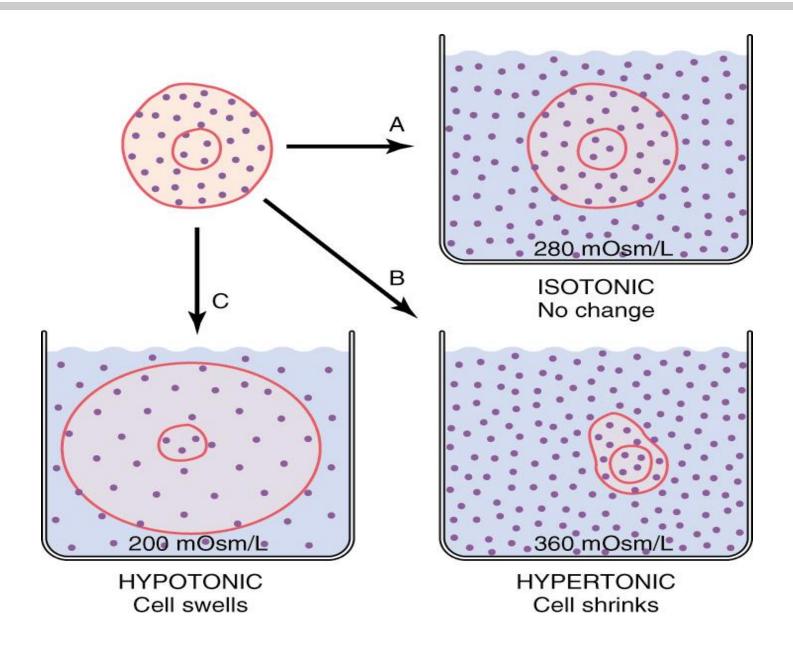




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#### Osmosis





## Osmosis

#### • If <u>environment</u> is:

- <u>Hypertonic</u>:
  - MORE SOLUTES outside cell
  - MORE WATER IN CELL
  - over time, cell <u>loses</u> water

#### <u>Isotonic</u>:

- same
- No change in cell volume
- <u>Hypotonic</u>:
  - LESS SOLUTES outside cell
  - LESS WATER IN CELL, more solutes in cell.
  - over time, cell <u>gains</u> water

#### **\***Isotonic solution :

- (no swells or shrink)
- 0.9% solution of sodium chloride .
- same in and out .
- ★ Hypotonic solution :
   (swelling)↓ 0.9%
   in is higher than out .
- **\* Hypertonic solution :** (shrink) 10.9%
   out is higher than in

**Glucose and other solutions administered for nutritive purposes** 

• People who can not take adequate amount of food.

- Slowly.
- Prepared in isotonic solution.

• Water is excreted.

## Homeostasis (1+2)

- At the end of this session, the students should be able to:
- Understand the concept and importance of homeostasis.
- Understand how the steady state is monitored.
- Identify and describe the compensatory responses to any change in the steady state.
- Identify and describe the disturbances of volumes of ECF and ICF.

### Homeostasis

 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

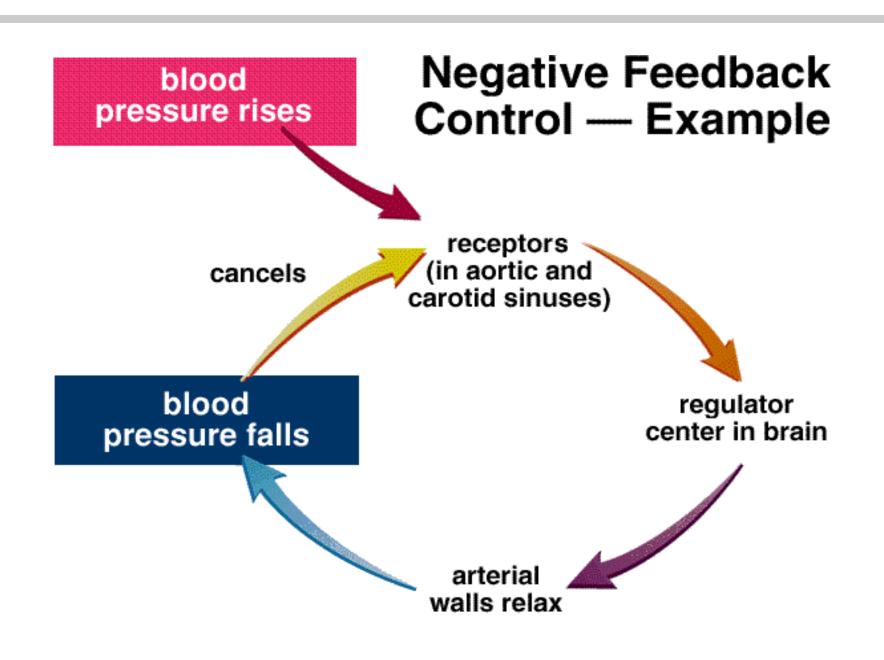
#### **Homeostatic Control Mechanisms**

- 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

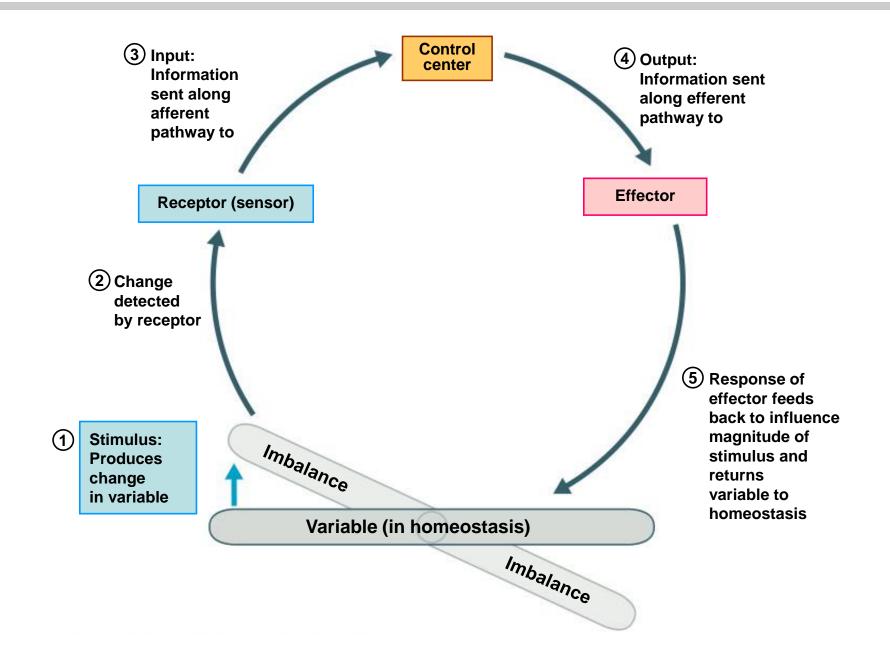
- sensory input.
- central nervous system.
- motor out put.



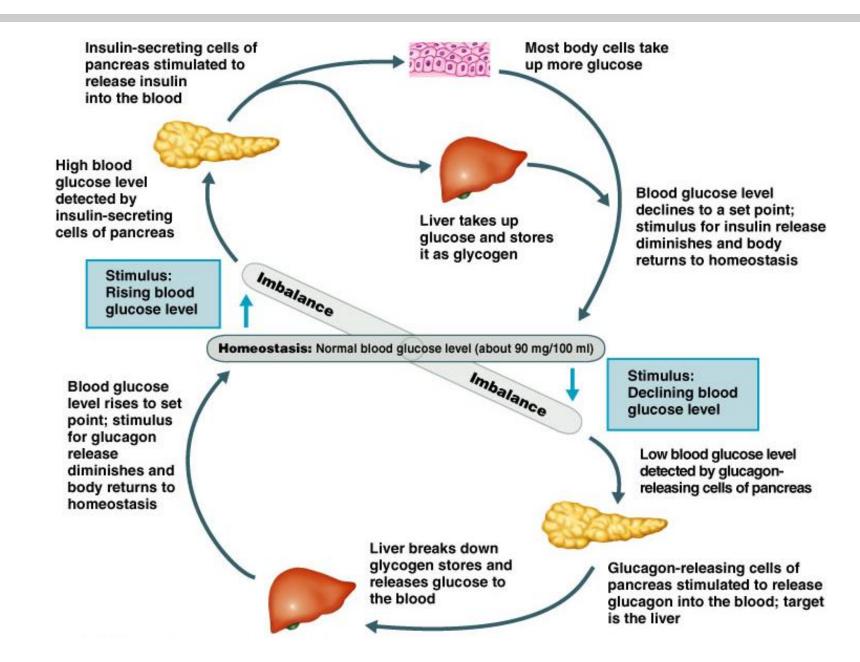
2. Hormonal system of regulation.

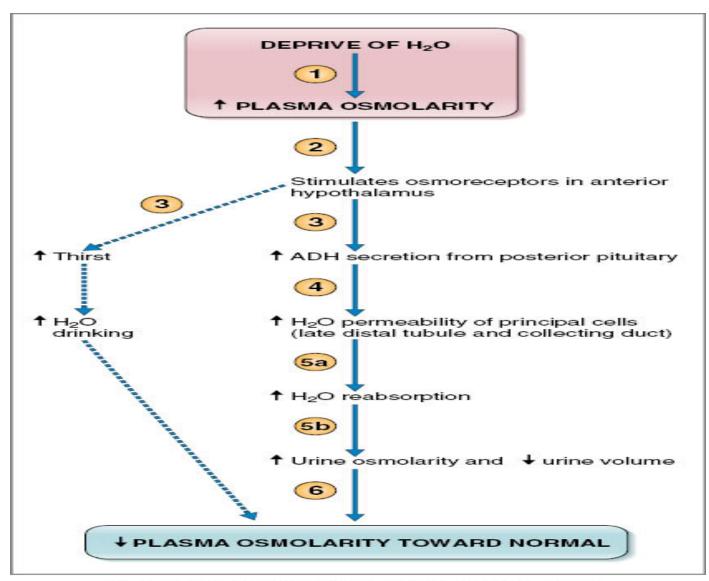
Endocrine gland.
Pancreas, thyroid
e.g. : insulin control glucose level.

#### **Homeostatic Control Mechanisms**

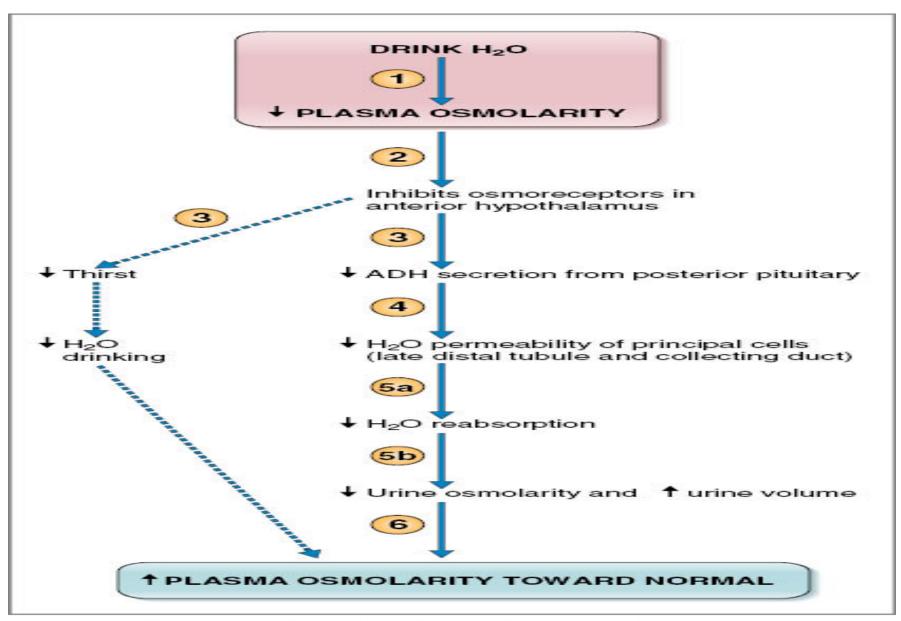


#### Feedback





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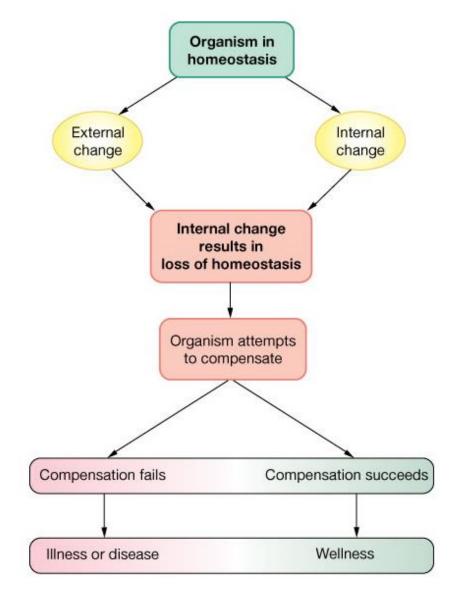
#### **Homeostatic Imbalance**

## • **Disturbance** of homeostasis or the body's normal equilibrium

### **Homeostasis & Controls**

- 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 .
- I in ECF volume.
- † in ICF volume.

#### **Volume Expansion**

#### 1. - Infusion of isotonic NaCl.

## - **ECF volume.**

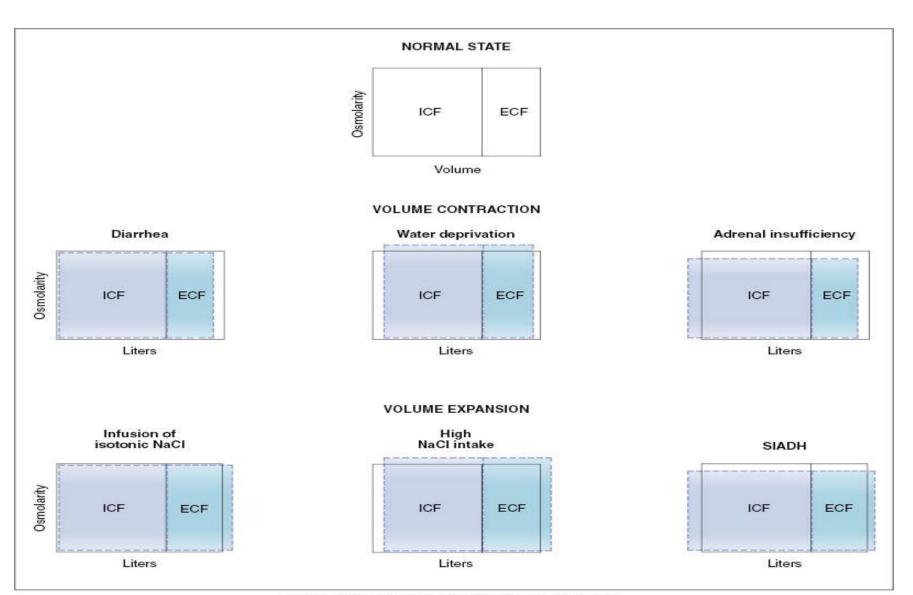
- No change in osmolarity.
- Isomotic expansion .

2. High NaCl intake.

- teating salt.
- **† osmolarity** in both.
- volume of ICF.
- **volume of ECF** .
- hyperosmotic volume expansion.

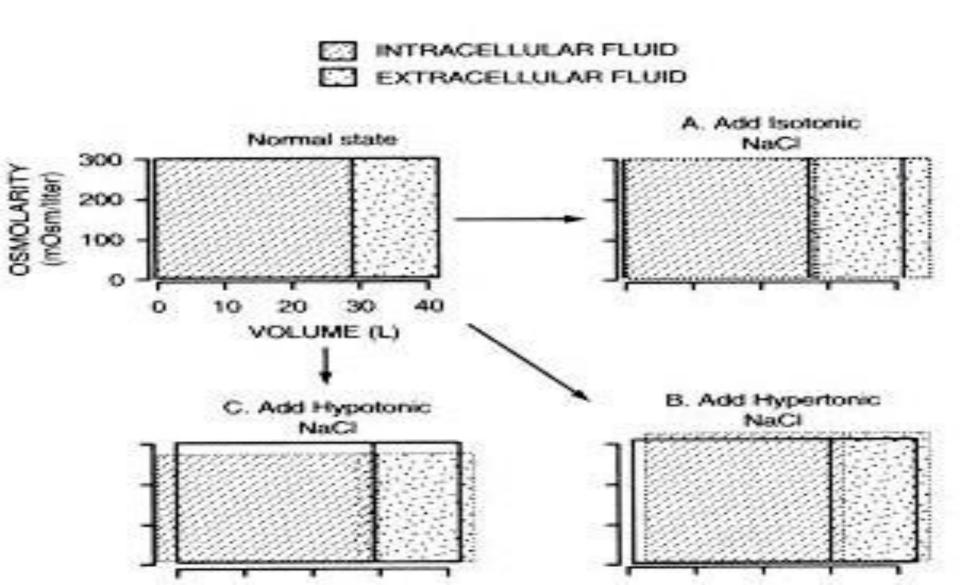
# 3- Syndrome of inappropriate antidiurtic hormone (SIADH):

- volume
- | osmolarity

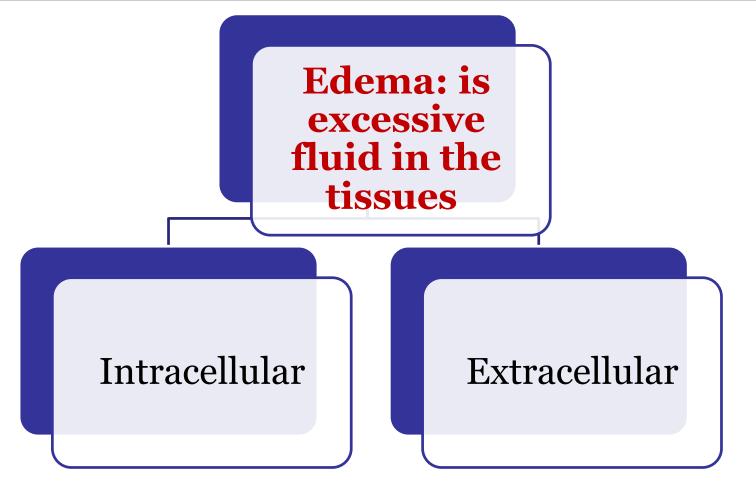


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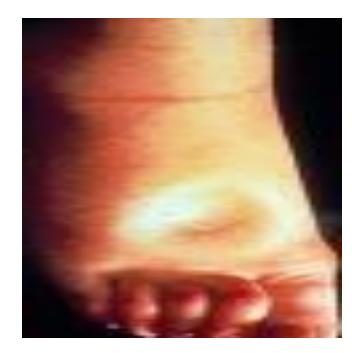
# **Effect of adding saline solution to the ECF**







Edema occurs mainly in the extracellular fluid compartment





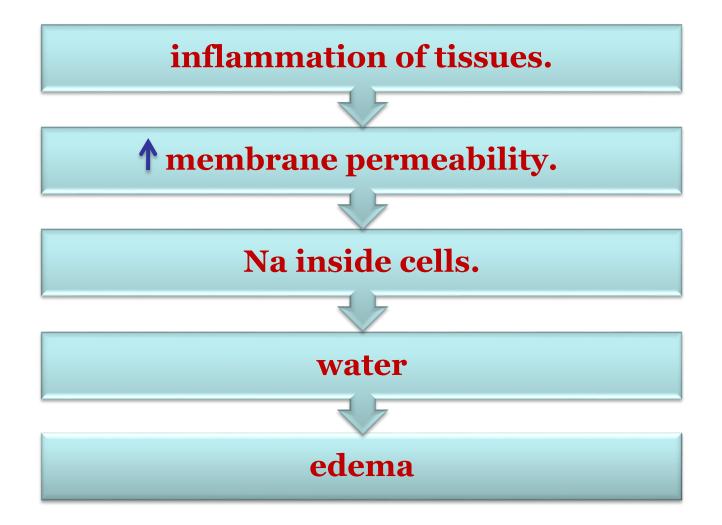


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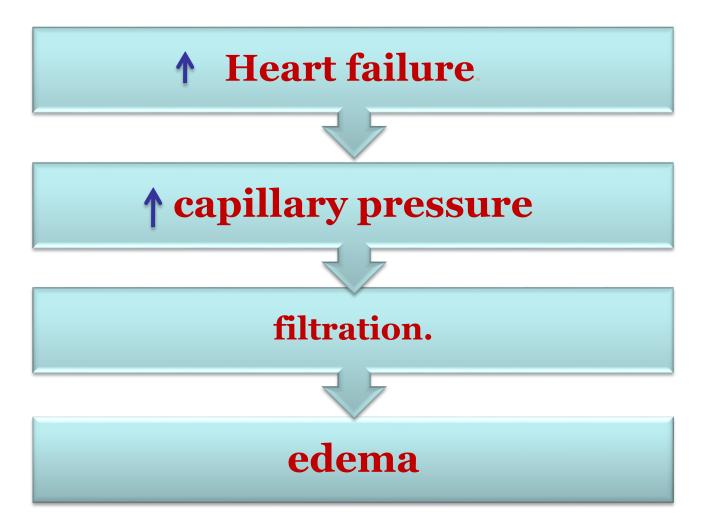


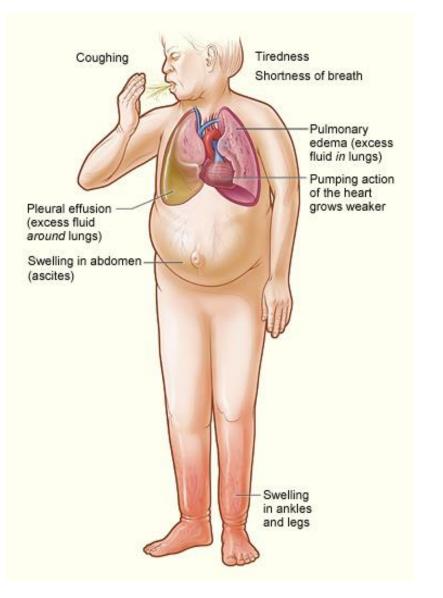
## **Intracellular Edema:**



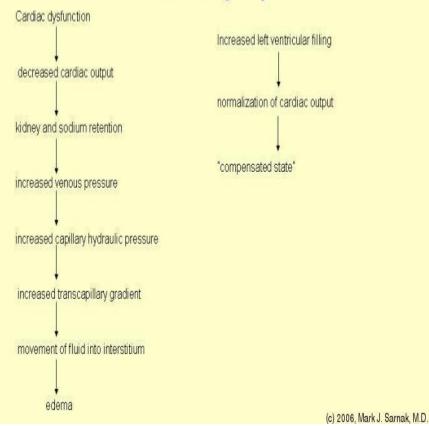
## **Extracellular Edema:**

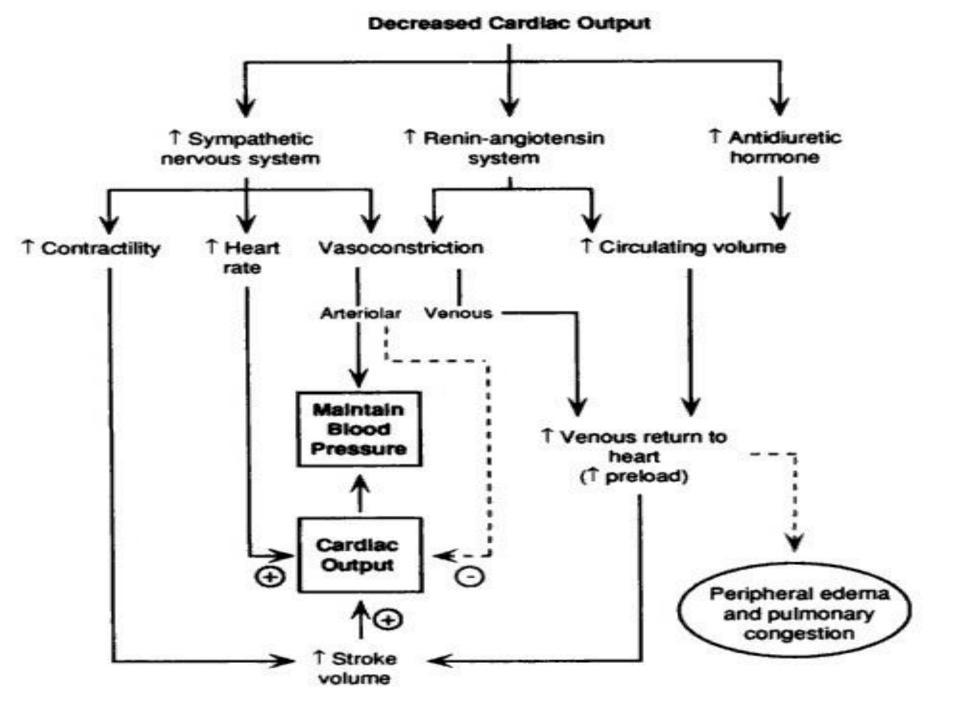
#### *common clinical cause is excessive capillary fluid filtration.*





# Pathophysiology of edema in heart failure (HF)





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.

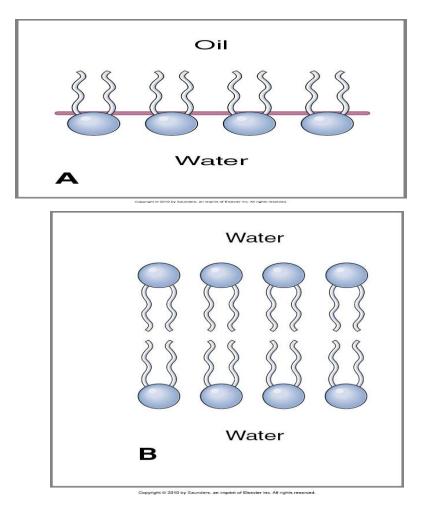
#### **Cell Membrane**

- 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 .

# Protein Phospholipids Cholesterol lipid Glycolipid Carbohydrates

# The Cell Membrane Phospholipids Consist Of :

- 1. Glycerol head (hydrophilic).
- Two fatty acid "tails" (hydrophobic).



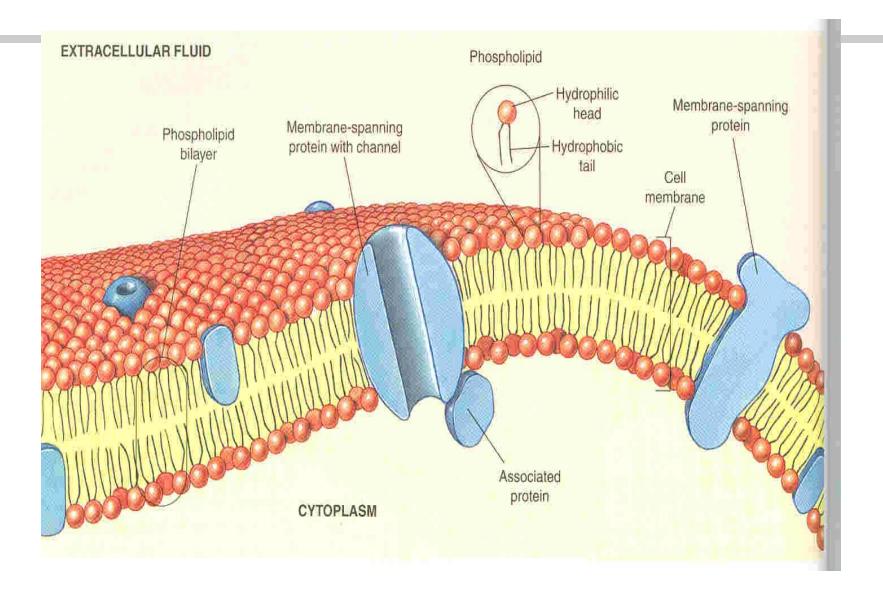
 Heads (hydrophilic) facing ICF and ECF and tails (hydrophobic) face each other in the interior of the bilayer.

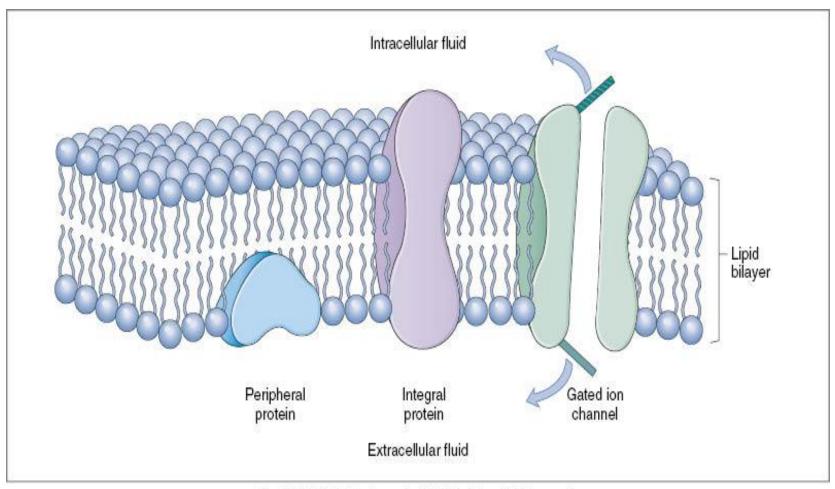
• Amphipathic.

#### **The Cell Membrane Proteins.**

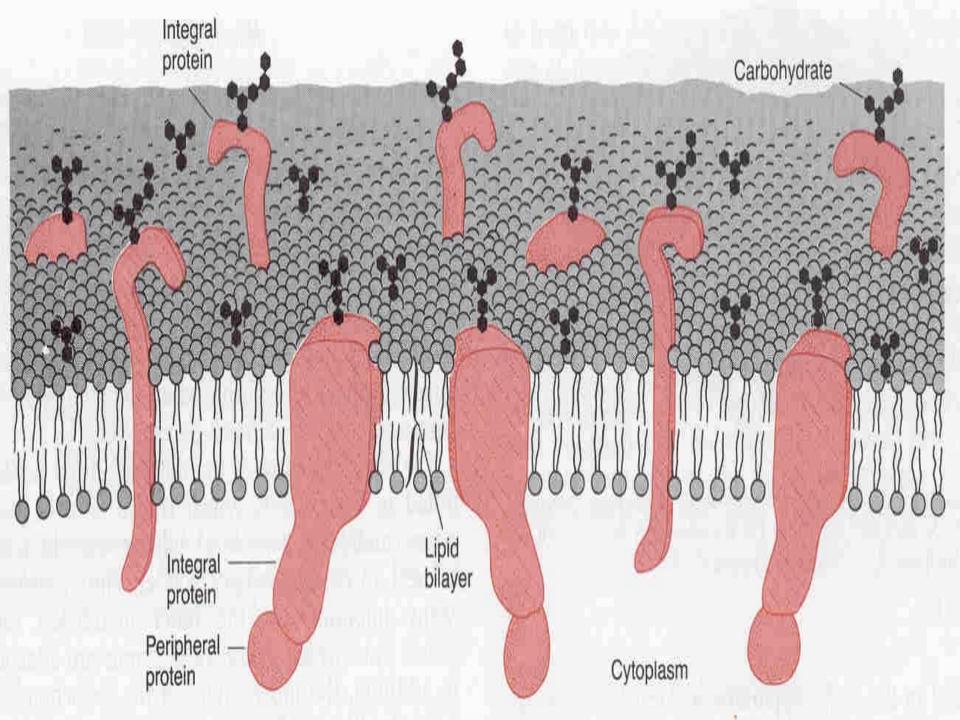
- **1. Integral proteins** span the membrane . Proteins provide structural channels or pores.
- Peripheral proteins (carrier proteins)

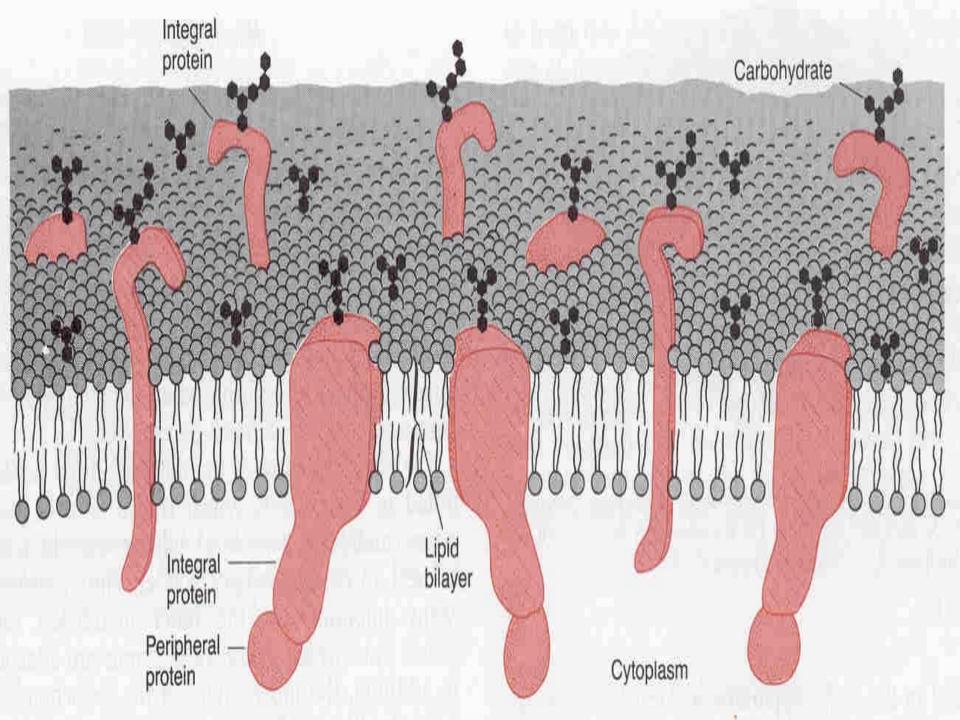
   Present in one side.
  - Hormone receptors ..





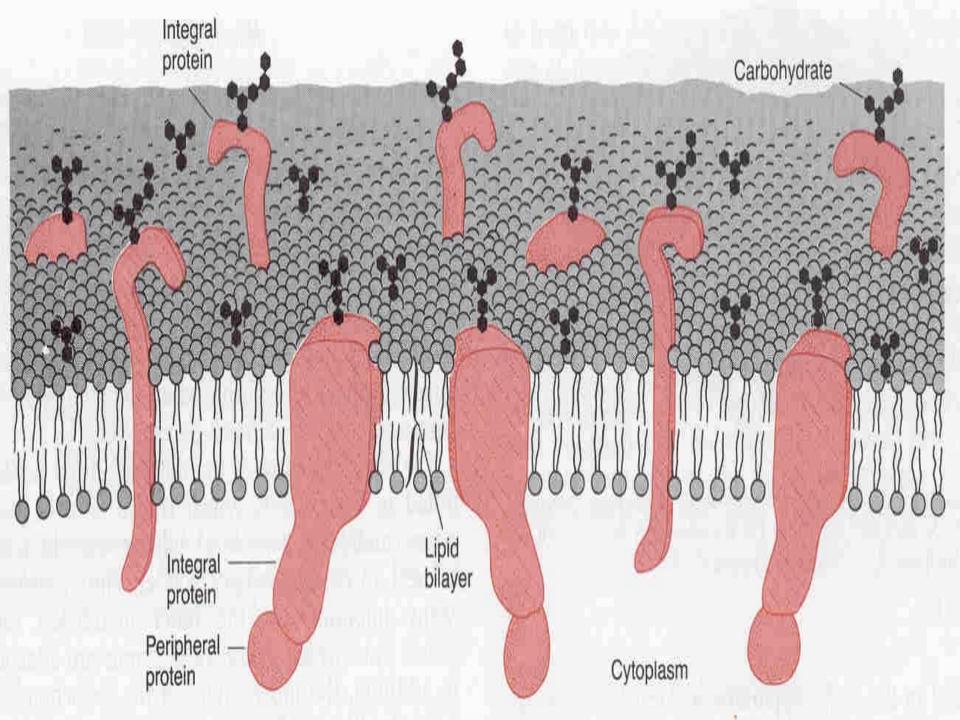
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#### The Cell Membrane Carbohydrates:

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



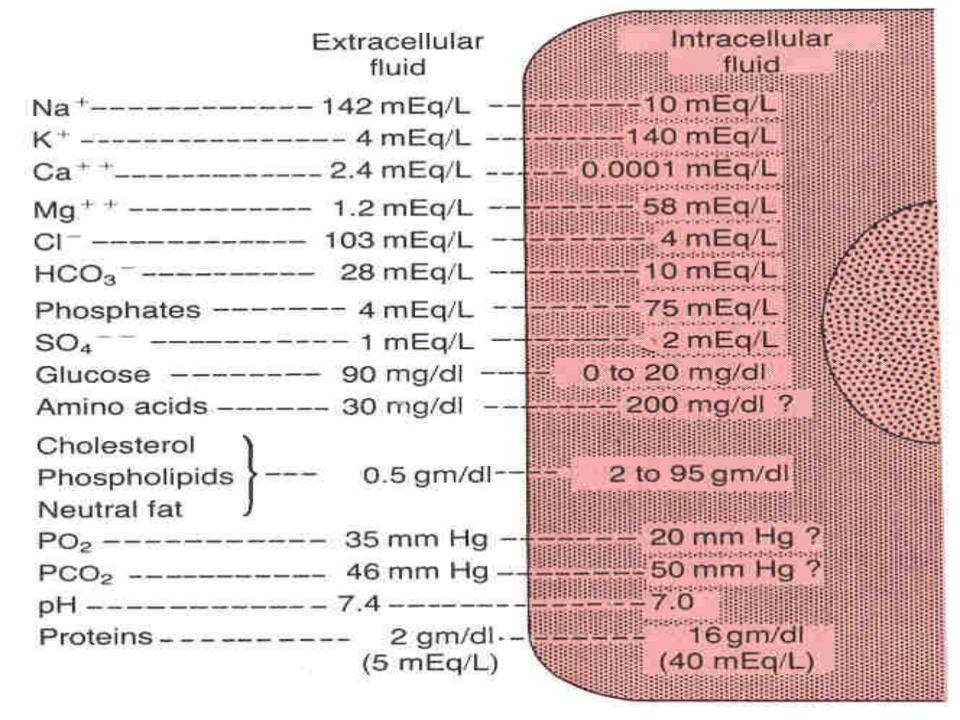
- Attaches cell to each others.
- Act as receptors substances. (help ligend to recognize its receptor ).
- Some enter in to immune reactions.
- Give most of cells overall –ve surface.

# **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 (O2, CO2, OH...



# **Types Of Membrane Transport**

- 1- Diffusion
- a)- Simple diffusion.
- b)- Facilitated diffusion.
- 2- Active transport.
- a)- Primary active transport.
- b)- Secondary active transport.
- 3- Osmosis.

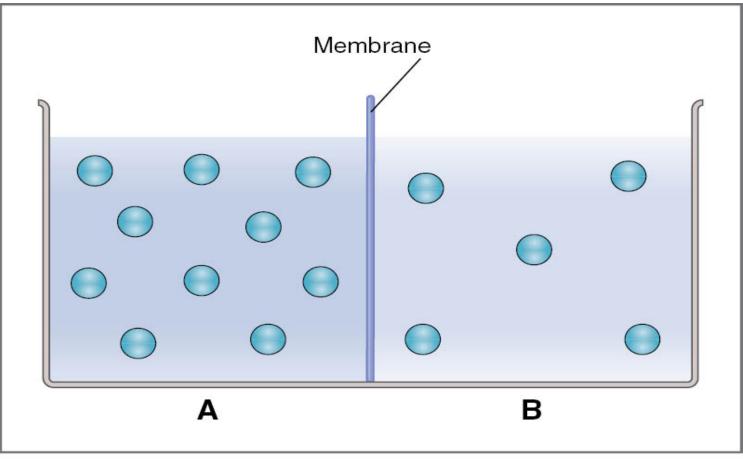
#### Diffusion

• Random movement of substance either through the membrane directly or in combination with carrier protein <u>down</u> an electrochemical gradient.

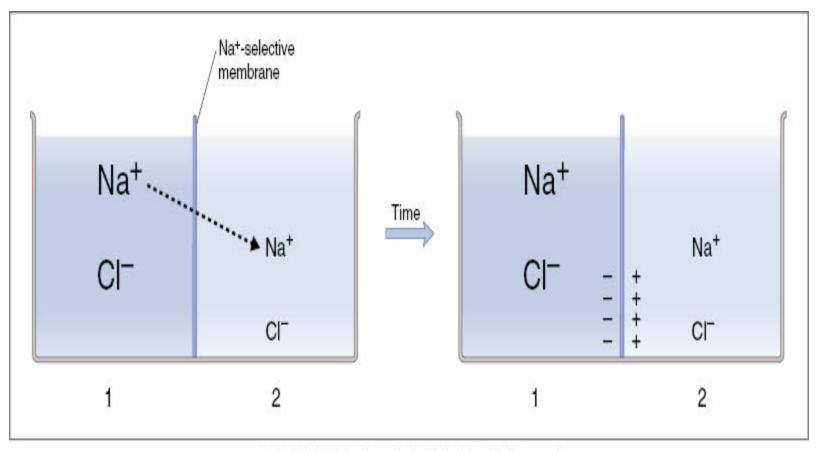
- 1- Simple diffusion.
- 2- Facilitated diffusion.

- Non carrier mediated transport down an electrochemical gradient.
- **Diffusion of nonelectrolytes** (uncharged) from high concentration to low concentration.

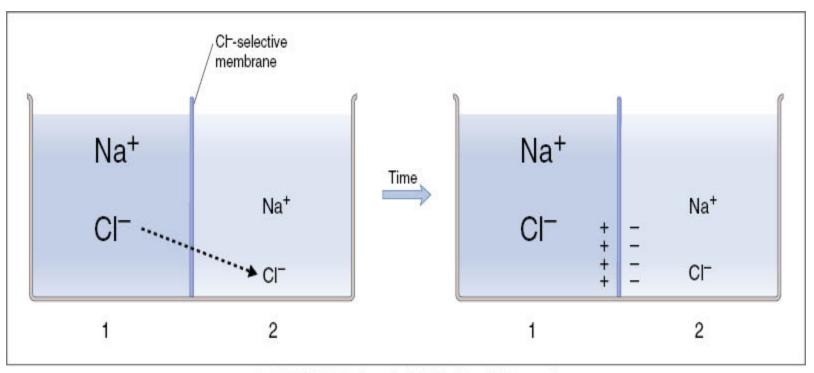
• **Diffusion of electrolytes** (charged) depend on both chemical as will as electrical potential difference.



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# **Rate Of Simple Diffusion Depend 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:

<sup>†</sup> concentration  $\longrightarrow$  † binding of protein

If all protein is occupied we achieve full saturation.

## 2- Stereopecificity:

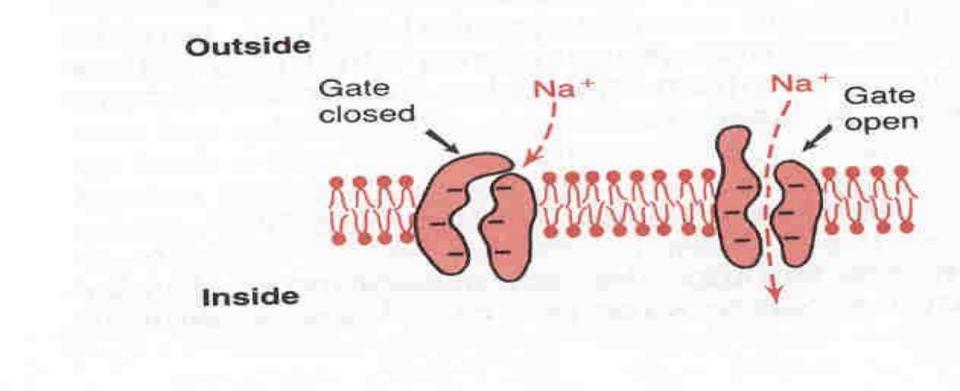
The binding site recognize a specific substance D-glucose but not L-glucose

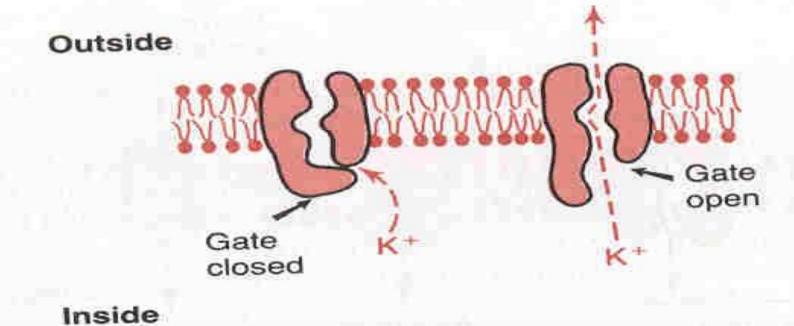
## **3- Competition:**

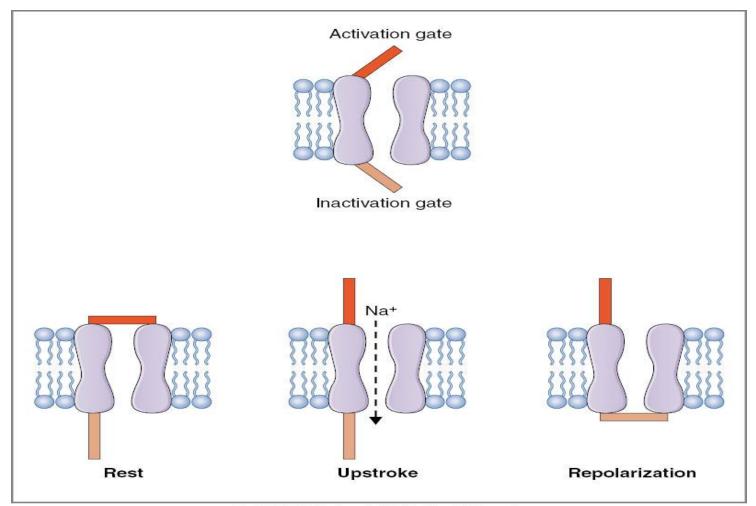
# Chemically similar substance can compete for the same binding site.

D-galactose D-glucose.

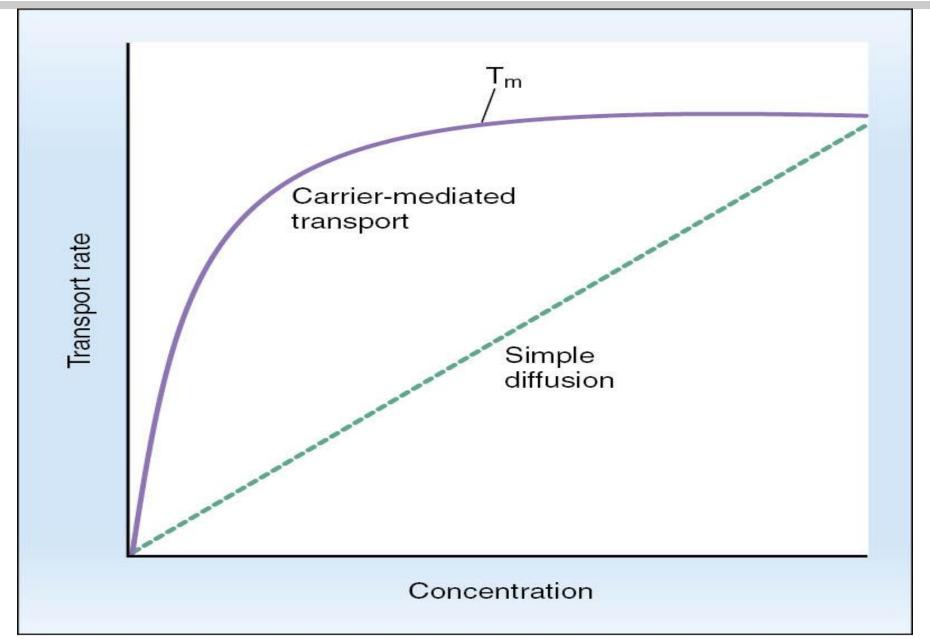
Substance  $\rightarrow$  binding site  $\rightarrow$  substance protein complex  $\longrightarrow$  conformational changes release of substance







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• Glucose, most of amino acids.

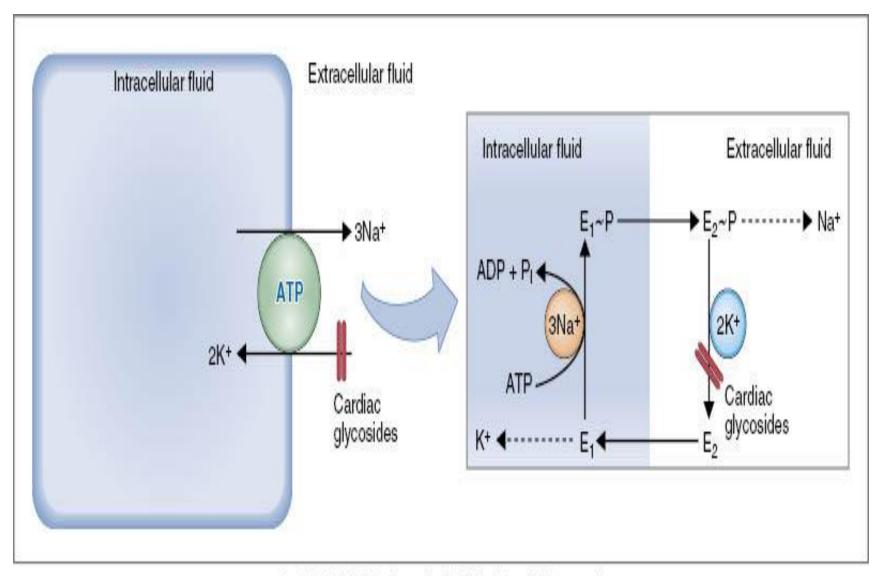
 Transport (uphill) → against electrochemical gradient.
 Required energy → direct. indirect.

• Required carrier – protein.

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

#### A. - Sodium-Potassium pump (Na-K pump).

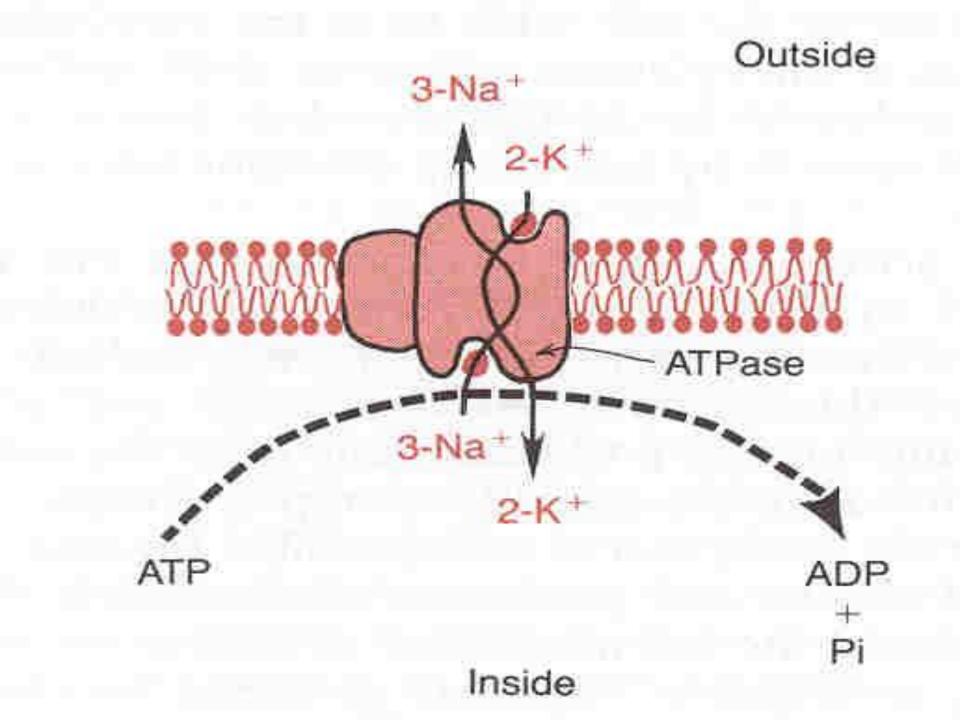
- its present in all cell membranes.
- Na in →out.
- K out  $\longrightarrow$  in.



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### **Characteristic Of The Pump:**

- 1. Carrier protein is formed from  $\alpha$  and  $\beta$  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.



- 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<sup>2</sup>+ ATPase).

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

#### **Function:**

Maintaining a low Ca<sup>2</sup>+ concentration inside the cell.

• C. - Primary active transport of hydrogen lons H+-K ATPase.

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

#### 2) Secondary Active Transport:

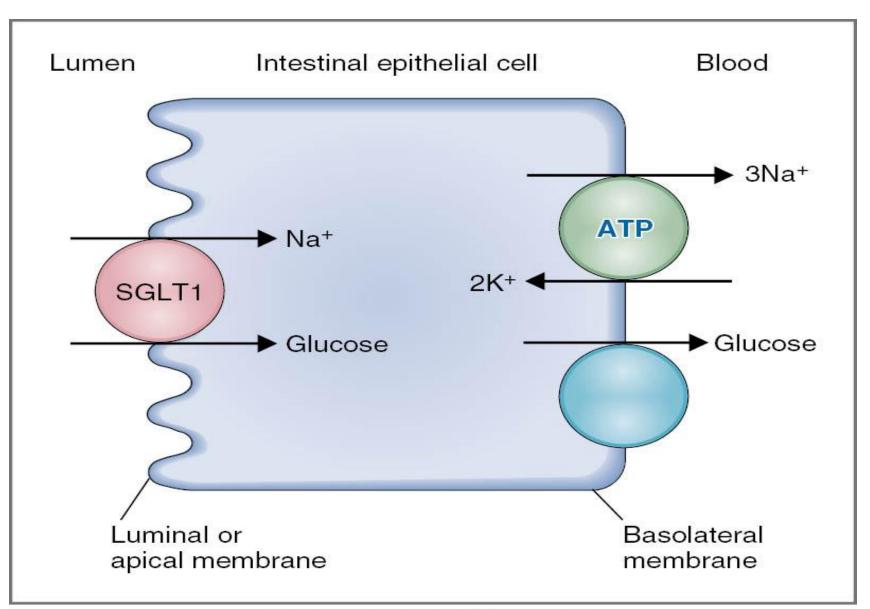
#### Co- transport and countertransport:

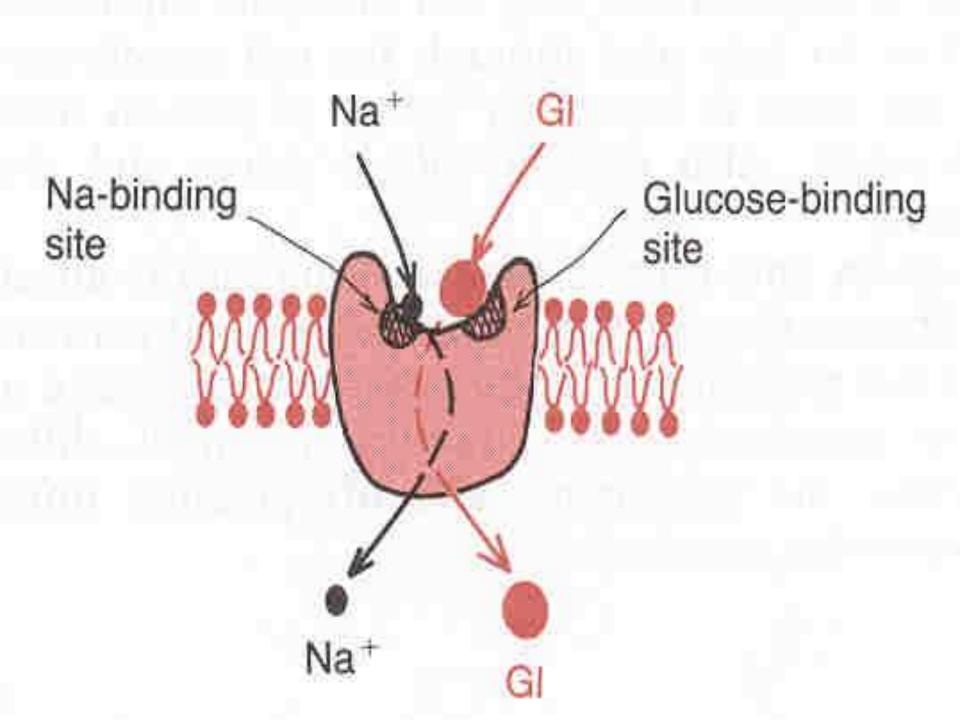
is transport of one or more solutes against an electrochemical gradient ,coupled to the transport of another solute down an electrochemical gradient .

- "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.

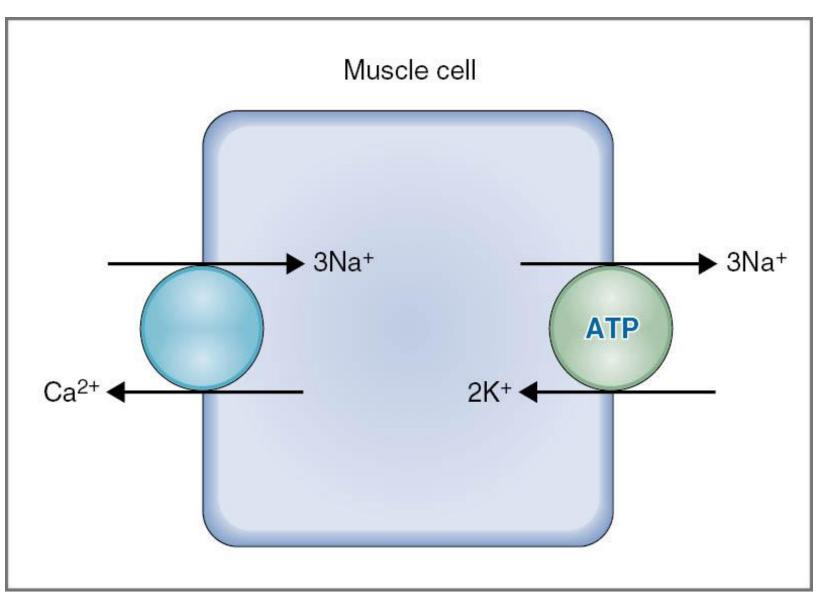




- Countertransport:
- Na is moving to the interior causing other substance to move out.

Ca<sup>2</sup>+ - Na+ exchange.
 (present in many cell membranes)

• Na –H+ exchange in the kidney.



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