# Dr. Nervana Mostafa

MB BS, MD, PhD (UK)

Professor of Physiology College of Medicine, KKUH, KSU

nbayoumy@ksu.edu.sa

# Cell membrane structure & transport across cell membrane

# objectives

- 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.
- Differentiate between passive and active transport mechanisms and give examples on each.

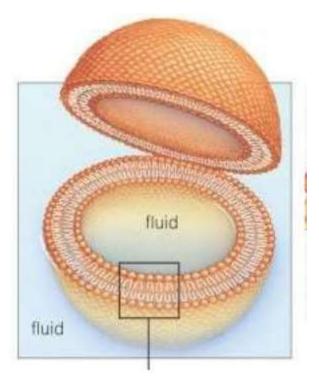
**#Study source for this lecture: (Guyton & Hall Textbook of Medical Physiology, 13**<sup>th</sup> edition) #

#### **Cell Membrane**

Envelops the cell.

Thin, pliable and elastic.

• 7 - 10 nanometer thick.



Also, referred to as the plasma membrane.

# Composition

```
<u>Lipoprotein</u>
protein 55%
```

```
lipid 42% phospholipids 25% cholesterol 13% glycolipid 4%
```

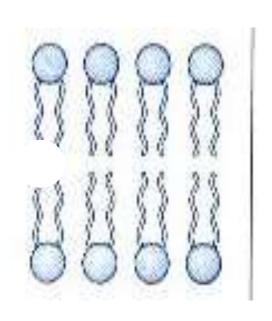
carbohydrates 3%

# The Cell Membrane Phospholipids Consist Of:

**1. Glycerol head** (hydrophilic).

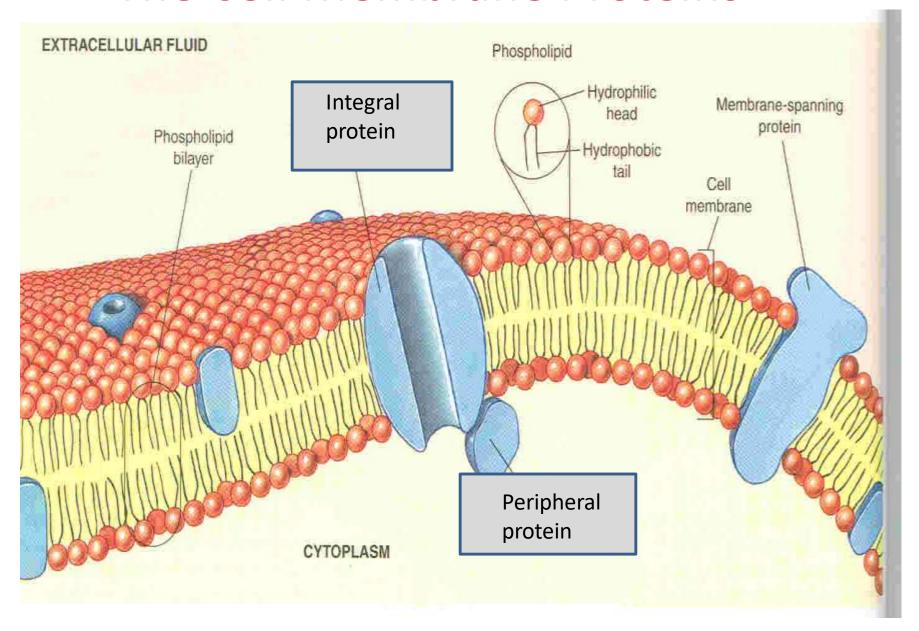
2. Two fatty acid "tails" (hydrophobic).

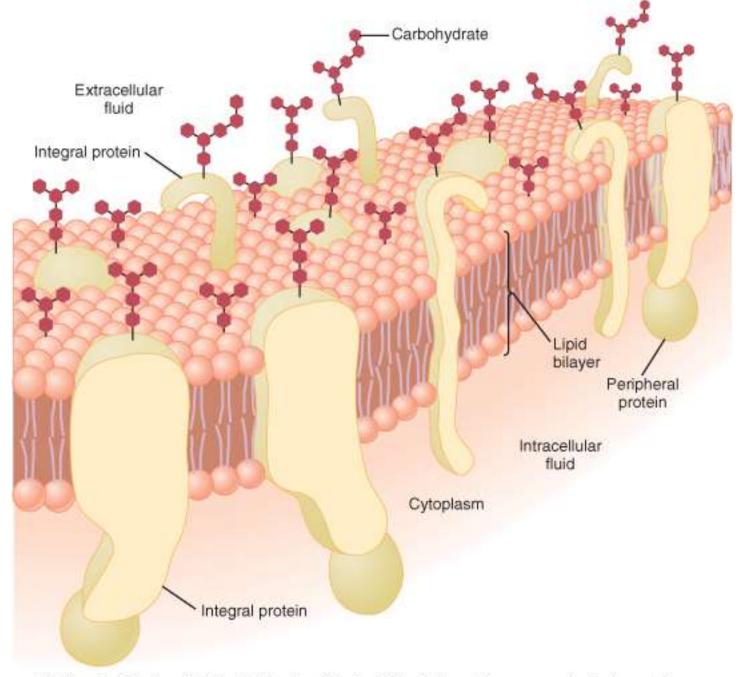
**ECF** 



**ICF** 

### **The Cell Membrane Proteins**





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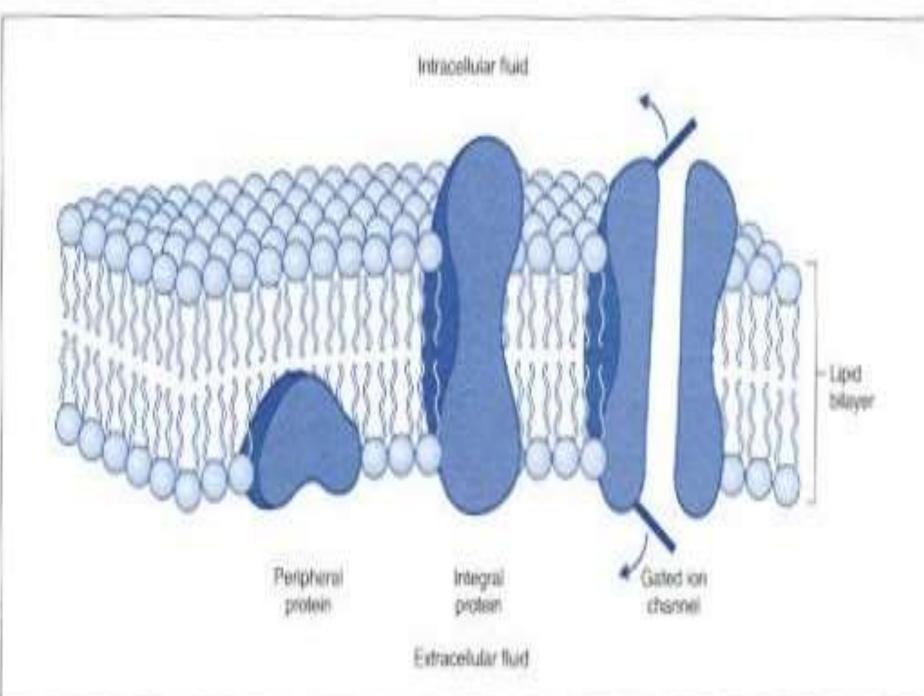
# **The Cell Membrane Proteins:**

#### 1. Integral proteins

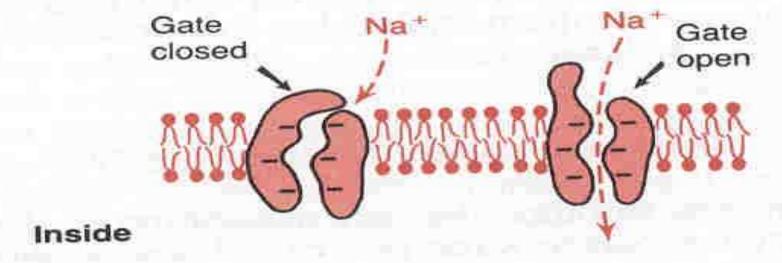
- Span the whole thickness of the membrane .
- Proteins provide structural **channels** or **pores**.
- Carrier proteins.

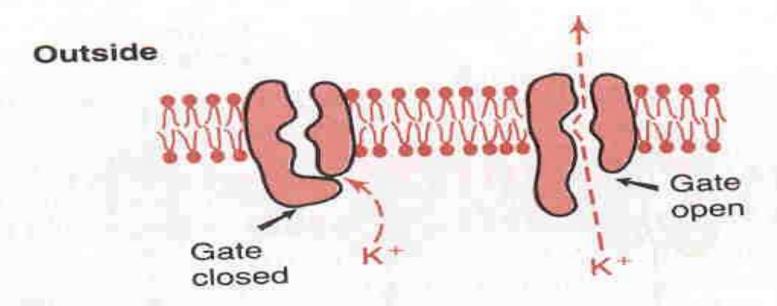
#### 2. Peripheral proteins

- -Present in one side.
- Hormone receptors .
- Cell surface antigens.



#### Outside

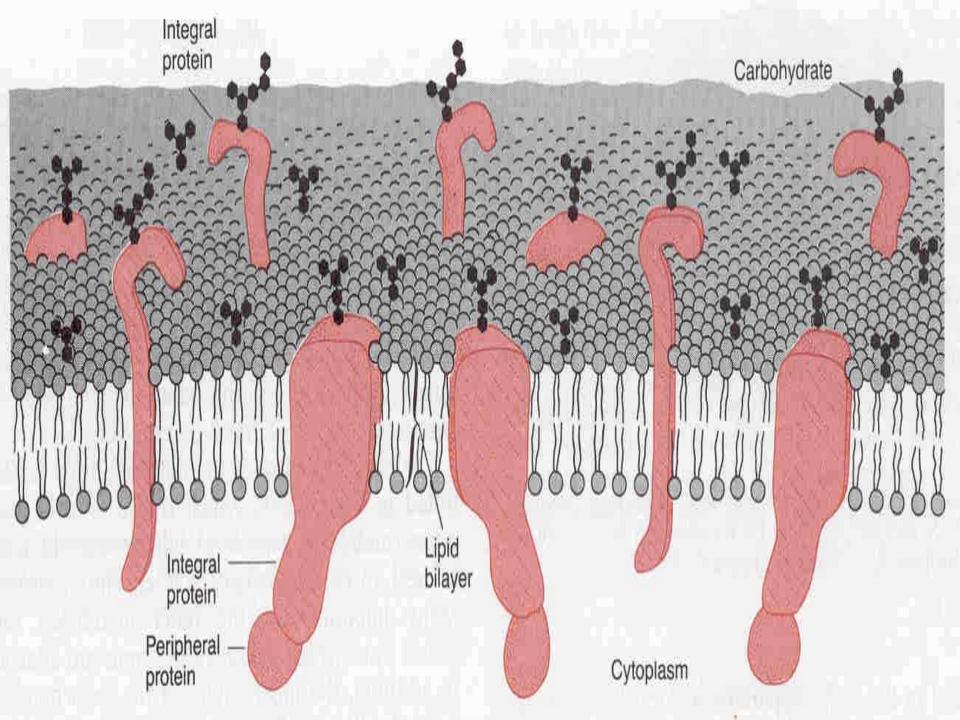




#### Inside

#### **The Cell Membrane Carbohydrates:**

- Glycoproteins (most of it) and Glycolipids.
- Proteoglycans (mainly carbohydrate substance bound together by protein).
- "glyco" part is in the surface (hydrophilic).
- Glycocalyx (Carbohydrate molecules protrude to the outside of the cell forming a loose carbohydrate coat "glycocalyx".



# **Function Of Carbohydrates:**

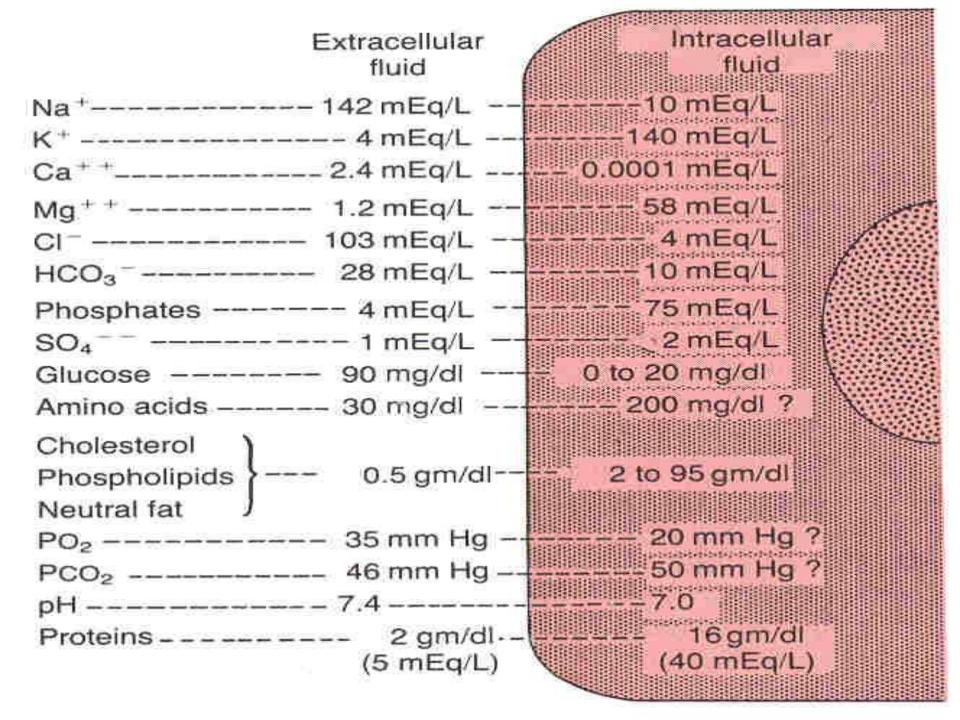
- Attaches cell to each others.
- Act as receptors substances (help ligend to recognize its receptor).
- Some enter in to immune reactions.
- Give most of cells overall –ve surface.

## **Transport across the Cell Membrane**

Cell membrane is selectively permeable.

- Through the proteins.
  - Water-soluble substances e.g. ions, glucose ...

- Directly through the lipid bilayer.
  - Fat-soluble substance (O2, CO2, N2, alcohol...



## **Types Of Membrane Transport**

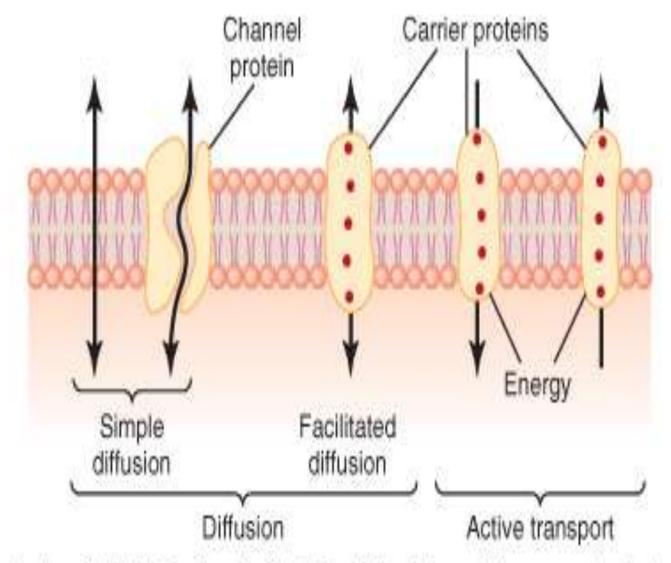
#### 1- Diffusion

- a) simple diffusion.
- b) facilitated diffusion.

#### 2- Active transport.

- a) primary active transport.
- b) secondary active transport.

#### 3-Osmosis.



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#### **Diffusion**

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

- 1- Simple diffusion.
- 2- facilitated diffusion.

- Simple and facilitated diffusion Do NOT require input of energy
- = powered by concentration gradient or electrical gradient.
- Active transport = uses energy = utilizes ATP.

# **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 will as, electrical potential difference.

#### Rate Of Simple Diffusion Depend On:

- 1- Amount of substance available.
- 2- The number of opening in the cell membrane for the substance (pores).
- 3- Chemical concentration difference.
- 4- Electrical potential difference.
- 5- Molecular size of the substance.
- 6- Lipid solubility.
- 7- Temperature.

# TABLE 3-1 Factors Influencing the Rate of Net Diffusion of a Substance across a Membrane (Fick's Law of Diffusion)

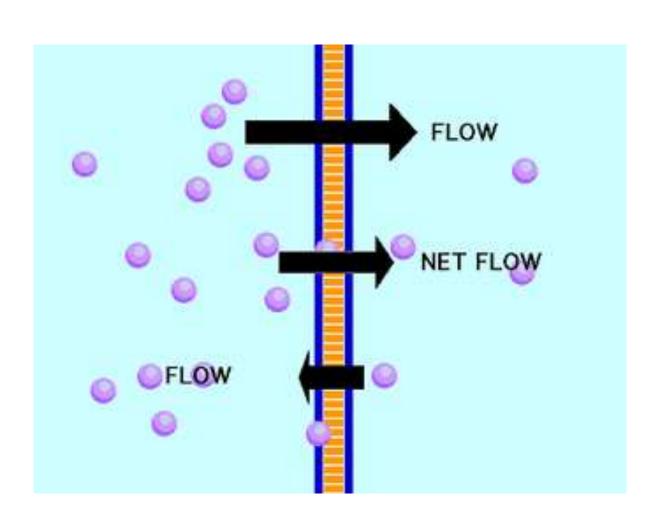
Factor	of Net Diffusion
$\uparrow$ Concentration gradient of substance ( $\Delta C$ )	1
↑ Surface area of membrane (A)	1
Membrane permeability	1
Molecular weight of substance (MW)	<b>+</b>
$\uparrow$ Distance (thickness) ( $\Delta X$ )	1 1
† Temperature	1

cont...

#### Rate of diffusion = PXA(C1-C2)

- 1. P = Permeability coefficient.
- a. Temperature b. Size of molecule
- c. Solubility in lipids d. Thickness of membrane
- 2. A = surface area.
- 3. (C1-C2) = gradient difference:
  - a. Concentration difference
  - b. Electrical difference.
  - c. Pressure difference.

# **Net Flow**



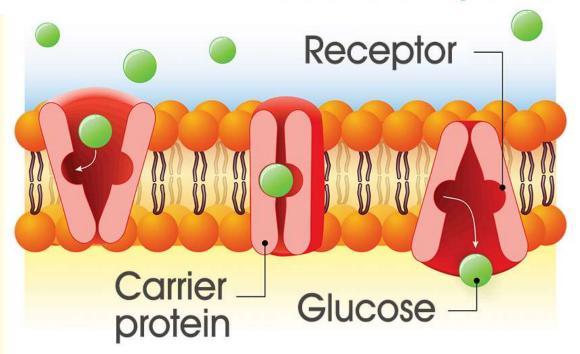
#### **Facilitated Diffusion**

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

e.g. glucose & amino acids.

#### Extracellular space

Facilitated diffusion—the process that allows selective movement in and out of the cell membrane.



Cytoplasm

# Features Of Carrier Mediated Transport (Facilitated diffusion)

#### 1- saturation:

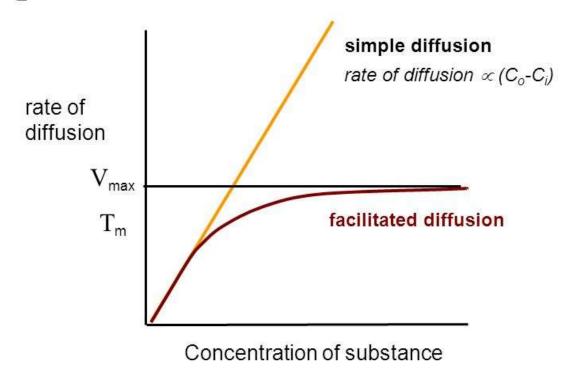
concentration — binding of protein
If all protein carriers are occupied, full saturation is achived.

i.e. The rate of diffusion reaches a maximum (Vmax) when all the carriers are functioning as rapidly as possible.

#### 2- stereopecificity:

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

#### Simple vs. Facilitated



What limits maximum rate (Vmax) of facilitated diffusion? Number of carriers

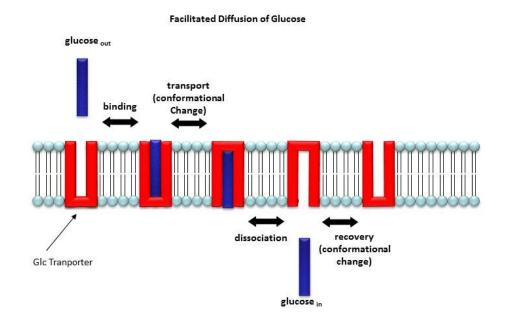
#### **3- Competition:**

Chemically similar substances can compete for the same binding site.

D- galactose / D-glucose.

\_\_\_\_\_

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



# **Active Transport:**

 Transport (<u>uphill</u>) — against electrochemical gradient.

Required carrier – protein.

# 1- Primary Active Transport:

-Energy is supplied directly from ATP.

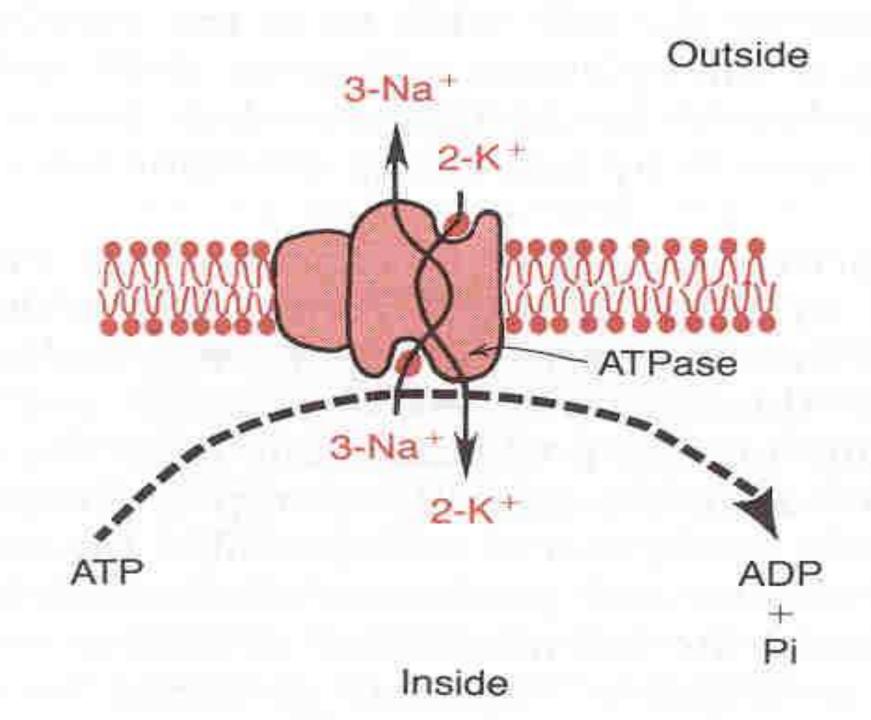
$$ATP \longrightarrow ADP + P + energy.$$

- A. Sodium-Potassium pump (Na<sup>+</sup>- K<sup>+</sup> pump).
  - it's present in all cell membranes.
  - 3 Na<sup>+</sup> in → out.
  - 2 K<sup>+</sup> out  $\longrightarrow$  in.

#### Discovery

 Na<sup>+</sup>/K<sup>+</sup>-ATPase pump was discovered by <u>Jens</u> <u>Christian Skou</u> in 1957.

 In 1997, he received the <u>Nobel Prize in</u> Chemistry.



# Characteristic of Na<sup>+</sup>/K<sup>+</sup>-ATPase 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.

#### **Function:**

1. Maintaining Na<sup>+</sup> and K<sup>+</sup> concentration difference.

2. It's the basis of nerve signal transmition.

3. Maintaining negative potential inside the cell.

4. Maintains a normal cell volume.

# B. primary active transport of calcium (Ca \*\* 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 ions H+-K+ ATPase.

- stomach.
- kidneys.
- pump to the lumen.
- H<sup>+</sup>-K<sup>+</sup> ATPase inhibitors, are used to treat ulcers (e.g. omeprazole).

## 2) Secondary Active Transport:

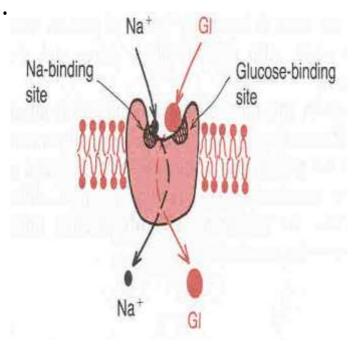
- Co- transport and counter-transport:
- is transport of one or more solutes against an electrochemical gradient, coupled with the transport of another solute down an electrochemical gradient.
- "downhill" solute is Na<sup>+</sup>.

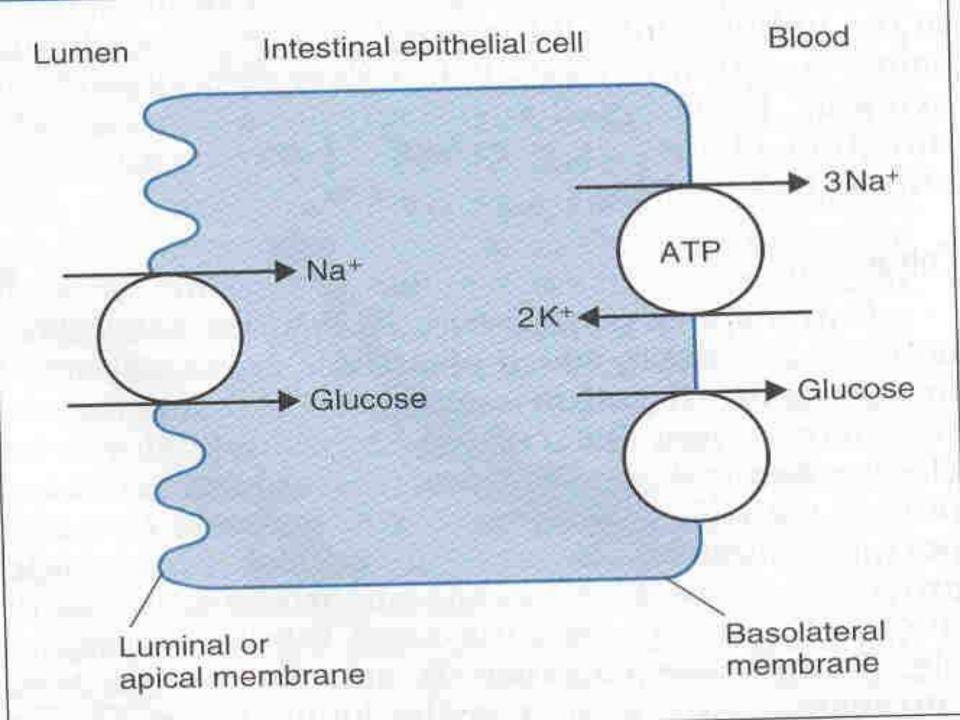
- Energy is supplied indirectly form primary transport.

#### Co-transport:

- All solutes move in the same direction "inside cell".

- e.g.
  - Na<sup>+</sup>- glucose Co-transport.
  - Na<sup>+</sup>- amino acid Co-transport.
  - present in the intestinal tract & kidneys.





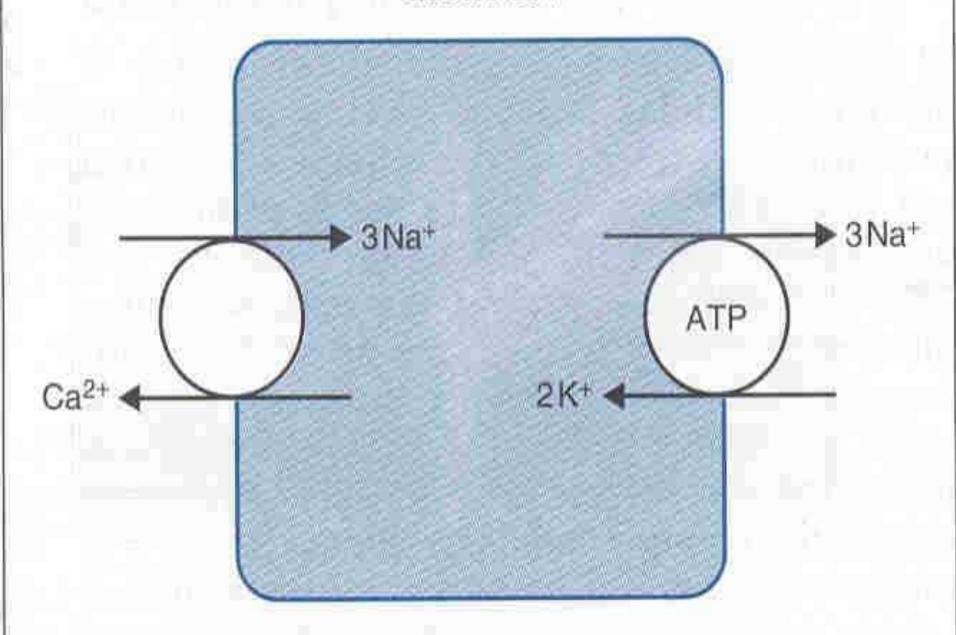
#### **Counter-transport:**

 Na<sup>+</sup> is moving to the interior of the cell causing other substance to move out.

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

Na<sup>+</sup>- H<sup>+</sup> exchange in the kidney.

#### Muscle cell



# **Body Fluids & Electrolytes**

#### **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 (ECF), interstitial fluid, trans-cellular fluid and total
   body water (TBW).
- 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.

Human body contain 50-70% water.

• E.g.

— 70 kg man has 42 L of water.

– (Kg of water = Liter of water)

#### PERCENTAGE OF WATER IN THE BODY



#### **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.
- Total water content declines throughout life.
- 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.

## Daily intake of water

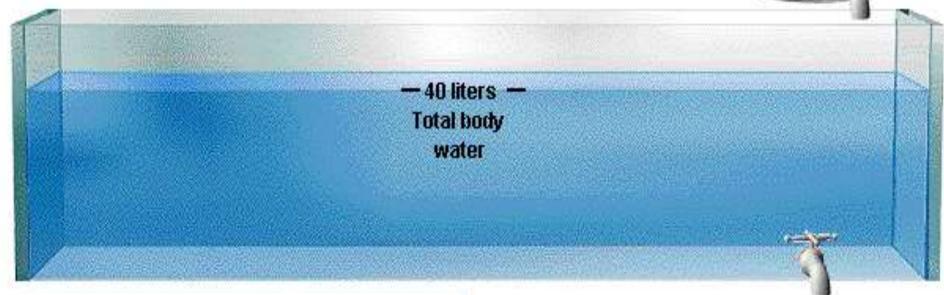
## TABLE 20-1 DAILY INTAKE AND OUTPUT OF WATER (in mi/day)

	Normal	Prolonged, Honvy Exercise
Intake		
Fluids ingested	2100	7
From metabolism	200	_200
Total intake	2300	?
Output	3115050	
Insensible—Skin	350	350
Insensible—Lungs	350	650
Sweat	100	5000
Feces	100	100
Urine	1400	500
Total output	2300	6600

#### WATER TANK ANALOGY

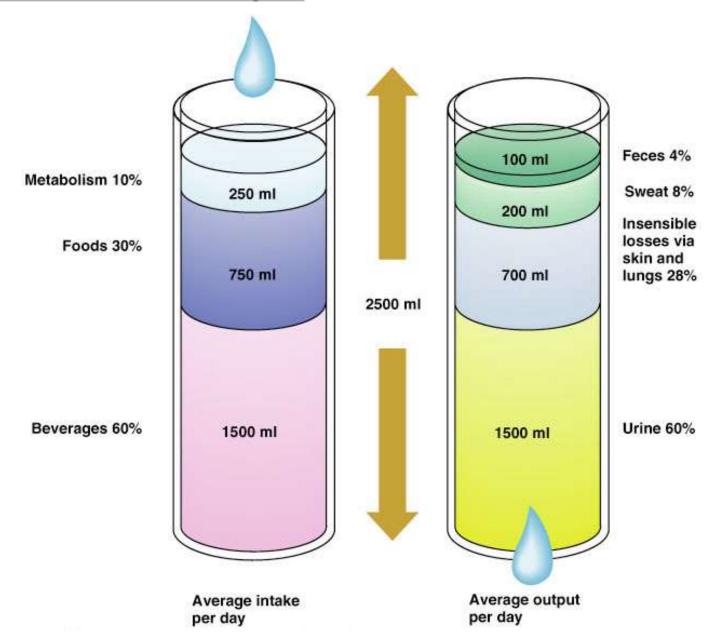
Maintaining water homeostasis is a balancing act. The amount of water taken in must equal the amount of water lost.







#### **Water Intake and Output**



### Regulation of Water Intake

**Climate** 

**Habits** 

Level of physical activity.

## Regulation of Water Intake

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

#### **Factors that affect the TBW**

#### **Physiological factors:**

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

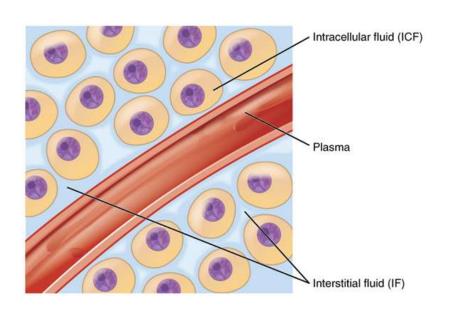
#### **Pathological factors:**

- Vomiting
- Diarrhea
- Diseases with excessive loss of water (DM, excessive sweating,....
- Blood loss

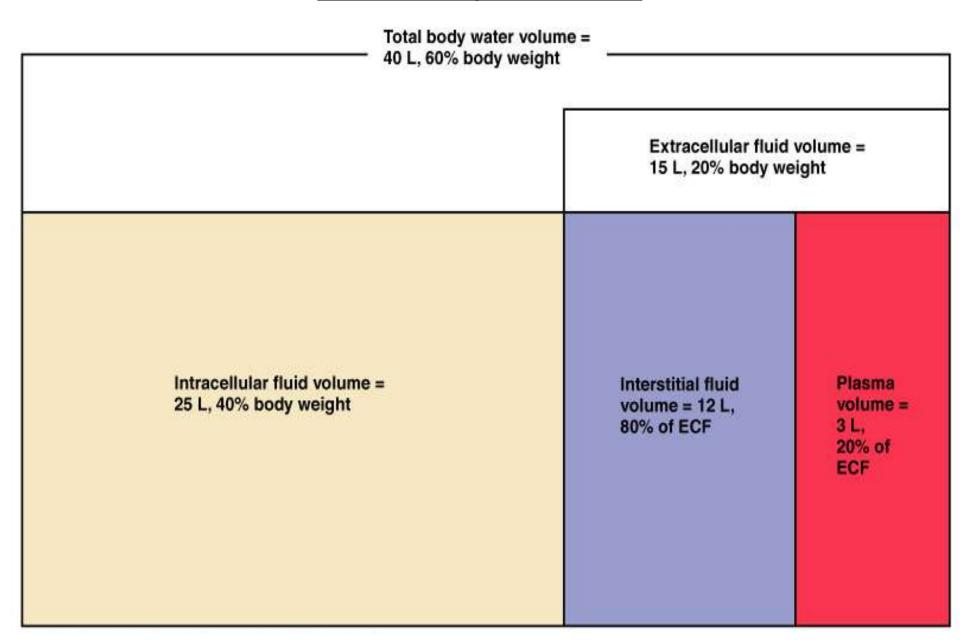
#### Fluid Compartments

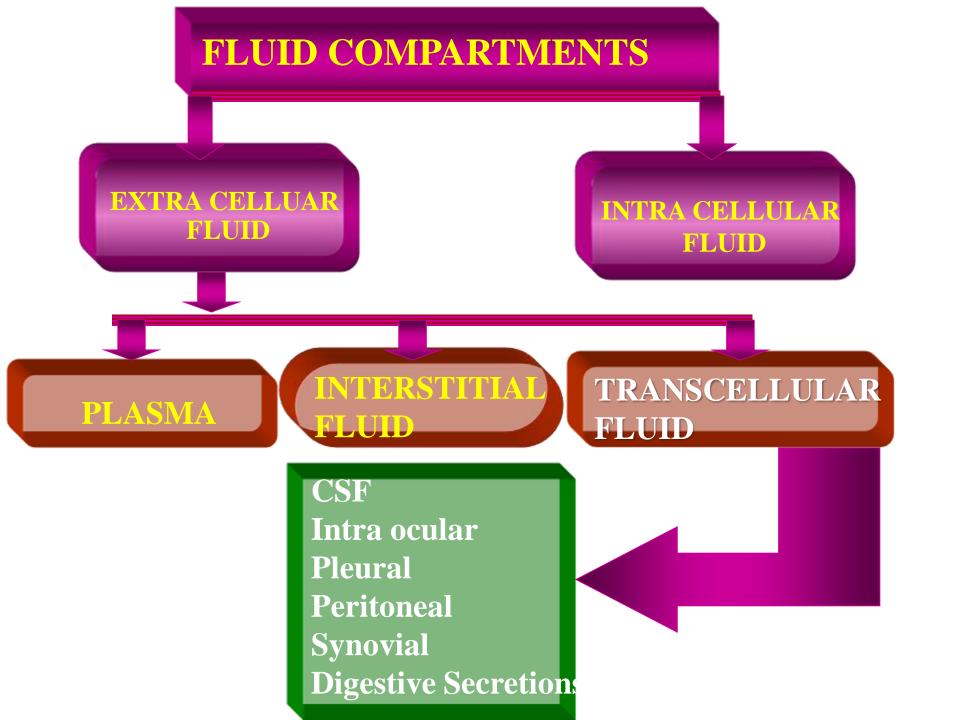
Water occupies two main fluid compartments:

- —Intracellular fluid (ICF)
- —Extracellular fluid (ECF)
  - Plasma
  - Interstitial fluid (IF)



#### **Fluid Compartments**





## 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.

#### e.g.

- 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.

#### concentration

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)

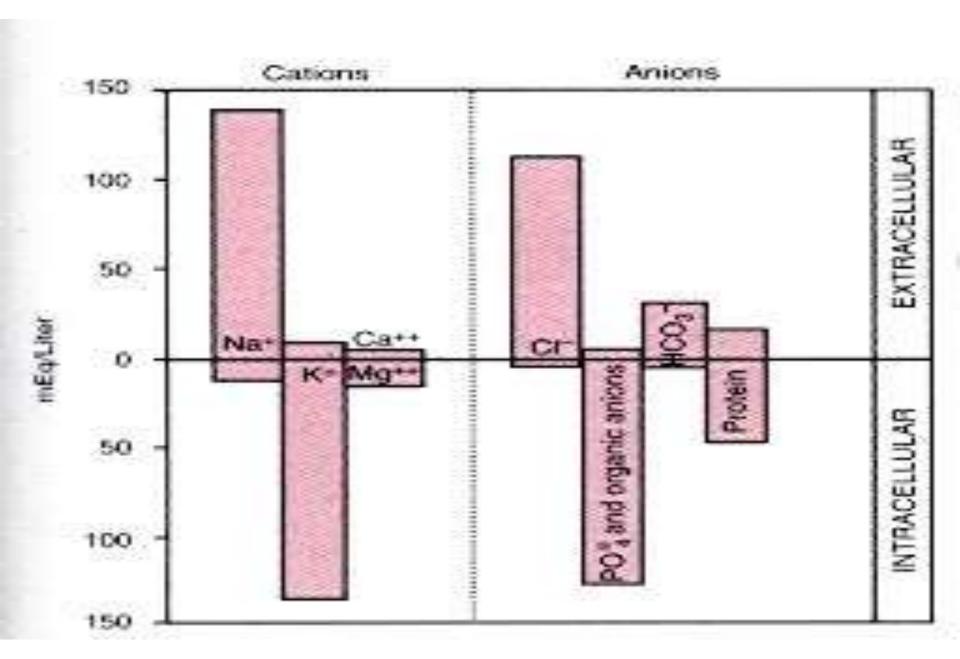
1mM=1/1000 M

• 1mOsm=1/1000 Osm

## **Electrolyte Concentration**

- Expressed in milliequivalents per liter (mEq/L), a measure of the number of electrical charges in one liter of solution.
- mEq/L = (concentration of ion in [mg/L]/the atomic weight of ion) × number of electrical charges on one ion.
- For single charged ions, 1 mEq = 1 mOsm
- For bivalent ions, 1 mEq = 1/2 mOsm

#### Constituents of ECF and ICF



#### TABLE 20-2 OSMOLAR SUBSTANCES IN EXTRACELLULAR AND INTRACELLULAR FLUIDS

	Plasma (m0sm/bler of H <sub>2</sub> D)	Interstitial	Introcellulo
Na+	142	139	14
K+	4.2	4.0	140
Ca**	1.3	1.2	0
Mg*	0.8	0.7	20
CI-	108	108	4
HCO,	24	28.3	10
HPO,, H,PO,-	2	2	11
so,	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	100		5
Hexose monophosphate			3.7
Glucose	5.6	5.6	3.7
Protein	1.2	0.2	1997
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.

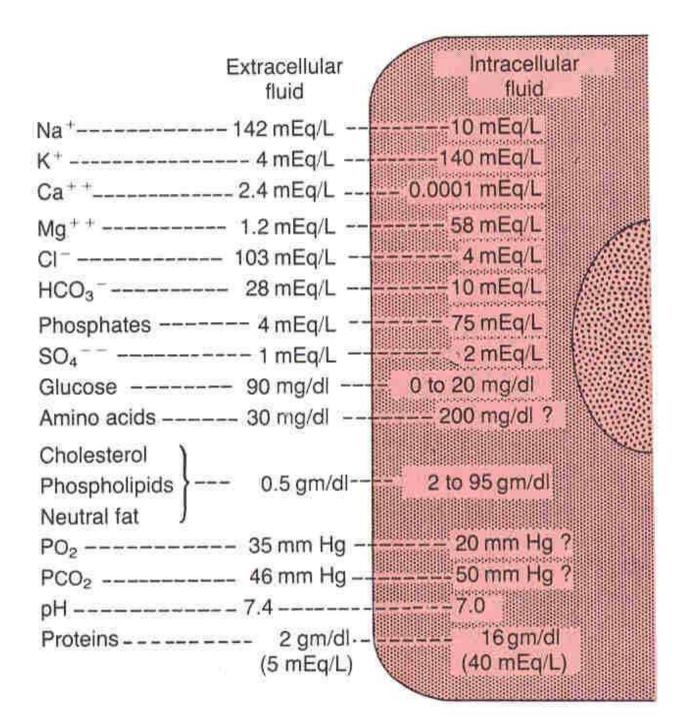
- Extracellular fluids are similar (except for the high protein content of plasma)
  - Sodium is the chief cation
  - Chloride is the major anion

Intracellular fluid has 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% above normal.

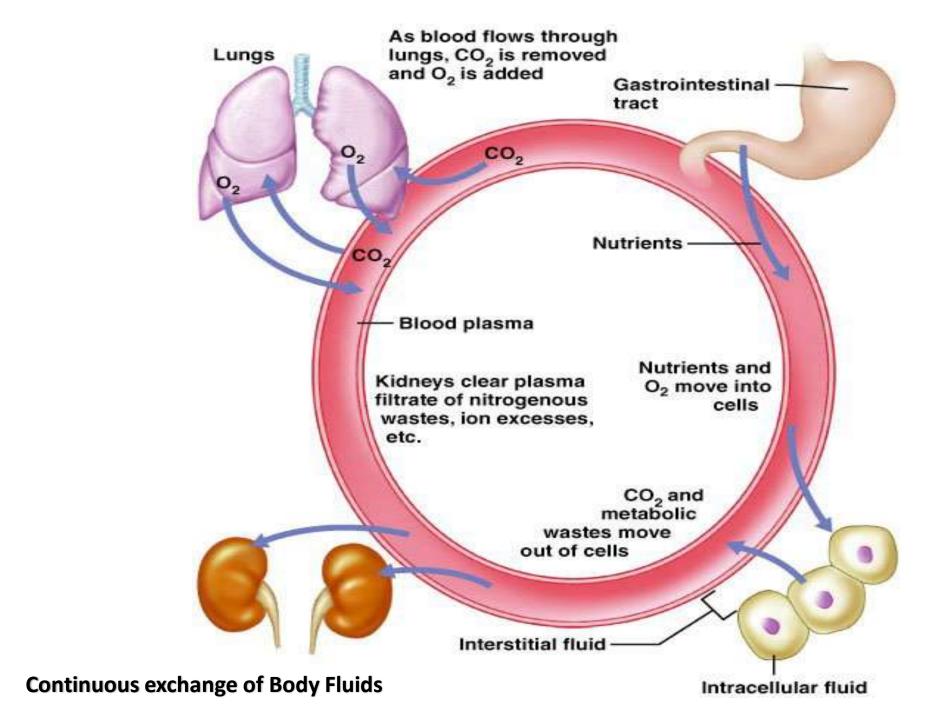
#### **Hypernatremia:**

increase in Na concentration in ECF.

#### **Hyponatremia:**

decrease in Na concentration in the ECF.





#### Mechanisms for Movement

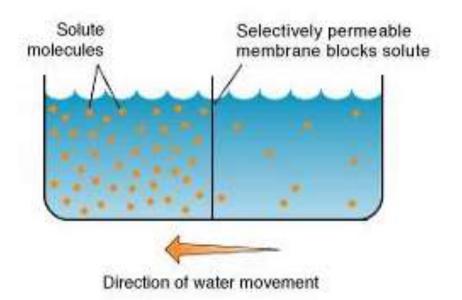
- 3 general mechanisms:
- 1. simple diffusion (passive)
- 2. Facilitated transport (passive)
- 3. Active transport

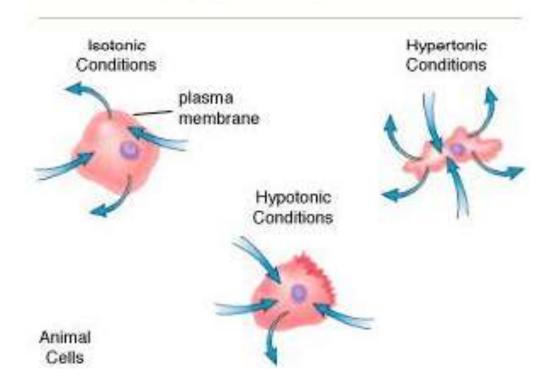
#### osmosis

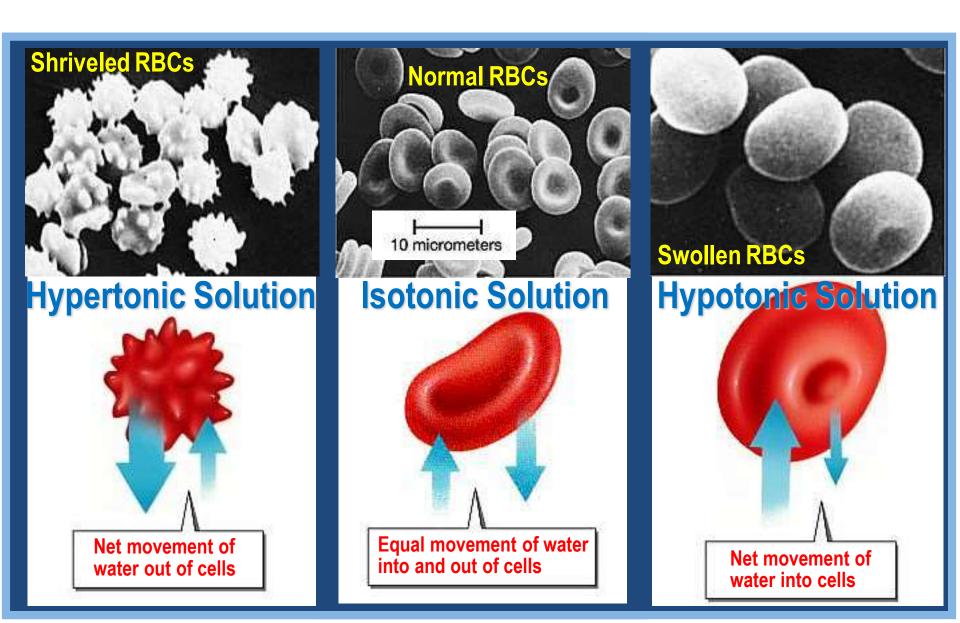
 Net diffusion of water from a region of high water concentration to region of low water concentration.

# 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







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

#### - Isotonic:

- same
- No change in cell volume

#### – <u>Hypotonic</u>:

- LESS SOLUTES outside cell
- LESS WATER IN CELL, more solutes in cell.
- over time, cell gains water

#### Isotonic solution :

- (not swell 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) 10.9%
- out is higher than in

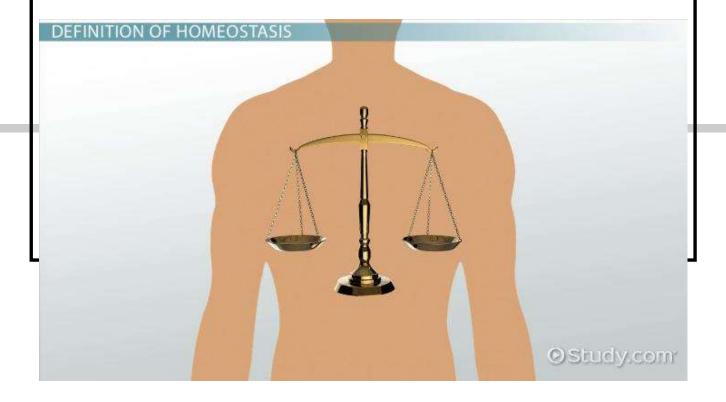
# Glucose and other solutions administered for nutritive purposes

 People who can not take adequate amount of food.

Slowly.

Prepared in isotonic solution.

## **Homeostasis**



#### 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.

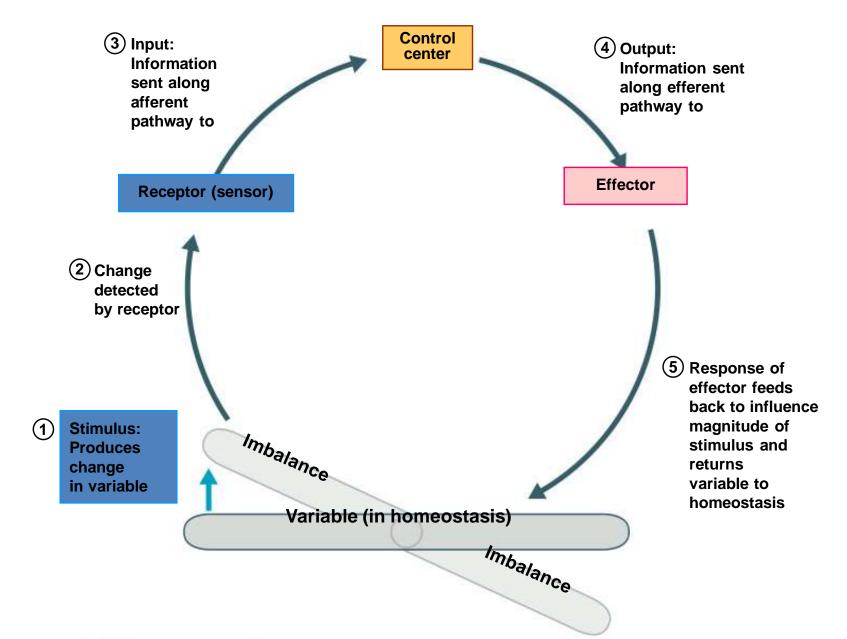
### 2. Hormonal system of regulation.

- Endocrine gland.

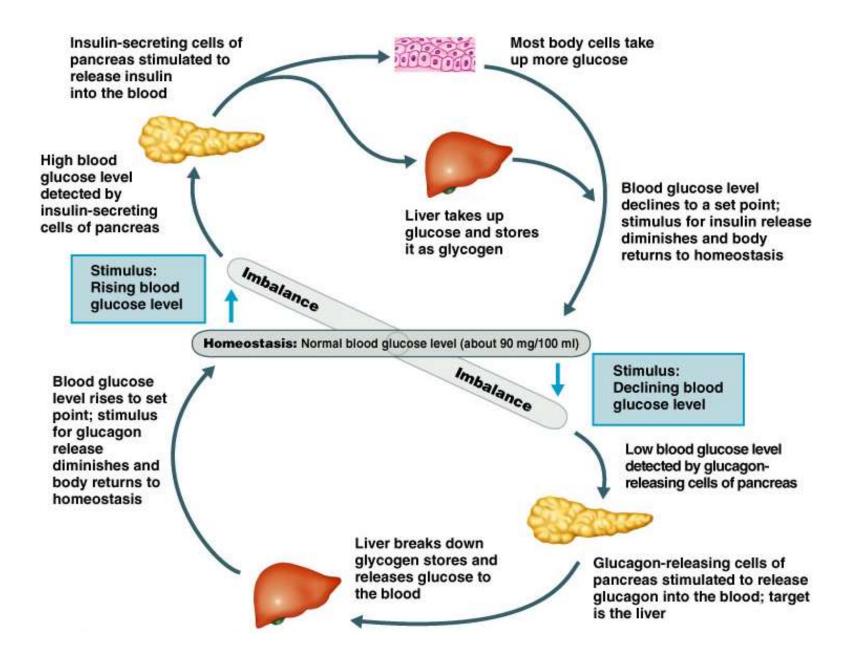
Pancreas, thyroid

e.g.: insulin control glucose level.

# Homeostatic Control Mechanisms



### Feedback



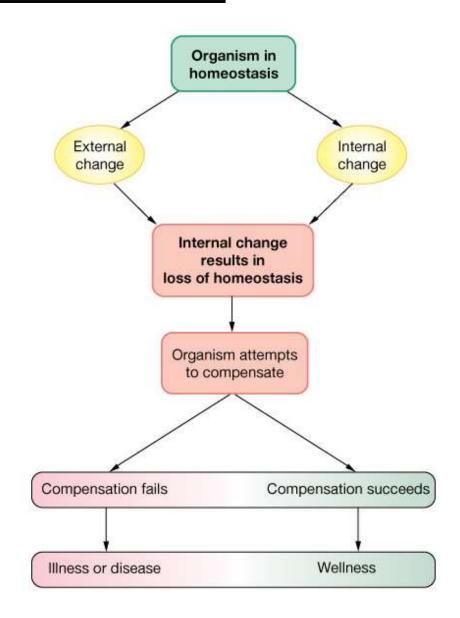
#### Homeostatic Imbalance

• Disturbance of homeostasis or the body's normal equilibrium.

#### **Homeostasis & Controls**

- Successful compensation
  - Homeostasis reestablished

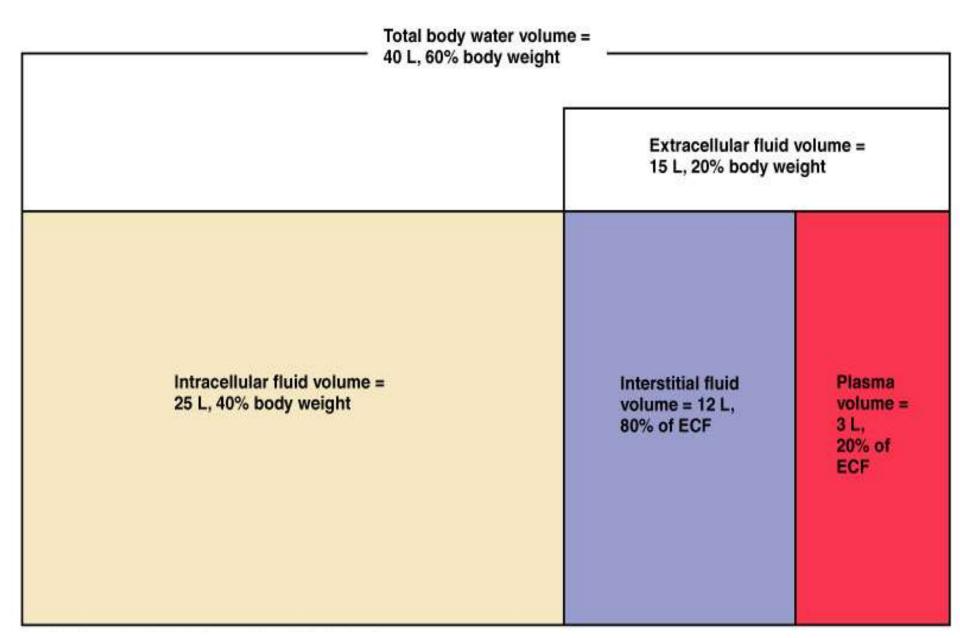
- Failure to compensate
  - Pathophysiology
    - Illness
    - Death



#### Lecture 4

# Changes in The Body Fluid Compartments (ECF & ICF) and Edema

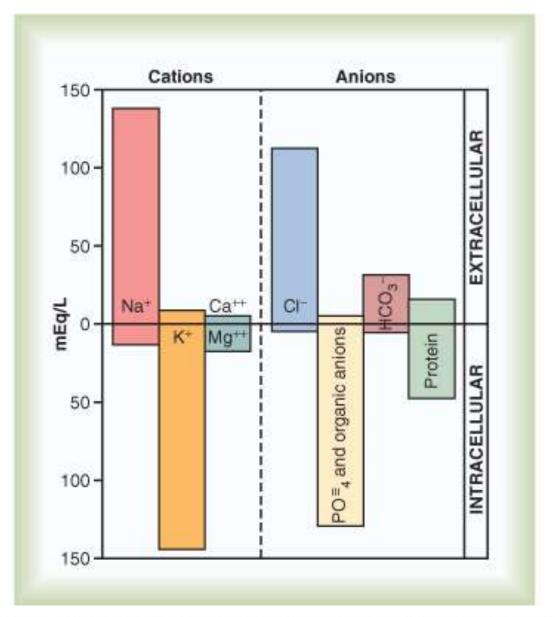
#### Fluid Compartments

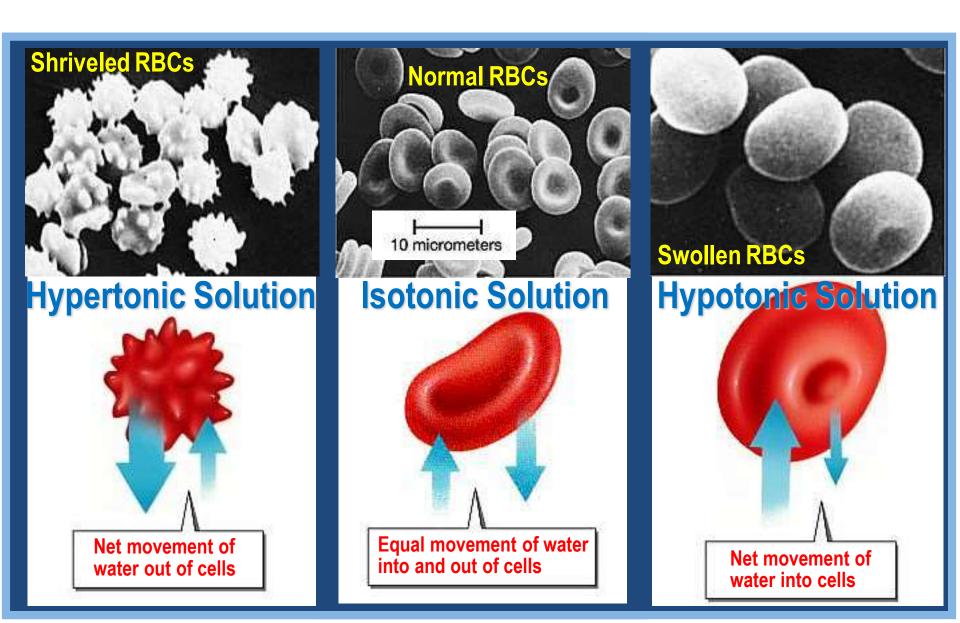


#### TABLE 20-2 OSMOLAR SUBSTANCES IN EXTRACELLULAR AND INTRACELLULAR FLUIDS

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Mg*	0.8	0.7	20
CI <sup>2</sup>	108	108	4
HCO,	24	28.3	10
HPO, H,PO,	2	2	11
50,	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	No.		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
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#### Constituents of ECF and ICF





# Volumes And Osmolarities of ECF and ICF In Abnormal States.

- Some factors can cause the change:
  - dehydration

- intravenous infusion (IV)

- abnormal sweating.
- etc..

Changes in volume :

1. Volume contraction.

2. Volume expansion.

# Changes in volume

#### **Volume contraction**

removing

1- isotonic solution.

2- *hypertonic* solution.

3- *hypotonic* solution.

### **Volume expansion**

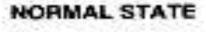
Adding

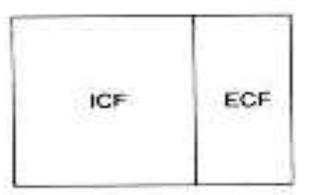
1- *isotonic* solution.

2- *hypertonic* solution.

3- *hypotonic* solution.

# 1- Loss of iso-osmotic fluid e.g. Diarrhea







# **Volume contraction:**

#### 1. Diarrhea.

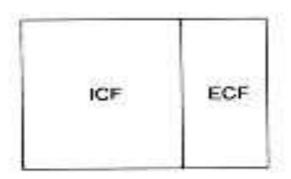
- osmolarity of fluid lost ≈ osmolarity of ECF

(loss of isosmotic fluid).

- ↓volume in ECF.

- ↓ arterial pressure.

# 2. Loss of hypotonic solution e.g. Water deprivation NORMAL STATE



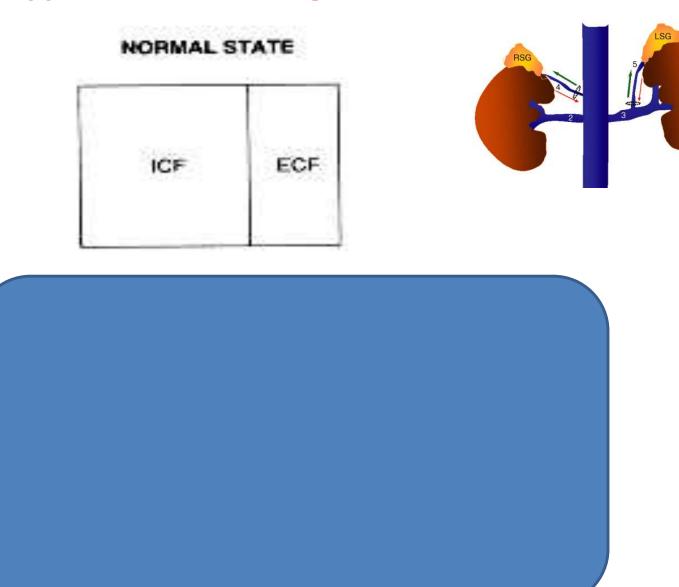
## 2. Water deprivation:

- Osmolarity and volume will change.

- Osmolarity in both ECF and ICF.

- Volume in both ECF and ICF.

### 3- Loss of hypertonic sol. e.g. Adrenal insufficiency

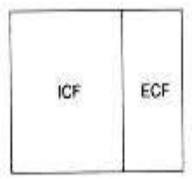


# 3. Loss of hypertonic solution e.g. Adrenal insufficiency:

i.e. Aldosterone deficiency.

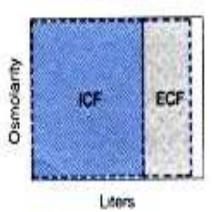
- ↓- Na<sup>+</sup> in the ECF.
- |- osmolarity in both .
- in ECF volume.

#### NORMAL STATE

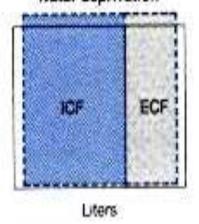


### **VOLUME CONTRACTION**

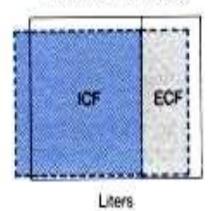
## Diarrhea



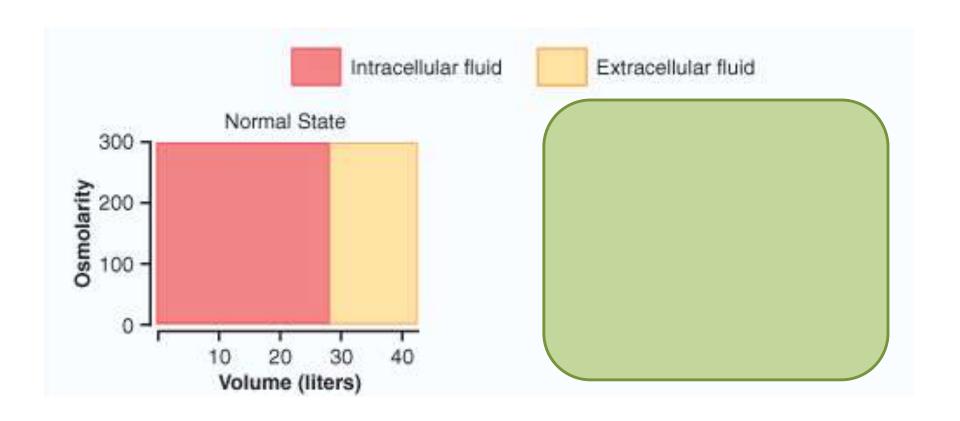
### Water deprivation



### Adrenal insufficiency



# **Volume Expansion**



## 1. Adding of isotonic NaCl.

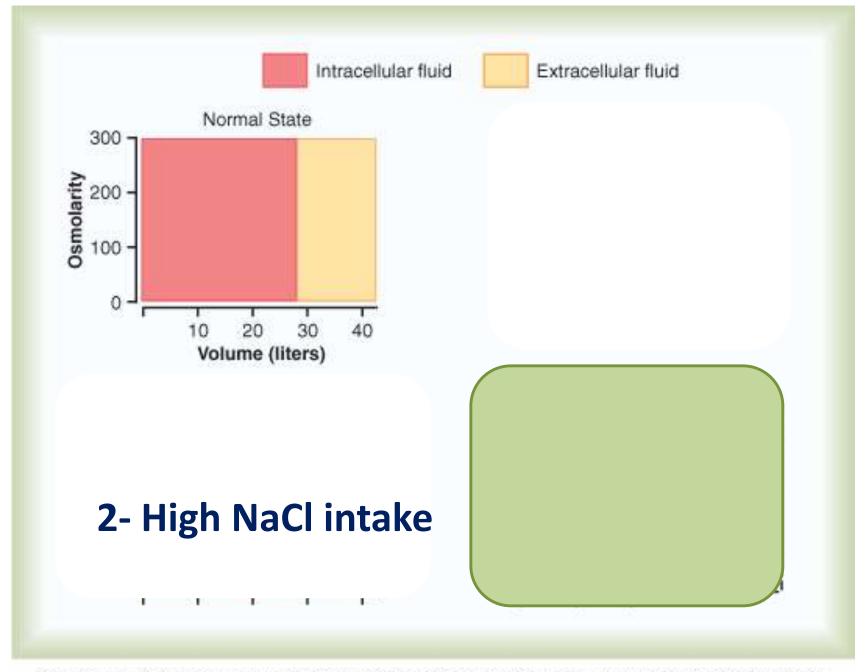
# **Volume Expansion**

1. Infusion of isotonic NaCl.

† - in ECF volume.

- No change in osmolarity.

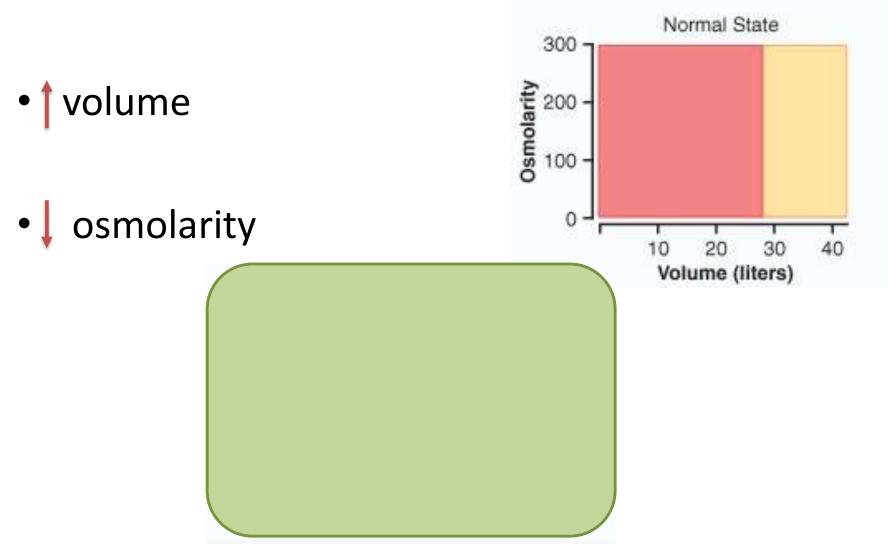
- Isomotic expansion .

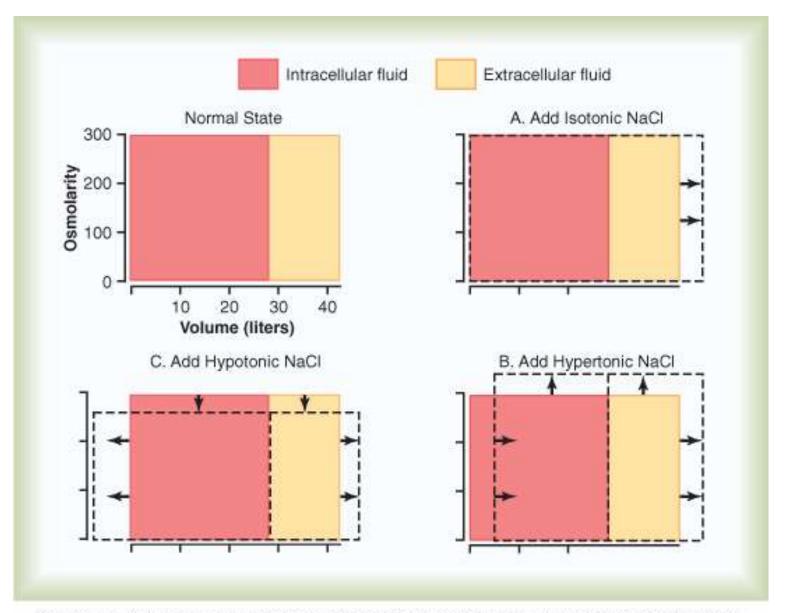


## 2. High NaCl intake.

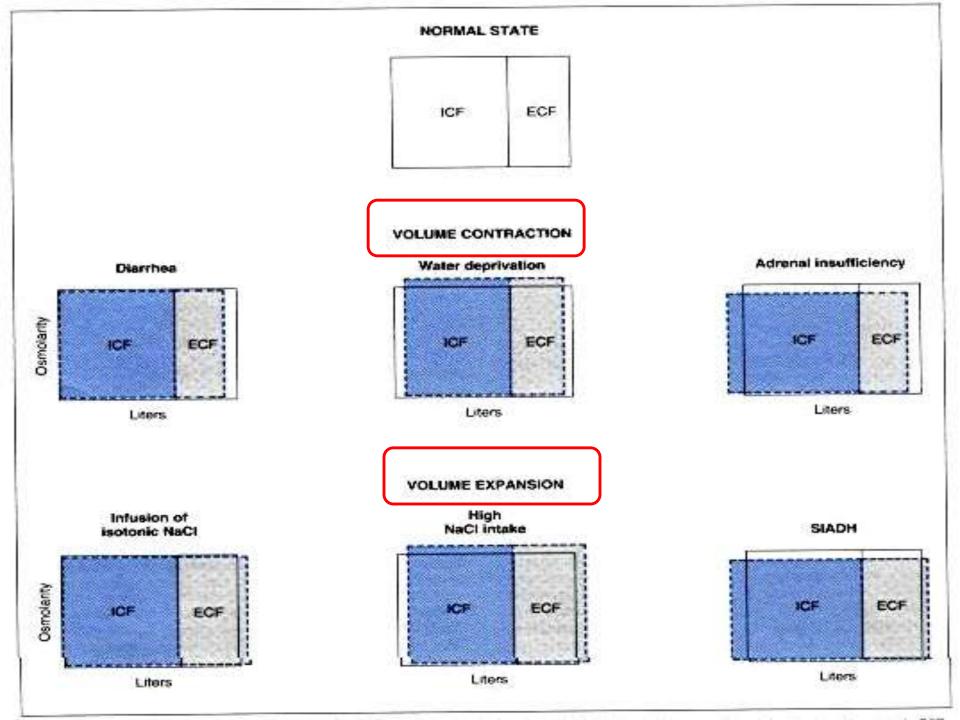
- teating salt.
- osmolarity in both.
- volume of ICF.
- volume of ECF.
- hyperosmotic volume expansion.

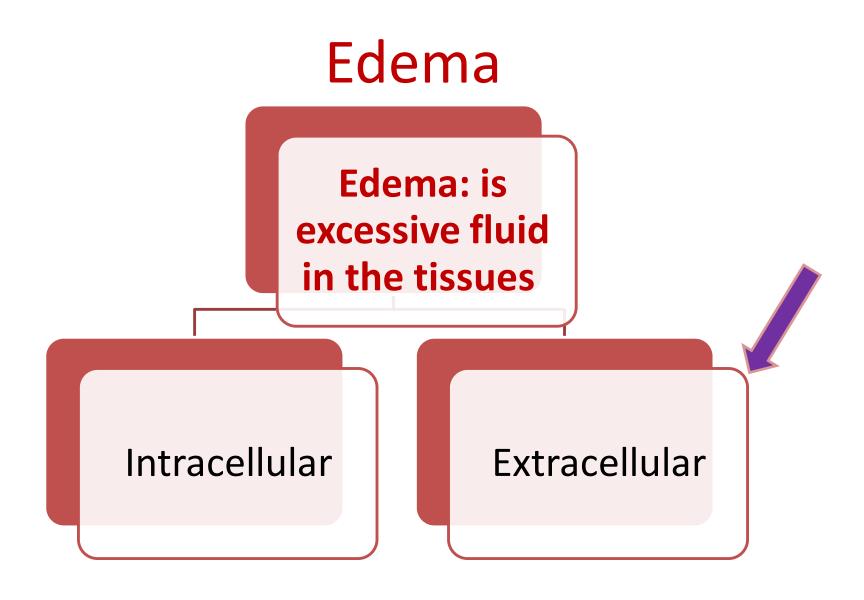
# 3- Adding hypotonic solution e.g. Syndrome of inappropriate antidiurtic hormone (SIADH)





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Edema occurs mainly in the ECF compartment

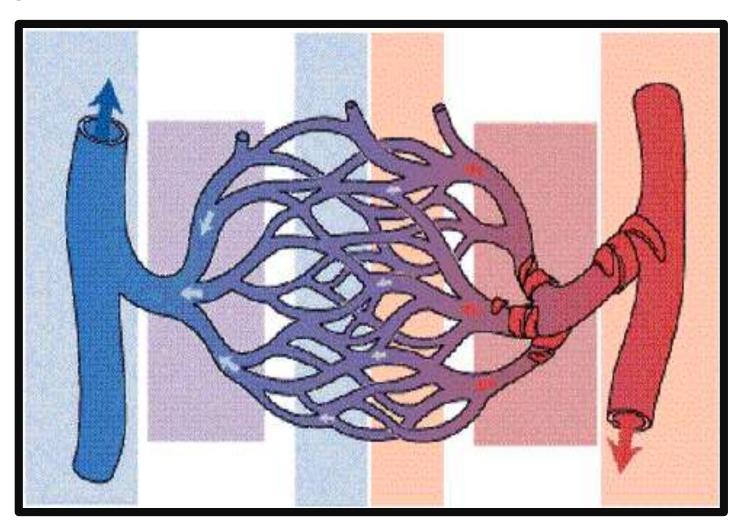






## **Extracellular Edema**

common clinical cause is excessive capillary fluid filtration.



## **Intracellular Edema:**

