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Human Physiology

Introduction

working definition of physiology:

Physiology is the study of the ***function*** of organisms as integrated systems of molecules, cells, tissues, and organs, in health and disease.

TEXTBOOK OF

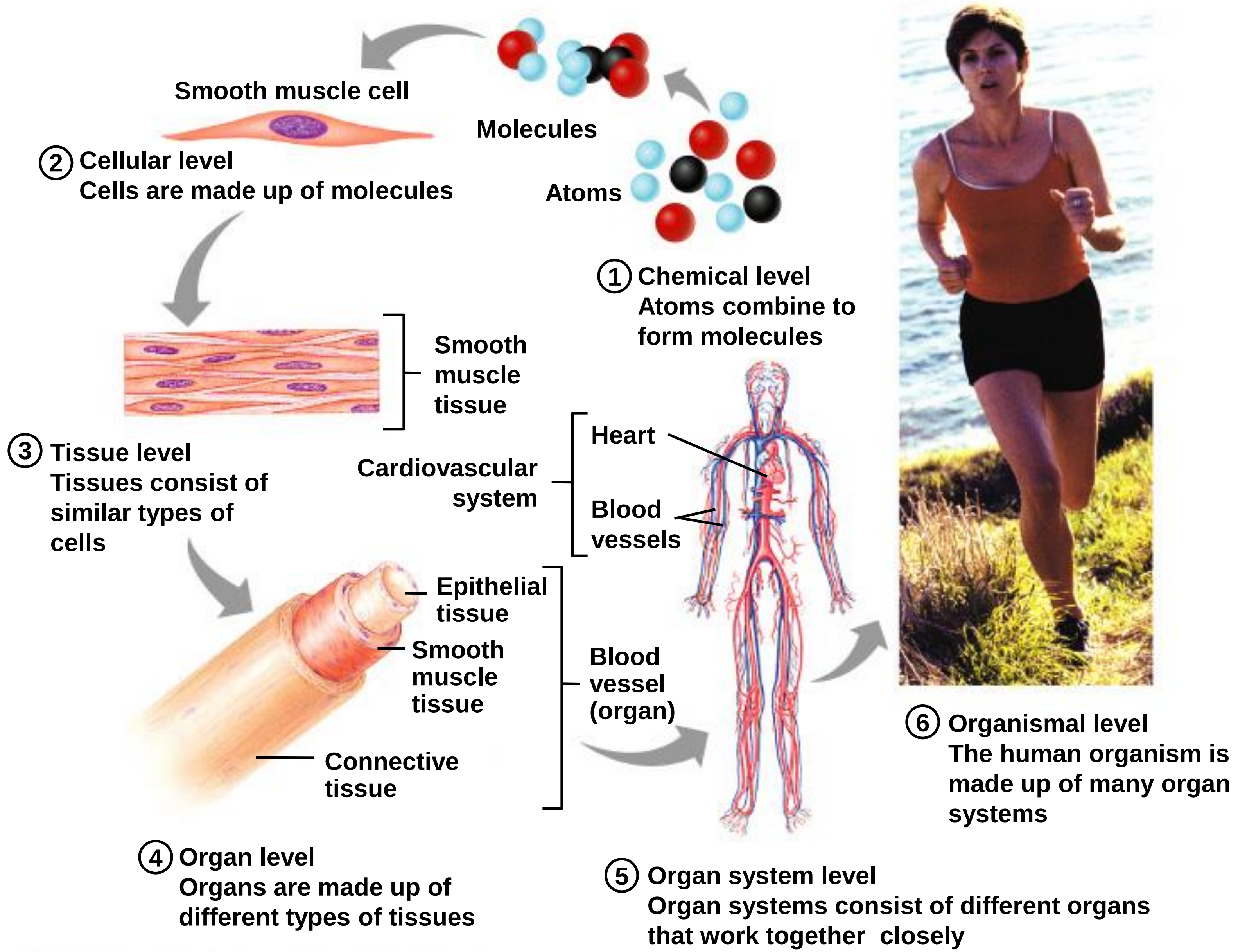
Medical Physiology

ELEVENTH EDITION

GUYTON & HALL

- **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 & Electrolytes

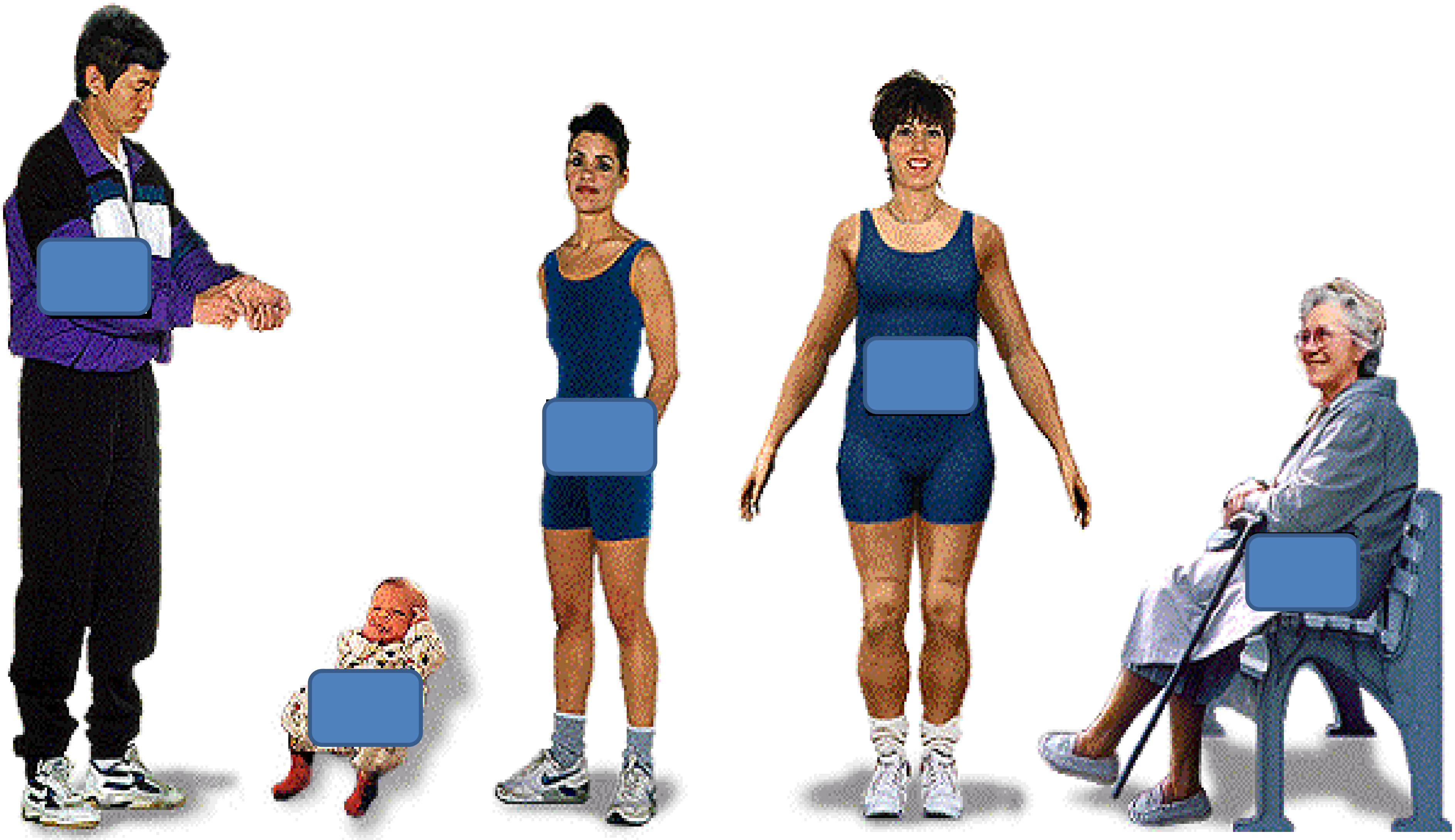
objectives

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 = L 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.

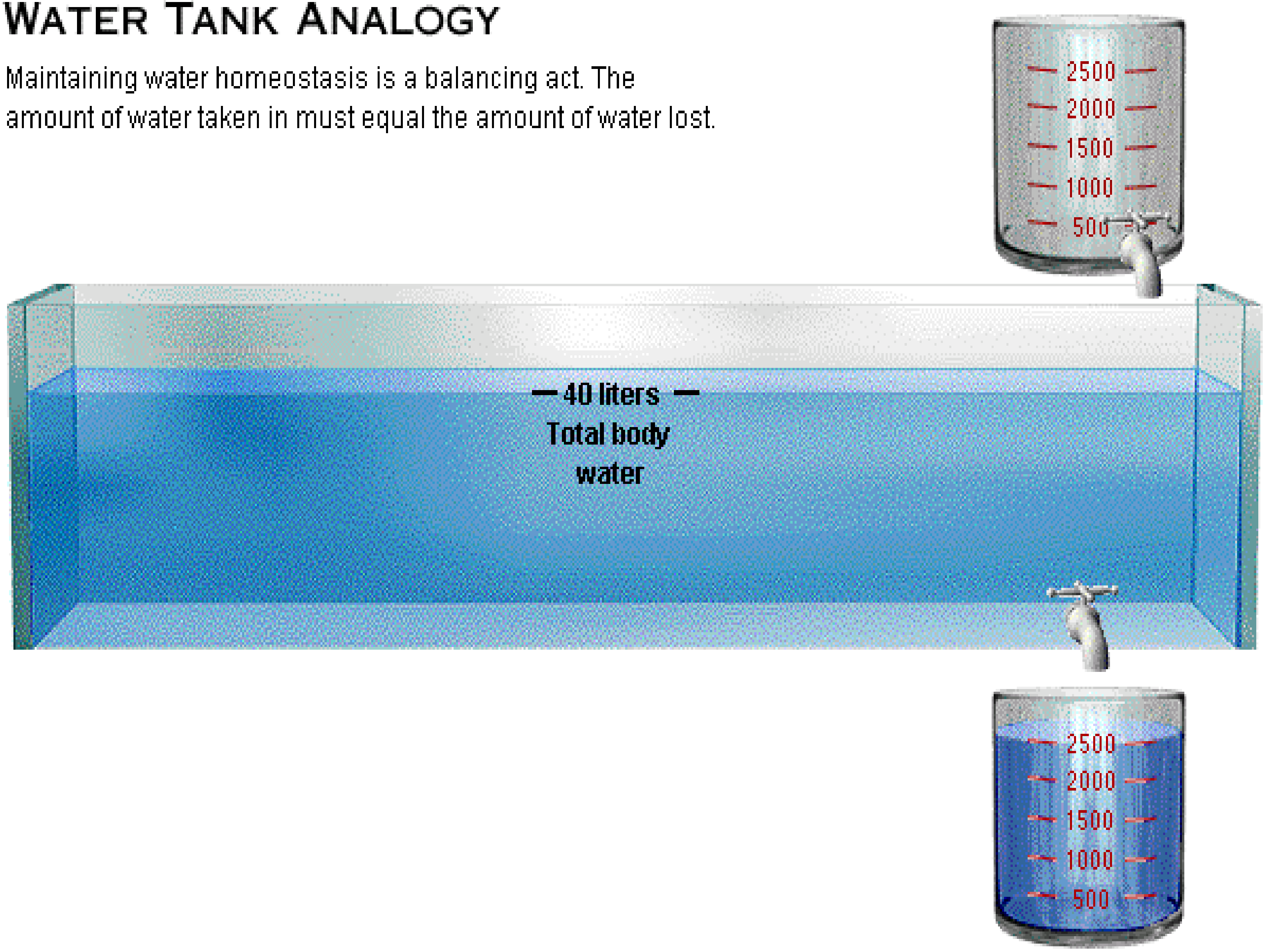
Daily intake of water

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

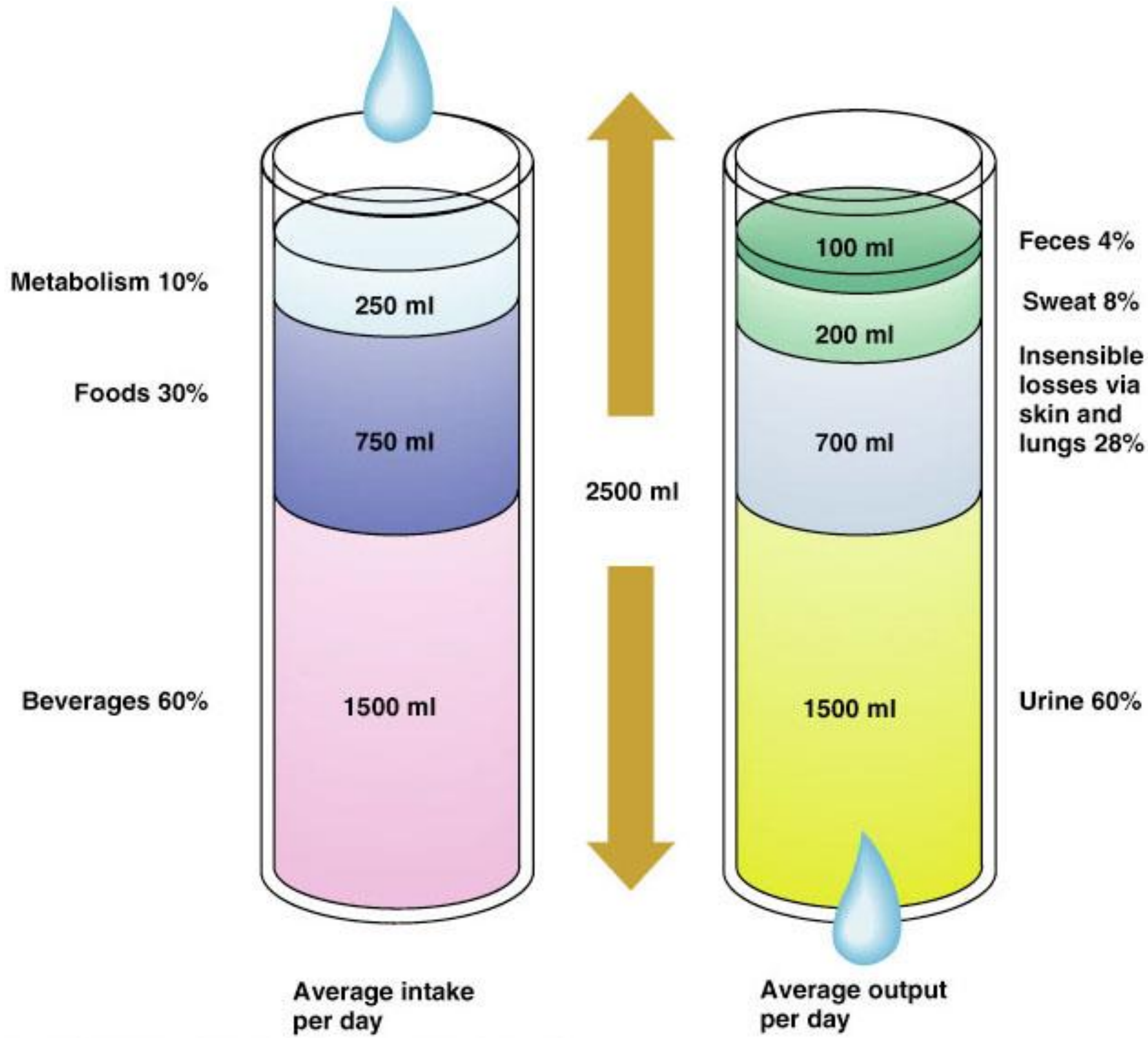
	Normal	Prolonged, Heavy Exercise
Intake		
Fluids ingested	2100	?
From metabolism	200	200
Total intake	2300	?
Output		
Insensible—Skin	350	350
Insensible—Lungs	350	650
Sweat	100	5000
Feces	100	100
Urine	1400	500
Total output	2300	6600

Water 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:

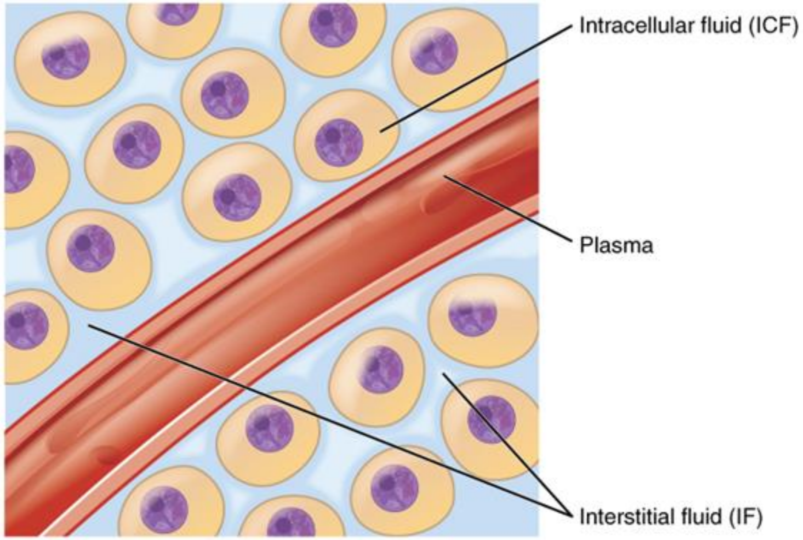
- Age
- Sex
- Body fat
- Climate
- Physical activity

Pathological factors:

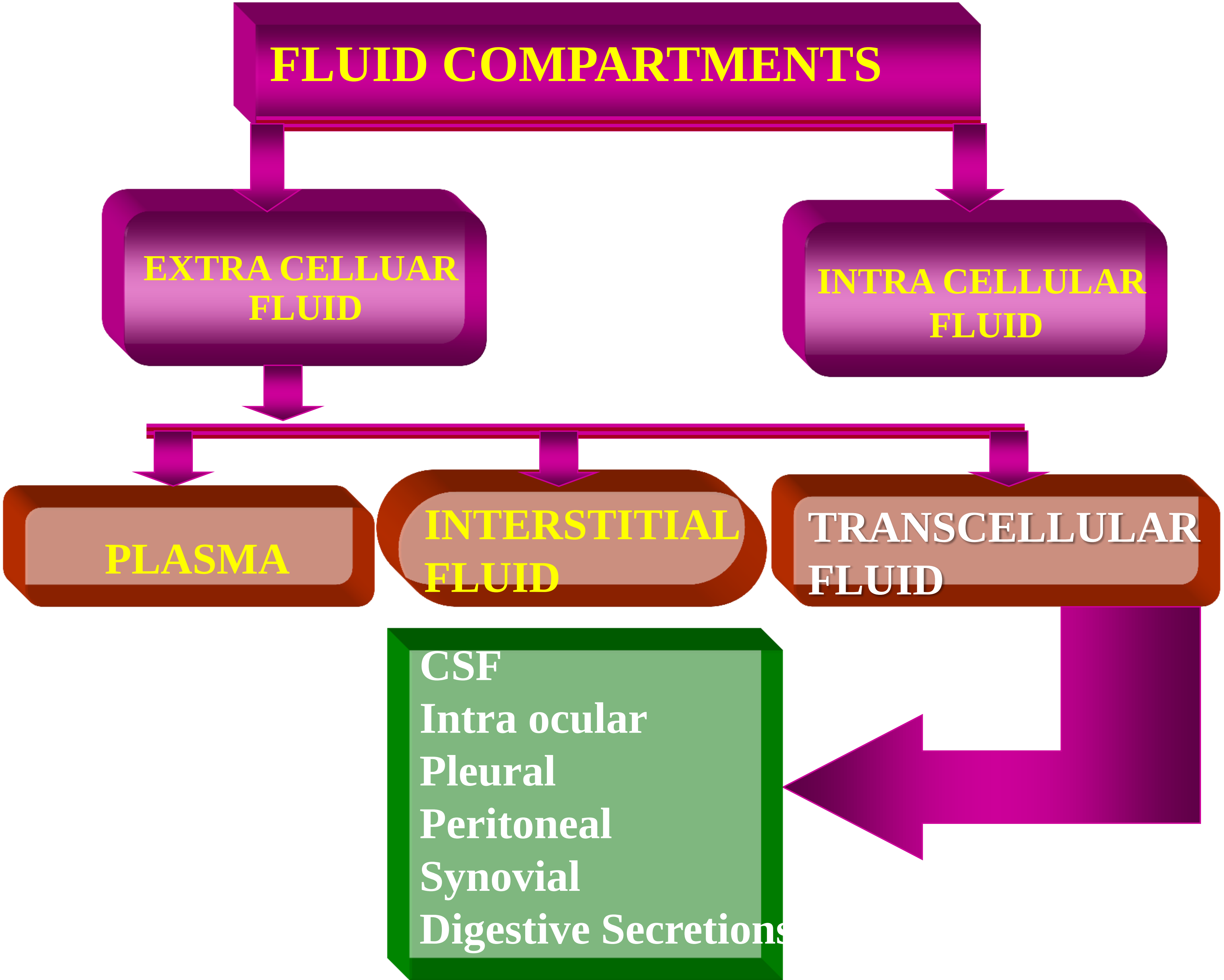
- Vomiting
- Diarrhea
- Diseases with excessive loss of water (DM, excessive sweating,….
- Blood loss

Fluid Compartments

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



Fluid Compartments


FLUID COMPARTMENTS
EXTRA CELLUAR FLUID
INTRA CELLULAR FLUID
PLASMA
INTERSTITIAL FLUID
TRANSCELLULAR FLUID
CSF
Intra ocular
Pleural
Peritoneal
Synovial
Digestive Secretions

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

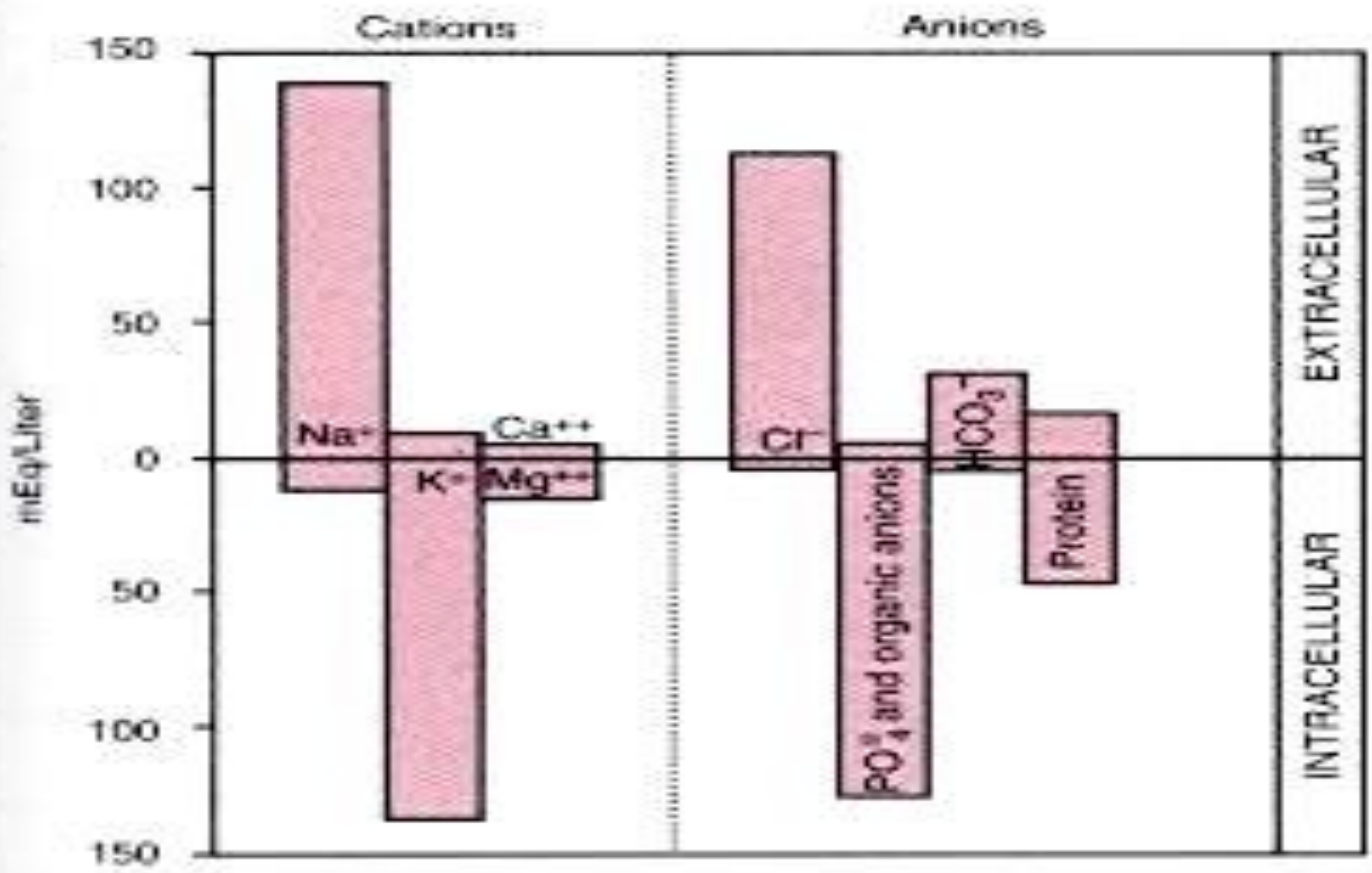


TABLE 20–2 OSMOLAR SUBSTANCES IN EXTRACELLULAR AND INTRACELLULAR FLUIDS

	Plasma (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

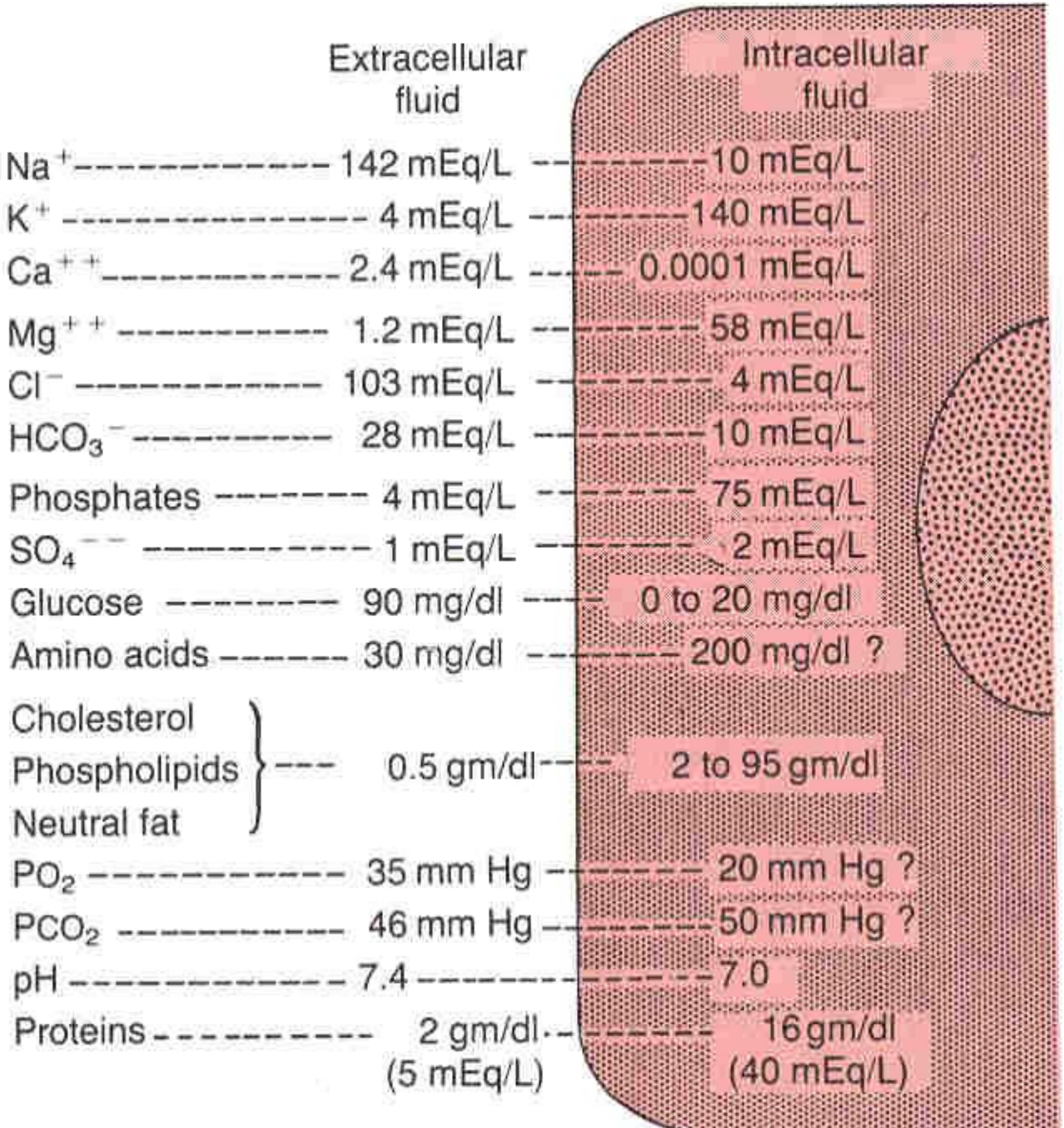
- Each fluid compartment of the body has a distinctive pattern of electrolytes.

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

- **Intracellular 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)



Extracellular fluid
Intracellular fluid
Na+ 142 mEq/L 10 mEq/L
K+ 4 mEq/L 140 mEq/L
Ca++ 2.4 mEq/L 0.0001 mEq/L
Mg++ 1.2 mEq/L 58 mEq/L
Cl− 103 mEq/L 4 mEq/L
HCO3− 28 mEq/L 10 mEq/L
Phosphates 4 mEq/L 75 mEq/L
SO4−− 1 mEq/L 2 mEq/L
Glucose 90 mg/dl 0 to 20 mg/dl
Amino acids 30 mg/dl 200 mg/dl ?
Cholesterol
Phospholipids 0.5 gm/dl 2 to 95 gm/dl
Neutral fat
PO2 35 mm Hg 20 mm Hg ?
PCO2 46 mm Hg 50 mm Hg ?
pH 7.4 7.0
Proteins 2 gm/dl (5 mEq/L) 16 gm/dl (40 mEq/L)

- **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.**

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Lecture 3

Homeostasis

Fluid Compartments

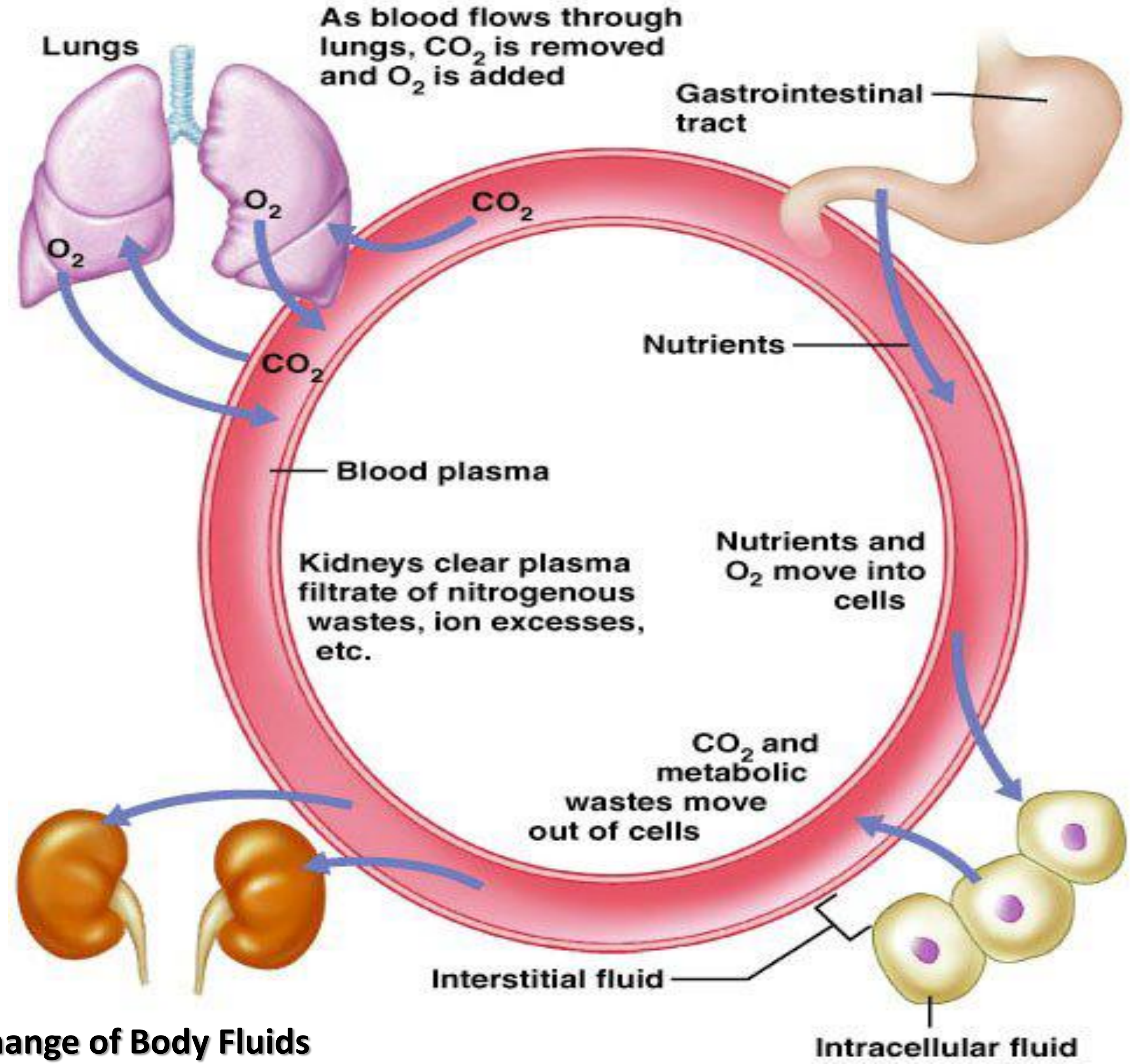
Extracellular and Intracellular Fluids

- Ion fluxes are restricted and move selectively by active transport.

- Nutrients, respiratory gases, and wastes move Unidirectionally.

- Plasma is the only fluid that circulates throughout the body and links external and internal Environments

- Osmolalities of all body fluids are equal; changes in solute concentrations are quickly followed by osmotic changes



Continuous exchange of Body Fluids

Mechanisms for Movement

- **3 general mechanisms:**

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

osmosis

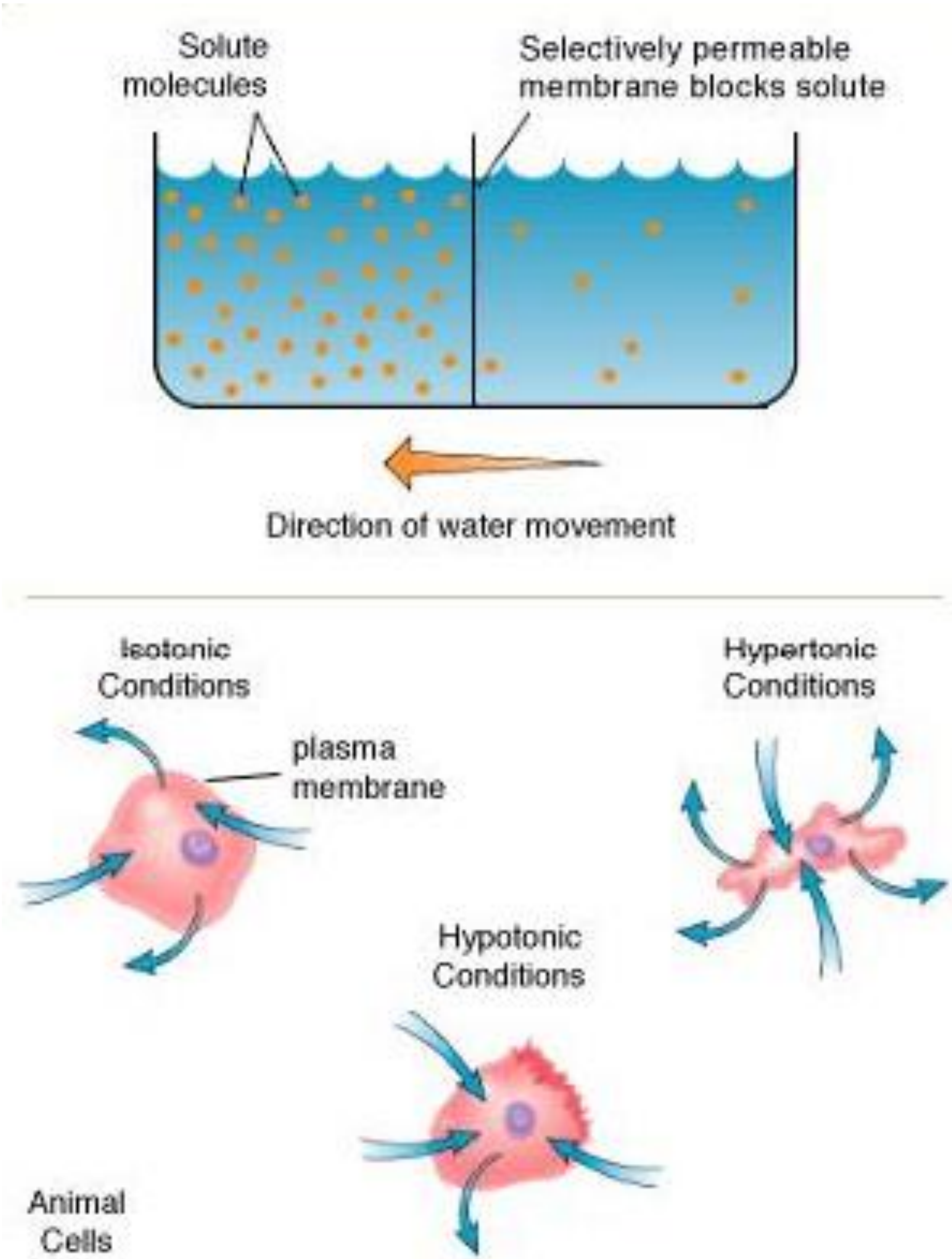
- **Net diffusion of water from a region of high water concentration to region of low water concentration.**

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.**

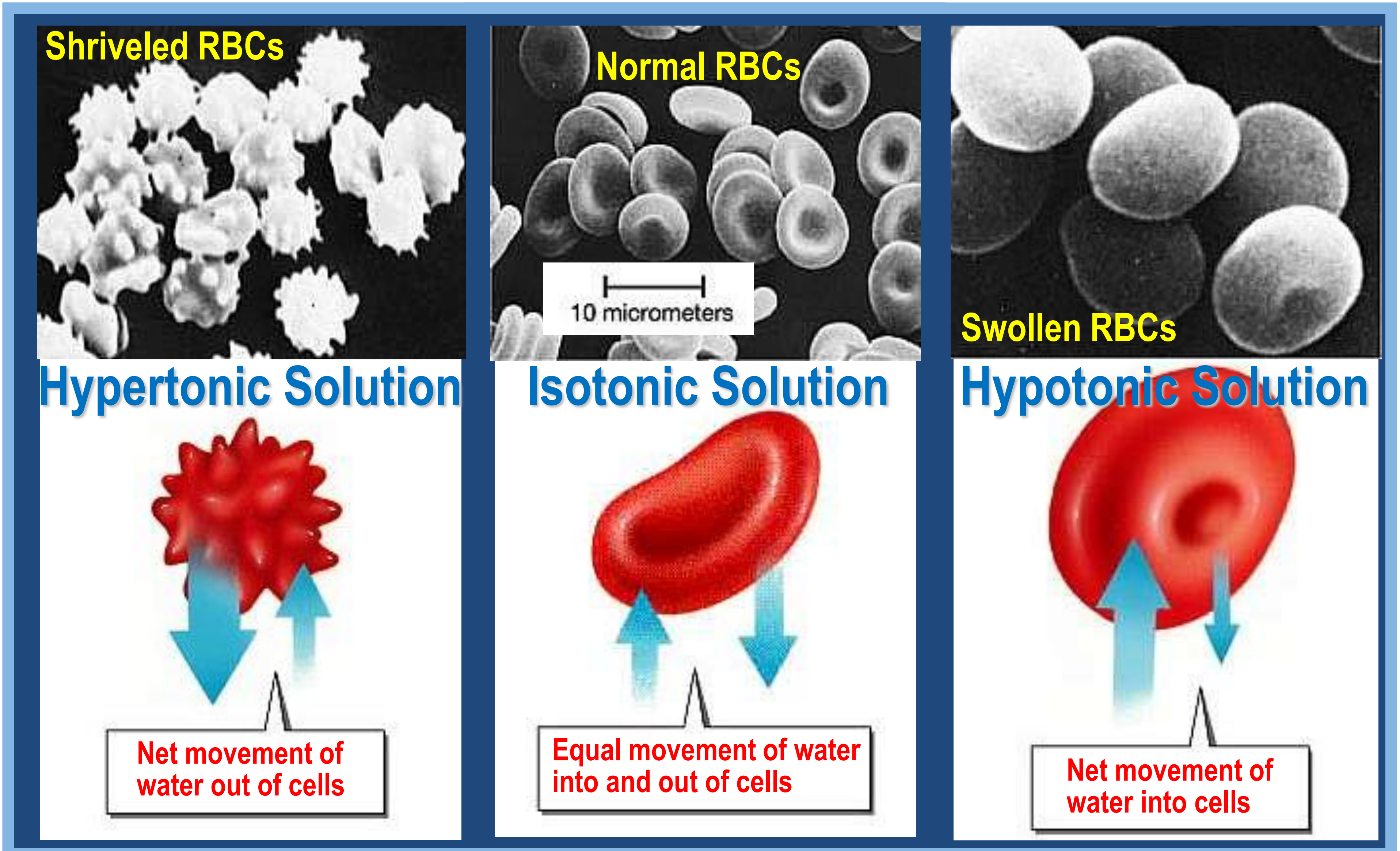
- **Intracellular osmolarity = extracellular osmolarity .**
- **≈ 300 mosm/L**

Osmosis



Solute molecules
Selectively permeable membrane blocks solute
Direction of water movement
Isotonic Conditions
plasma membrane
Hypertonic Conditions
Hypotonic Conditions
Animal Cells

Osmosis


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

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 :

- (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) ↑ 0.9%
- 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 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.**

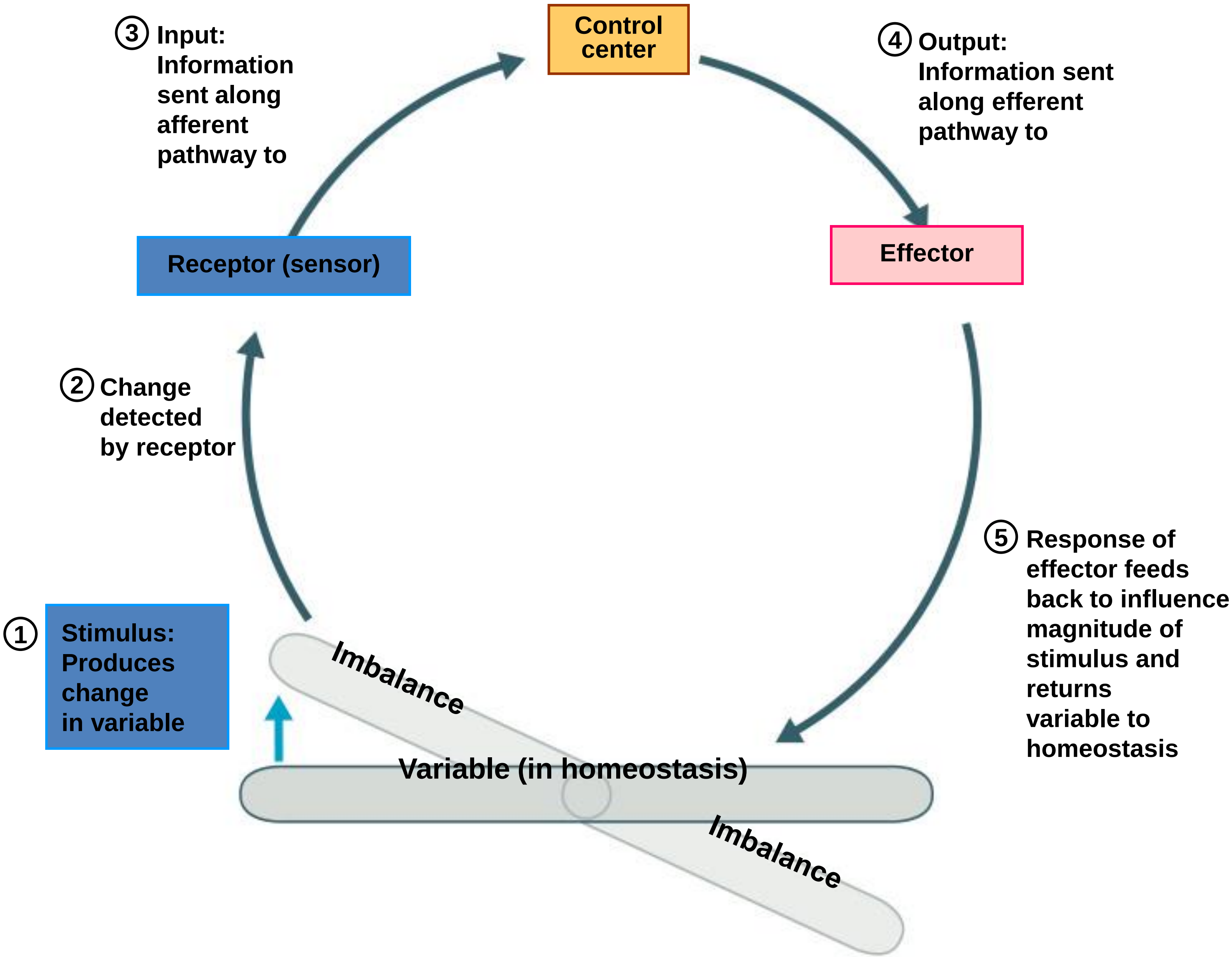
2. Hormonal system of regulation.

- **Endocrine gland.**

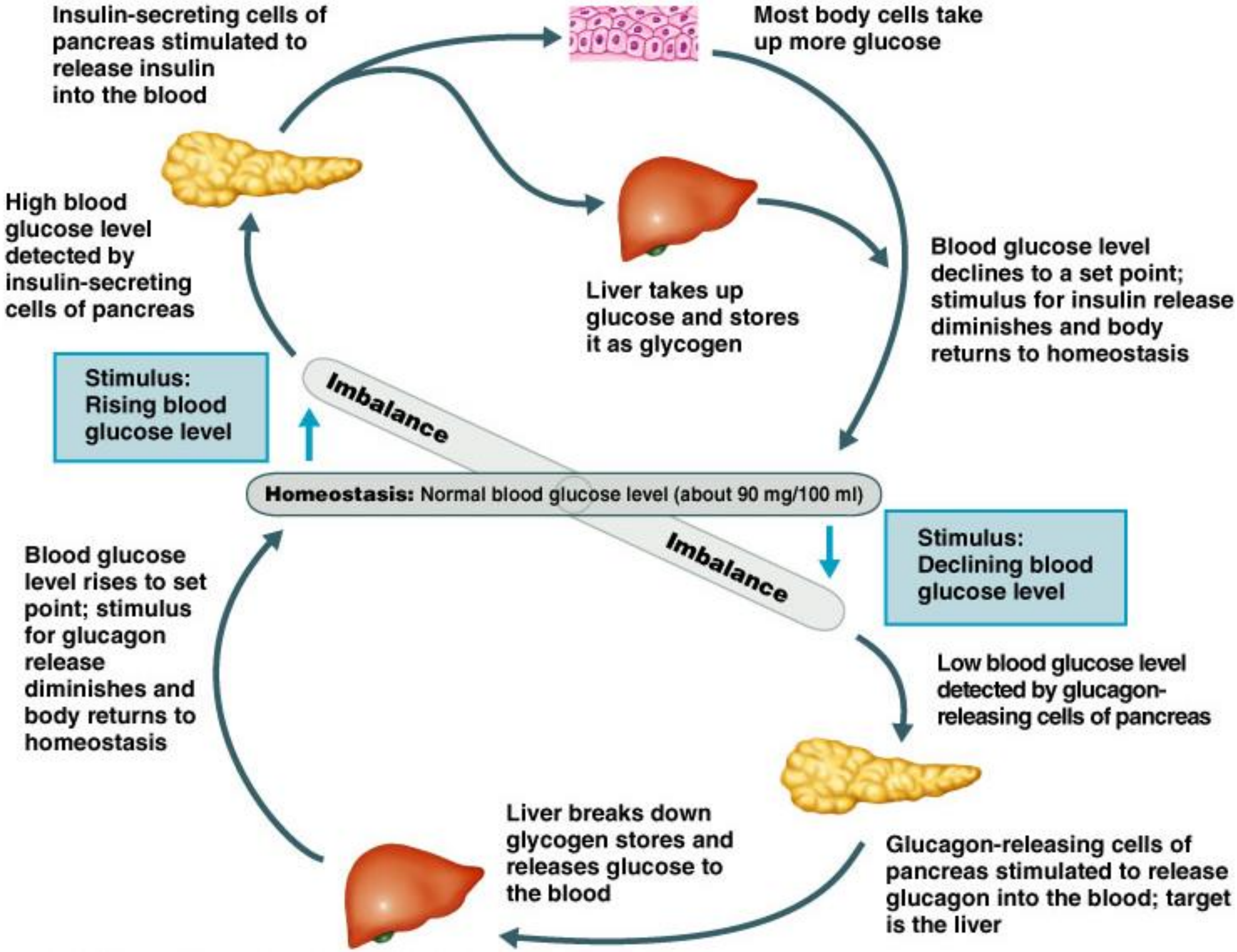
  Pancreas, thyroid

e.g. : insulin control glucose level.

Homeostatic Control Mechanisms



Feedback



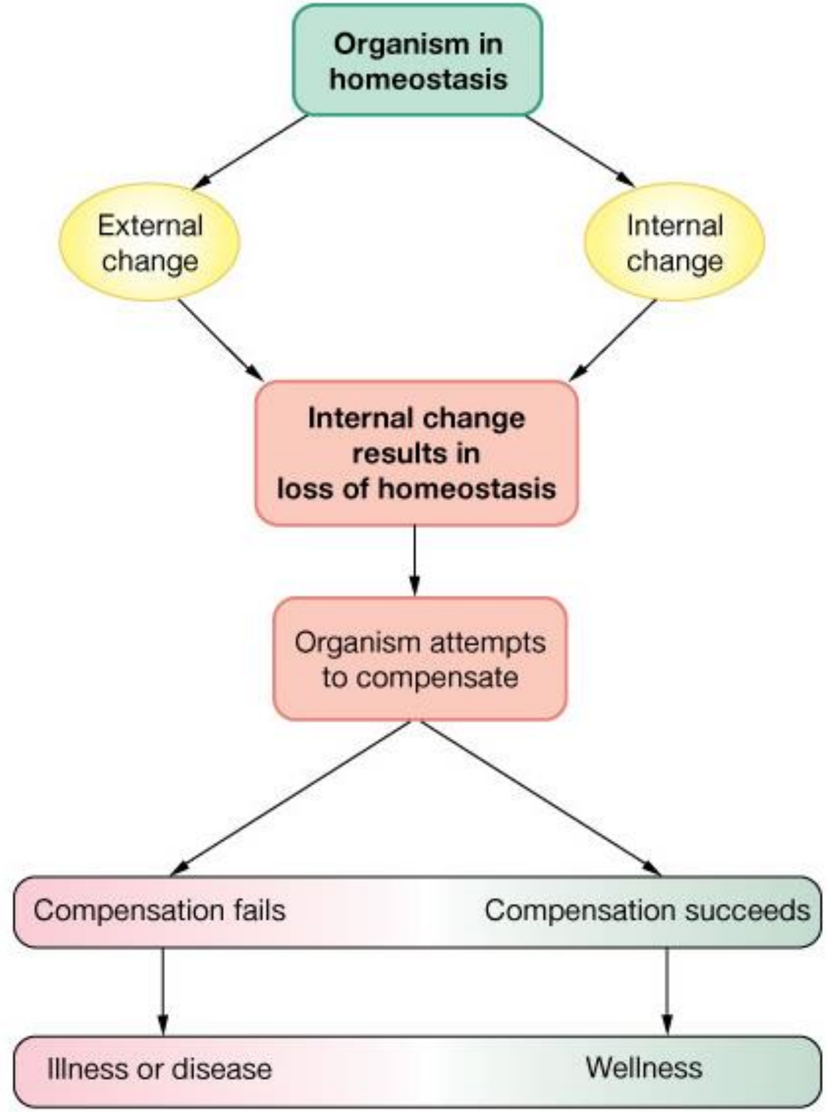
Insulin-secreting cells of pancreas stimulated to release insulin into the blood
Most body cells take up more glucose
High blood glucose level detected by insulin-secreting cells of pancreas
Liver takes up glucose and stores it as glycogen
Blood glucose level declines to a set point; stimulus for insulin release diminishes and body returns to homeostasis
Stimulus: Rising blood glucose level
Imbalance
Homeostasis: Normal blood glucose level (about 90 mg/100 ml)
Imbalance
Stimulus: Declining blood glucose level
Blood glucose level rises to set point; stimulus for glucagon release diminishes and body returns to homeostasis
Low blood glucose level detected by glucagon-releasing cells of pancreas
Liver breaks down glycogen stores and releases glucose to the blood
Glucagon-releasing cells of pancreas stimulated to release glucagon into the blood; target is the liver

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

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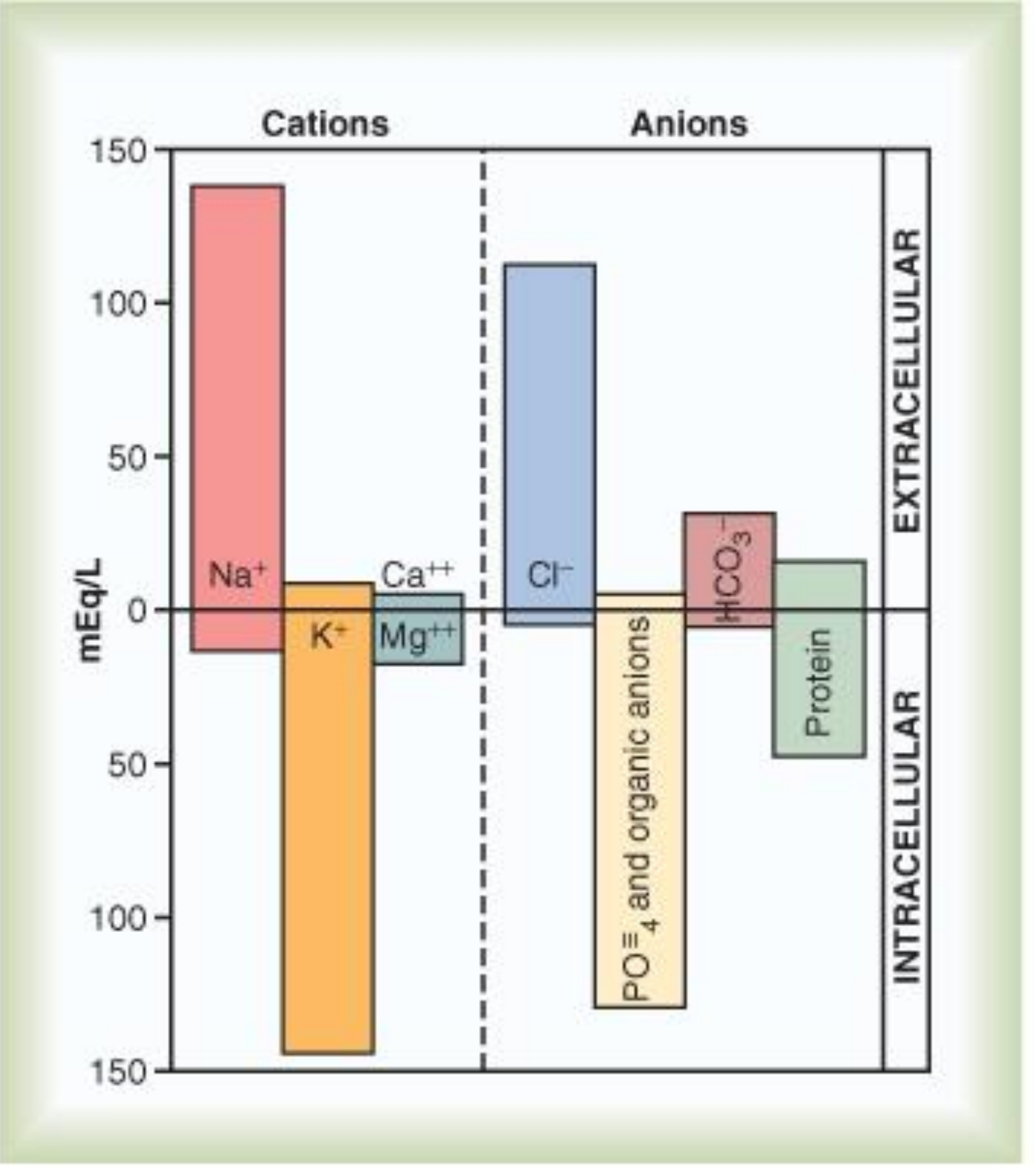
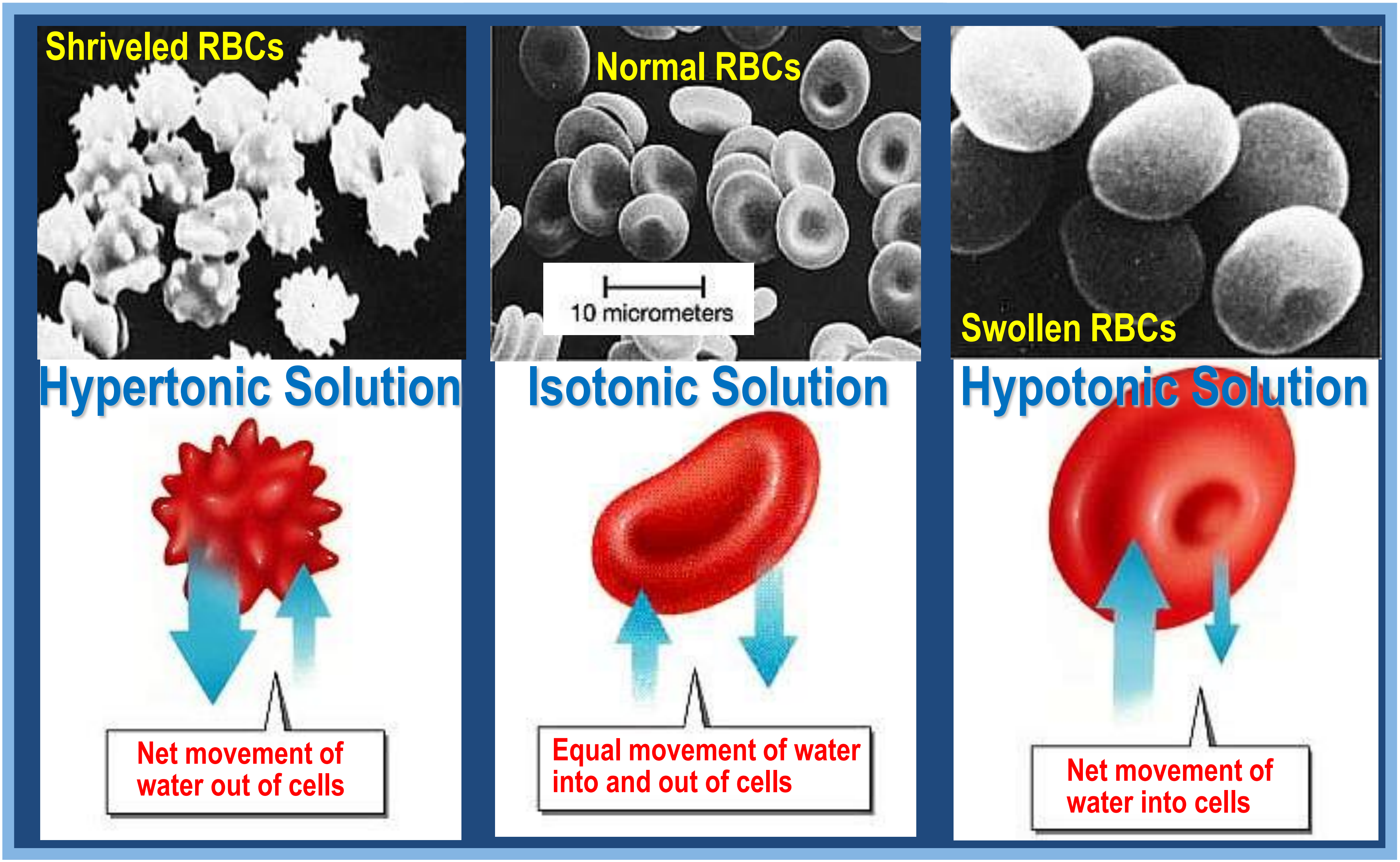
Constituents of ECF and ICF



Osmosis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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

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

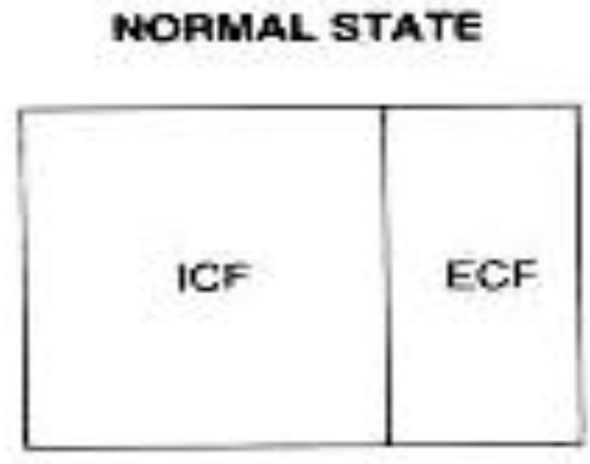
Adding

1- ***isotonic*** solution.

2- ***hypertonic*** solution.

3- ***hypotonic*** solution.

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



Volume contraction:

1. Diarrhea.

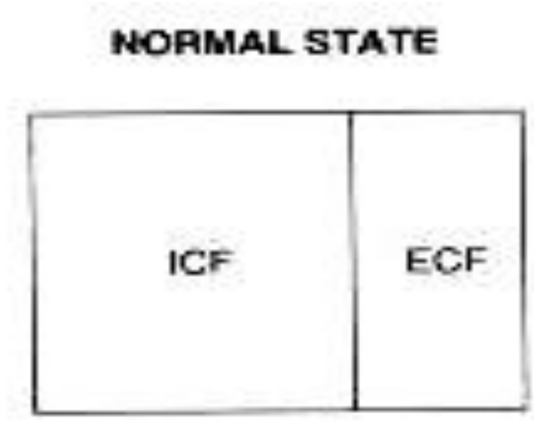
- osmolarity of fluid lost ≈ osmolarity of ECF

(loss of isosmotic fluid).

- ↓ volume in ECF.

- ↓ arterial pressure.

2. Loss of hypotonic solution
e.g. Water deprivation



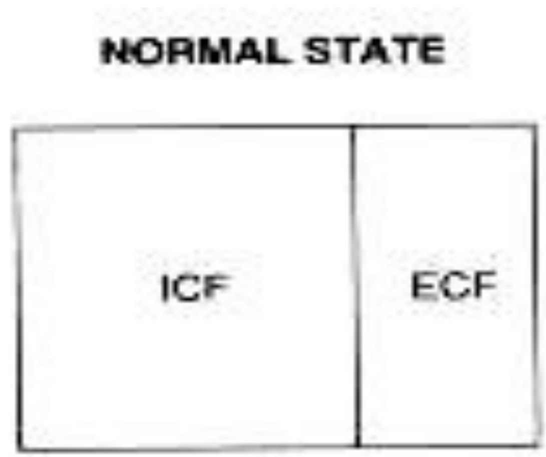
2. Water deprivation :

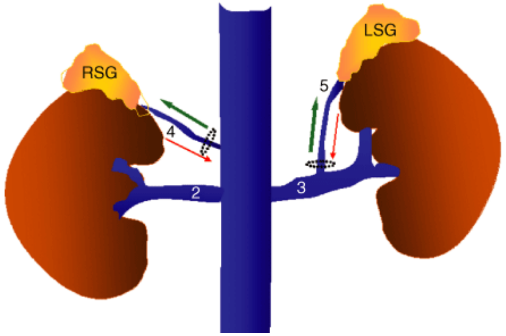
- Osmolarity and volume will change .

- ↑ Osmolarity in both ECF and ICF.

- ↓ Volume in both ECF and ICF.

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





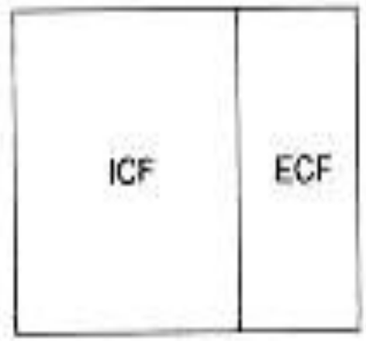
3. **Loss of hypertonic solution**

e.g. Adrenal insufficiency:

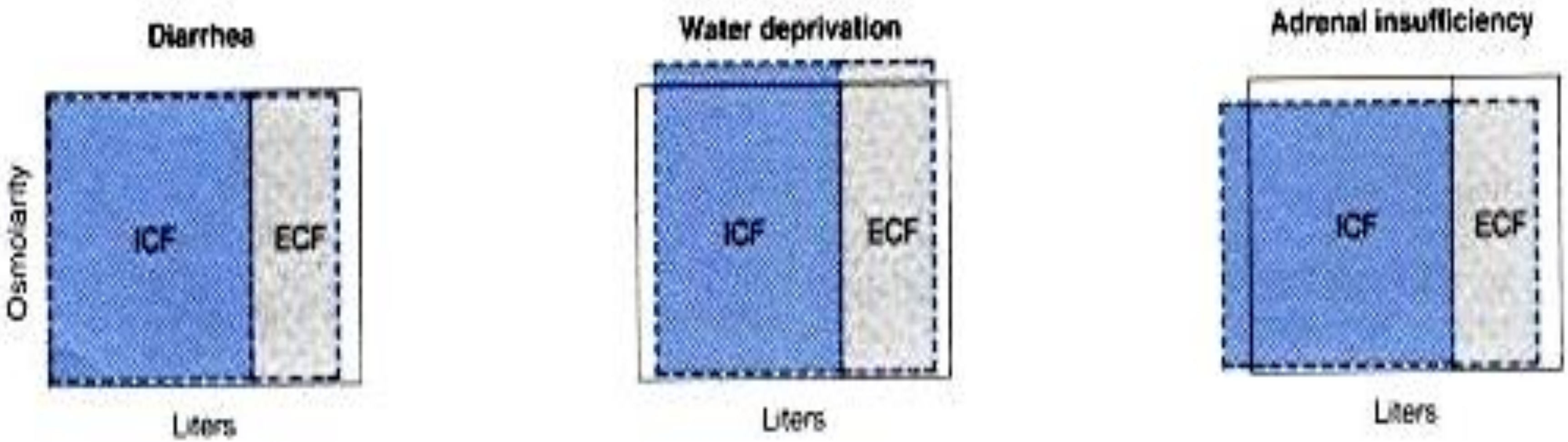
i.e. Aldosterone deficiency.

- ↓ - Na^+ in the ECF.
- ↓ - osmolarity in both .
- ↓ - in ECF volume.
- ↑ - in ICF volume.

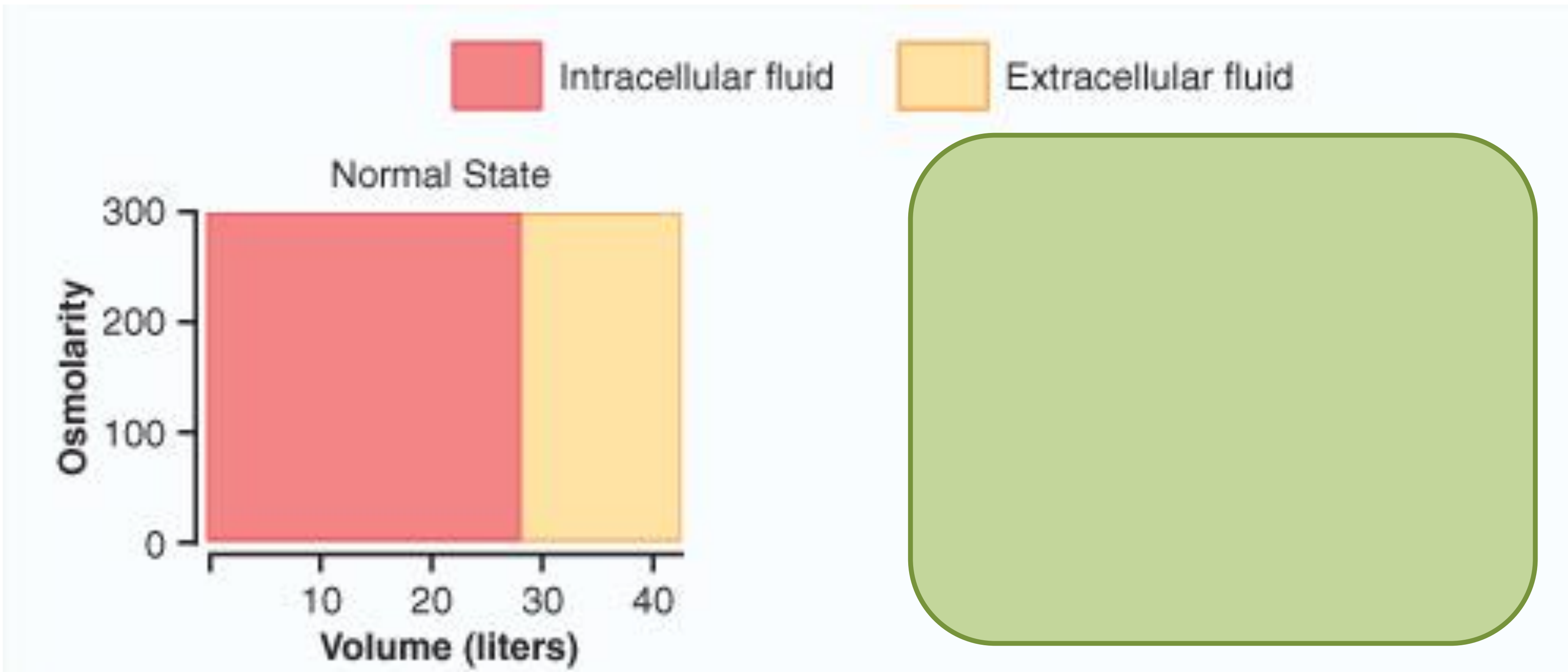
NORMAL STATE



VOLUME CONTRACTION



Volume Expansion



1. **Adding of isotonic NaCl.**

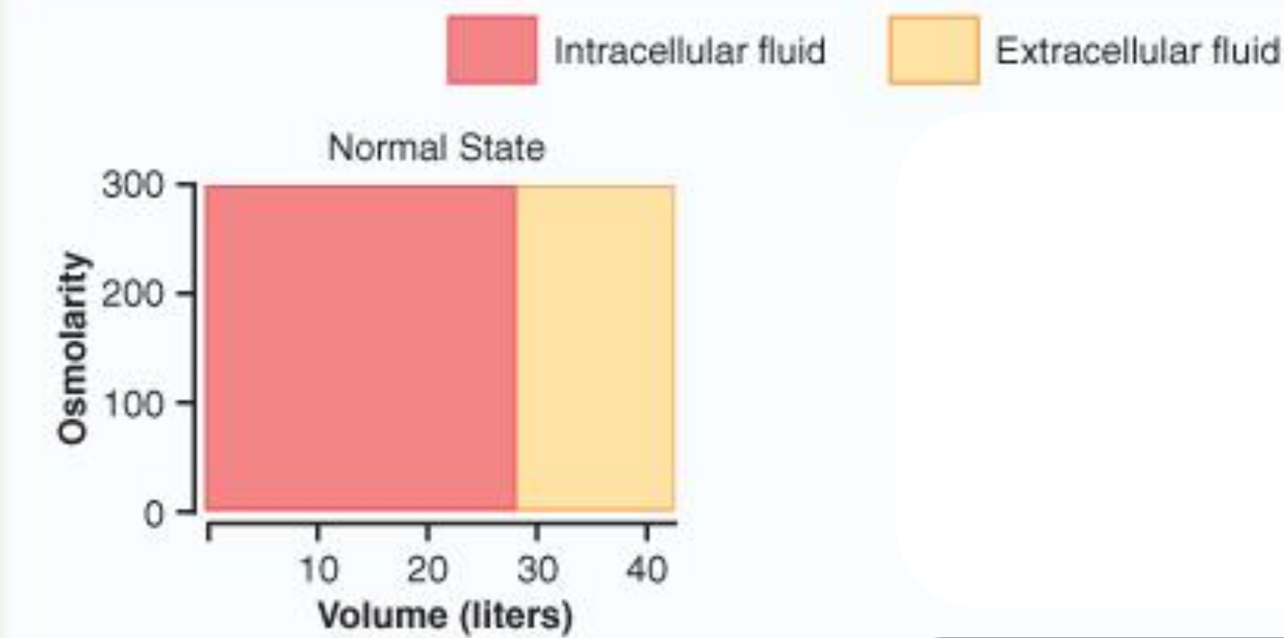
Volume Expansion

1. **Infusion of isotonic NaCl.**

↑ - in ECF volume.

- No change in osmolarity.

- ***Isomotic expansion*** .



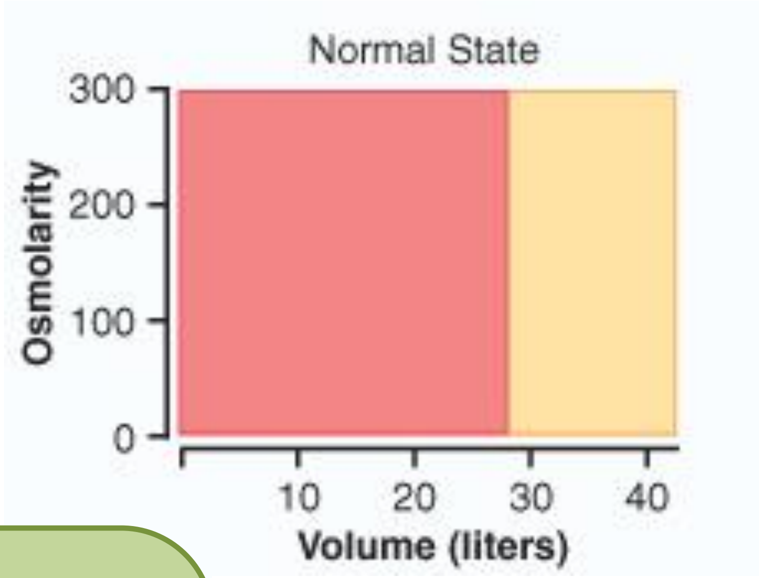
2- High NaCl intake

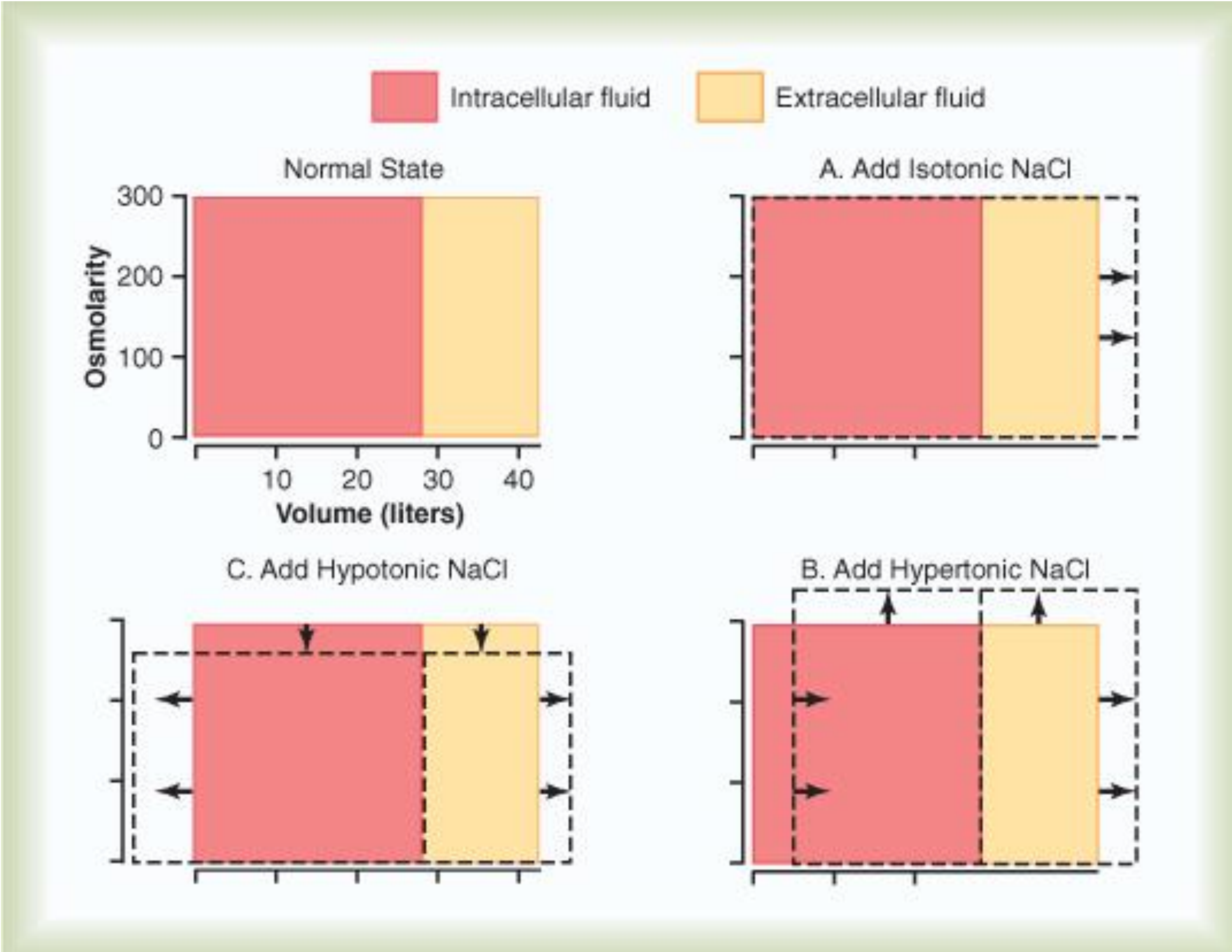
2. High NaCl intake.

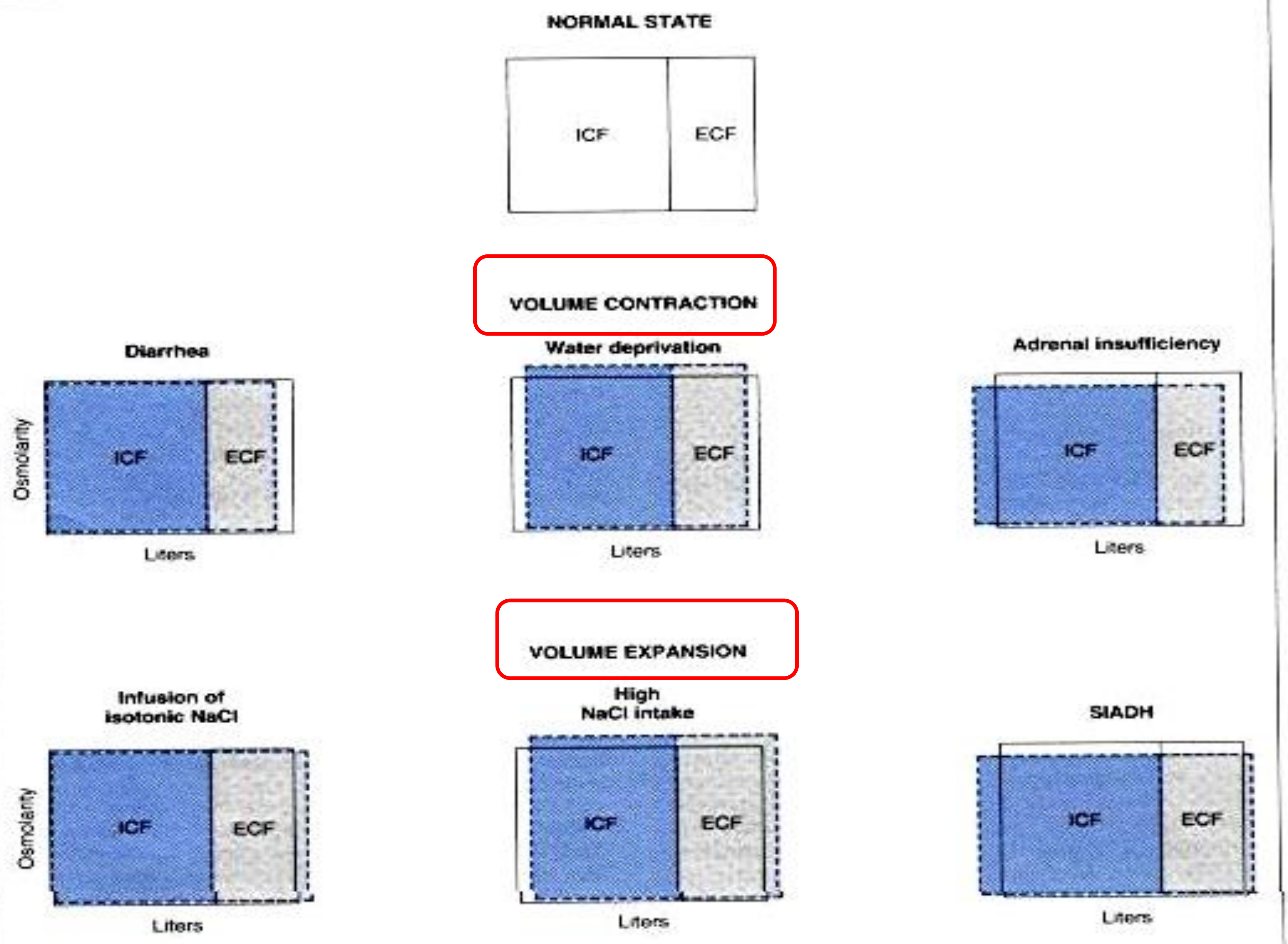
- ↑ eating salt.
- ↑ osmolarity in both.
- ↓ volume of ICF .
- ↑ volume of ECF .
- ***hyperosmotic volume expansion***.

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

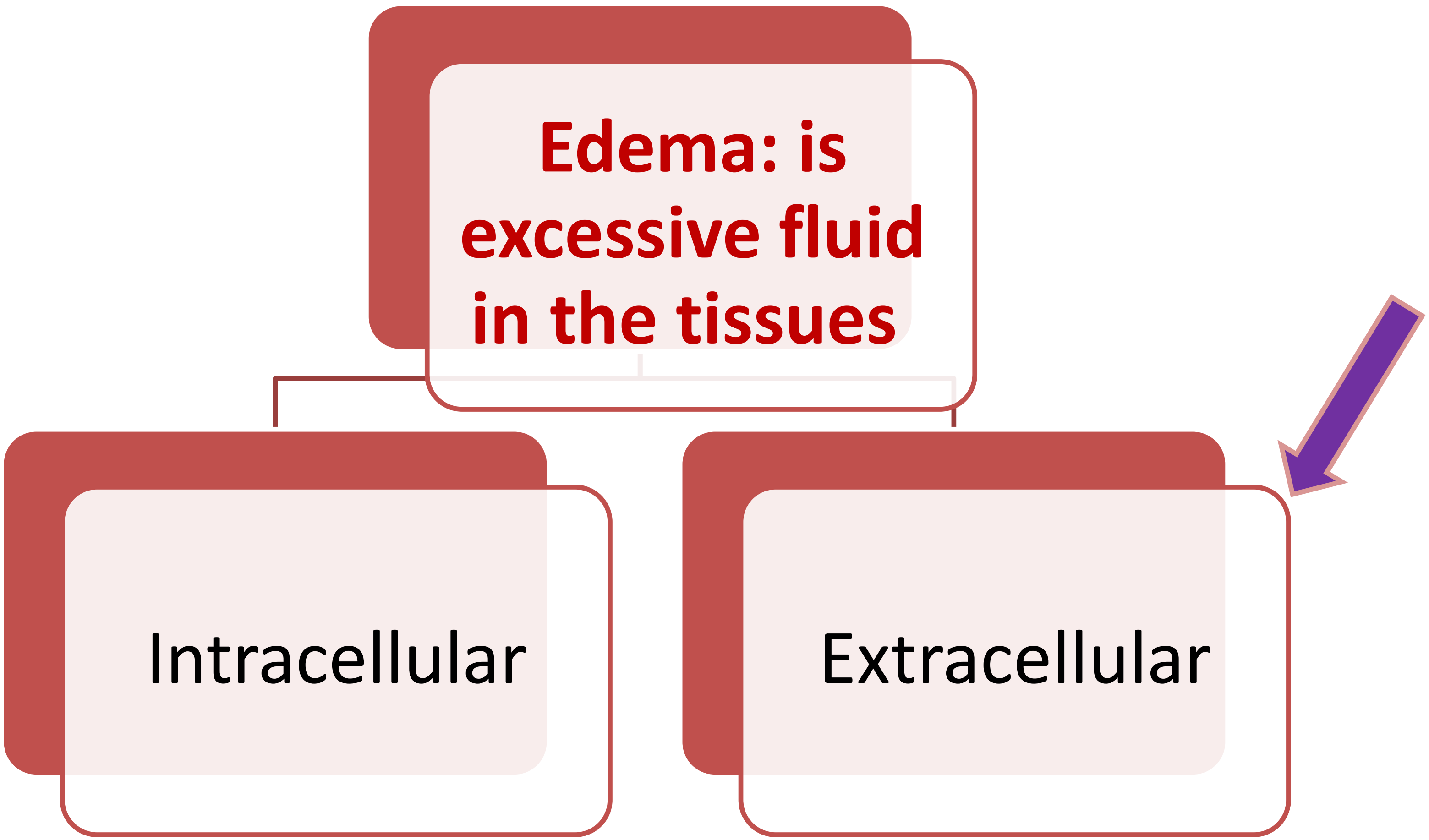
- ↑ volume
- ↓ osmolarity



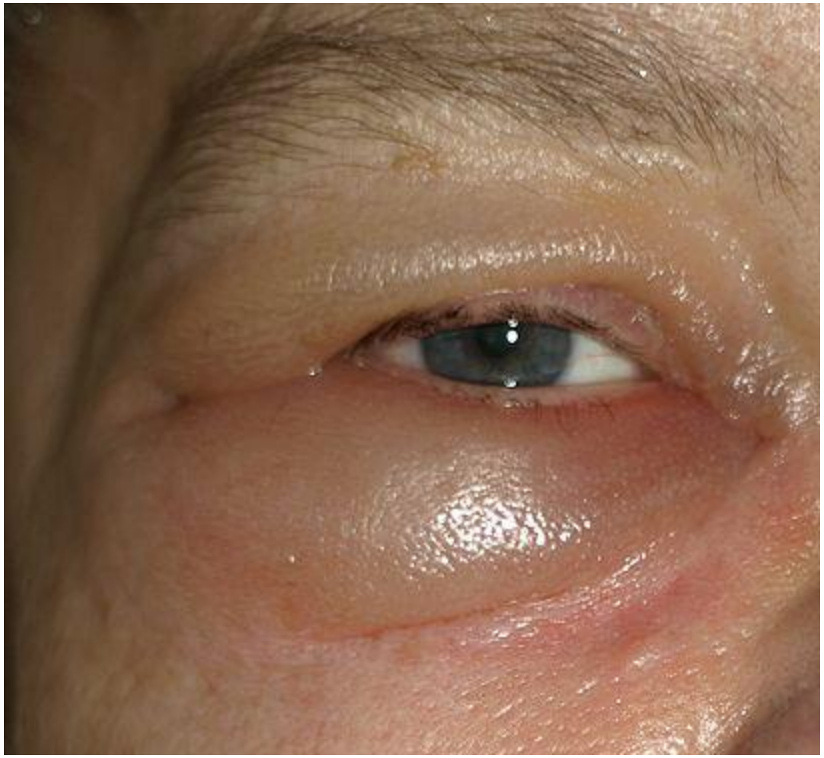

Intracellular fluid
Extracellular fluid
Normal State
300
200
100
0
Osmolarity
10
20
30
40
Volume (liters)
A. Add Isotonic NaCl
C. Add Hypotonic NaCl
B. Add Hypertonic NaCl


NORMAL STATE
ICF
ECF
VOLUME CONTRACTION
Diarrhea
Osmolarity
ICF
ECF
Liters
Water deprivation
ICF
ECF
Liters
Adrenal insufficiency
ICF
ECF
Liters
VOLUME EXPANSION
Infusion of
isotonic NaCl
Osmolarity
ICF
ECF
Liters
High
NaCl intake
ICF
ECF
Liters
SIADH
ICF
ECF
Liters

Edema

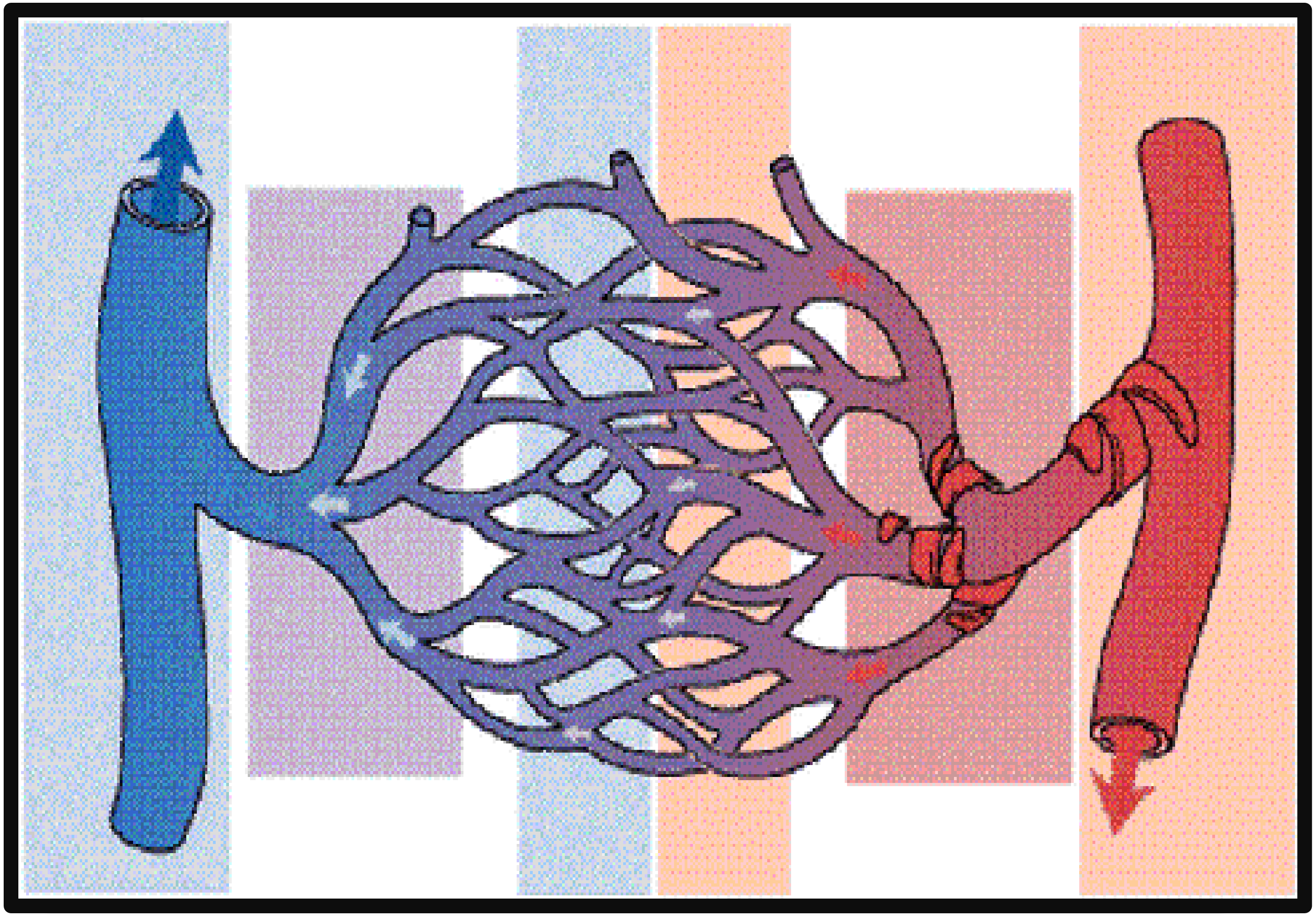


- **Edema occurs mainly in the ECF compartment**



Extracellular Edema

common clinical cause is excessive capillary fluid filtration.



Intracellular Edema:

inflammation of tissues.

↓

↑ membrane permeability.

↓

Na inside cells.

↓

water

↓

edema

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Lecture 2

Cell membrane structure and transport across cell membrane

objectives

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

- Envelops the cell.
- Thin, pliable and elastic.
- 7 - 10 nanometer thick.
- Also, referred to as the plasma membrane .

Composition

protein 55%

phospholipids 25%
cholesterol 13%
glycolipid 4%

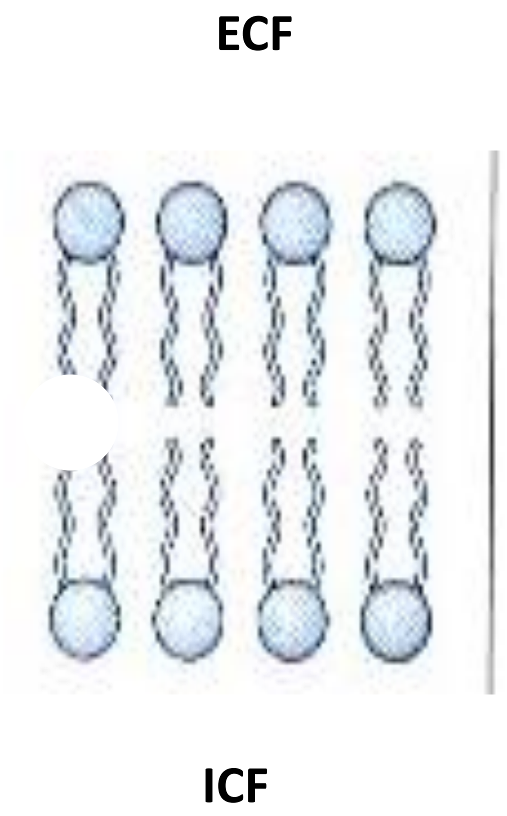
} lipid

carbohydrates 3%

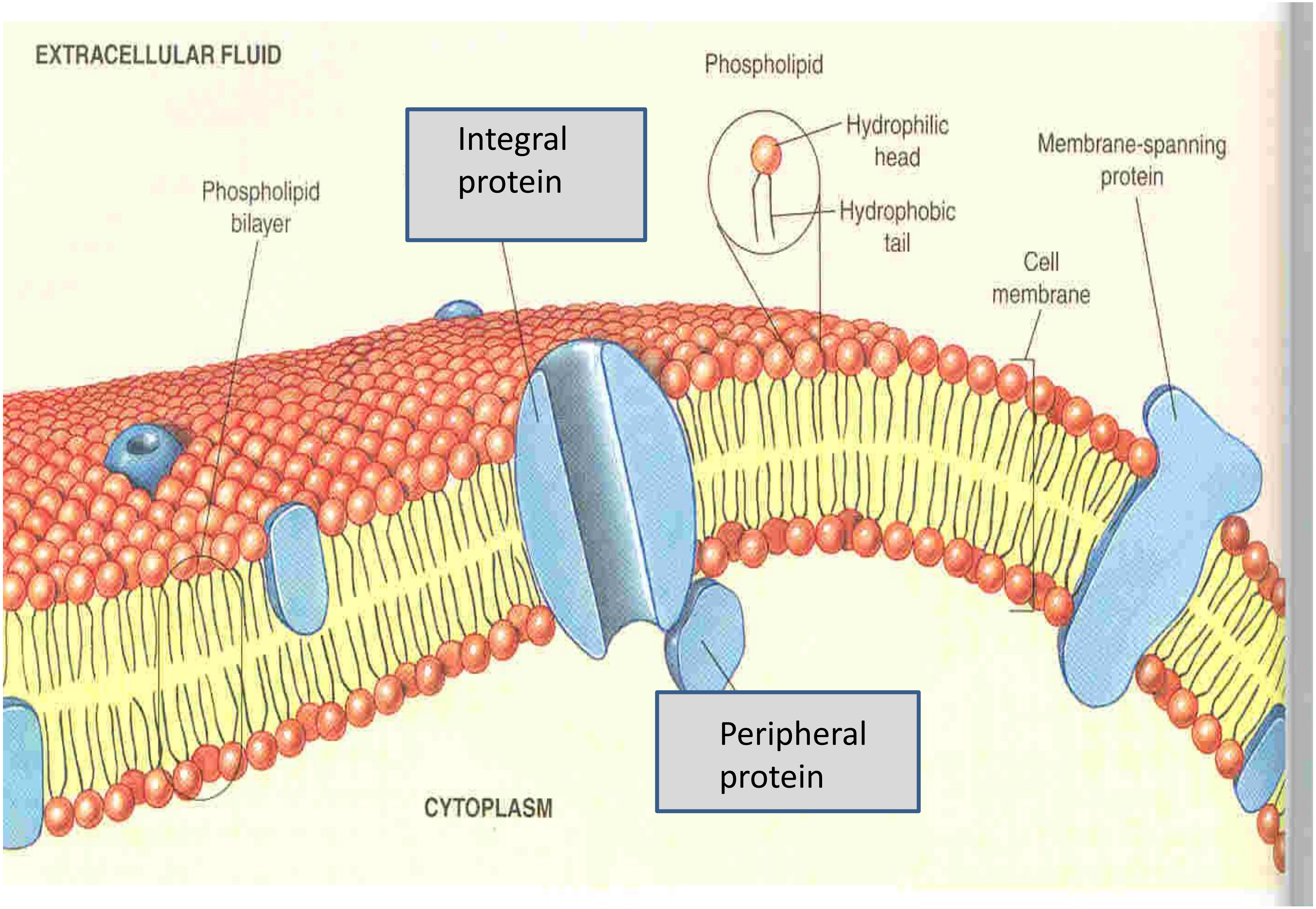
The Cell Membrane Phospholipids Consist Of :

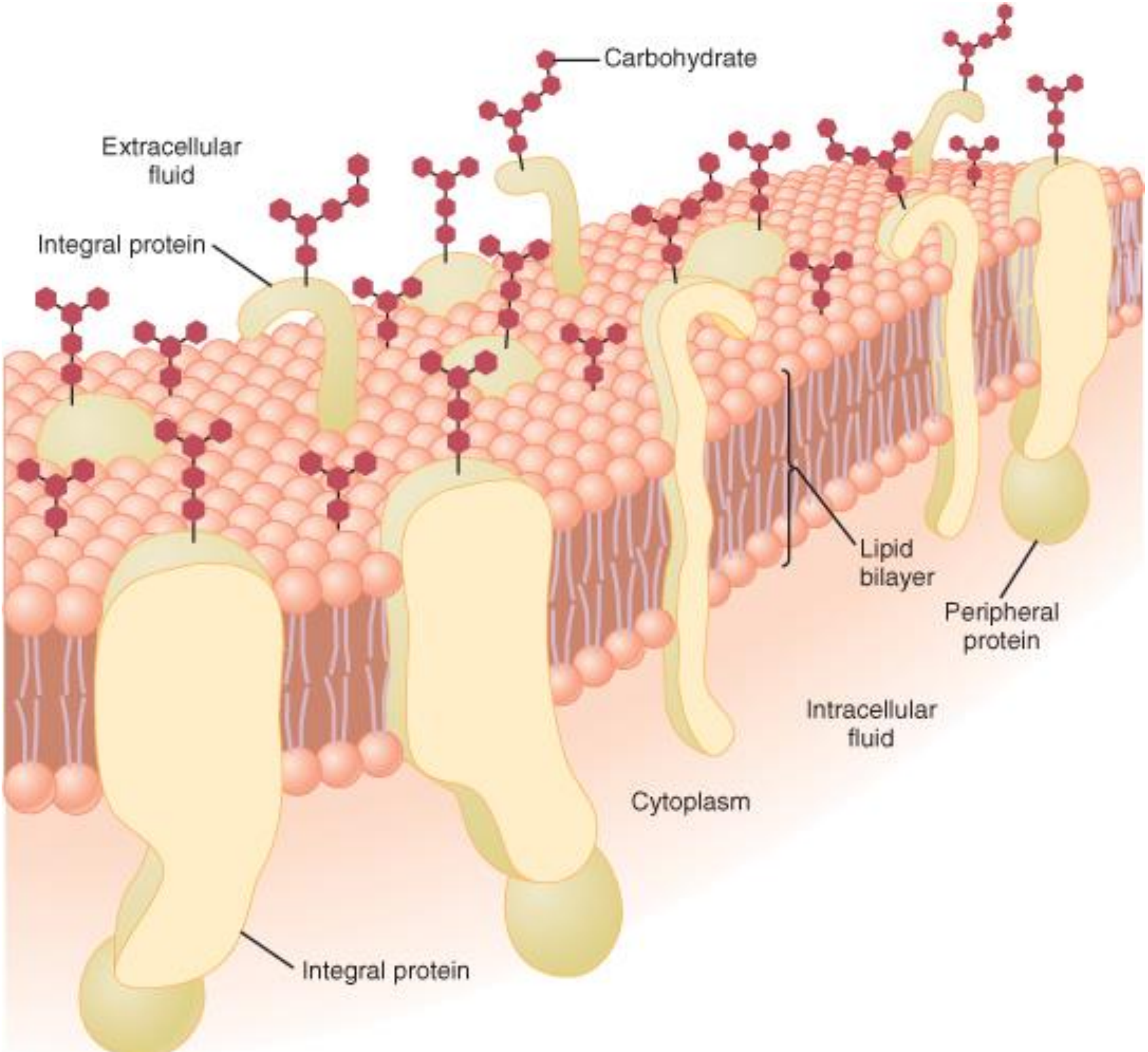
1. Glycerol head (hydrophilic).

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



The Cell Membrane Proteins




Carbohydrate
Extracellular fluid
Integral protein
Lipid bilayer
Peripheral protein
Intracellular fluid
Cytoplasm
Integral protein

The Cell Membrane Proteins.

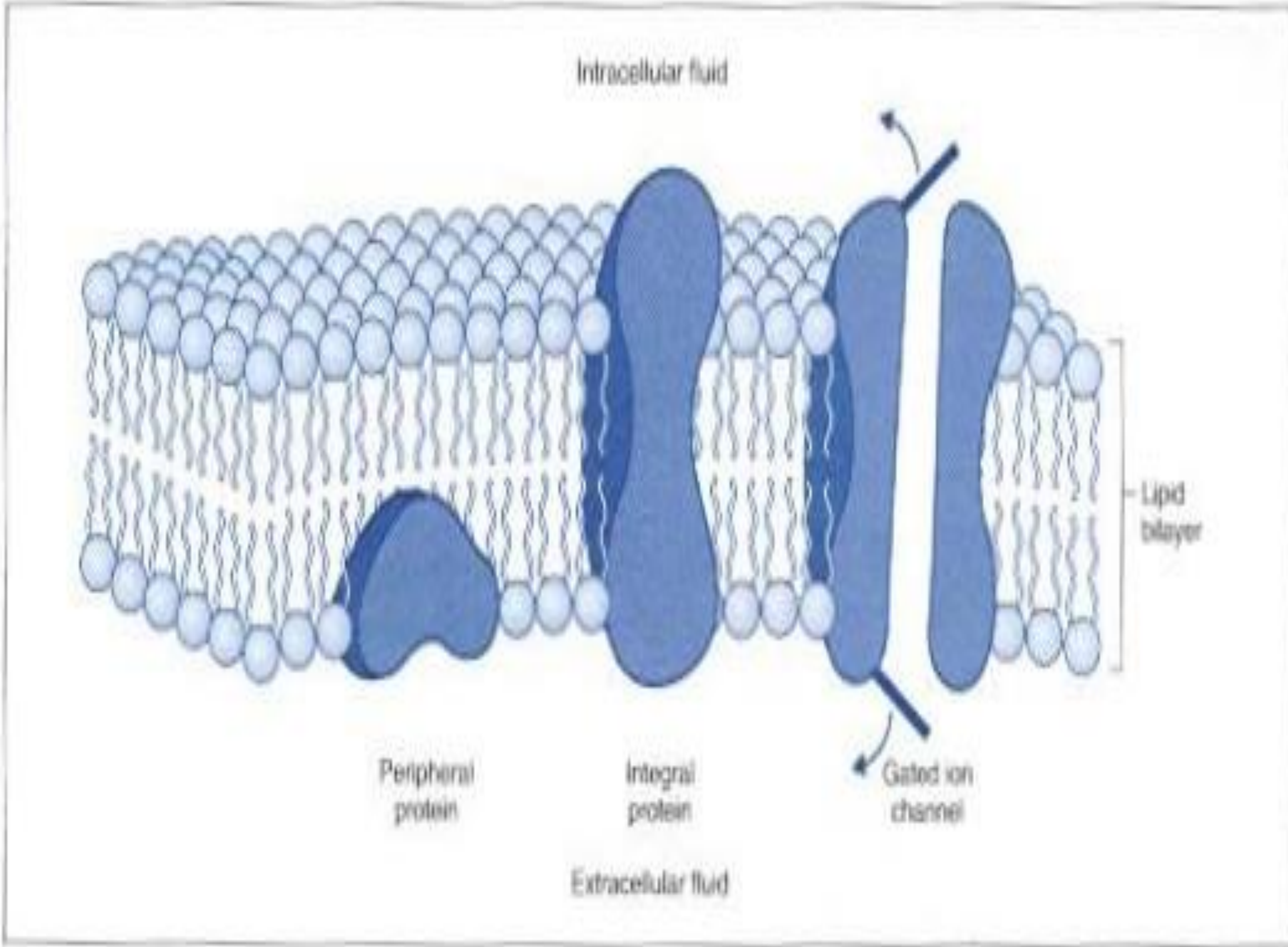
1. **Integral proteins** span the membrane .

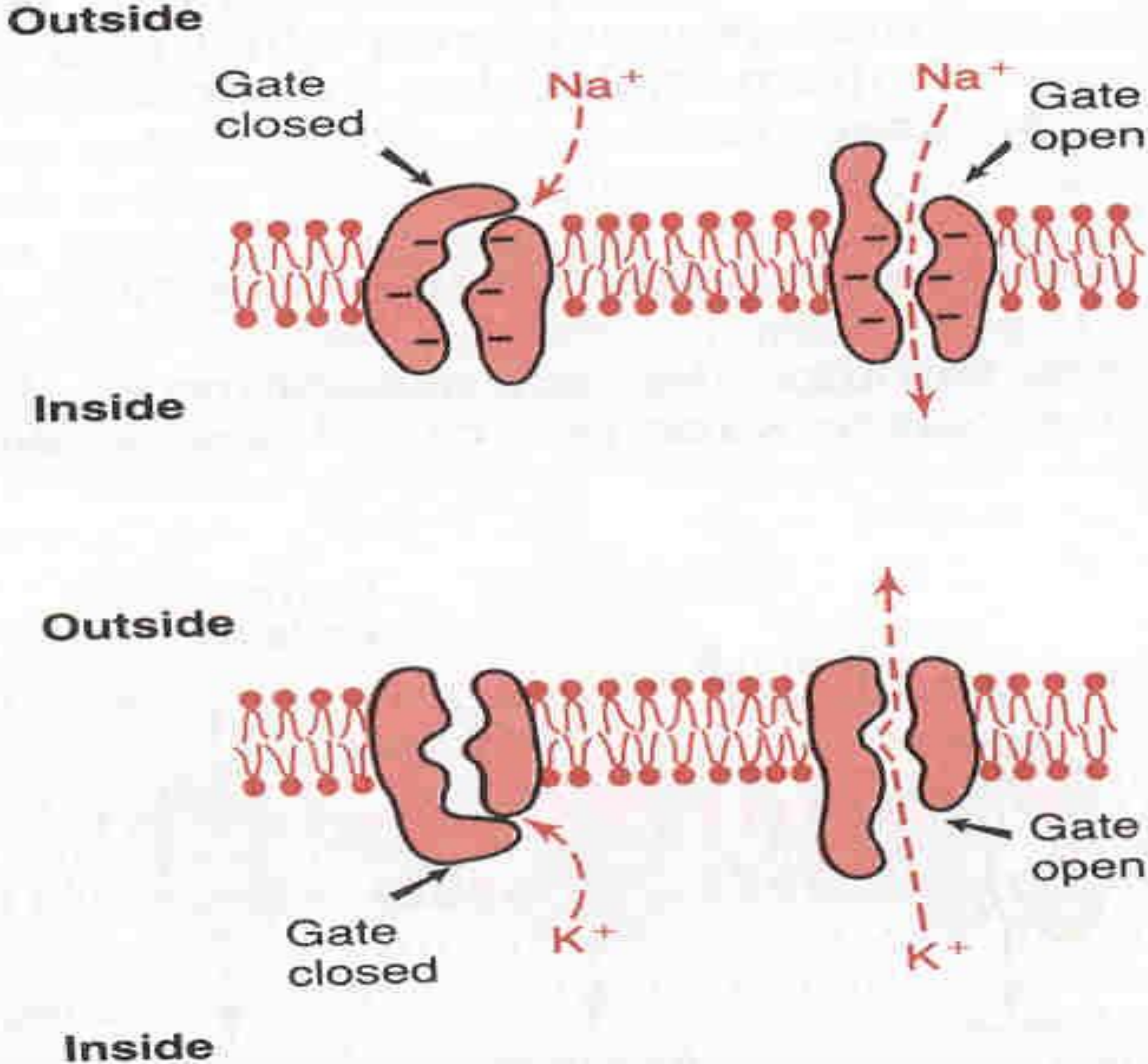
- Proteins provide structural **channels** or **pores**.
- **Carrier** proteins

2. **Peripheral proteins**

-Present in one side.

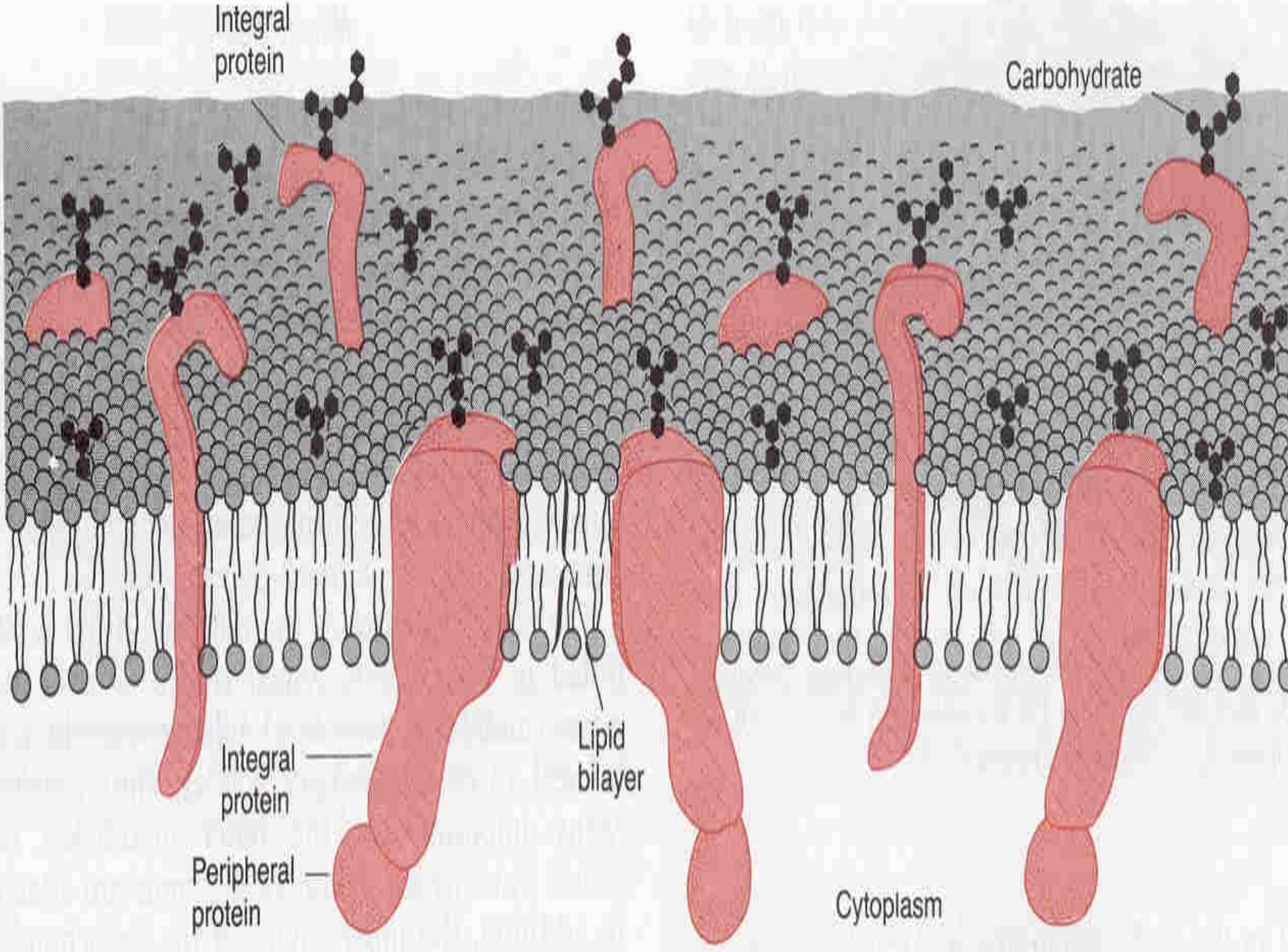
- Hormone receptors .
- Cell surface antigens .


Intracellular fluid
Lipid bilayer
Peripheral protein
Integral protein
Gated ion channel
Extracellular fluid


Outside
Gate
closed
Na+
Na+
Gate
open
Inside
Outside
Gate
open
Gate
closed
K+
K+
Inside

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.


Integral protein
Carbohydrate
Integral protein
Peripheral protein
Lipid bilayer
Cytoplasm

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 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, N2, alcohol..

	Extracellular fluid	Intracellular fluid
Na^{+}	142 mEq/L	10 mEq/L
K^{+}	4 mEq/L	140 mEq/L
Ca^{++}	2.4 mEq/L	0.0001 mEq/L
Mg^{++}	1.2 mEq/L	58 mEq/L
Cl^{-}	103 mEq/L	4 mEq/L
HCO_3^{-}	28 mEq/L	10 mEq/L
Phosphates	4 mEq/L	75 mEq/L
SO_4^{--}	1 mEq/L	2 mEq/L
Glucose	90 mg/dl	0 to 20 mg/dl
Amino acids	30 mg/dl	200 mg/dl ?
Cholesterol, Phospholipids, Neutral fat	0.5 gm/dl	2 to 95 gm/dl
PO_2	35 mm Hg	20 mm Hg ?
PCO_2	46 mm Hg	50 mm Hg ?
pH	7.4	7.0
Proteins	2 gm/dl (5 mEq/L)	16 gm/dl (40 mEq/L)

Types Of Membrane Transport

1- Diffusion

a) simple diffusion.

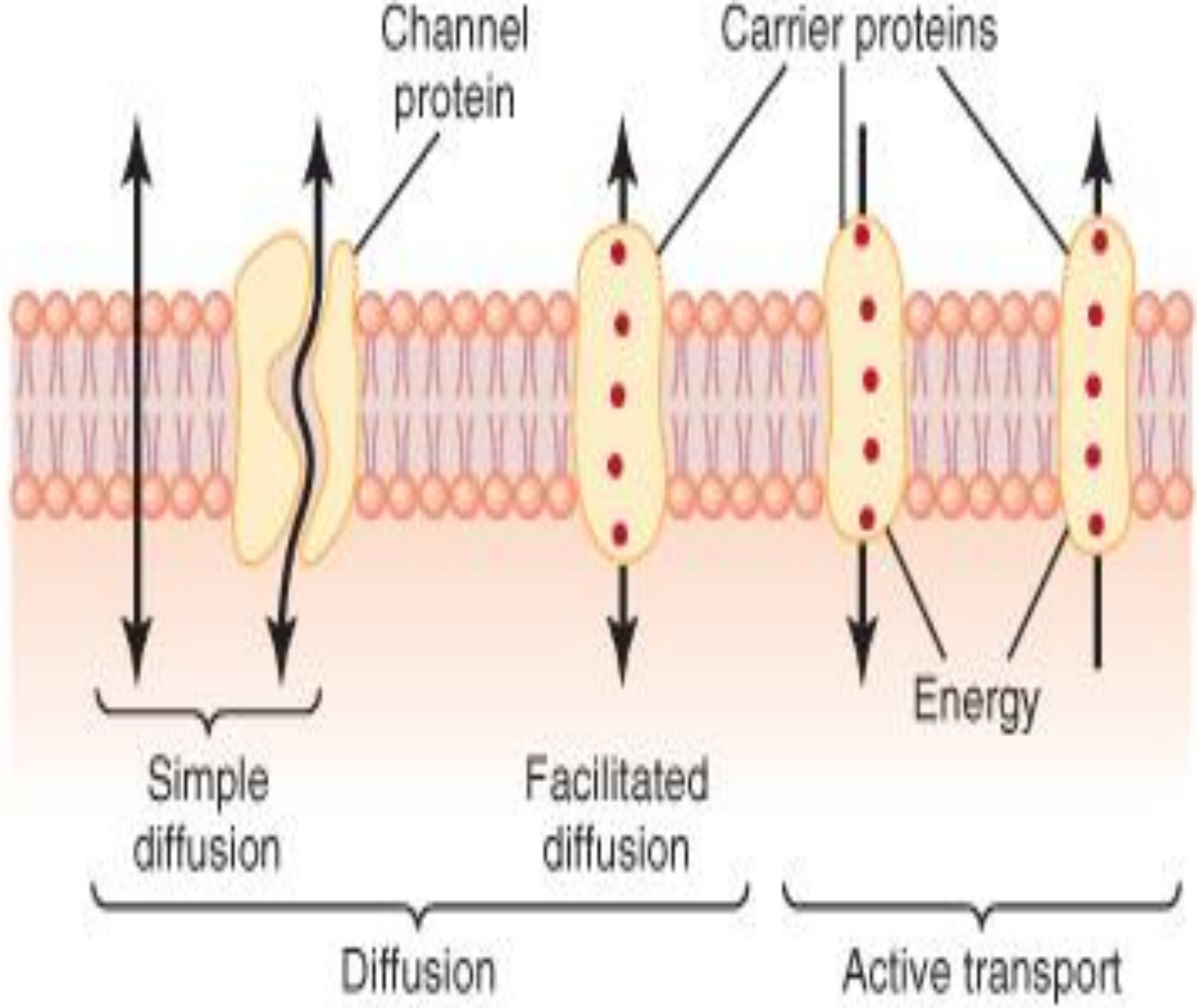
b) facilitated diffusion.

2- Active transport.

a) primary active transport.

b) secondary active transport.

3- Osmosis.


Channel protein
Carrier proteins
Energy
Simple diffusion
Facilitated diffusion
Diffusion
Active transport

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 diffusion & facilitated transport don't require input of energy = powered by concentration gradient or electrical gradient.
- Active transport = directly uses 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).

selective gating system

3- Chemical concentration difference.

net diffusion= P x A (Co-Ci)

4- Electrical potential difference.

$EPD = \pm\ 61 \log C1/C2$

5- Molecular size of the substance.

6- Lipid solubility.

7- Temperature.

Facilitated Diffusion

- Carrier mediated transport down an electrochemical gradient.
- E.g. glucose & amino acids.

Features Of Carrier Mediated Transport (Facilitated diffusion)

1- saturation:

↑ concentration ⟶ ↑ binding of protein

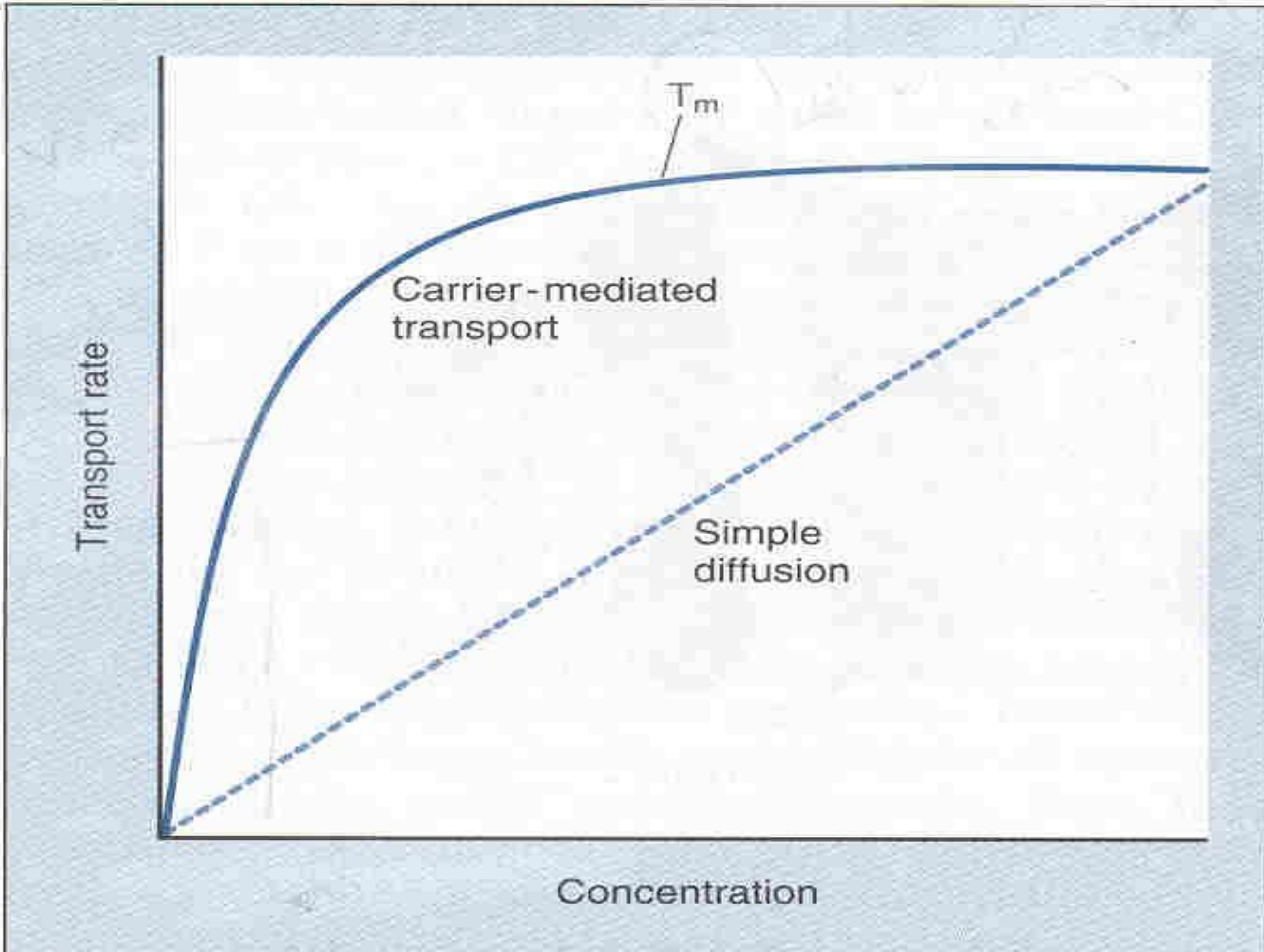
If all protein is occupied we achieve full saturation.

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.



T_m
Carrier-mediated transport
Simple diffusion
Transport rate
Concentration

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

Active Transport:

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

1- Primary Active Transport:

-Energy is supplied directly from ATP.

ATP → ADP +P+ energy.

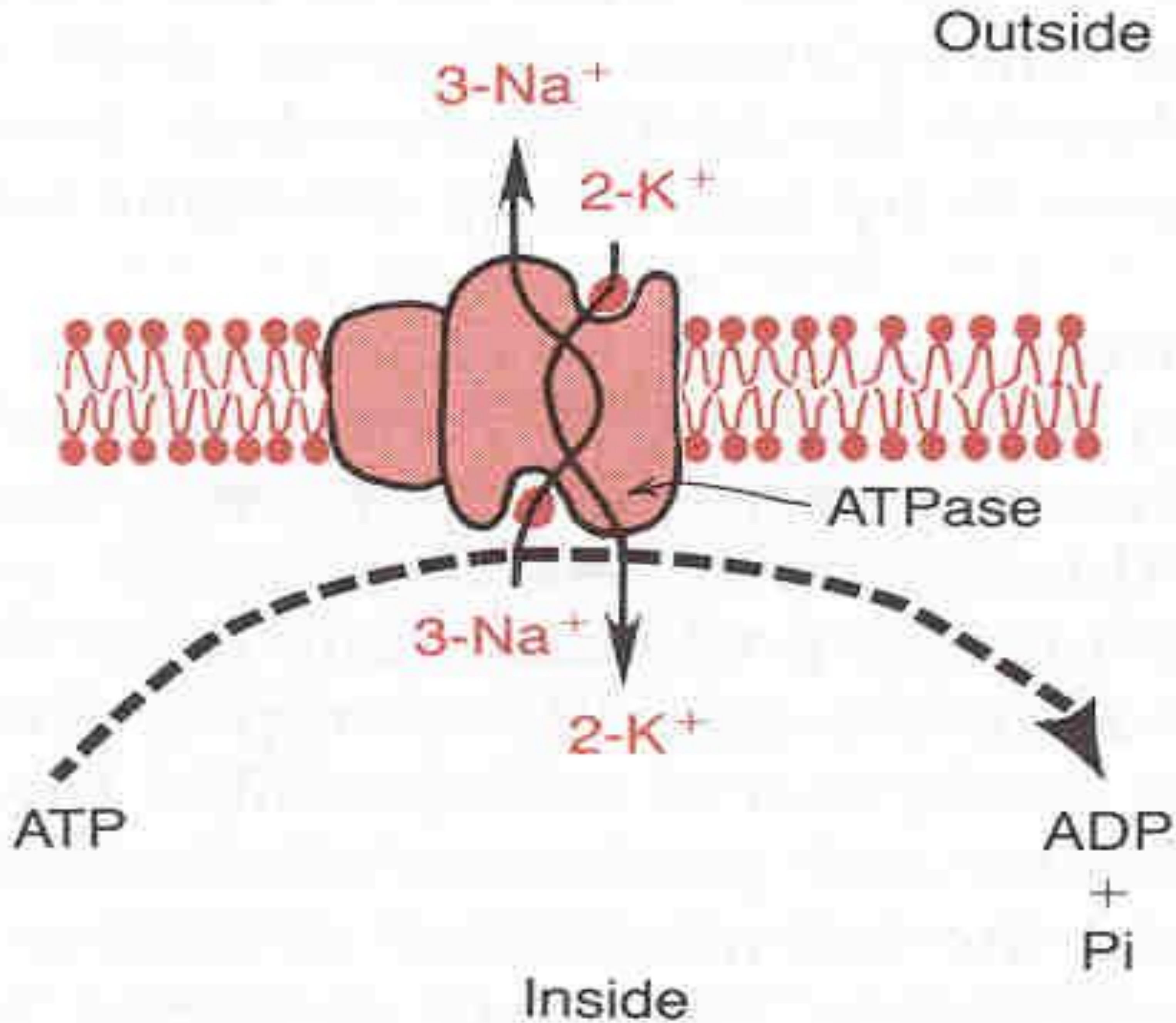
A. - **Sodium-Potassium pump (Na^+-K^+ pump).**

- its present in all cell membranes.
- 3 Na^+ in → out.
- 2 K^+ out → in.

Discovery

- Na^+/K^+-ATPase was discovered by Jens Christian Skou in 1957.

- In 1997, he received one-half of the Nobel Prize in Chemistry .



Outside
3-Na+
2-K+
ATPase
3-Na+
2-K+
ATP
ADP
+
Pi
Inside

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 transmtion .

3. Maintaining –ve potential inside the cell.

4. Maintains a normal cell volume.

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 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.

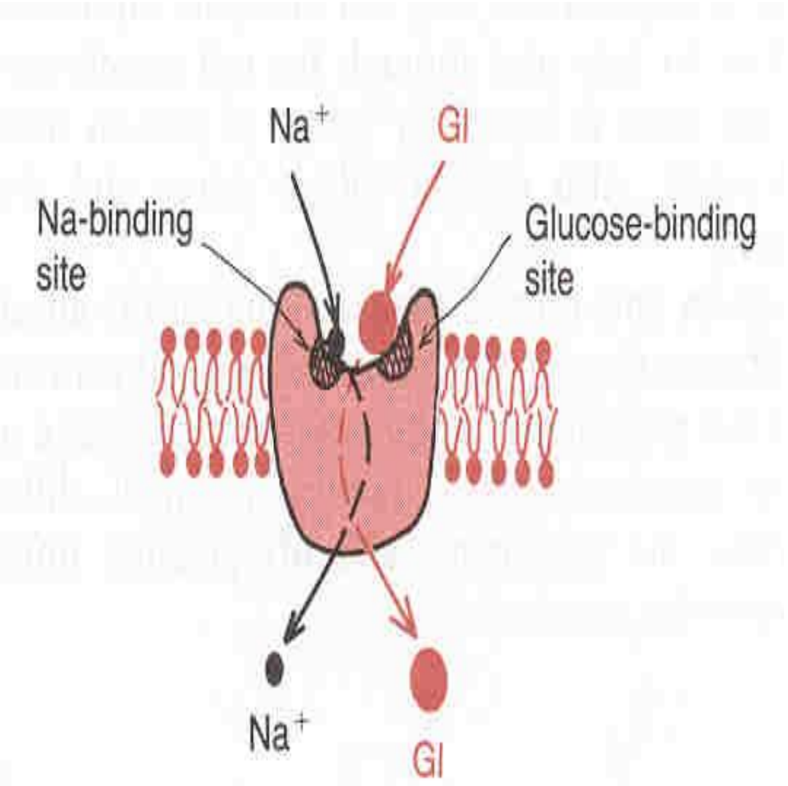
- **Co-transport:**

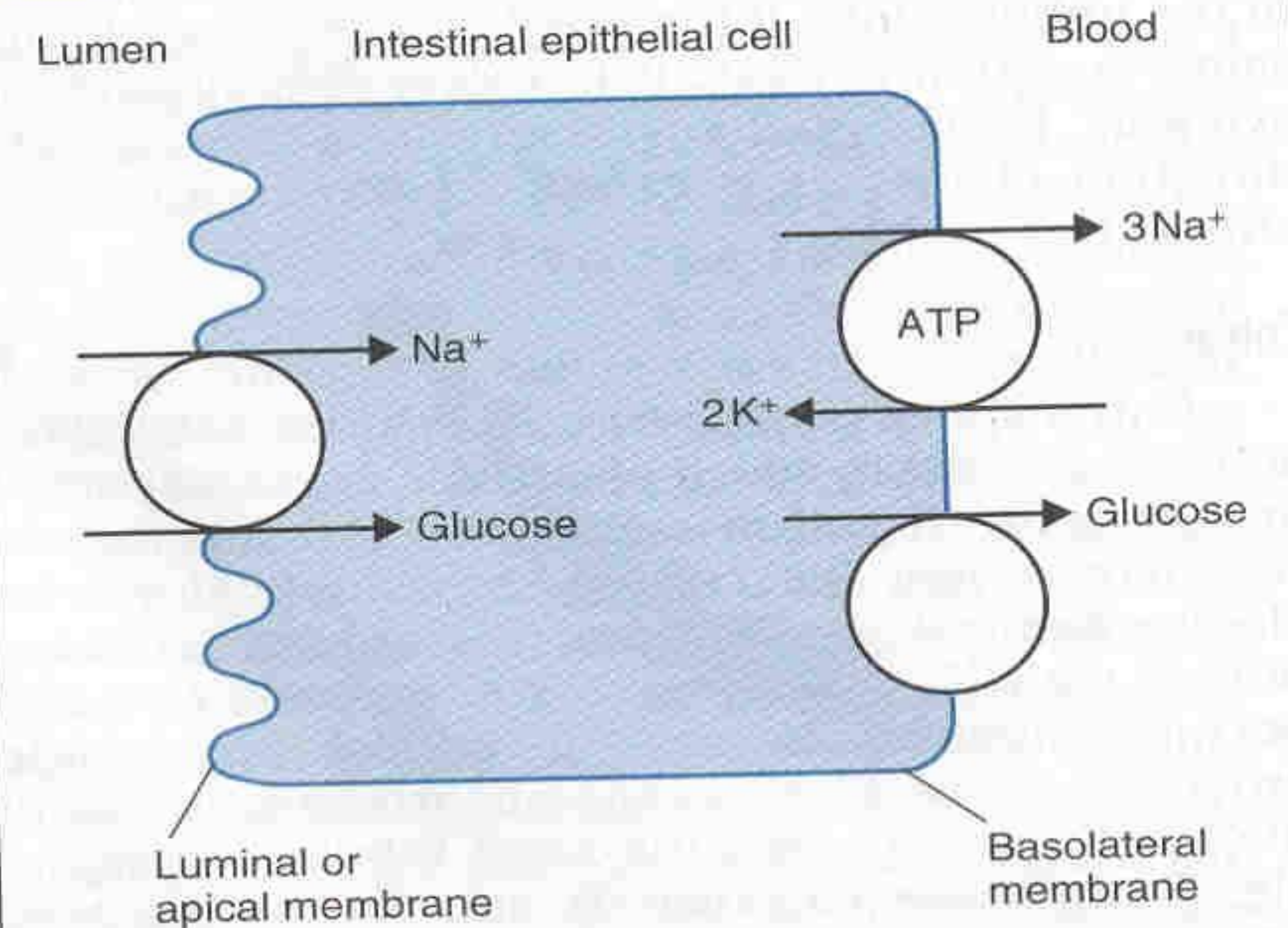
  - All solutes move in the same direction " inside cell".

  - e.g. – Na^+ - glucose Co-transport.

    - Na^+ - amino acid Co-transport.

    - in the intestinal tract kidney.



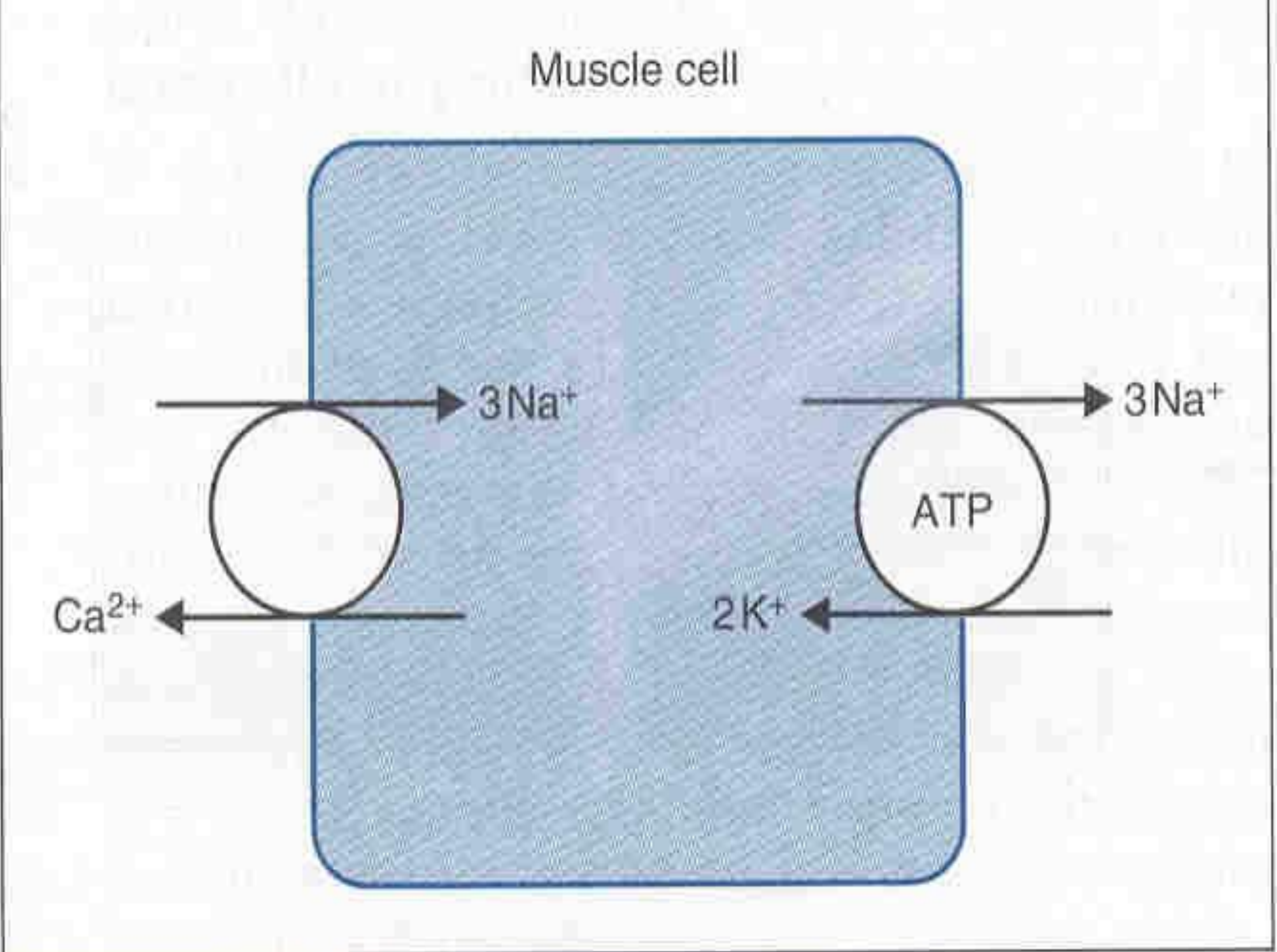

Lumen
Intestinal epithelial cell
Blood
3 Na+
ATP
Na+
2K+
Glucose
Glucose
Luminal or
apical membrane
Basolateral
membrane

- **Countertransport:**
- 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.


Muscle cell
3Na⁺
3Na⁺
ATP
Ca²⁺
2K⁺