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Basic Principles and Perspectives in Medical Chemistry and Biochemistry

Fluid, Electrolyte, and Acid-Base Balance

Part-1- Fluid and Electrolyte Balance

1st Medical and Biochemistry (BIQC-101) Lecture

by

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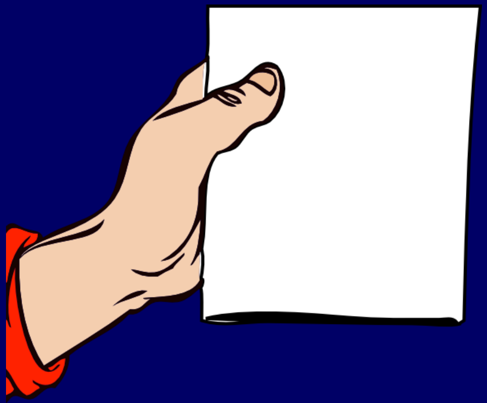
Fluid and Electrolyte Balance

Learning Objective

1. Define body fluid and electrolytes.
2. Know the volumes and main composition of body fluids.
3. List the factors that determine body water content and describe the effect of each factor.
4. Describe the role of the body systems in regulating the body's fluid composition and volume.
5. Describe mechanisms that regulate water intake and hormonal controls of water output in urine.

List of Content



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Introduction

- The chemical reactions of life take place in aqueous solutions.
- The dissolved substances in a solution are called **solutes**.
- In the human body, solutes vary in different parts of the body, but may include proteins, lipids, carbohydrates, and, very importantly, electrolytes.
- Often in medicine, an electrolyte is referred to as a mineral dissociated from a salt that carries an electrical charge (an ion). For instance, sodium ions (Na^+) and chloride ions (Cl^-) are often referred to as **electrolytes**.
- In the body, water moves through semi-permeable membranes of cells and from one compartment of the body to another by a process called osmosis. **Osmosis** is basically the diffusion of water from regions of higher concentration to regions of lower concentration, along an osmotic gradient across a semi-permeable membrane. As a result, water will move into and out of cells and tissues, depending on the relative concentrations of the water and solutes found there. An appropriate balance of solutes inside and outside of cells must be maintained to ensure normal function.

Body Water Content

- Human beings body are mostly water, ranging from about 75 percent of body mass in infants to about 50–60 percent in adult men and women, to as low as 45 percent in old age.
- The percent of body water changes with development, because the proportions of the body given over to each organ and to muscles, fat, bone, and other tissues change from infancy to adulthood.
- Your brain and kidneys have the highest proportions of water, which composes 80–85 percent of their masses. In contrast, teeth have the lowest proportion of water, at 8–10 percent.

Fluid Compartments

1. **The intracellular fluid (ICF) compartment** is the system that includes all fluid enclosed in cells by their plasma membranes.
2. **Extracellular fluid (ECF)** surrounds all cells in the body. Extracellular fluid has two primary constituents:
   1) The fluid component of the blood (called plasma)
   2) The interstitial fluid (IF)

Intracellular Fluid

- The ICF lies within cells and is the principal component of the cytosol /cytoplasm.
- The ICF makes up about 60 percent of the total water in the human body, and in an average-size adult male, the ICF accounts for about 25 liters) of fluid .

Extracellular Fluid

- Extracellular fluid (ECF) or extracellular fluid volume (ECFV) usually denotes all the body fluid that is outside of the cells. The extracellular fluid can be divided into two major sub-compartments: interstitial fluid (surrounds the cells) and blood plasma (holds the blood cells).
- The volume of ECF is typically 15L (of which 12L is interstitial fluid and 3L is plasma).
- Transcellular fluid is the portion of total body water contained within the epithelial-lined spaces. Examples of this fluid are cerebrospinal fluid, ocular fluid, joint fluid. The function of transcellular fluid is mainly lubrication of these cavities

Composition of Body Fluids

- The compositions of the two components of the ECF—plasma and IF—are more similar to each other than either is to the ICF.
- Both blood plasma and IF has high concentrations of sodium, chloride, bicarbonate, and protein. but IF has less concentration of protein.
- In contrast, the ICF has elevated amounts of potassium, phosphate, magnesium, and protein. Overall, the ICF contains high concentrations of potassium and phosphate, whereas both plasma and the ECF contain high concentrations of sodium and chloride.

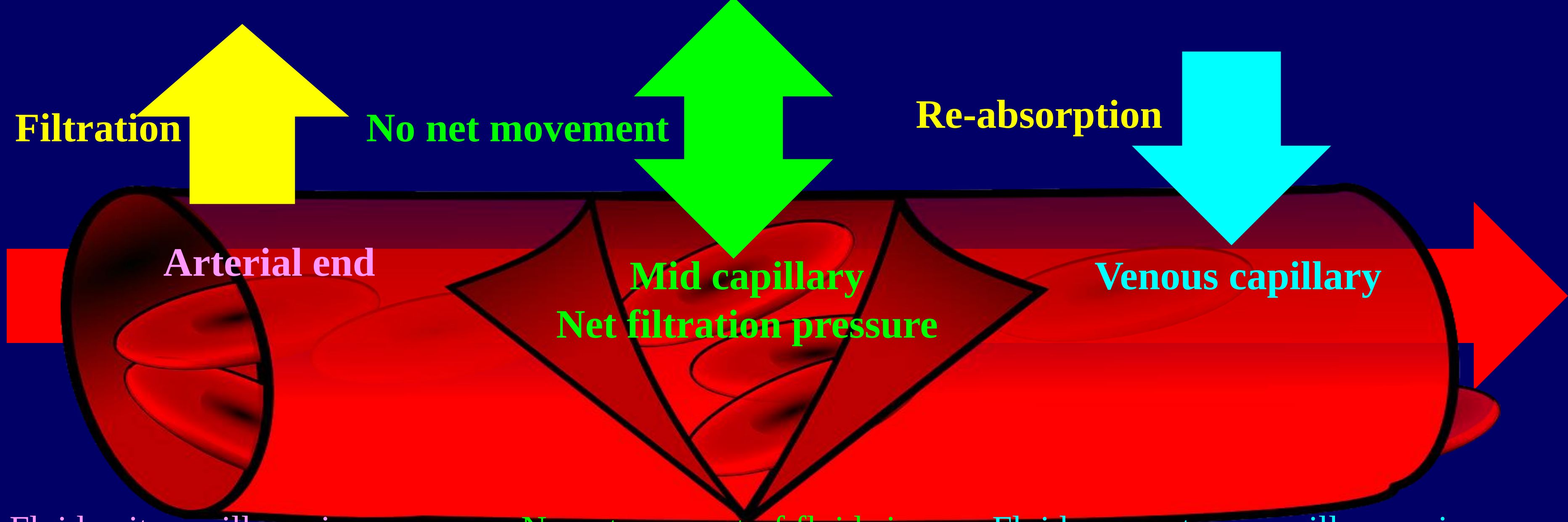
Ions	Extracellular Fluid		Intracellular (mOsm/L H2O)
	Plasma (mOsm/L H2O)	Interstitial (mOsm/L H2O)	
Na+	142	139	19
K+	4.2	4.0	140
Ca++	1.3	1.2	0
Mg++	0.8	0.7	20
Cl−	106	108	4
HCO3 −	2	2	10
HPO4 − ,H2PO4 −	0.5	0.5	11
SO4 −	0.5	0.5	1
Glucose	5.6	5.6	0
Protein	1.2	0.2	4

Fluid Movement between Compartments

Fluid moves through compartments depends on several variables factors :-

- ❖ Extracellular fluid is separated among the various compartments of the body by **semi-permeable membranes**. These membranes are hydrophobic and repel water; however, there such way that fluids can move between body compartments.
- ❖ There are small gaps in membranes, such as the tight junctions, that allow fluids and small ions and molecules to pass through membranes by way of **pressure gradients**:

1. **Hydrostatic pressure:** is generated by the contractions of the heart during systole. It pushes water out of the small tight junctions in the capillaries. The water potential is created due to the ability of the small solutes to pass through the walls of capillaries.
2. **Osmotic pressure**: This buildup of solutes induces **osmosis**. The water passes from a high concentration (of water) outside of the vessels to a low concentration inside of the vessels, in an attempt to reach an equilibrium. The osmotic pressure drives water back into the vessels. Because the blood in the capillaries is constantly flowing, equilibrium is never reached.



Fluid exits capillary since capillary hydrostatic pressure is greater than blood osmotic pressure

No net moment of fluid since capillary hydrostatic pressure =blood osmotic pressure

Fluid re-enter capillary since capillary hydrostatic pressure is less than blood osmotic pressure

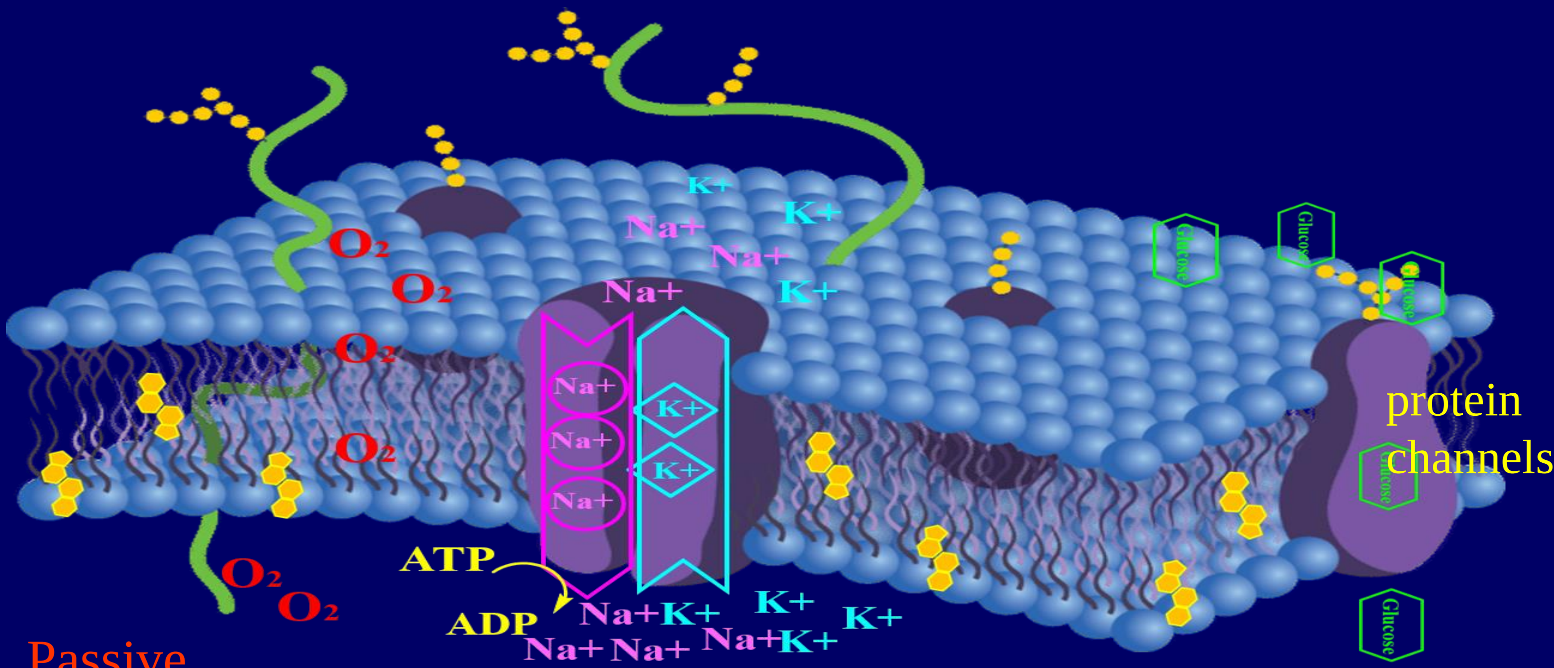
- The balance between the two forces (hydrostatic and osmotic presser) differs at different points on the capillaries. At the arterial end of a vessel, the hydrostatic pressure is greater than the osmotic pressure, so the net movement favors water and other solutes being passed into the tissue fluid.
- At the venous end, the osmotic pressure is greater, so the net movement favors substances being passed back into the capillary.

- Hydrostatic pressure is especially important in governing the movement of water in the nephrons of the kidneys to ensure proper filtering of the blood to form urine. As hydrostatic pressure in the kidneys increases, the amount of water leaving the capillaries also increases, and more urine filtrate is formed. If hydrostatic pressure in the kidneys drops too low, as can happen in dehydration, the functions of the kidneys will be impaired, and less nitrogenous wastes will be removed from the bloodstream. Extreme dehydration can result in kidney failure.
- Fluid also moves between compartments along an osmotic gradient. Recall that an osmotic gradient is produced by the difference in concentration of all solutes on either side of a semi-permeable membrane. The magnitude of the osmotic gradient is proportional to the difference in the concentration of solutes on one side of the cell membrane to that on the other side. Water will move by osmosis from the side where its concentration is high (and the concentration of solute is low) to the side of the membrane where its concentration is low (and the concentration of solute is high). In the body, water moves by osmosis from plasma to the IF (and the reverse) and from the IF to the ICF (and the reverse). In the body, water moves constantly into and out of fluid compartments as conditions change in different parts of the body.

For example, if you are sweating, you will lose water through your skin. Sweating depletes your tissues of water and increases the solute concentration in those tissues. As this happens, water diffuses from your blood into sweat glands and surrounding skin tissues that have become dehydrated because of the osmotic gradient. Additionally, as water leaves the blood, it is replaced by the water in other tissues throughout your body that are not dehydrated. If this continues, dehydration spreads throughout the body. When a dehydrated person drinks water and rehydrates, the water is redistributed by the same gradient, but in the opposite direction, replenishing water in all of the tissues.

Solute Movement between Compartments

- The movement of some solutes between compartments is **active**, which consumes energy and is an active transport process, whereas the movement of other solutes is **passive**, which does not require energy. Active transport allows cells to move a specific substance against its concentration gradient through a **membrane protein**, requiring energy in the form of ATP. For example, the sodium-potassium pump employs active transport to pump sodium out of cells and potassium into cells, with both substances moving against their concentration gradients.
- Passive transport of a molecule or ion depends on its ability to pass through the membrane, as well as the existence of a concentration gradient that allows the molecules to diffuse from an area of higher concentration to an area of lower concentration. Some molecules, like gases, slip fairly easily through the cell membrane;
- Polar molecules like glucose, amino acids, molecules enter and leave cells using **facilitated transport**, whereby the molecules move down a concentration gradient through specific protein channels in the membrane. This process does not require energy. For example, glucose is transferred into cells by glucose transporters that use facilitated transport .



1. Passive diffusion

2. Active transport against concentration gradient with input of energy

3. Facilitated diffusion with carrier protein (large molecule i.e. glucose)

Osmolality and Osmolarity.

- The osmolal concentration of a solution is called **osmolality** when the concentration is expressed as osmoles per kilogram of water; it is called **osmolarity** when it is expressed as osmoles per liter of solution.
- In dilute solutions such as the body fluids, these two terms can be used almost synonymously because the differences are small.
- In most cases, it is easier to express body fluid quantities in liters of fluid rather than in kilograms of water. Therefore, most of the calculations used clinically and the calculations expressed in medical sciences are based on osmolarities rather than **osmolalities.**
- The osmolarity of solutions containing a single type of solute (for example: just glucose or just sodium chloride) can be calculated from the following equation:

Osmolarity = Molarity * n * Φ

n: osmole =*number of particles that dissociated from the solute molecule*

Φ : *osmotic coefficient of the solute*

- The osmolarity of solutions containing many different type of solutes (for example: glucose and sodium chloride) can be calculated from the following equation:

Osmolarity = SUM OF ALL (molarity x n x Φ) OF EACH SOLUTE

Osmotic pressure can be calculated from the following equation: $\pi = n * \Phi * c * R * T$

π =Osmotic pressure. It is measured in units of Pascals (symbol Pa) or bars.

n = Osmole =Number of ions produced when the solute undergoes dissociation. It is also called the dissociation factor or the van't Hoff factor. Most typically, it ranges from **1** (for substances that cannot be dissociated) to **3**.

Φ =Osmotic coefficient of the given solute. It is a unitless factor dependent on the type of substance. Its value is most often **close to 1.**

R =Universal gas constant. It is equal to 8.314 J/(K•mol)

T =Temperature, measured in Kelvins (symbol K).

Example: The osmotic pressure of a 0.9 percent sodium chloride solution is calculated as follows:

A 0.9 percent solution means that there is 0.9 gram of sodium chloride per 100 milliliters of solution, or 9 g/L.

Because the molecular weight of sodium chloride is 58.5 g/mol, the molarity of the solution is 9 g/L divided by 58.5 g/mol, or about 0.154 mol/L.

Because each molecule of sodium chloride is equal to 2 osmoles, the osmolarity of the solution is 0.154 × 2 X 0.93 =0.286 osm/L

Solute	n of osmole	M.W.	Φ
NaCl	2	58.5	0.93
KCl	2	74.6	0.92
HCl	2	36.6	0.95
NH_4Cl	2	53.5	0.92
$NaHCO_3$	2	84.0	0.96
$NaNO_3$	2	85.0	0.90
KSCN	2	97.2	0.91
KH_2PO_4	2	136.0	0.87
$CaCl_2$	3	111.0	0.86
$MgCl_2$	3	95.2	0.89
Na_2SO_4	3	142.0	0.74
K_2SO_4	3	174.0	0.74
$MgSO_4$	2	120.0	0.58
Glucose	1	180.0	1.01
Sucrose	1	342.0	1.02
Maltose	1	342.0	1.01
Lactose	1	342.0	1.01

Example: What is the osmotic pressure of a solution prepared by adding 13.65 g of sucrose ($C_{12}H_{22}O_{11}$) to enough water to make 250 mL of solution at 25 °C?

Mw of sucrose = 342

$n_{sucrose}$ = 13.65 g x 1 mol/342 g

$n_{sucrose}$ = 0.04 mol

$M_{sucrose} = n_{sucrose}/Volume_{solution}$

$M_{sucrose}$ = 0.04 mol/(250 mL x 1 L/1000 mL)

$M_{sucrose}$ = 0.04 mol/0.25 L

$M_{sucrose}$ = 0.16 mol/L

$\pi = n * \Phi * c * R * T$

=1 x 0.16 mol/L x 0.08206 L·atm/mol·K x 298 K

Example: Calculate the osmlarity of blood. The concentration os solution are:-

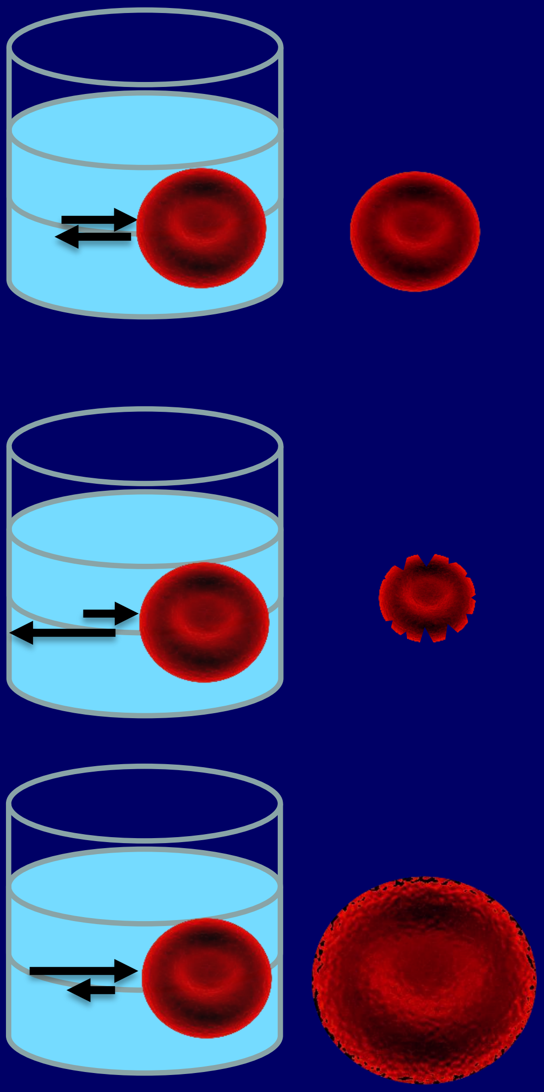
[Soduim chloride] = 0.140 mol/L.

[Glucose]=180 mg/100mL.

[Blood urea nitrogen]=20 mg/100 mL

Fluid Types

1. **Isotonic :**An isotonic solution exerts the same osmotic pressure as red blood cells. is known as a “physiological solution”. of 5.0% glucose or 0.90% NaCl is used medically because each has a solute concentration equal to the osmotic pressure equal to red blood cells.
2. **Hypotonic:** The solute concentration outside the cell is greater than that inside the cell, the solution is hypertonic. water will flow out of the cell, and **crenation** results.
3. **Hypertonic:** **T**he solute concentration outside the cell is less than that inside the cell, the solution is hypotonic. water will flow into the cell, and **hemolysis** results.



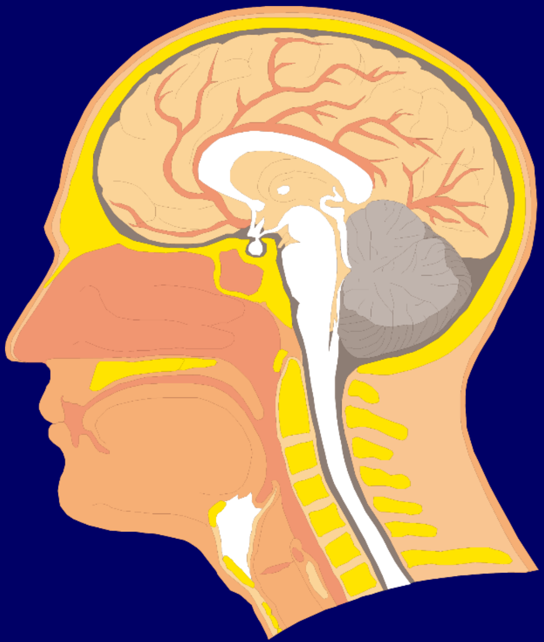
Body Water Homeostasis

- Fluid can enter the body as preformed water, ingested food and drink, and, to a lesser extent, as metabolic water that is produced as a by-product of aerobic respiration and dehydration synthesis.
- The input of water through ingested fluids is approximately 2500 ml/day.
- A constant supply is needed to replenish the fluids lost through normal physiological activities, such as **respiration**, **sweating**, and **urination**.
- Water generated from the biochemical metabolism of nutrients provides a significant proportion of the daily water requirements but it provides only a small fraction of a human's necessary intake. In the normal resting state.
- **Body water homeostasis** is regulated mainly through ingested fluids, which, in turn, depends on **thirst**.

Body Water Homeostasis

Hypothalamus-Mediated Thirst

- Thirst is the basic instinct or urge that drives an organism to ingest water.
- Thirst is a sensation created by the **hypothalamus**, the thirst center of the human body. Thirst is an important component of blood volume regulation, which is slowly regulated by homeostasis.
- An **osmoreceptor** is a sensory receptor that detects changes in osmotic pressure and is primarily found in the hypothalamus of most homeothermic organisms.
- Osmoreceptors detect changes in plasma osmolarity (that is, the concentration of solutes dissolved in the blood).

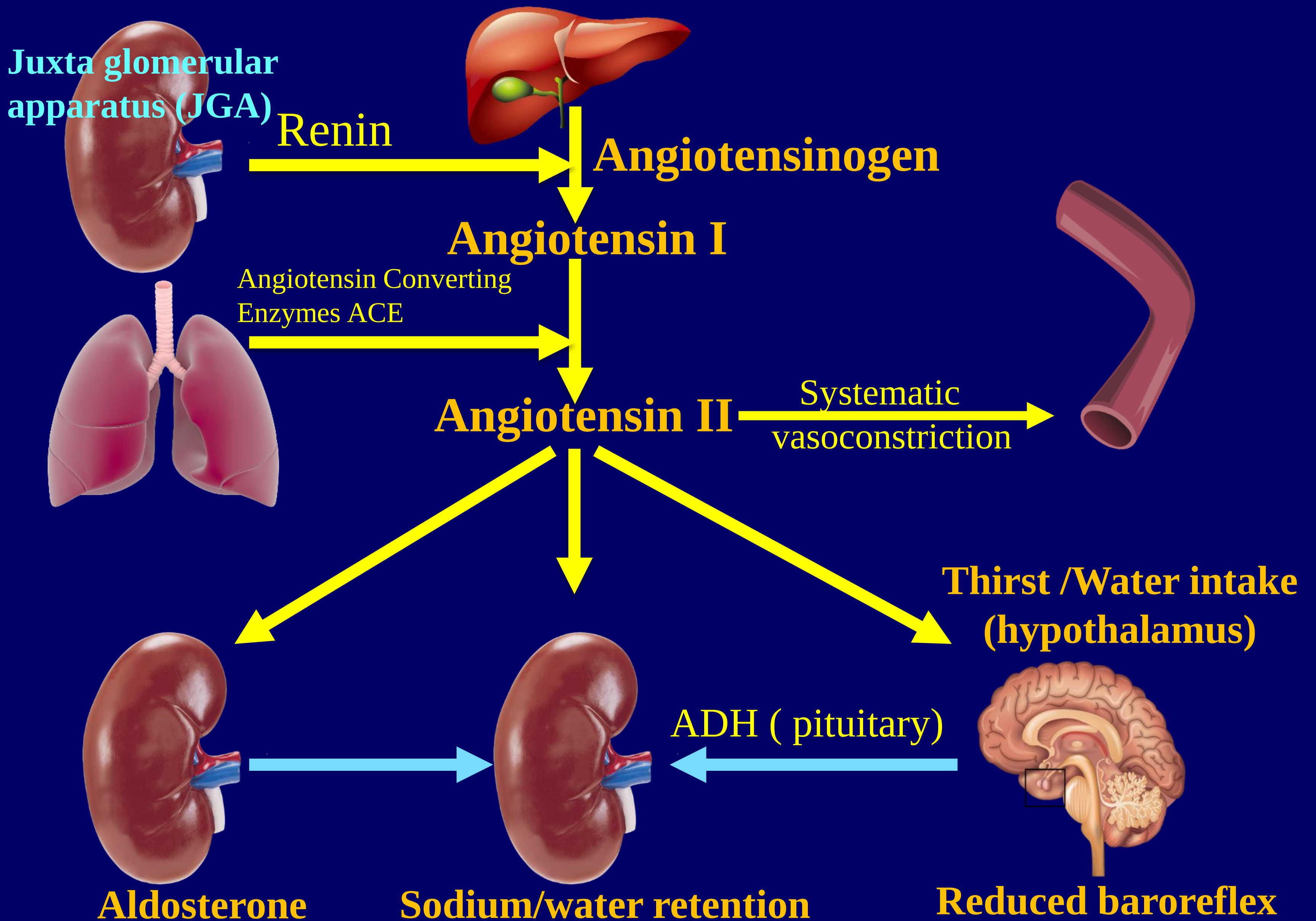


- When the osmolarity of blood changes (it is more or less dilute), water diffusion into and out of the osmoreceptor cells changes. That is, the cells expand when the blood plasma is more dilute and contract with a higher concentration.
- When the osmoreceptors detect high plasma osmolarity (often a sign of a low blood volume), they send signals to the hypothalamus, which creates the biological sensation of thirst.
- Osmoreceptors also stimulate vasopressin (antidiuretic hormone ADH) secretion, which starts the events that will reduce plasma osmolarity to normal levels.

Renin–Angiotensin System-Mediated Thirst

- Another way through which thirst is induced is through **angiotensin II**, one of the hormones involved in the renin–angiotensin system.
- The renin–angiotensin system is a complex homeostatic pathway that deals with blood volume as a whole, as well as plasma osmolarity and blood pressure.
- The macula densa cells in the walls of the ascending loop of Henle of the nephron is another type of osmoreceptor; however it stimulates the juxtaglomerular apparatus (JGA) instead of the hypothalamus.
- When the macula densa is stimulated by high osmolarity, The JGA releases renin into the bloodstream, which cleaves angiotensinogen into angiotensin I. Angiotensin I is converted into angiotensin II by **Angiotensin-converting Enzyme (**ACE) in the lungs.
- Angiotensin II acts on the hypothalamus to cause the sensation of thirst. It also causes vasoconstriction, and the release of aldosterone to cause increased water reabsorption in a mechanism that is very similar to that of ADH.

Renin- Angiotensin –Aldosterone System (RAAS)



Electrolytes

Electrolytes are minerals that carry an electric charge cations and anions (when they are dissolved in a liquid such as blood.

Sodium

- Major extracellular cation ,normal range of serum sodium 135 - 145 mEq/L,
- Combines with chloride and bicarbonate to help regulate acid-base balance.
- When sodium intake increases (Hypernatremia) , extracellular fluid concentration also rises so:-

1) Increased serum Na+ increases thirst and the release of ADH, which triggers kidneys to retain water.
2) Aldosterone also has a function in water and sodium conservation when serum Na+ levels are low.
3) Sodium-Potassium Pump: sodium-potassium pump maintains normal concentrations.

Calcium

- 99% in bones, 1% in serum and soft tissue, works with phosphorus to form bones and teeth, role in cell membrane permeability, affects cardiac muscle contraction, participates in blood clotting. Serum calcium $<$ 8.9- 10.1 mg/dl.

Potassium

- ❖ Major intracellular cation, untreated changes in K+ levels can lead to serious neuromuscular and cardiac problems , Normal K+ levels = 3.5 - 5 mEq/L
- ❖ Potassium ions and hydrogen ions exchange freely across cell membranes:
- ✓ **Acidosis :-** Hyperkalemia, serum K+ < 3.5 mEq/L (K+ moves out of cells)
- ✓ **Alkalosis :-** Hypokalemia, serum K+ > 5 mEq/L (K+ moves into cells)
- ❖ Balancing Potassium

1) Most K+ ingested is excreted by the kidneys.
2) Sodium/Potassium Pump use ATP to pump potassium into cells and pumps sodium out of cells to reach creates a balance.
3) Aldosterone secretion causes Na+ reabsorption and K+ excretion.

Magnesium

- ❖ Helps produce ATP, play a role in protein synthesis & carbohydrate metabolism, helps cardiovascular system function (vasodilation), regulates muscle contractions
- ❖ serum Mg++ level < 1.5- 2.5 mEq/L.

Chloride

- ❖ Major extracellular anion, maintain water balance, secreted in the stomach as hydrochloric acid, aids carbon dioxide transport in blood
- ❖ Chloride level 96 -106 mEq/L.

Phosphorus:

- The primary anion in the intracellular fluid, crucial to cell membrane integrity, muscle function, neurologic function and metabolism of fats and protein., functions in ATP formation, platelet function and formation of bones and teeth.
- Hypophosphatemia, serum phosphorus < 2.5 mg/dl, respiratory alkalosis (hyperventilation), elevated parathyroid hormone
- Hyperphosphatemia , serum phosphorus > 4.5 mg/dl, hypoparathyroidism, respiratory acidosis

thank you!