كلية المستقبل الجامعة الاهلية
قسم الصيدلة

Lecture: 1 of Pharmaceutical Chemistry

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Major Intra and Extra Cellular Electrolytes

Electrolytes: Substances whose molecules dissociate into ions when they are placed in water. Electrolytes are classified as:

1. Cations (Positively charged particles):

- Sodium (Na^+),
- Potassium (K^+),
- Calcium (Ca^{++})
- Magnesium (Mg^{++})

2. Anions (Negatively charged particles):

- Bicarbonate (HCO_3^-)
- Chloride (Cl^-)
- Phosphate (PO_4^{-3})

Composition of fluid compartments

1. Extracellular fluid (ECF): Na^+ primary cation and Cl^- primary anion in ECF compartments

2. Intracellular fluid (ICF): K^+ primary cation and phosphate (PO_4^{-3}) primary anion in ICF compartments

Electrochemical Equivalence

Electrolytes measured in milligrams/deciliter (mg/dL) or in millmoles/liter (mmol/L)

Electrolytes Functions

- Volume and osmotic regulation
- Myocardial rhythm and contractility
- Cofactors in enzyme activation
- Regulation of ATPase ion pumps
- Acid-base balance
- Blood coagulation
- Neuromuscular excitability
- ATP generation from glucose

Osmolality

The net movement of water across a membrane that is permeable only to water depends on the concentration gradient of particles (either ions or molecules) across that membrane, and is known as the osmotic gradient. Water moves easily across cell membrane separating ECF from ICF. Osmolality is the concentration of osmotically active particles per unit weight of water. Osmosis is flow of solvent across semi-permeable membrane from low solute concentration to higher solute concentration. Osmotic pressure is the driving pressure for water to change the

concentration of osmotically active particles. Osmotic pressure is the same on both sides of the cell membrane. Water moves across cell membrane to maintain osmolality of ECF & ICF; even if it causes the cells to shrink or expand in volume The following formula has the benefit of being easy to calculate plasma osmolality (all concentrations must be in mmol/L):

Calculated osmolality = 2 [Na^+] + 2 [K^+] + [glucose] + [urea]

This formula includes all the low molecular weight solutes contributing to plasma osmolality. Values for Na^+ and K^+ are doubled so as to allow for their associated anions, such as chloride.

Regulation of water balance

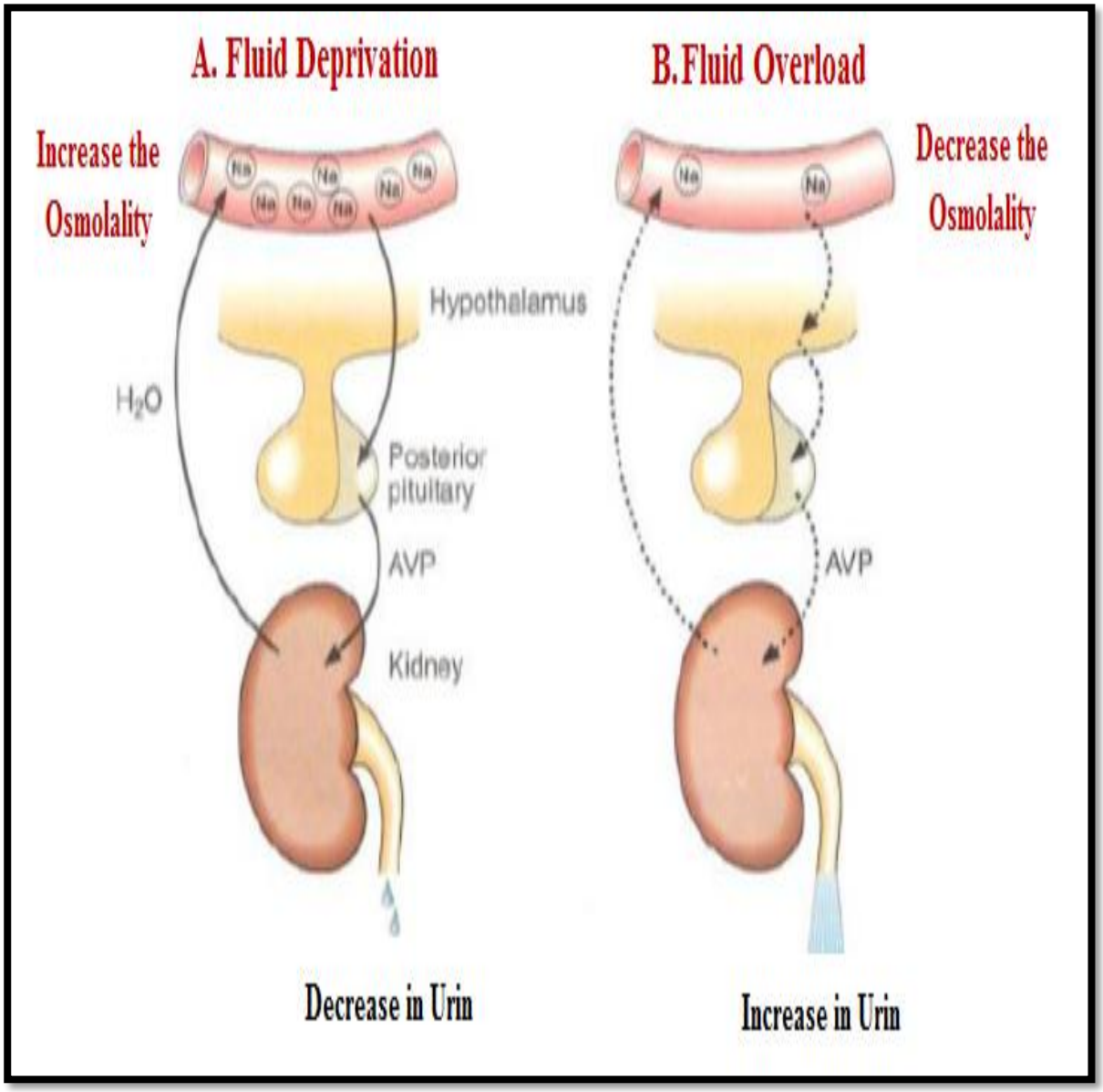
1. Arginine vasopressin (anti-diuretic hormone)

Water balance is regulated by arginine vasopressin (AVP) which also called anti-diuretic hormone (ADH). AVP is a hormone produced by posterior pituitary gland. It tightly regulates water excretion by the kidneys, AVP causes water to be retained by the kidneys. Osmolality in ICF is equal to that in ECF. Specialized cells in hypothalamus are involved in maintaining the osmolality between ICF and ECF. A rising osmolality promotes the secretion of AVP while a declining osmolality decrease the secretion of AVP.

A. In case of fluid deprivation (increase the osmolality) results in stimulation of AVP secretion causing increase of water reabsorption by kidney and reduction in urine flow to conserve body water (return normal osmolality).

B. In case of fluid overload (decrease the osmolality) results in inhibition of AVP secretion causing decrease of water reabsorption by kidney and increase in urine flow to conserve body water (return normal osmolality).

By regulating water excretion or retention, AVP maintains normal concentrations of electrolytes within the body.



2. Fluid shifts

Rapid water movements between ECF and ICF in response to an osmotic gradient. If ECF osmotic concentration increases, ECF becomes hypertonic to ICF, water moves from inside cells to ECF. While if ECF osmotic concentration decreases, ECF becomes hypotonic to ICF, water moves from ECF into cells.

Electrolyte and Electrolyte Replacement Therapy

1. Sodium (Na^+) (Normal value 135-145 mmol/L)

Sodium is the main ECF cation that maintains ECF concentration & volume, primary determinant of ECF osmolality and transmits nerve & muscle impulses. The regulation of sodium level depend on sodium intake and sodium loss, the sodium intake varies among individuals depending on habits, taste and availability while sodium loss is made mainly by kidney and the remaining excreted in sweat and feces.

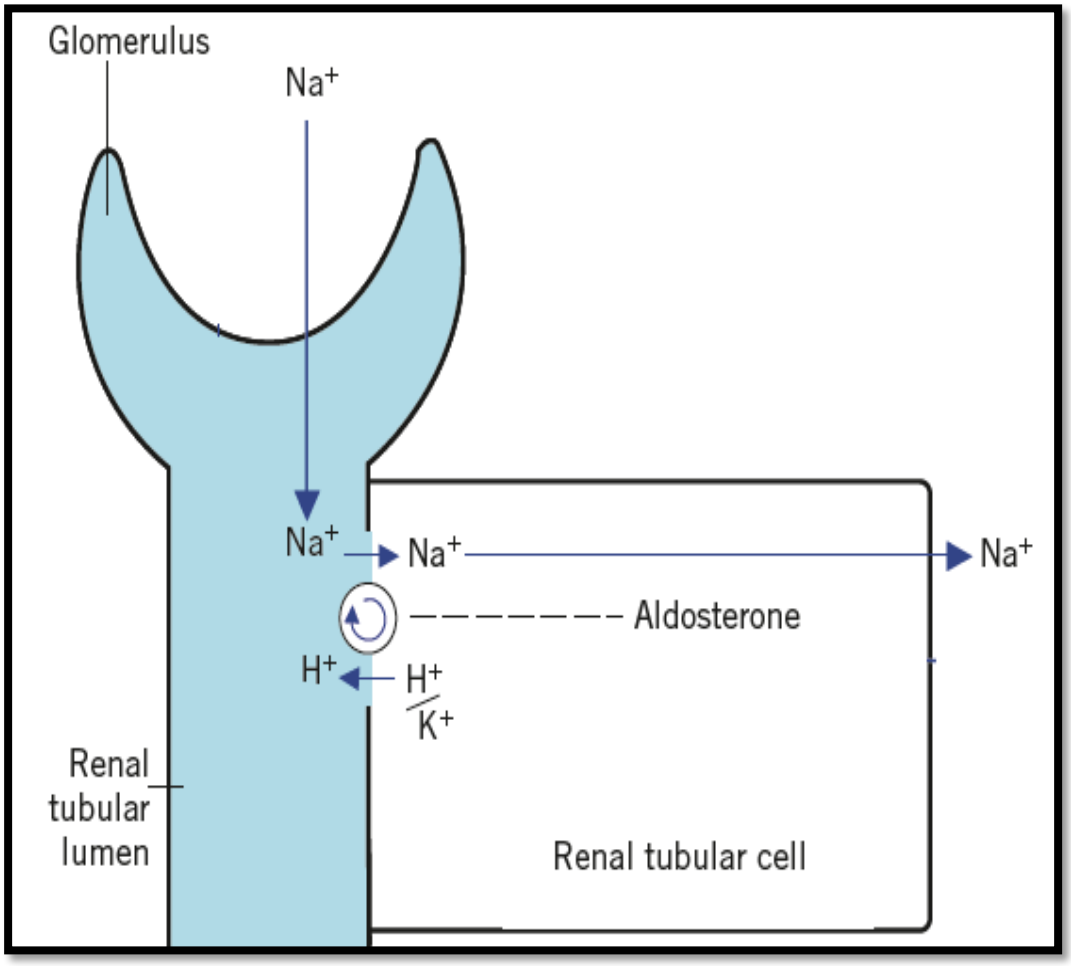
Regulation of sodium level

The plasma concentration of sodium depends on:

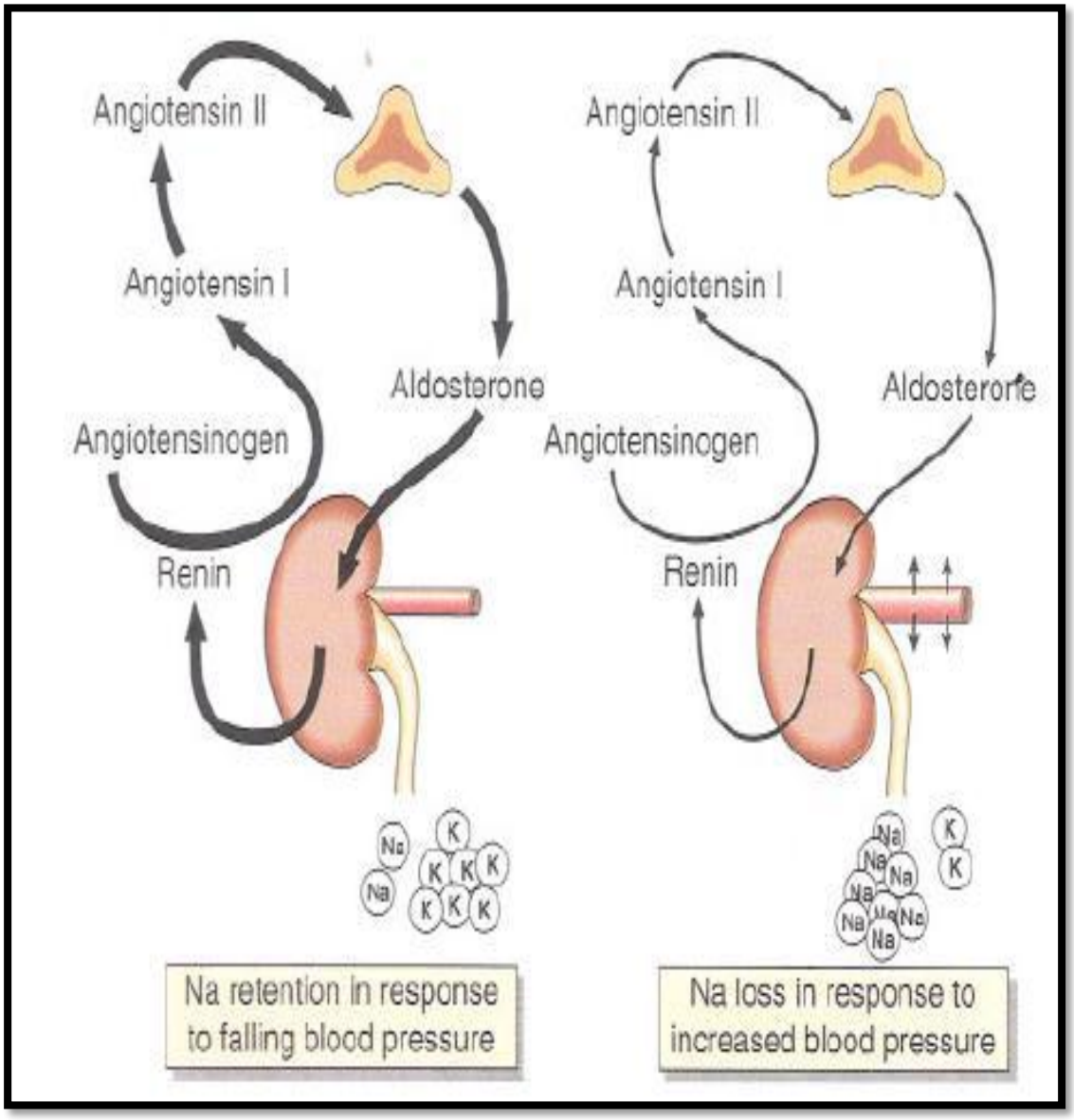
1. Intake of water in response to thirst
2. Excretion of water due to blood volume or osmolality changes
3. Renal regulation of sodium, kidneys can excrete Na^+ depending on ECF and blood volume, the renal regulation of sodium done by renin-angiotensin-aldosterone system and atrial natriuretic factor.

Aldosterone

Aldosterone is a hormone produce in the adrenal cortex, it decreases urinary sodium excretion by increasing re-absorption of Na^+ in renal tubules in exchange for tubule excretion of K^+ and H^+. Aldosterone also decreases loss of Na^+ in sweat glands and mucosal cells of the colon, but in normal circumstances these effects are minimal.



The major stimulus for secretion of aldosterone are volume and osmolality of ECF. Specialized cells in juxtaglomerular apparatus of kidneys detect decrease in blood pressure and secrete renin, renin is an enzyme that converts angiotensinogen (produced in liver) to angiotensin I, angiotensin I is converted to angiotensin II by angiotensin converting enzyme (ACE), angiotensin II then act on adrenal cortex to produce aldosterone, aldosterone acts on kidney tubules causing reabsorption of Na^+ in exchange for excretion of K^+, and H^+.



Regulation of sodium excretion by aldosterone

Atrial Natriuretic Factor (ANF)

Atrial Natriuretic Factor (ANF) is a polypeptide hormone secreted by cardiocytes in the right atrium of the heart thus, it is a cardiac hormone. ANF increases urinary sodium excretion.

Hyponatremia

Hyponatremia represents a decrease in plasma sodium concentration below 135 mmol/L.

Causes of hyponatremia

1. Excessive sodium losses

a. Gastrointestinal losses (vomiting and diarrhea)

b. Adrenal insufficiency (e.g. Addison's disease)

c. Potassium depletion, K^+ normally excreted, if none, then Na

2. Excessive water intake in relation to output

a. Excessive water drinking

b. Increased ADH level (SIADH)

c. Renal failure (Increased water retention)

d. Excess water gains from hypotonic IV fluids (D5W, 0.25 or 0.45 NaCl)

Symptoms of hyponatremia

- Seizures, coma, encephalopathy and cramping

Hypernatremia

Hypernatremia represents an increase in plasma sodium concentration above 145 mmol/L.

Causes of hypernatremia

a. Sodium gain from excessive intake (salt tablets, food and medications)

b. Excess water loss (diarrhea, sweating and burn) resulting in dehydration

c. Hyperaldosteronism

d. Diabetes insipidus (ADH deficiency and increase water loss)

e. IV hypertonic saline

Symptoms of hypernatremia

- Tachycardia
- Weakness and muscle aches
- Headache, nausea and vomiting, and confusion