WATER AND ELECTROLYTES

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ELECTROLYTES

- Are ions capable of carrying an electric charge (cations or anions)
- The dietary requirements for electrolytes vary widely; some need to be Consumed only in small amounts. Others, such as calcium, potassium and Phosphorus, are excreted continuously and must be ingested regularly to Prevent deficiency
- They are involved in many processes:
  - Volume and osmotic pressure (Na, K, Cl)
  - Myocardial rhythm and contractility (K, Mg, Ca)
  - Cofactors in enzyme activation (Mg, Ca, Zn)
  - Regulation of ATPase ion pump (Mg)
  - Acid-base balance (HCO_3, K, Cl)
  - Blood coagulation (Ca, Mg)
  - Neuromuscular excitability (K, Ca, Mg)
  - Production and use of ATP from glucose (Mg, PO_4)

WATER

- In a 70-kg man, the total body water is about 42L (60%), ICF(28L) and ECF (14 L, plasma (3.5 L) and interstitial fluid (10.5L))
- Daily water intake is 1.5-2L
- Women have lower water content than men (more fat)
- Importance of water in human body:
  - Transport nutrient to the cells
  - Determine cell volume by its transport into and out of cells
  - Remove waste products (urine)
  - Body coolant (sweating)

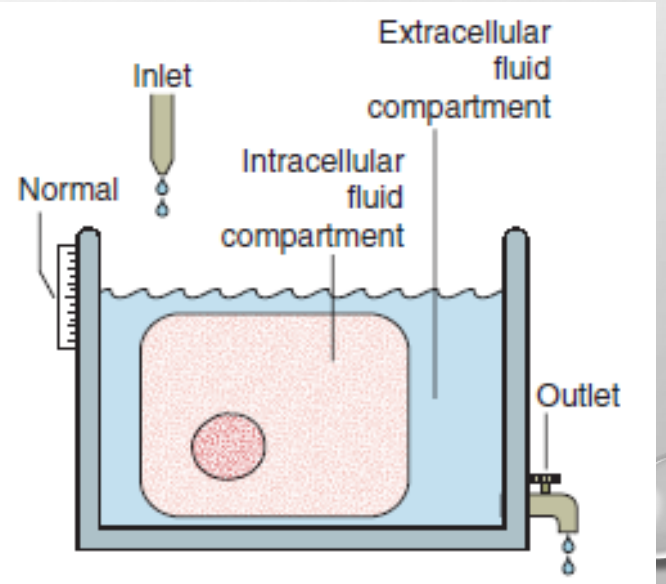

Fig 6.2 **Water tank model of body fluid compartments.**

WATER

- The concentration of ions inside the cells and in plasma is maintained by passive diffusion and active transport through ATPase-dependent ion pump
- Most biological membranes are permeable to water but not ions
- Water and sodium output
  - Kidneys and gastrointestinal tract
  - Sweat and expired air: about 1L daily
- Factors that affect the flow of water across the membrane
  - Ions and proteins at one side of the membrane
  - Blood pressure

CLINICAL FEATURES OF HYDRATION PROBLEMS

Table 6.1 **The principal clinical features of severe hydration disorders**

Feature	Dehydration	Overhydration
Pulse	Increased	Normal
Blood pressure	Decreased	Normal or increased
Skin turgor	Decreased	Increased
Eyeballs	Soft/sunken	Normal
Mucous membranes	Dry	Normal
Urine output	Decreased	May be normal or decreased
Consciousness	Decreased	Decreased

CONTROL OF WATER BALANCE

- Both intake and loss of water are controlled by osmotic gradient across cell membrane in the brain hypothalamic osmoreceptor centre
- These centres control thirst and secretion of antidiuretic hormone (ADH)=AVP (arginine vasopressin hormone)
- Thirst is the major defense mechanism against hyperosmolality and hypernatremia
- Antidiuretic hormone:
  - Is polypeptide with $t_{1/2}$ of 20 min
  - Synthesized by the hypothalamus and secreted by the posterior pituitary
  - 2% increase in osmolality lead to 4 times increase in ADH
  - Low blood pressure and severe hypovolemia stimulate ADH release
  - Stress due to vomiting, nausea and pain may increase ADH secretion
  - ADH act by increasing the reabsorption of water in cortical and medullary collecting tubules

CONTROL OF WATER BALANCE

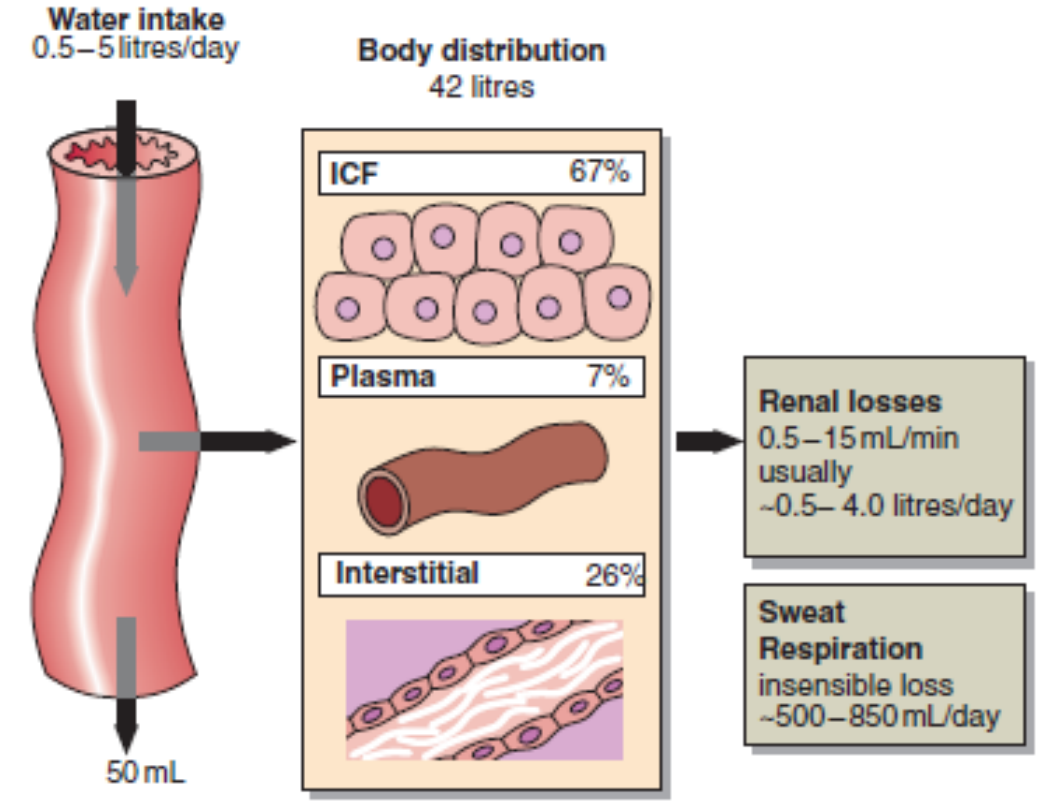

Fig 7.1 **Normal water balance.**

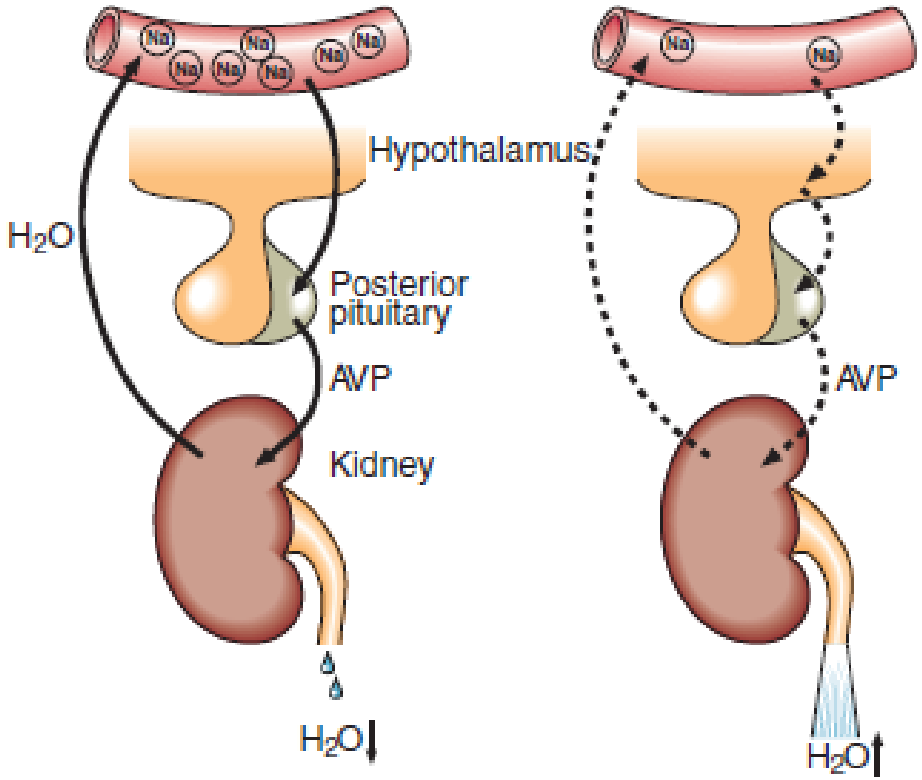

Fig 7.2 **The regulation of water balance by AVP and osmolality.**

CONTROL OF WATER BALANCE

- Hypernatremia rarely occurs in a person with a normal thirst mechanism and access to water, it becomes a concern in:
  - Infants
  - Unconscious patients
  - Anyone who is unable to drink or ask for water.
  - People who are older than 60 where osmotic stimulation of thirst progressively diminished
  - In the older patient with illness and diminished mental status, dehydration becomes increasingly likely example of the effectiveness of thirst in preventing dehydration
- A patient with diabetes insipidus (no ADH) may excrete 10 L of urine daily, but as water intake matches output, plasma sodium remains normal

OSMOLALITY

- Physical property based on the conc. of solutes (in mmol) per kg of solvent (w/w). This affect different properties of solution as:
  - Freezing point depression
  - Vapor pressure decrease
- Increase in osmolality will induce secretion of ADH enzyme while decrease in osmolality will lead to turning off ADH secretion
- Osmolal gap is the difference between the measured osmolality and the calculated osmolality
- Osmolal gap indirectly indicates the presence of osmotically active substances other than sodium, urea, or glucose, such as ethanol, methanol, ethylene glycol, lactate, or β-hydroxybutyrate.

SIGNIFICANCE OF OSMOLALITY

- Because it is the parameter by which the hypothalamus responds
- It affects Na concentration as it represents 90% of osmotic activity in Plasma
- Na concentration is also affected by blood volume

DETERMINATION OF OSMOLALITY

- Osmolality may be measured in serum or urine.
- Plasma use is not recommended because osmotically active substances may be introduced into the specimen from the anticoagulant.
- Samples must be free of particulate matter to obtain accurate results.
- Turbid serum and urine samples should be centrifuged before analysis

DETERMINATION OF OSMOLALITY

- Osmometers are standardized by NaCl solution, then the freezing point of the sample is measured and this is compared to the calculated value as double of serum sodium or according to the following 2 formulas:

$$2\,Na + \frac{\text{glucose (mg/dL)}}{20} + \frac{\text{BUN (mg/dL)}}{3}$$

$$1.86\,Na + \frac{\text{glucose}}{18} + \frac{\text{BUN}}{2.8} + 9 \qquad \text{(Eq. 15-1)}$$

NORMAL RANGES

TABLE 15-1 REFERENCE RANGES FOR OSMOLALITY

Serum	275–295 mOsm/kg
Urine (24-h)	300–900 mOsm/kg
Urine/serum ratio	1.0–3.0
Random urine	50–1200 mOsm/kg
Osmolal gap	5–10 mOsm/kg

Electrolytes, Sodium (Na)

- Body contains about 3000 mmol of sodium mainly in ECF
- Sodium daily intake is about 60-150 mmol
- Sodium balance is regulated by blood flow and aldosterone (hormone secreted by adrenal cortex)

Electrolytes, Sodium (Na)

- Sodium is the most abundant cation in the ECF (90% of all extracellular cations) and largely determines the osmolality of the plasma.
- Sodium concentration in the ECF is much larger than inside the cells, because a small amount of sodium can diffuse through the cell membrane.
- To prevent equilibrium from occurring, active transport systems, such as ATPase-dependent ion pumps (moves 3 Na out of cell for each 2 K moving into the cell) are present in all cells

REGULATION OF SODIUM

- The plasma sodium concentration depends on: the intake and excretion of water and the renal regulation of sodium
- Three processes are of primary importance:

  (1) The intake of water in response to thirst, as stimulated or suppressed by plasma osmolality
  (2)the excretion of water, largely affected by ADH release in response to changes in either blood volume or osmolality

  (3) the blood volume status, which affects sodium excretion through aldosterone- angiotensin II and ANP (atrial natriuretic peptide)

- The kidneys have the ability to conserve or excrete large amounts of sodium, depending on the sodium content of the ECF and the blood volume, normally, 60-75% of filtered sodium is reabsorbed in the proximal tubule
- some sodium is reabsorbed in the loop and distal tubules (controlled by aldosterone) exchanged for K in the connecting segment and cortical collecting tubule.

REGULATION OF SODIUM

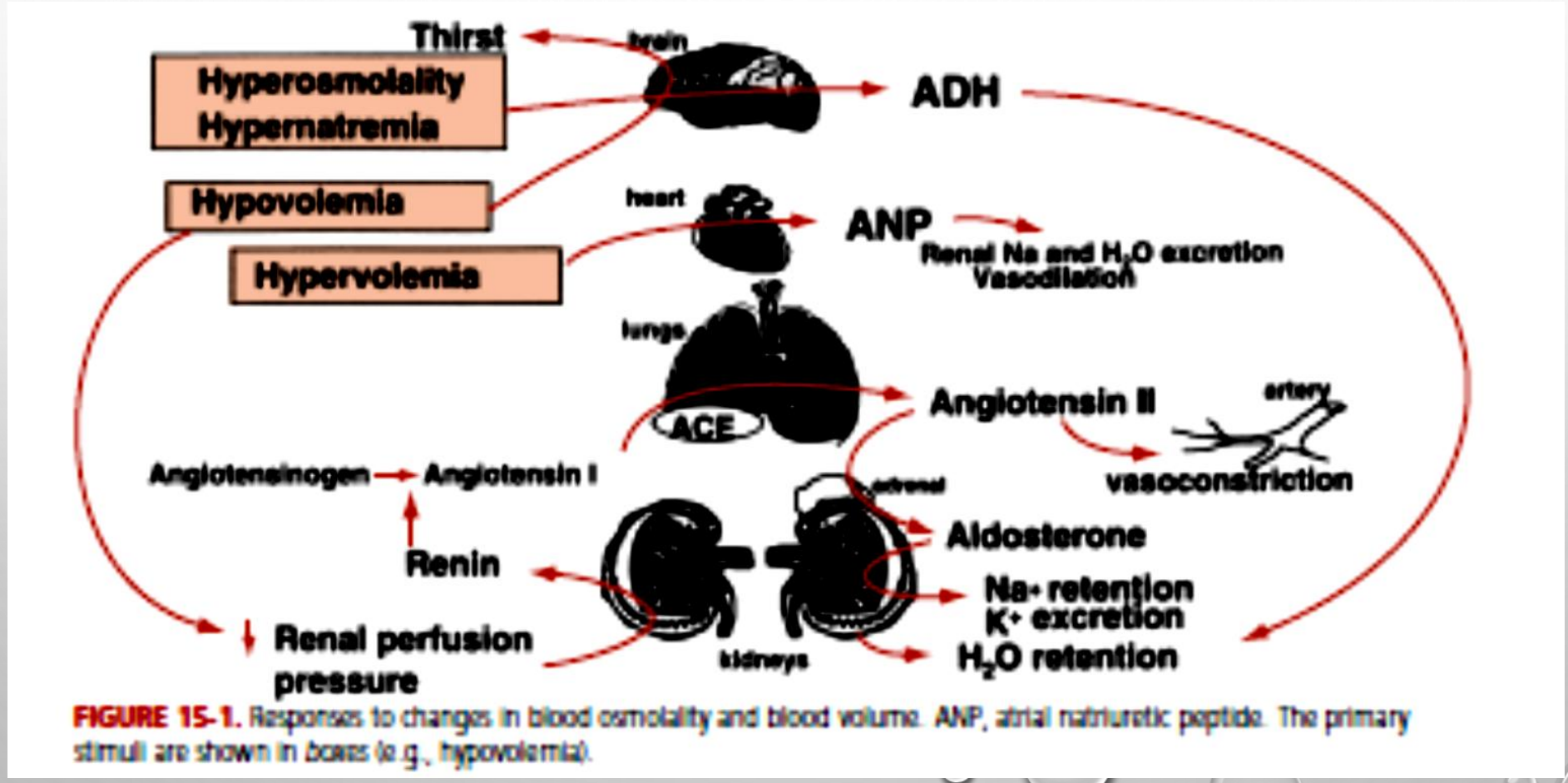

FIGURE 15-1. Responses to changes in blood osmolality and blood volume. ANP, atrial natriuretic peptide. The primary stimuli are shown in *boxes* (e.g., hypovolemia).

CAUSES OF HYPERNATREMIA

- Excess water loss
  - Diabetes insipidus
  - Renal tubular disorder
  - Prolonged diarrhea
  - Profuse sweating
  - Severe burns
- Decreased water intake
  - Older persons
  - Infants
  - Mental impairment
- Increased intake or retention
  - Hyperaldosteronism
  - Sodium bicarbonate excess
  - Dialysis fluid excess

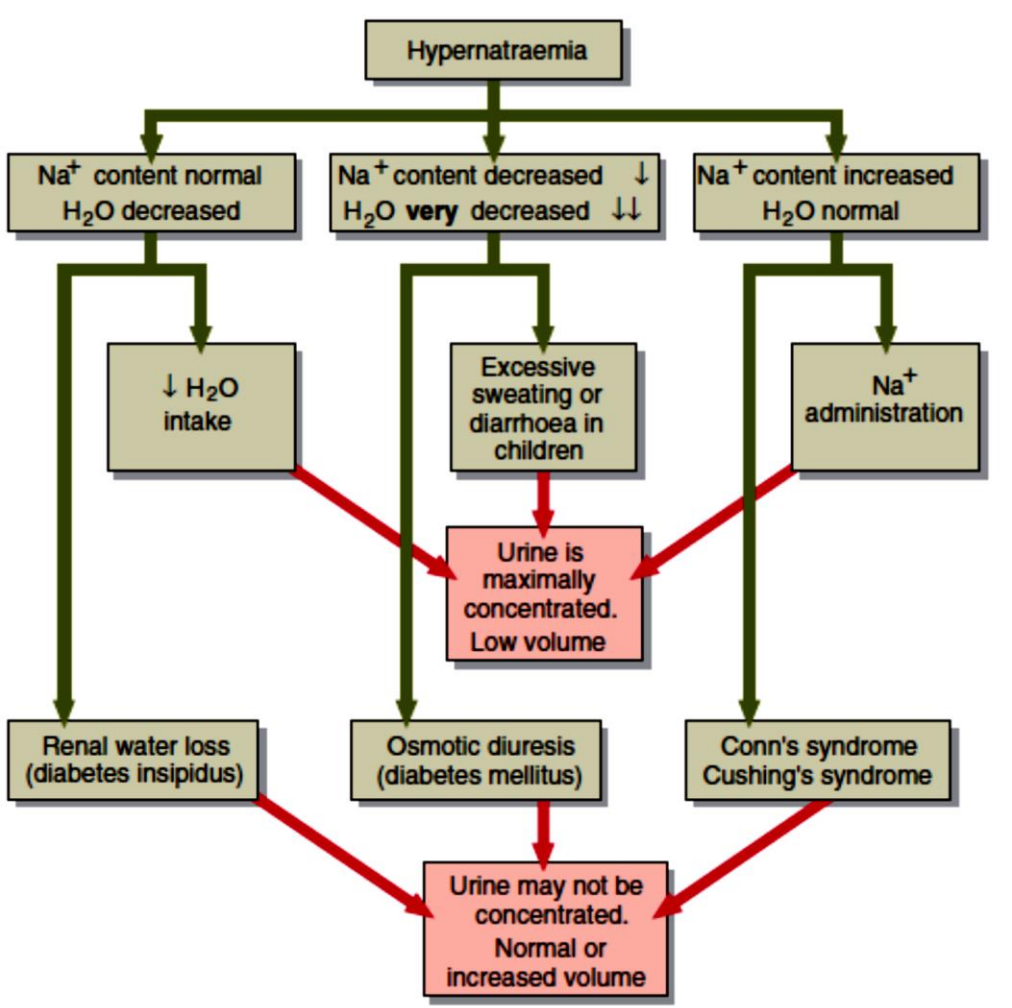

Fig 10.1 **The causes of hypernatraemia.**

HYPERNATREMIA (150 MMOL/L) RELATED TO URINE OSMOLALITY

- Urine osmolality <300 mosm/kg
  - Diabetes insipidus (impaired secretion of ADH respond to ADH) or kidneys cannot
- Urine osmolality 300-700 mosm/kg
  - Partial defect in ADH release or response to ADH
  - Osmotic diuresis
- Urine osmolality >700 mosm/kg
  - Loss of thirst
  - Insensible loss of water (breathing, skin)
  - GI loss of hypotonic fluid
  - Excess intake of sodium

SYMPTOMS OF HYPERNATREMIA

- Involve the central nervous system (CNS) hyperosmolar state which include: as a result of the
  - Altered mental status
  - Lethargy
  - Irritability
  - Restlessness.
  - Seizures
  - Muscle twitching, hyperreflexes
  - Fever, nausea or vomiting
  - Difficult respiration, and increased thirst.
- Serum sodium of more than 160 mmol/L is associated with a mortality rate of 60-75%

TREATMENT OF HYPERNATREMIA

- Treatment is directed at correction of the underlying condition that caused the water depletion or sodium retention.

- The speed of correction depends on the rate with which the condition developed

- Hypernatremia must be corrected gradually because too rapid a correction of serious hypernatremia (>160 mmol/L) can induce cerebral edema and death. The maximal rate should be 0.5 mmol/L per hour

HYPONATREMIA

- Hyponatremia is defined as a serum or plasma level <135 mmol/L.
- Levels below 130 mmol/l are clinically significant.
- Hyponatremia can be assessed by the cause for the decrease or with the osmolality level.

CAUSES OF HYPONATREMIA

- Increase sodium loss
  - Hypoadrenalism
  - Potassium deficiency (exchange in kidney)
  - Diuretic use (thiazide)
  - Ketonuria (sodium lost with ketones)
  - Salt losing nephropathy (with some renal tubular disorders)
- **These factors will increase the conc. of Na in urine to >20 mmol/L**
  - Prolong vomiting or diarrhea
  - Severe burns
- Increased water retention
  - Renal failure
  - Nephrotic syndrome
  - Hepatic cirrhosis
  - Congestive heart failure

CAUSES OF HYPONATREMIA

- Water imbalance

- Excess water intake (polydipsia, increased thirst): may cause mild or severe hyponatremia if water intake was chronic. In a normal individual, excess intake will not affect Na levels.

- SIADH causes an increase in water retention because of increased ADH production which is associated with pulmonary disease, malignancies, CNS disorders, infections.

- Pseudohyponatremia by measuring Na using indirect ISE (which dilutes sample prior to analysis), in a patient with hyperproteinemia or hyperlipidemia.

CLASSIFICATION OF HYPONATREMIA BY OSMOLALITY

- With low osmolality
  - Increased sodium loss
  - Increased water retention
- With normal osmolality increased nonsodium cations
  - Lithium excess
  - Increased -γ-globulins-cationic (multiple myeloma)
  - Severe hyperkalemia
  - Severe hypermagnesemia
  - Severe hypercalcemia, pseudohyponatremia
  - Hyperlipidemia
  - Hyperproteinemia
  - Pseudohyperkalemia as a result of in vitro hemolysis
- With high osmolality
  - Hyperglycemia
  - Mannitol infusion

SYMPTOMS OF HYPONATREMIA

- Symptoms depend on the serum level.
  - Between 125 and 130 mmol/l: symptoms are gastrointestinal
  - Below 125 mmol/l: more severe neuropsychiatric seen including nausea and vomiting, muscular weakness, headache, lethargy, and ataxia.
  - More severe symptoms also include seizures, coma, and respiratory depression

TREATMENT OF HYPONATREMIA

- Treatment is directed correction of the condition that caused either water loss or sodium loss in excess of water loss.
- Correcting severe hyponatremia too rapidly can cause cerebral myelinolysis while too slowly can cause cerebral edema
- Appropriate management of fluid administration is critical. Fluid administration and monitoring is required during treatment of the underlying cause of the hyponatremia.
- The measurement of urine osmolality is necessary to evaluate the cause of hypernatremia
- Chronic hyponatremia in an alert patient is indicative of hypothalamic disease

DETERMINATION OF SODIUM

- Sodium can be measured in serum, plasma, and urine.
- When plasma is used, lithium heparin, ammonium heparin, and lithium oxalate are suitable anticoagulants.
- Hemolysis does not cause significant change in serum or plasma values as a result of decreased levels of intracellular sodium. however, with marked hemolysis, levels may be decreased as a result of a dilutional effect
- Whole blood samples may be used with some analyzers.
- The specimen of choice in urine sodium analyses is a 24-hour collection.
- Sweat is also suitable for analysis.

POTASSIUM

- Potassium is the major intracellular cation in the body with a concentration 20 times greater inside the cells than outside
- Many cellular functions requires that the body maintains a low ECF concentration of K. As a result, only 2% of the body's total potassium circulates in the plasma
- Function of potassium in the body include
  - Neuromuscular excitability
  - Contraction of the heart
  - ICF volume
  - Hydrogen ion concentration

POTASSIUM

- The potassium ion concentration has a major effect on skeletal and cardiac muscles. A lower than normal difference increases cell excitability leading to muscle weakness.
- Severe hypokalemia can cause muscle excitability which may lead to paralysis or fatal cardiac arrhythmia
- Hypokalemia decreases cell excitability resulting in an arrhythmia or paralysis
- the heart may cease to contract in extreme case of hypokalemia or hyperkalemia
- Potassium concentration affects hydrogen ion concentration in the blood. In hypokalemia, when potassium ion is lost from the blood, sodium and hydrogen ions move to into the cells. The hydrogen ion concentration decreases in ECF resulting to alkalosis

FACTORS AFFECT K LEVEL IN ECF

- Three factors that influence the distribution of potassium between cells and ECF are:
- (1) **Potassium loss** frequently occurs whenever the NaK ATPase pump is inhibited by conditions such as:
  - (1) hypoxia
  - (2) hypomagnesemia
  - (3) or digoxin overdose
- (2) **Insulin** promotes acute entry of K ions into skeletal muscle and liver by increasing NaK ATPase activity
- (3) **Catecholeamines** such as epinephrine (β2-stimulator), promotes cellular entry of K whereas propranolol (β-blocker) impairs cellular entry of potassium .
- With preexisting condition such as **dietary deficiency** (or excess) can enhance the degree of hypokalemia (or hyperkalemia)but rarely the primary cause.

Factors affect K level in ECF

- **Exercise:** potassium is released from cells leading to increase by 0.3-1.2 mmol/L with mild to moderate exercise and 2-3 mmol/l with exhaustive exercise (reversed after several minutes of rest).
- **Hyperosmolality:** like in uncontrolled diabetes mellitus, causes water to diffuse from the cells carrying potassium ions leading to gradual depletion of potassium if kidney function is normal.
- **Cellular breakdown:** cellular breakdown releases K into the ECF like in severe trauma, tumor lysis syndrome and massive blood transfusion.

HYPOKALEMIA

- Hypokalemia is a plasma potassium concentration below the lower limit of the reference range
- Hypokalemia can occur with GI or urinary loss of potassium or with increased cellular uptake of K
- Common causes of hypokalemia like:
- GI loss occurs when GI fluid is lost through vomiting, diarrhea, gastric suction or discharge from intestinal fistula
- Increased potassium loss in the stool also occurs in certain tumors, malabsorption, cancer therapy and large doses of laxatives
- Renal loss of K can result from kidney disorders such as potassium losing nephritis and renal tubular acidosis (RTA). In RTA, as tubular excretion of H+ decreases, K excretion increases

HYPOKALEMIA, COMMON CAUSES

- **Hyperaldosteronism:** lead to hypokalemia and alkalosis
- **Magnesium deficiency:** inhibits NaK ATPase and enhances secretion of aldosterone (treated by Mg and K supplement)
- **Alkalemia and insulin**: increase the cellular uptake of K
- **Drug induced:** thiazide diuretics and corticosteroids are the most important, carbanoxolone has mineralocorticoid activity
- **Alkalosis:** may cause a shift of potassium from the ECF to the ICF (0.1 increase in pH leads to 0.4 mmol/l decrease in potassium)

SYMPTOMS OF HYPOKALEMIA

- Mild hypokalemia (3-3.4 mmol/L) is asymptomatic
- Weakness, fatigue and constipation at K< 3 mmol/l
- Muscle weakness and paralysis that interfere with breathing
- Dangerous for patients with cardiovascular disease as it may cause arrhythmia leading to sudden death in some patients

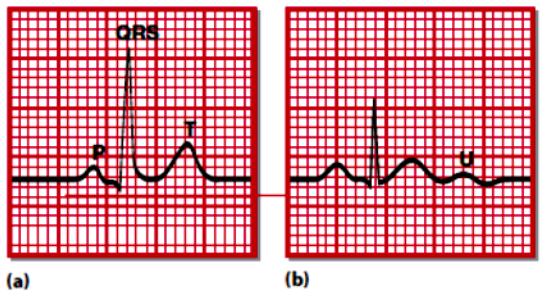

Fig 12.1 **Typical ECG changes associated with hypokalaemia. (a)** Normal ECG (lead II). **(b)** Patient with hypokalaemia: note flattened T-wave. U-waves are prominent in all leads.

TREATMENT

- Potassium salt are unpleasant to take orally and are usually given prophylactically in an enteric coating
- Severe potassium depletion often has to be treated by intravenous potassium
- Intravenous potassium should not be given faster than 20 mmol/hour except in extreme cases and under ECG monitoring
- Mild chronic hypokalemia can be treated by diet rich K (dried fruits, nuts, banana and orange juice)

HYPERKALEMIA

- Hyperkalemia is the commonest and most serious electrolyte emergency encountered in clinical practice.

- Hyperkalemia causes muscle weakness that may be preceded by paraesthesiae. However, the first manifestation may be cardiac arrest.

- Above 7.0 mmol/l there is a serious risk of cardiac arrest. However, the ECG changes in hyperkalaemia may mimic other conditions such as myocardial infarction, thus, it is important to check the serum potassium concentration in patients after cardiac arrest

CAUSES OF HYPERKALEMIA

- **Renal failure.** The kidneys may not be able to excrete when the glomerular filtration rate is very low. The acidosis associated with renal failure contributes to the problem.

- **Mineralocorticoid:** this the most frequently seen in Addison's disease or in patient receiving aldosterone antagonists. In these patients, there is an increase in total body potassium

- **Acidosis:** Hyperkalemia results from the redistribution of potassium from the intracellular to the extracellular fluid space

CAUSES OF HYPERKALEMIA

- **Potassium release from damaged cells:** because of the very high potassium concentration inside cells, cell damage can give rise to a very high serum potassium as occurs in trauma and malignancy

- **Diabetes mellitus:** fast shift of potassium from cells to the blood due to insulin deficiency in addition to hyperosmolality that pulls water to outside the cells

- **Various drugs:** specially in patients with renal insufficiency or diabetes mellitus as captopril (ACEI), NSAID, digoxin, spironolactone, cyclosporine and heparin therapy

- **Warming after surgery** leads to release of K from cells, hypothermia may cause hypokalemia

PSEUDOHYPERKALEMIA

- Refers to elevation in the measured potassium concentration potassium movement out of cells during or after the drawing of the blood specimen.
- The commonest cause is hemolysis. This can occur due to mechanical trauma during venopuncture. Hemolysis is characterized by release of potassium from red blood cells.
- A small amount of potassium is released from white blood cells and platelets during normal clotting
- In patient with grossly elevated white cells and platelets due to hematological malignancies, the amount of potassium released is much greater
- Pseudohyperkalemia should be suspected when there is no apparent cause for hyperkalemia and there are no ECG changes reflecting altered cardiac muscle contractility

SYMPTOMS OF HYPERKALEMIA

- Muscle weakness at K conc of 8 mmol/l
- Tingling, numbness and mental confusion
- Cardiac arrhythmia and cardiac arrest at conc of 6-7 mmol/l which alter ECG
- Fatal cardiac arrest at conc > 10 mmol/l

TREATMENT OF HYPERKALEMIA

- Treatment should be started if K > 6-6.5 or if ECG changes occur
- An infusion of calcium gluconate may be given to potential of myocardial cells reduce threshold
- the commonest form of treatment of acute hyperkalemia is the infusion of sodium carbonate, insulin and glucose to move potassium ions into cells
- K can be removed by loop diuretics in good renal function
- Na polystyrene sulphonate enema which binds K secreted in the colon
- Dialysis is frequently necessary to treat severe hyperkalemia

COLLECTION OF THE SAMPLE

- Simultaneous collection and processing of serum and plasma specimens may help, the anticoagulant in plasma specimens prevents clotting from occurring.
- Care must be taken during drawing of blood as high platelet counts or when tourniquet is left for long time on the arm may increase the conc of K
- Whole blood samples should be stored at room temperature (not iced) or rapid centrifugation of the sample to remove cells
- Specimen used may include serum, plasma, whole blood or 24-hr-urine sample
- Reference ranges of potassium are:
  - Serum and plasma 3.4-5.0 mmol/l
  - Urine (24-hr) 25-125 mmol/day