SODIUM BALANCE – Overview

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How are solute and solvent related to solution?

- **Solution** is made up of **Solute** and **Solvent**,
- **Concentration** of solution is a ratio of two variables:
  - Amount of Solvent (*Water*),
  - Amount of Solute (e.g., **Na**\(^+\) ions),
- **Molar concentration** = Amount of Solute in 1000ml of solution,
- Molar concentration is represented as \([\ ]\),
- Concentration of solution can change when either or both variables change For example:
  - Solution containing \([\text{Na}^+]\) of 140mmol/L may become 130mmol/L if amount of **Na**\(^+\) ions in solution is reduced or amount of Solvent (water) is increased;
What are the electrolytes (Solutes) in ECF and ICF?

• Na\(^+\) is Principal Cation in ECF,
• K\(^+\) is Principal Cation in ICF,
• Proteins and Phosphates are the main Anions in ICF,
• Cl\(^-\) ions & HCO\(_3^-\) ions are main Anions in ECF,
• Na\(^+\) is highest in ECF; it contributes to plasma Osmolality,
• Urea & Creatinine are measured with plasma electrolytes because they provide an indication of Renal Function,
• Increase in plasma [Urea] and [Creatinine] indicates decrease in Glomerular Filtration Rate in the kidneys;

• How are the Solvent (Water) and Solutes regulated?
How is water (solvent) balance regulated?

- Water balance is regulated by Arginine Vasopressin (AVP)
- AVP: hormone produced by Posterior Pituitary Gland;
- AVP tightly regulates water excretion by kidneys;
- Osmolality in ICF is equal to that in ECF;
- Specialized cells in Hypothalamus maintain Osmolality between ICF and ECF;
- When Hypothalamus detects differences in Osmolality between ICF and ECF it regulates secretion of AVP;
• Regulation is as follows:
  • Rising Osmolality promotes secretion of AVP,
  • Declining Osmolality switches off secretion of AVP,
  • AVP causes water to be retained by the kidneys,
• Fluid deprivation results in stimulation of AVP secretion causing reduction in Urine Flow Rate to about 0.5 ml/min to conserve body water;
• Within ONE hour after drinking about 2 liters of water, Urine Flow Rate may rise to about 15 ml/min as AVP secretion is Shut Down;
• By regulating water Excretion or Retention, AVP maintains normal concentrations of Electrolytes within the body (Figs. 1a & 1b)
Figs. 1a & 1b: Regulation of water balance by AVP: Increased Osmolality activates AVP secretion and reduces urine flow rate; Decreased Osmolality inhibits secretion of AVP and increases urine flow rate;
SODIUM BALANCE

• Amount consumed should equal amount loss per day;
• Total Sodium in body is made up of:
  • Non-Exchangeable Sodium = 25% of Total Sodium;
  • Exchangeable sodium = 75% of Total Sodium;
• Non-Exchangeable Sodium is in Bone and Cartilage and has slow turnover rate;
• Most Exchangeable Sodium is in ECF;
• Exchangeable Sodium circulates in Plasma as Na⁺;
• Normal range of Na⁺ in plasma = 135 to 145mmol/L;
• Plasma [Na⁺ ] does not indicate Sodium balance;
• Plasma [Na⁺ ] primarily reflects body water content;
Sodium intake and Sodium loss:

Sodium Intake:
- By individuals vary, depending on Habits, Taste, Availability;
- Health individuals: Total body sodium does not change even if intake falls to 5mmol/day or increases to 750mmol/day;

Sodium Loss:
- Loss of sodium varies among individuals;
- Sodium is excreted mainly via the Kidneys;
- Some is lost in sweat (5 mmol/day) and feces (5 mmol/day);
- GIT is major route of pathological Sodium loss;
- **Diarrhea** and **Vomiting** may result in death from Salt loss and Water Depletion in **Pediatric Cases**;
What factors regulate Sodium excretion?

• Sodium Excretion is regulated by:
  • Intrinsic Renal Mechanisms,
  • Level of Aldosterone Secretion,
  • Secretion of Atrial Natriuretic Factor (ANF),
What is the role of Aldosterone in regulation of Sodium Balance?

• Aldosterone is a hormone produce in Adrenal Cortex;

• **Aldosterone:**
  
  • Decreases Urinary Sodium Excretion by Increasing the Re-absorption of Na\(^+\) in Renal Tubules in exchange for Tubule excretion of K\(^+\) and H\(^+\),
  
  • Decreases loss of Na\(^+\) in Sweat Glands and Mucosal Cells of the Colon, but in normal circumstances these effects are minimal;
How is secretion of Aldosterone regulated?

• Major stimulus for secretion of Aldosterone:
  • Volume of ECF, and Osmolality of ECF,
  • Specialized cells in Juxtaglomerular Apparatus of the Kidneys detect decrease in Blood Pressure and secrete **Renin**, 
• Renin converts **Angiotensinogen** to **Angiotensin I**;
• **Angiotensin Converting Enzyme** (ACP) in Lungs converts **Angiotensin I** to **Angiotensin II**;
• **Angiotensin II** acts on Adrenal Cortex to produce **Aldosterone**
• Aldosterone acts on Kidney Tubules causing reabsorption of **Na⁺** in exchange for excretion of **K⁺, and H⁺** (Fig. 2)

• Action of Angiotensin II is terminated by **Angiotensinasis**;
Fig. 2: Regulation of Sodium balance by Aldosterone?
What is the role of Atrial Natriuretic Factor (ANF) in regulation of Sodium balance?

- 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: **Natriuresis**;
- ANF regulates ECF volume,
- ANF regulates concentration of Sodium in plasma,
What is Osmolality (Osmolarity)?

• Osmolality: concentration of **osmotically active** particles in solution,
  • particles that cannot cross semi-permeable membrane,
• Water moves across cell membrane separating ECF from ICF;
• Osmosis is flow of solvent across semi-permeable membrane from low solute concentration to higher solute concentration,
• Osmotic pressure: driving force for water to change the concentration of osmotically active particles,
• Osmolality of ICF = Osmolality of ECF: Isotonic solutions,
• Water moves across cell membrane to maintain Osmolality of ECF & ICF; even if the cells shrink or expand in volume,
How is Osmolality of Serum or Plasma calculated?

- Osmotically active solutes are used:
- Simple formula for calculating Osmolality:
  \[
  \text{Serum Osmolality} = 2[\text{Na}^+] 
  \]
  (Unit is \text{mmol/kg}, \text{or mOsmol/Kg} \text{ or mOsmol/L}; \text{Unit for Plasma or Serum Sodium ion is mmol/L});
- Simple formula is used only when Plasma [\text{Urea}] and [\text{Glucose}] are within the reference ranges;
- \textbf{NB}: Normal Osmolality of Serum or Plasma (other body fluids except urine) is \textbf{285 to 295 mmol/kg (285 to 295 mOsmol/L)};
Example for calculating Osmolality

**Normal Conditions** (Plasma or Serum [Urea] and [Glucose] are within normal range)

- ECF Osmolality can be roughly estimated as:

\[ P_{osm} = 2 \cdot [\text{Na}]_p = 270 - 290 \text{ mOsm} \]

Where \( P_{osm} \) is plasma Osmolality; since intracellular Osmolarity is the same as extra-cellular Osmolality under normal conditions, this also provides an estimate of intracellular Osmolality.
Example for calculation of Osmolality

Clinical Laboratory Measurement:

• Plasma Osmolarity measured in Clinical laboratory also includes [Glucose] and [Urea];
• Normally the contribution from Glucose and Urea is small;
• Under certain Pathological conditions, the concentrations of these substances can be very high;
• Plasma Osmolality measured in clinical laboratory:

\[ P = 2[Na^+] + 2[K^+] + [\text{Glucose}] + [\text{Urea}] \]

(\(P = \) Plasma or Serum Osmolality)

• Glucose and BUN normally contribute about 5mOsm each (about 2%) of Plasma Osmolarity measured in the clinical lab.
How is effective Osmole different from ineffective Osmole?

- **Ineffective Osmole:**
  - Urea crosses the semi-permeable cell membranes just as easily as water, therefore it does not contribute to redistribution of water between ECF and ICF;

- **Effective Osmoles:**
  - Glucose, Na$^+$ and Anions associated with Na$^+$ do not cross the semi-permeable membrane;
  - They have concentration gradients across the cell membrane and are osmotically active;
  - They determine the distribution of water between ECF and ICF;
How is Effective Osmole calculated?

Two ways for calculating Effective Osmole:

• Effective Osmole:
  \[ P \text{ (effective)} = 2[Na^+] + [\text{Glucose}] \]

• Effective Osmole:
  \[ P \text{ (effective)} = P \text{ (measured)} - [\text{Urea}] \]

  (\(P = \) plasma or serum Osmolality)
What is Osmolal Gap and how is it calculated?

**OSMOLAL GAP (OG):**

- Difference between Measured Osmolality (MO) and Calculated Osmolality (CO)

\[
\text{Osmolal Gap (OG)} = \text{MO} - \text{CO}
\]

- Large positive OG helps to identify presence in serum of osmotically active substances, e.g., Ethanol, Methanol, Iso-propanol, Ethylene Glycol and Acetone,

- Proper interpretation of OG also requires knowledge of Anion Gap (AG), and blood pH

\[
\text{Anion Gap} = [\text{Na}^+] - \{[\text{HCO}_3^-] + [\text{Cl}^-]\}
\]
What is HYponatraemia?

• **Hyponatraemia**: significant fall in $[\text{Na}^+]$ below the reference range for plasma or serum;
  • (what is the reference range for Serum $[\text{Na}^+]$ in PMGH?)

• **“Hypo-Osmolality”** is synonymous with **Hyponatraemia** because $\text{Na}^+$ is major cation in ECF in sufficient amount such that a decrease in concentration would significantly affect the Osmolality;
List two possibilities of Hyponatraemia?

• Hyponatraemia due to Fluid **Retention:**
  • More fluid than normal is retained in the body compartments and dilutes the constituents in ECF causing **Hyponatraemia**; *(Fig. 3a)*

• Hyponatraemia due to **Loss of Na\(^+\) ions:**
  • When loss of **Na\(^+\) ions** exceeds loss of fluid, Hyponatraemia may result, *(Fig. 3b)*
  • Example: Loss of fluid (vomiting or fistulae) that contain **Na\(^+\) ions** are replaced simply by water;
Fig. 3a: Fluid retention in ECF & ICF causing Hyponatraemia
Fig. 3b: Sodium loss resulting in Hyponatraemia [Gwa et al 1999]
• Water tank model in **Fig. 3a & 3b** emphasizes that biochemical observation of Hyponatraemia gives no clear explanation about the volume of the ECF compartment;

• Both laboratory results of these patients indicate Hyponatraemia, with no indication of fluid retention or loss of Sodium;

• **Thus, the courses of Hyponatraemia should be made by proper History taking and Clinical Examination of the Patient, not by assessing the laboratory results alone;**
• Some patients with reduced ECF volume may present with either Reduced, Increased or Normal Plasma Sodium concentration (Figure 4a, 4b, 4c),

• These diagrams clearly indicates that Clinicians MUST always give greater emphasis and attention to History, Signs and Symptoms of the Patients not to Laboratory results on plasma Sodium alone;
Fig. 4a: Reduced ECF with Hyponatraemia (low plasma Sodium conc.);
Fig. 4b: Reduced ECF with Hypernatraemia (high plasma Sodium conc.);
Fig. 4c: Reduced ECF with Normal plasma Sodium conc. (Gwa et al 1999)
What are some causes of Hyponatraemia with fluid retention?

- **Decreased water excretion: Examples:**
  - Nephrotic Syndrome,
  - Renal Failure;

- **Increased Water Intake: Examples:**
  - Inappropriate IV Saline,
  - Compulsive water drinking,
TAKE NOTE:

• If fluid loss is not apparent from the Clinical history of a patient then the reason for the Hyponatraemia is usually WATER RETENTION;

• Hyponatraemia due to water overload without decrease in total body Sodium is the commonest Biochemical disturbance encountered in clinical practice;

• Further consideration of Hyponatraemia of this type, depends on whether the patient has Edema:

• Two possible conditions are:
  • Edematous Hyponatraemia,
  • Non-Edematous Hyponatraemia,
EDEMATOUS HYPONATRAEMIA

• Patients with generalized Edema have an increase in both Total Body Sodium and Water:

• Some causes of Edema:

• Heart Failure:
  • Effective blood volume may be reduced because pumping action of the heart is unable to maintain a satisfactory circulation of Blood and ECF;

• Hypo-albuminaemia,
  • Effective blood volume is reduced because Hypo-albuminaemia lowers Plasma Oncotic Pressure, which disrupts normal exchange of solutes and fluid in capillary bed reducing circulation of Blood and ECF;
  • Edema occurs if albumin concentration falls very low;
• In response to reduced effective blood volume, **aldosterone** is secreted and causes Sodium retention to allow the ECF volume to expand;

• Reduction in effective blood volume is one of the Non-Osmotic Stimuli for the secretion of AVP and consequently water is retained;

• Hyponatraemia results from the Retention of relatively more water than Sodium in the ECF;
What are some causes of Hypo-albuminaemia?

• **Decreased biosynthesis** of albumin due to:
  • Liver disease;
  • Loss of albumin exceeds biosynthetic capacity of liver as occurs in Nephrotic syndrome;
  • Malnutrition or Mal-absorption;

• **Abnormal distribution or dilution:**
  • Over-hydration or if there is increased capillary permeability as occurs in Septicemia;

• **Abnormal excretion or degradation:**
  • Nephrotic Syndrome, Protein-losing Enteropathies, Burns, Haemorrhage and Catabolic states;
NON-EDEMATOUS HYPONATRAEMIA

• Patients with Non-Edematous Hyponatraemia have normal total body Sodium and exhibit the features of Syndrome of Inappropriate Anti-diuresis (SIAD)

• Patients are Hyponatraemic, Normotensive, have normal Glomerular Filtration Rate (GFR) and normal serum Urea and Creatinine concentrations;

• Urine Flow Rate is usually less than 1.5 liter/day;
• SIAD may occur in conditions such as:
  • Infections, e.g. Pneumonia,
  • Malignancy, e.g. Carcinoma of Bowel or Lung,
  • Trauma, e.g. Abdominal Surgery,
  • Drug-induced, e.g. Thiazide Diuretics, Chlorpropamide
    • Patients suffering from any of the above may have Non-Osmotic AVP stimulation and, if they are exposed to excessive water loads, in the form of oral drinks or intravenous glucose solutions, they will become Hyponatraemic;
HYPONATRAEMIA DUE TO SODIUM LOSS

• Occurs during Pathological Sodium Loss
• May be from GIT or Urine
• Vomiting (severe and protracted as occurs in Pyloric Stenosis)
• Diarrhoea;
• Fistula
Urinary loss of Sodium may be due to

- Aldosterone deficiency due to failure of the Adrenal Glands (Addison’s disease);
- Drugs that antagonize Aldosterone action;
- Initially in such patients:
  - Sodium loss is accompanied by Water loss and Serum Sodium ion concentration remains normal;
  - As Sodium loss proceeds, the reduction in ECF and blood volume stimulates AVP secretion;
  - Non-osmotic control of AVP secretion overrides osmotic control mechanism;
  - Increased AVP secretion causes water retention and thus the patient becomes Hyponatraemic;
  - Patient becomes Hyponatraemic because a deficit of Isotonic Sodium-containing fluid is replaced only by water, either Orally or Intravenously;
- In all cases patients should be given Oral Rehydration Solution,
REFERENCES


WATER (FLUID) BALANCE (STEADY STATE)

• Amount of daily water intake varies among individuals;
• Amount of daily water loss varies among individuals;
• Water loss is normally seen as changes in volume of urine production;
  • Urine Flow Rate can vary widely in a very short time;
• **To maintain water balance:**
  • Amount of daily water intake must equal amount of daily water loss,
• Disruption of balance may cause:
  • Net water gain: Over hydration; or
  • Net water loss: Dehydration
How much fluid (water) is contained in the body?

• Water/Fluid is a major body constituent;
• Average person (70 kg) contains about 42 liters of Total Body Water (TBW);
• TBW is about 60% of total body weight;
• TBW separated into 2 major compartments;
  • Extra-Cellular Fluid Compartment (ECF),
  • Intra-Cellular Fluid Compartment (ICF),
    • Fig. 1: Water tank model illustration ECF, ICF, TBW,
Fig. 1: Schematic diagram of water tank model to illustrate body fluid compartments [Gwa et al 1999]
What are the major fluid compartments in the body?

- Major fluid compartments (Fig. 2):
  - Intra-Cellular Fluid Compartment (ICF): Volume of Fluid Inside Cells;
    - ICF constitute about 66.6% of TBW,
  - Extra-Cellular Fluid Compartment (ECF): Volume of Fluid Outside Cells;
    - ECF constitute about 33.3% of TBW,
  - ECF made up of **Plasma** and **Interstitial Fluid**
    - Plasma: about 25% of ECF,
    - Interstitial Fluid: about 75% of ECF,
What are the major sources and routes of fluid intake?

• Some major sources of fluid intake:
  • Water Drinking;
  • Water contained in various foodstuffs;
  • Metabolic water;
What are some major routes in the body for fluid loss?

- Some major routes of fluid loss:
  - Urinary loss,
  - Fecal loss
- Insensible water loss: evaporation from Respiratory Tract and Skin Surface (sweat is sensible since it has a purpose);

- Sweat Losses:
  - Room temperature: sweating is 25% of H$_2$O loss;
  - Cold environments: H$_2$O loss in sweat decreases;
  - Warm environments, exercise: sweat losses increases;
- Pathological losses: vascular bleeding, vomiting, and diarrhea;
What are some consequences of fluid loss?

• Selective loss of fluid from ICF or ECF gives rise to distinct signs and symptoms:
  • Loss of ICF can cause Cellular Dysfunction: leads to Lethargy, Confusion and Coma;
  • Loss of ECF: leads to Circulatory Collapse, Shock, Renal shutdown;
  • Loss of TBW: similar effects as loss of ICF or ECF;
• Signs of (substantial) fluid loss is spread across ICF & ECF;
How is the state of hydration of a patient assessed?

- State of Hydration indicates volume depletion or Volume expansion of body fluid compartments;
- It is assessed Clinically by appropriate Clinical signs;
- It involves:
  - History taking to identify water intake and water loss;
  - Signs and Symptoms indicating,
    - Dehydration (loss of fluid),
    - Over-hydration (accumulation of fluid)
- Figs 3a & 3b: illustrate effect of Volume Depletion and Volume Expansion on water thank model of body fluid compartments,
Fig. 3a: Dehydration: Loss of fluid in ICF & ECF due to increased urinary output; Fig. 3b: Overhydration: Increased fluid intake resulting in increased fluid volume in ICF and ECF [Gwa et al 1999]