WATER & SODIUM BALANCE – An Overview

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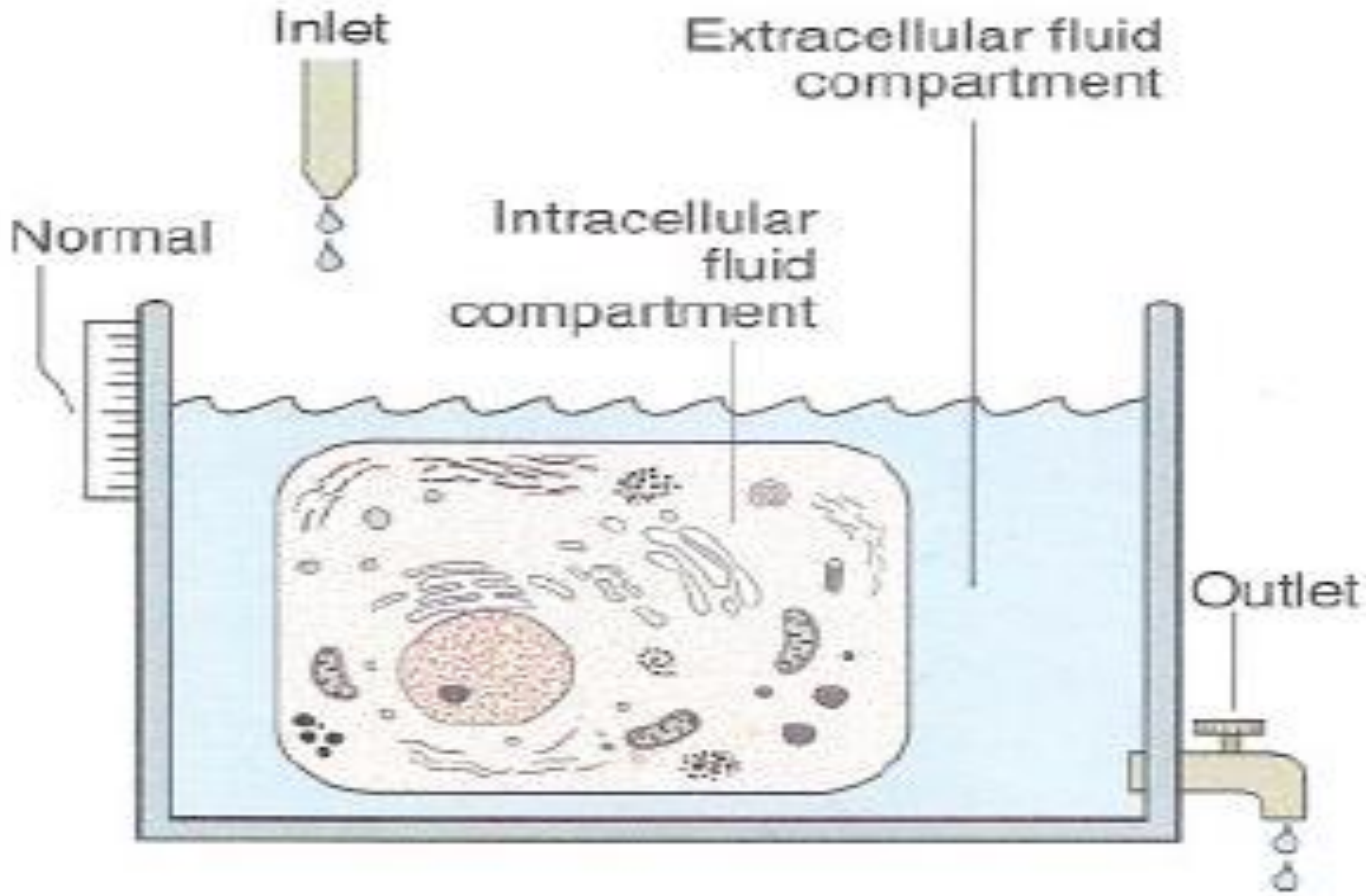
WATER (FLUID) BALANCE (STEADY STATE)

- 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?

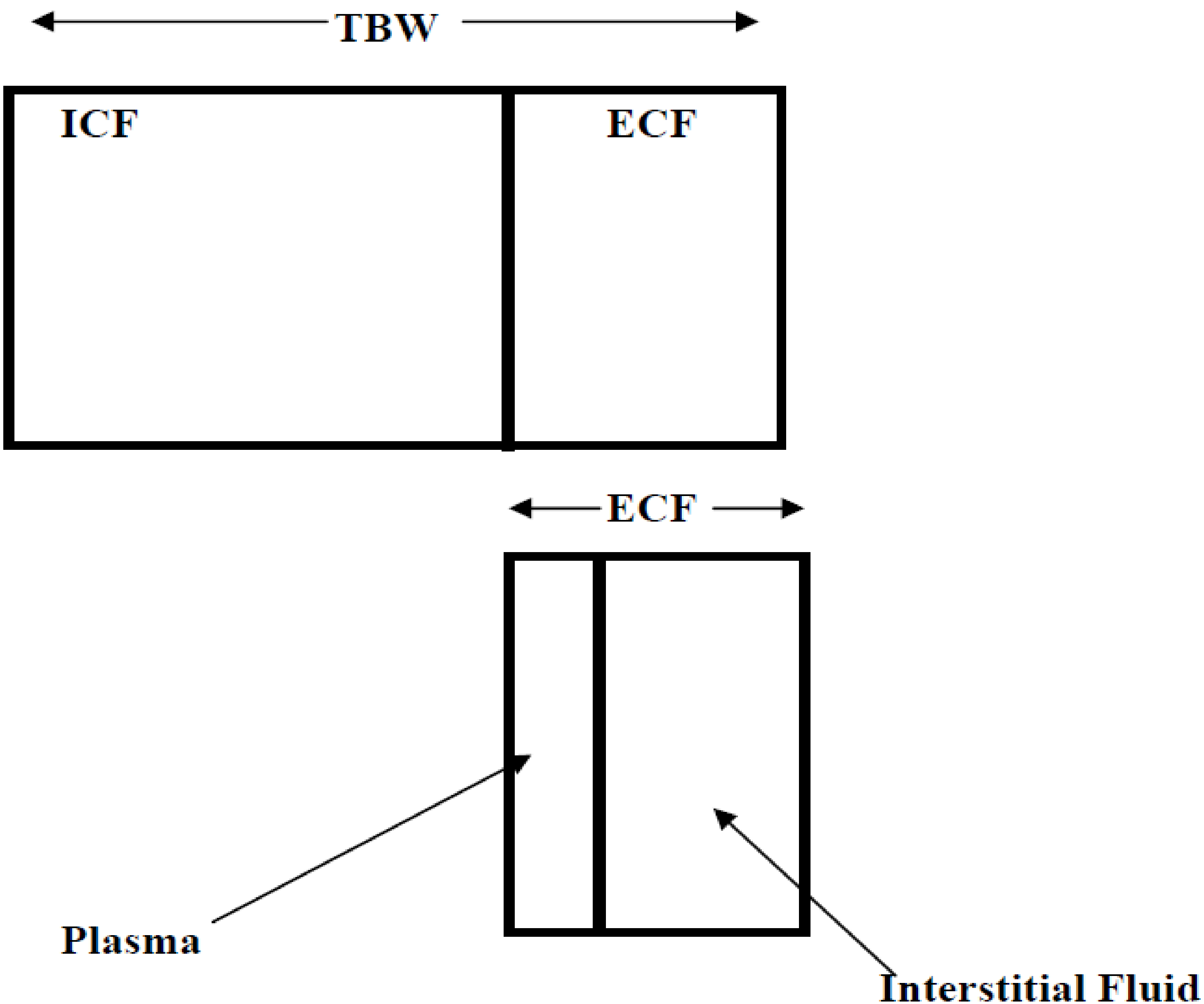
- Water/Fluid is a major body constituent;
- An average person (Wt 70 kg) contains about 42 liters of Total Body Water (TBW);
- TBW is about 60% of the total body weight;
- TBW is separated into two major compartment;
  - Extra-Cellular Fluid Compartment (ECF)
  - Intra-Cellular Fluid Compartment (ICF)
    - **Fig. 1**: Water tank model illustration ECF, ICF, TBW

Fig. 1: Schematic diagram of water tank model to illustrate body fluid compartments [1]



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 is made up of **Plasma** and **Interstitial Fluid**
  - Plasma is about 25% of ECF
  - Interstitial Fluid is about 75% of ECF


TBW
ICF
ECF
ECF
Plasma
Interstitial Fluid

What are the major sources and routes of fluid intake?

- Some major sources of fluid intake:
- Water Drinking;
- Water contained in our various foodstuffs;
- Metabolic water;

What are some of the major routes in the body for fluid loss?

- Some major routes of fluid loss:
- Urinary loss, Fecal loss
- Insensible water loss – such as evaporation from the Respiratory Tract and Skin Surface (not including sweat which is sensible since it has a purpose)

- Sweat Losses –
  - At normal room temperature, sweating accounts for about 25% of heat losses;
  - In cold environments, H_2O losses in sweat decreases;
  - In warm environments, or with exercise, sweat losses increases;
- Pathological losses: vascular bleeding, vomiting, and diarrhea;

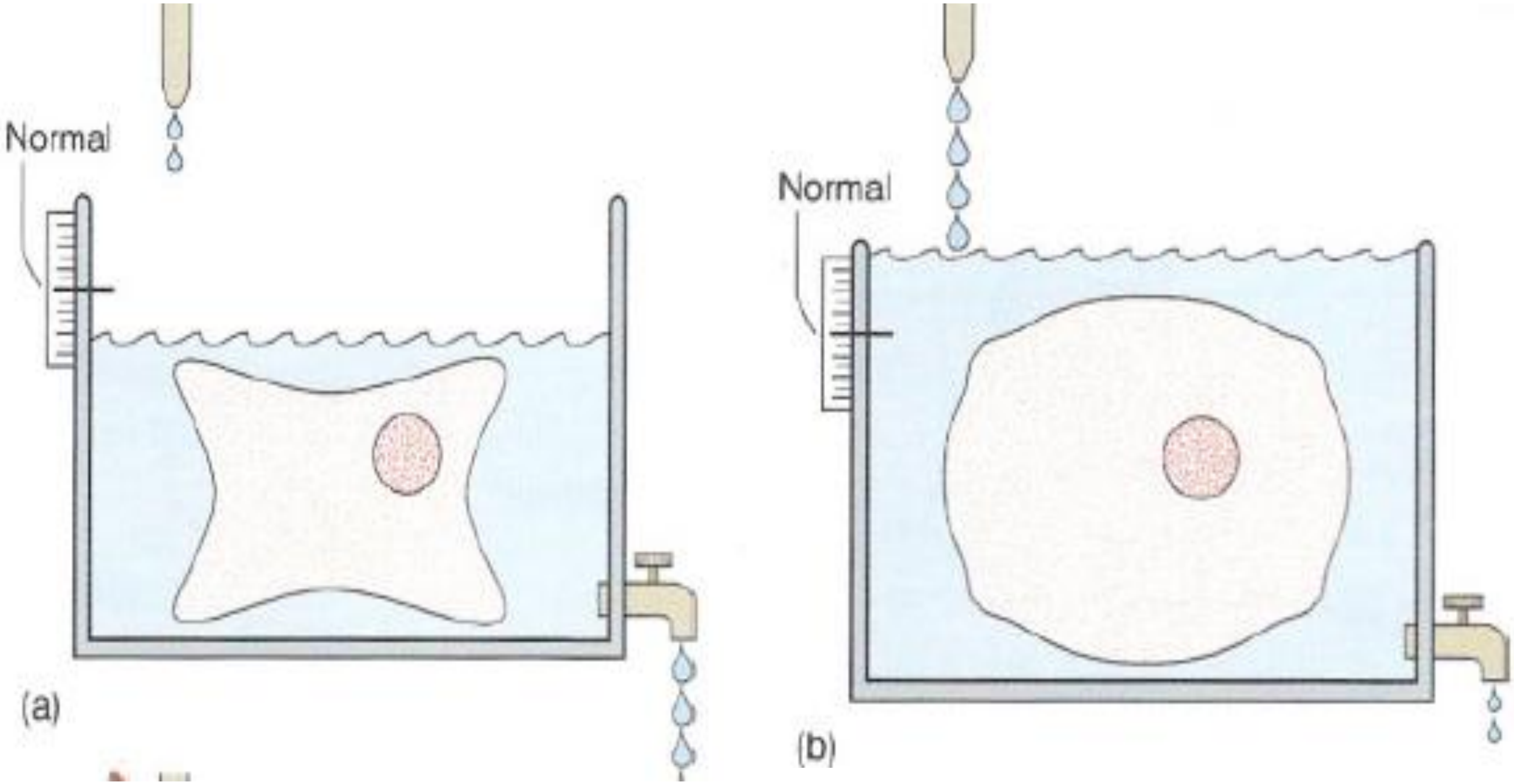
What are some of the consequences of fluid loss?

- Selective loss of fluid from either ICF or ECF compartments gives rise to distinct signs and symptoms:
- Loss of ICF can cause Cellular Dysfunction: resulting in Lethargy, Confusion and Coma;
- Loss of ECF can lead to Circulatory Collapse, Shock, Renal shutdown;
- Loss of TBW produces 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 usually assessed on Clinical grounds by looking for appropriate Clinical signs; it involves:
  - History taking to identify water intake and water loss;
  - Signs and Symptoms indicating
    - Dehydration (loss of fluid) or
    - Over-hydration (accumulation of fluid in compartments)
- **Fig 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 [1]



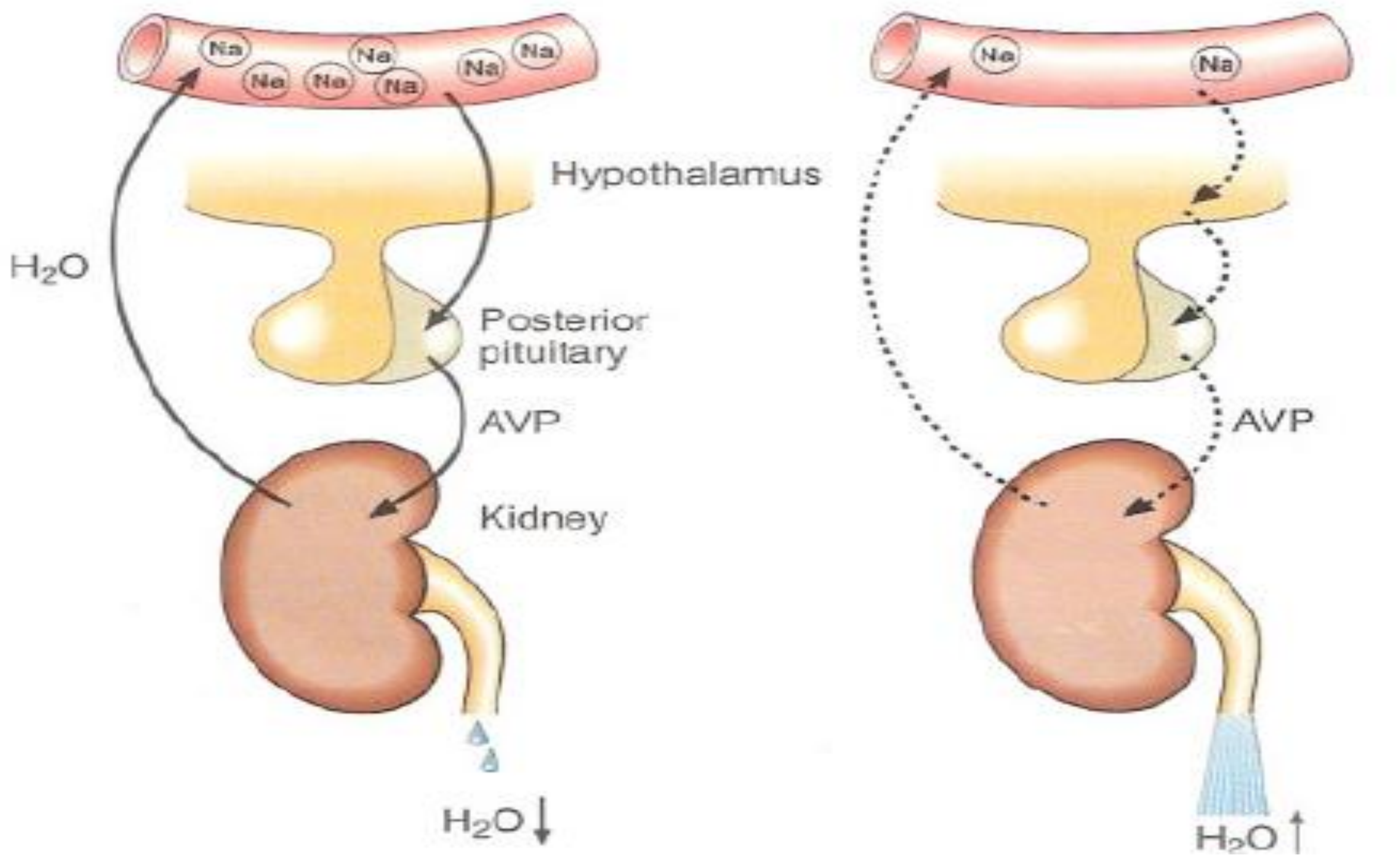
How is water balance regulated?

- Water balance is regulated by Arginine Vasopressin (AVP; also called Anti-Diuretic Hormone, ADH);
- AVP is a hormone produced by Posterior Pituitary Gland;
- AVP tightly regulates water excretion 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;
- When the Hypothalamus detects differences in the Osmolality between ICF and ECF it regulates the secretion of AVP from Posterior Pituitary gland;

- Regulation is as follows:
  - **A rising Osmolality promotes the secretion of AVP,**
  - **A declining Osmolality switches off the 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 as little as 0.5 ml/min in order to conserve body water;
- Within ONE hour after drinking about 2 liters of water, the 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 (**Figure 4**)

Fig. 4: Regulation of water balance by Arginine Vasopressin (AVP):
Increased Osmolality activates production of AVP and reduces urine flow rate;
Decreased Osmolality inhibits production of AVP and increases urine flow rate; [1]



SODIUM BALANCE

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

Sodium intake and Sodium loss:

Sodium Intake:

- Varies among individuals 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 in feces (5 mmol/day);
- GIT is the major route of pathological Sodium loss;
- Diarrhea and vomiting may result in death from Salt and Water Depletion in Pediatric Cases;

What factors regulate Sodium excretion?

- Sodium Excretion is regulated by:
  - Intrinsic Renal Mechanisms,
  - Suppression of Aldosterone Secretion,
  - Stimulation of Secretion of Atrial Natriuretic Factor (ANF)

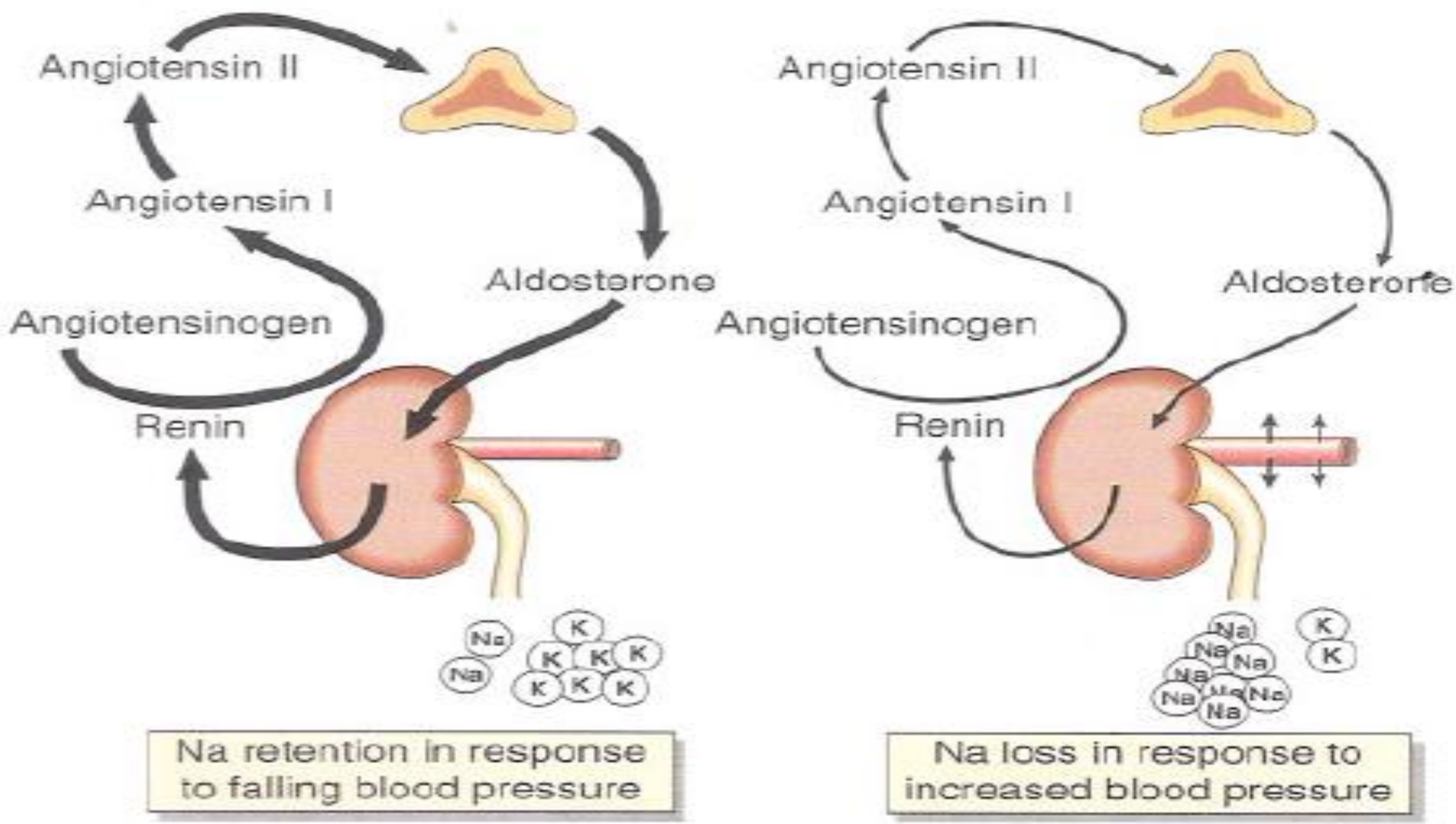
What is the role of Aldosterone in regulation of Sodium Balance?

- Aldosterone is a hormone produce in the Adrenal Cortex;
- Aldosterone 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;

How is secretion of Aldosterone regulated?

- Major stimulus for secretion of Aldosterone:
  - Volume of ECF,
  - Osmolality of ECF,
- Specialized cells in Juxtaglomerular Apparatus of Kidneys detect decrease in Blood Pressure and secrete Renin,
- Renin converts Angiotensinogen (produced in Liver) to Angiotensin I;
- Angiotensin I is converted to Angiotensin II by Angiotensin Converting Enzyme (ACP);
- 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^+ (Fig. 5)**

Fig. 5: Regulation of Sodium balance by Aldosterone? [1]



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 are the electrolytes in the ECF and ICF?

- Na^+ is the Principal Cation in ECF,
- K^+ is the Principal Cation in ICF,
- Proteins and Phosphates are the main Anions in ICF,
- Chloride (Cl^-) & Bicarbonate (HCO_3^-) are the main Anions in ECF,
- Na^+ are present at highest concentration in ECF and make the largest contribution to total plasma Osmolality,
- Despite the low amount of K^+ in ECF, changes in Plasma K^+ conc. is very important and may have life threatening consequences;
- Urea and Creatinine are measured with Plasma Electrolytes because they provide an indication of Renal Function,
- Increase in concentrations of Urea and Creatinine usually indicates a decrease in Glomerular Filtration Rate in the kidneys;

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 Solute (e.g., **Na^+** ions) and
  - Amount of Solvent (Water),
- Concentration of solution can change when either or both variables change For example:
  - **Na^+** ion concentration of 140mmol/l may becomes 130mmol/l if the amount of **Na^+** ions in the solution is reduced or the amount of solvent (water) is increased;

What is Osmolality (Osmolarity)?

- Osmolality is the concentration of osmotically active particles in a solution,
  - particles that cannot cross semi-permeable membrane
- Water moves easily 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 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,
- Osmolality of ICF equals Osmolality of the ECF: Isotonic solutions,
- Water moves across cell membrane to maintain Osmolality of ECF & ICF; even if it causes the cells to shrink or expand in volume,

How is Osmolality of Serum or Plasma calculated?

- Concentrations of osmotically active solutes are used:
- Simple formula for calculating Osmolality :

Serum Osmolality = 2 x [Serum Sodium ions] = 2[Na^+]

  - (Unit for Osmolality is **mmol/kg,** or **mOsmol/Kg** or **mOsmol/L**; Unit for Plasma or Serum Sodium ion is **mmol/L**);

- Simple formula is used when Concentrations of Plasma **Urea** and **Glucose** are within the reference ranges;
- If either or both are abnormally high, then concentration of either or both (in mmol/L) must be used in the calculation of Osmolality;
- **NB**: Normal Osmolality of Serum or Plasma (and other body fluids except urine) is in the range **285 to 295 mmol/kg** (**285 to 295 mOsmol/L**);

Example for calculating Osmolality

Normal Conditions (i.e., Plasma or Serum concentrations of Urea and Glucose are within normal range)

- ECF Osmolality can be roughly estimated as: →

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

{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 contributions from 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:

$$P = 2[Na^+] + 2[K^+] + [Glucose] + [Urea]$$

(**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)**

Osmolal Gap (OG) = MO – CO

- Large positive OG helps to identify presence in serum of osmotically active substances, such as, Ethanol, Methanol, Iso-propanol, Ethylene Glycol and Acetone
- Proper interpretation of OG also requires knowledge of **Anion Gap (AG)**, and blood pH

$$\textbf{Anion Gap} = [Na^+] - \{[HCO_3^-] + [Cl^-]\}$$

What is HYPONATRAEMIA?

- **Hyponatraemia** is a significant fall in the concentration of Na^+ ions below the reference range for plasma or serum;
  - (what reference range is used for Serum Na^+ ion in PMGH?)

- **"Hypo-Osmolality"** is synonymous with **Hyponatraemia**

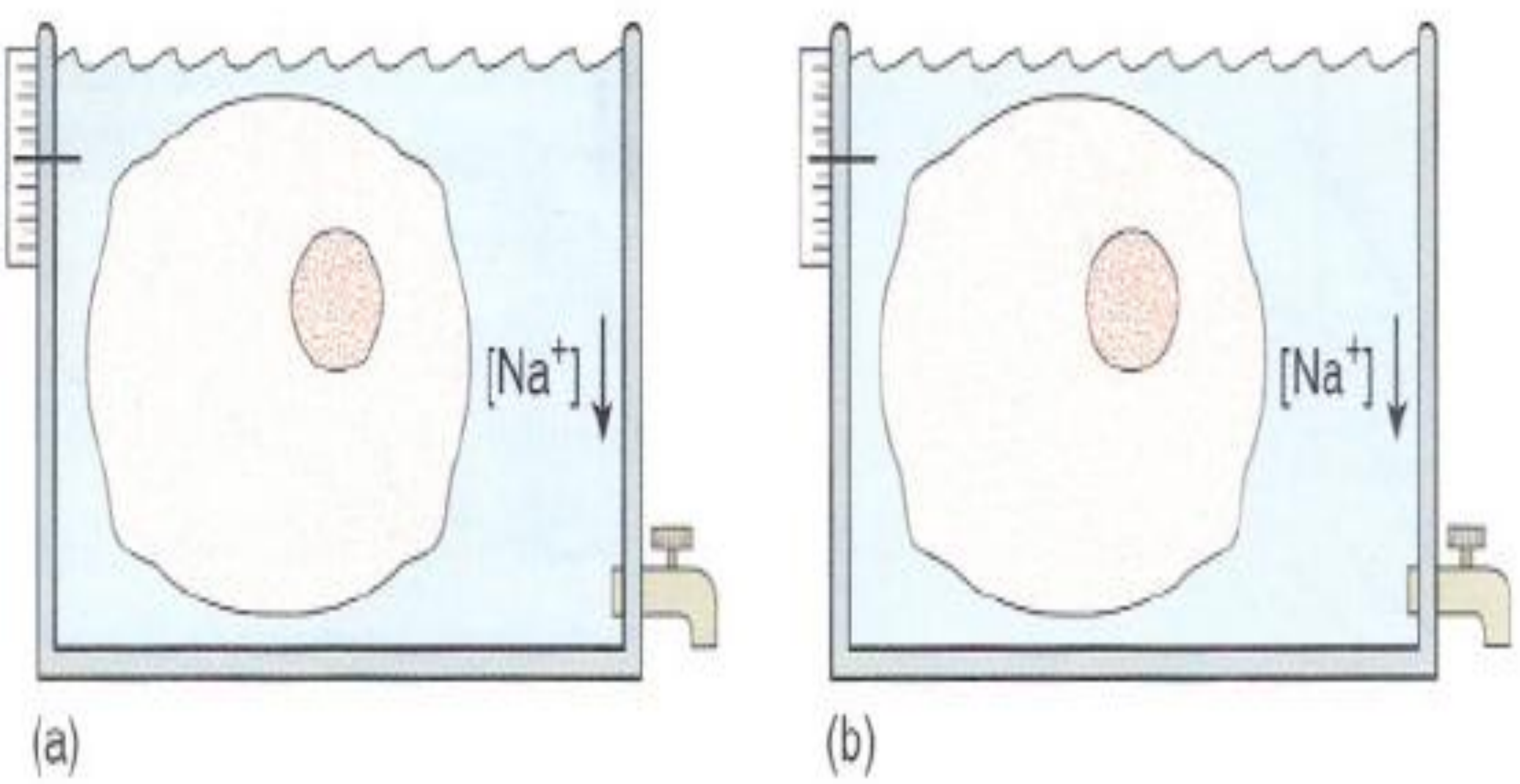
because **Na^+ ion** is the major cation in the ECF in sufficient amount such that a decrease in concentration would significantly affect the Osmolality;

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. 6a**)

- Hyponatraemia due to **Loss of Na^+ ions :**
  - When loss of **Na^+** ions exceeds loss of fluid, Hyponatraemia may result, (**Fig. 6b**)
  - Example: Loss of fluid (vomiting or fistulae) that contain **Na^+ ions** are replaced simply by water;

Fig. 6a: Fluid retention in ECF & ICF causing Hyponatraemia
Fig. 6b: Sodium loss resulting in Hyponatraemia [1]

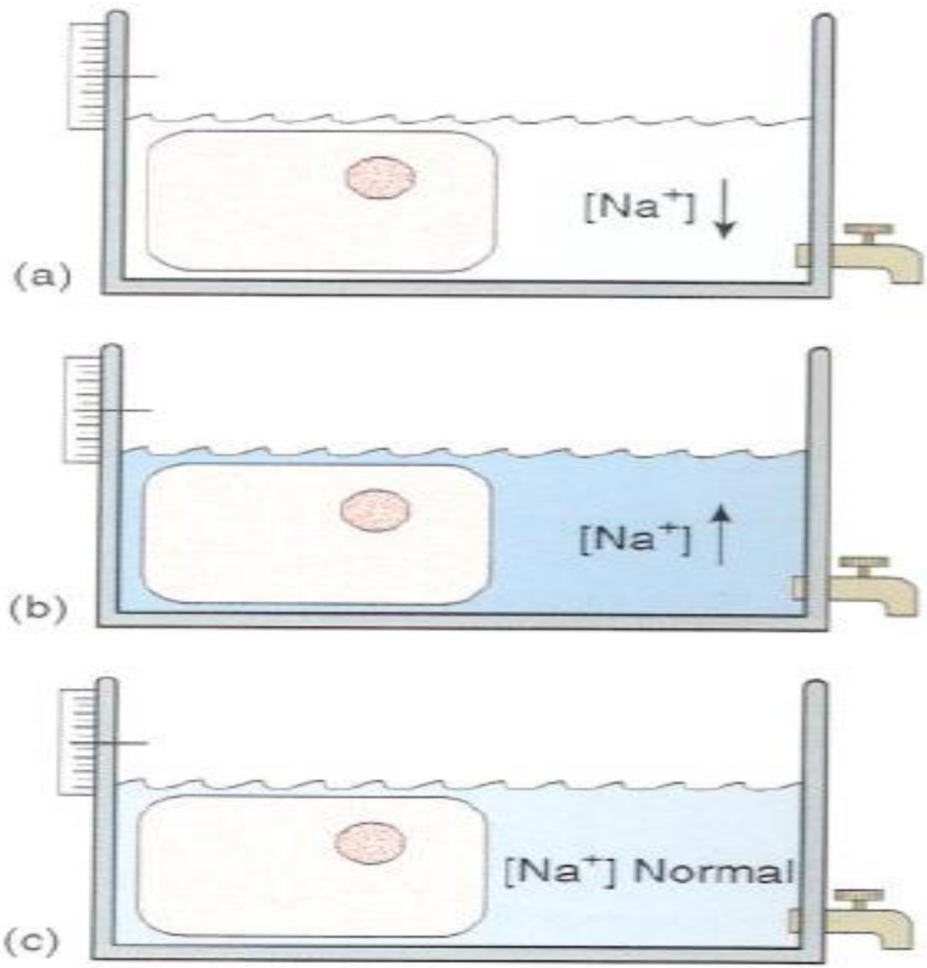


- Water tank model in **Fig. 6a & 6b** emphasizes that Biochemical observation of Hyponatraemia gives no clear explanation about the Volume of the ECF compartment;
- Both laboratory results of these patients indicate Hyponatraemia, with no indication of fluid retention or loss of Sodium;
- **Thus, the 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 7a, 7b, 7c**),

- **These diagrams clearly indicates that Clinicians MUST always give greater emphasis and attention to History, Signs and Symptoms of the Patients not to the Laboratory results on plasma Sodium alone;**

Fig. 7a: Reduced ECF with Hyponatraemia (low plasma Sodium conc.);
Fig. 7b: Reduced ECF with Hypernatraemia (high plasma Sodium conc.);
Fig. 7c: Reduced ECF with Normal plasma Sodium conc.



What are some of the 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:

- In general 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 a 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 **Oedema**:
- Two possible conditions are:
  - **Oedematous Hyponatraemia**
  - **Non-Oedematous Hyponatraemia**

OEDEMATOUS HYPONATRAEMIA

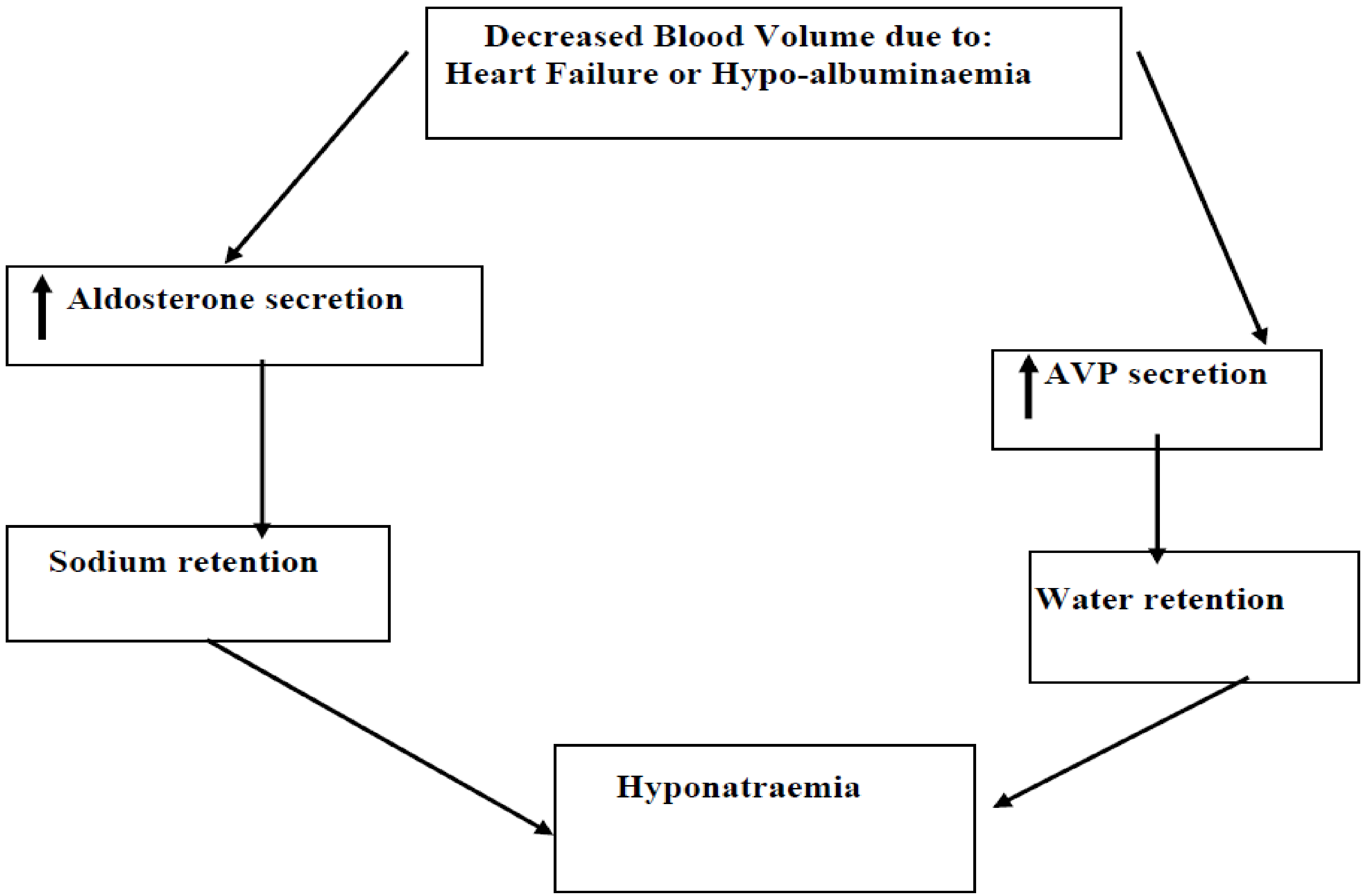
- Patients with generalized Oedema have an increase in both Total Body Sodium and Water:
- Some causes of Oedema:
- **Heart Failure:**
    - Effective blood volume may be reduced because pumping action of the heart is unable to maintain a satisfactory circulation of Blood and ECF;
- **Hypo-albuminaemia**,
    - Effective blood volume may be reduced because Hypo-albuminaemia lowers Plasma Oncotic Pressure, which disrupts normal exchange of solutes and fluid in capillary bed resulting in unsatisfactory circulation of Blood and ECF;
    - Albumin makes the biggest contribution to plasma Oncotic pressure;
    - Oedema occurs if blood 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 (Arginine Vasopressin) and consequently water is retained;

- **Hyponatraemia results from the Retention of relatively more water than Sodium in the ECF;**

Sequence of events leading to the development of Hyponatraemia in Patient with Oedema is schematically presented below:



What are some of the causes of Hypo-albuminaemia?

- **Decreased biosynthesis** of albumin due to:
  - Liver disease causing inadequate biosynthesis of Albumin;
  - 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 Septicaemia;
- **Abnormal excretion or degradation:**
  - Nephrotic Syndrome, Protein-losing Enteropathies, Burns, Haemorrhage and Catabolic states;

NON-OEDEMATOUS HYPONATRAEMIA

- Patients with Non-Oedematous 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 concentration;
- 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

Table below shows electrolyte composition of GIT

Fluid	Na^+ (mmol/L)	K^+ (mmol/L)	Cl^- (mmol/L)
Gastric juice	70	10	110
Small intestine fluid	120	10	100
Diarrhoea	50	30	50
Rectal mucus	100	40	100
Bile, Pleural and Peritoneal Fluids	140	5	100

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

SUMMARY

- Water is lost as Urine and as obligatory "Insensible" losses from skin and lungs;
- Na^+ ions may be lost in prolonged vomiting, diarrhea and intestinal fistulae,
- AVP regulates Renal water loss and causes changes in Osmolality of body fluid compartments;
- Aldosterone regulates Renal Na^+ ion and Na^+ content in ECF,
- Changes in Na^+ ion content in ECF cause changes in ECF volume because of the combined actions of AVP and Aldosterone,
- Hyponatraemia due to water retention is the commonest biochemical disturbance encountered in clinical practice,
- In some patients non-osmotic regulation of AVP overrides the osmotic regulatory mechanism, resulting in water retention, which is a non-specific feature of illness,

- Patients with Hyponatraemia without oedema, but have normal serum urea and creatinine and blood pressure, have water overload,
- Patients with Hyponatraemia and with Oedema are likely to have both water and sodium overload,
- Hyponatraemia may occur in patient with Gastrointestinal or Renal fluid losses, causing Sodium depletion,
- Low Sodium concentration in serum may occur because water retention is stimulated by increased AVP secretion,
- Patients with Hyponatraemia due to Sodium depletion may show clinical signs of fluid loss such as Hypotension, such patients usually do not have Oedema,

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