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**WATER (FLUID) AND SODIUM BALANCE – An Overview**

**WATER (FLUID) BALANCE / WATER (FLUID) STEADY STATE:**

- ❑ Amount of daily water intake varies among individuals
- ❑ Amount of daily water loss also 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 implies:
  - Body will have either a net water gain or a net water loss
  - **Fig 1** shows schematic representation of Normal water balance

**What are the major sources of intake of water (fluid)?**

- ❑ Water Drinking
- ❑ Water contained in Food
- ❑ Metabolic water (production of CO<sub>2</sub> and H<sub>2</sub>O)

**What are some of the major route of water (fluid) loss?**

- ❑ Urinary loss; Fecal loss
- ❑ Insensible H<sub>2</sub>O loss – such as evaporation from Respiratory Tract and Skin surface (excluding 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<sub>2</sub>O losses in sweat decrease
  - In warm environments, or with exercise, sweat losses increase
- ❑ Pathological losses – Include: Vascular Bleeding, Vomiting and Diarrhea

**What are the body fluid compartments?**

- ❑ Water is the major body constituent
  - Average person (70 kg) contains about 42 liters of Total Body Water
- ❑ Total body water is separated into 2 major compartments:
  - Intracellular Fluid Compartment (ICF): Volume of fluid inside cells
  - Extracellular Fluid Compartment (ECF): Volume of fluid outside cells
- ❑ Water Tank model can be used to illustrate body fluid compartments (**Fig. 2**)

**Does loss of fluid affect fluid compartments?**

- ❑ Selective loss of fluid from either ICF or ECF compartments gives rise to distinct signs and symptoms

- ❑ Loss of fluid from ICF (Intracellular fluid loss) can cause cellular dysfunction, which is most notably evident as Lethargy, Confusion and Coma
- ❑ Loss of fluid from ECF (Extracellular fluid loss), such as blood loss, can lead to Circulatory Collapse, Renal Shutdown and Shock
- ❑ Loss of Total Body Fluid usually produce similar effects as indicated above
- ❑ Signs of (substantial) fluid loss, is usually spread across both ECF and ICF compartments

### **How is the state of hydration of a patient assessed?**

- ❑ State of Hydration of a patient (i.e., Volume depletion or Volume expansion of body fluid compartments), is usually assessed on Clinical grounds:
  - History taking to identify water intake and water loss
  - Signs and Symptoms indicating Dehydration or Over hydration
- ❑ **Figures 3a & 3b** illustrate effect of Volume Depletion and Volume Expansion on water tank model of body fluid compartments

### **How is water balance regulated by AVP? Fig. 4**

- ❑ Arginine Vasopressin (AVP; also called Anti-Diuretic Hormone, ADH) is a hormone produced by Posterior Pituitary Gland
- ❑ AVP tightly regulates water excretion by the kidneys
- ❑ Osmolality in Intracellular fluid is equal to that in Extracellular fluid
- ❑ Specialized cells in Hypothalamus play a role in maintaining the Osmolality between Intracellular and Extracellular fluid
- ❑ These specialized cells can detect differences between their Intracellular Osmolality and that of the Extracellular fluid and adjust 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 endogenous 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**)

### **SODIUM BALANCE:**

#### **What is exchangeable and non-exchangeable sodium? (Fig. 5)**

- ❑ Total Sodium in the body can be separated into Exchangeable and Non-Exchangeable
- ❑ About 25% of total Sodium is Non-Exchangeable
  - Non-Exchangeable Sodium is incorporated into tissues such as bone and cartilage and has slow turnover rate

- ❑ About 75% of total Sodium is exchangeable
  - Most exchangeable sodium is in ECF
  - Sodium circulates in Plasma as Free Sodium Ions ( $\text{Na}^+$ )
  - Normal plasma or serum Sodium concentration is between 135 and 145mmol/L
  - Plasma or Serum sodium concentration does not reflect the state of Sodium balance
  - Plasma or Serum sodium concentration primarily reflects body water content

### **Sodium Intake:**

- ❑ Intake of sodium is variable and depends on many factors: Habits, Taste
- ❑ In a healthy individual total body sodium does not change even if intake falls to as little as 5mmol/day or greater than 750mmol/day

### **Sodium Loss:**

- ❑ Loss of sodium is just as variable as sodium intake
- ❑ For healthy individuals:
  - Urinary Sodium Excretion equals Sodium Intake
  - Most sodium excretion is via the kidneys
  - Some sodium is lost in sweat (on average about 5 mmol/day), and in the feces (about 5 mmol/day)
- ❑ In disease state GIT is often the major route of sodium loss
- ❑ This is a very important Clinical point, especially in Pediatric Cases, as Infantile Diarrhea may result in death from Salt and Water Depletion

### **What factors regulate sodium excretion?**

- ❑ Sodium excretion is controlled by:
  - Intrinsic Renal Mechanisms,
  - Suppression of Aldosterone Secretion and
  - Stimulation of Secretion of Atrial Natriuretic Factor (ANF)

### **What is the role of Aldosterone in regulation of sodium balance?**

- ❑ Aldosterone decreases Urinary Sodium Excretion by Increasing Re-absorption of  $\text{Na}^+$  in the Renal Tubules in exchange for Tubule excretion of  $\text{K}^+$  and  $\text{H}^+$
- ❑ Aldosterone does not concentrate the urine, because it exchanges one ion for another
- ❑ Aldosterone stimulates Sodium conservation by Sweat Glands and Mucosal Cells of the Colon, but in normal circumstances these effects are minimal

### **How is the secretion of Aldosterone controlled? (Fig. 6)**

- ❑ Volume of ECF is a major stimulus for secretion of Aldosterone
- ❑ Specialized cells in the Juxtaglomerular Apparatus of the Nephron sense decreases in Blood Pressure and Secrete Renin,
- ❑ Renin converts Angiotensinogen (produced in the 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

### What are the functions of Atrial Natriuretic Factor (ANF) or Atrial Natriuretic Peptide?

- ❑ Atrial Natriuretic factor is a polypeptide hormone that is predominantly secreted by the Cardiocytes of the Right Atrium of the Heart – thus, it is referred to as Cardiac Hormone
- ❑ ANF increases urinary sodium excretion – thus it is said to produce **Natriuresis**
- ❑ ANF is also play a role in regulation of ECF volume and sodium concentration

### How do AVP and Thirst indirectly regulates Sodium balance?

- ❑ AVP (ADH) and Thirst do not regulate Sodium directly,
- ❑ AVP and Thirst control fluid balance via the regulation of water absorption in the collecting duct of the Nephron
- ❑ Absorption and excretion of water alters the concentration of Sodium in the ECF
- ❑ When large intake of water lowers Serum Sodium concentration to less than 135 mmol/L, cell volume receptors in the Hypothalamus inhibit the secretion of AVP, excess water is excreted and circulating Sodium is returned to normal levels
- ❑ AVP secretion and Thirst are stimulated by:
  - Hyper-Osmolality and Volume depletion by signals to the Baro-receptors and volume receptors in the great vessels and heart

### TAKE NOTE:

- ❑ Some important Physiological concepts:
  - Water remains in Extracellular compartment by the Osmotic effect of ions
  - Sodium ions (and Anions, mainly Chloride) are largely restricted to the extracellular compartment
  - Amount of Sodium in the ECF determines the volume of the compartment
  
- ❑ Aldosterone and AVP interact to maintain normal volume and concentration of ECF

### How does AVP and Aldosterone interaction affect Osmolality?

To understand this concept let us consider a patient who has been Vomiting and has Diarrhea from a GIT infection:

- ❑ With no intake the patient becomes Fluid depleted
  - Consequently both water and Sodium have been lost
  - Because the ECF volume is low, Aldosterone secretion is High
  - Thus, as the patient begins to take fluids orally, any salt ingested is maximally retained
  - As this raises the ECF Osmolality, AVP action then ensures that water is retained too
  - Aldosterone and AVP interaction will continue until ECF fluid volume and composition return to normal
    - Aldosterone regulating the Sodium, AVP regulating the water

### What are the Electrolytes in the ECF and ICF?

- ❑ Cations and Anions in solution in all body fluids
- ❑ Sodium ion ( $\text{Na}^+$ ) is the Principal Cation in ECF
- ❑ Potassium ion ( $\text{K}^+$ ) is the Principal Cation in ICF

- ❑ Proteins and Phosphates are the main Anions in the ICF
- ❑ Chloride ion ( $\text{Cl}^-$ ) and Bicarbonate ion ( $\text{HCO}_3^-$ ) are the main Anions in ECF
- ❑  $\text{Na}^+$  ions are present at highest concentration in ECF and make the largest contribution to the total plasma Osmolality
- ❑ Despite the low concentration of  $\text{K}^+$  ion in the ECF, changes in Plasma concentration of  $\text{K}^+$  ion is very important and may have life threatening consequences
- ❑ Urea and Creatinine concentrations are frequently measured with Serum or Plasma Electrolytes because they provide an indication of Renal Function
- ❑ Increase in concentrations of Urea and Creatinine usually indicates a decrease in the 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., Sodium ions) and amount of Solvent
  - Concentration of solution can change if either or both variables change
- ❑ For example:
  - Sodium ion concentration of 140mmol/l may become 130mmol/l because the amount of Sodium in the solution has fallen or the amount of solvent has increased

#### HYPONATRAEMIA:

- ❑ Hyponatraemia is a significant fall in Serum Sodium concentration below the reference range of about 135 – 145 mmol/L (what reference range is used for serum sodium in PMGH?)
- ❑ Hypo-Osmolality is synonymous with Hyponatraemia because Sodium is the only ion in the ECF in sufficient amount such that a decrease in concentration would significantly affect the Osmolality

#### What are the possible types of Hyponatraemia? (Figs. 7a & 7b)

- ❑ Hyponatraemia due to water retention:
  - More water than normal is retained in the body compartments and dilutes the constituents of the extracellular space causing Hyponatraemia
- ❑ Hyponatraemia due to Sodium loss:
  - When loss of sodium ions exceeds loss of water, hyponatraemia may result
    - Example: Loss of body fluids that contain Sodium are replaced simply by water

#### TAKE NOTE:

- ❑ Illustrations in **Figs. 7a & 7b** emphasizes that Biochemical observation of Hyponatraemia gives no information about the Volume of the ECF compartments
- ❑ Information on Volume of ECF compartments can only be obtained from Clinical Examination of the Patient
- ❑ Some patients with life-threatening Sodium depletion may present with a Normal Serum Sodium concentration (**Figure 8a, b, c**)

- ❑ Illustrations in **Figs. 8a, b, c** clearly indicates that the Clinician must always give greater emphasis and attention to the History, Signs, and Symptoms of the Patient than to the Laboratory results on Serum Sodium

#### **What is Osmolality (Osmolarity)?**

- ❑ It is the concentration of osmotically active particles in a solution, i.e., particles that cannot cross the semi-permeable membrane
- ❑ Water moves easily through the cell membrane that separate ECF from the ICF
  - Osmosis is the flow of solvent across a semi-permeable membrane from a low solute concentration to a higher solute concentration
  - Osmotic pressure is the driving pressure for water to move the given concentration of osmotically active particles
- ❑ Osmotic pressure must always be the same on both sides of a cell membrane,
- ❑ In the living cell, water moves across the membrane so as to keep the Osmolality the same, even if this water movement causes cells to shrink or expand in volume
- ❑ Osmolality of the ICF is always the same as the Osmolality of the ECF
  - The two compartments contain Isotonic solutions

#### **What is the unit for expressing Osmolality (Osmolarity)?**

- ❑ **Osmolality** of a solution is expressed in **mmol solute per kilogram (mmol/kg, or mOsmol/kg) of solvent** (which is usually water)
- ❑ **Osmolarity** of a solution is expressed in **mmol solute per liter (mmol/L or mOsmol/L) of solution**
- ❑ In humans, the Osmolality of serum (and other body fluids except urine) is in the range 285 to 295 mmol/kg (285 to 295 mOsmol/L)

#### **How is Osmolality measured and calculated?**

- ❑ Osmolality of serum or plasma sample can be measured directly, or it may be calculated if the concentrations of the major solutes are already known
- ❑ Osmolality can be calculated as follows:
  - **Serum Osmolality = 2 x molar concentration of serum Sodium ions**
- ❑ This simple formula for calculating Osmolality can be used ONLY if the serum concentrations of Urea and Glucose are within the reference ranges
- ❑ If either or both are abnormally high, the concentration of either or both (in mmol/l) must be added in to give the calculated Osmolality value
- ❑ **Normal Conditions:** Estimating and Calculating ECF Osmolarity:
  - Plasma Osmolarity is representative of ECF Osmolarity and is clinically accessible
  - ECF Osmolarity is dominated by  $[Na^+]$  and the associated Anions which are necessary to maintain Electro-neutrality
- ❑ Under **Normal conditions**, ECF Osmolarity can be roughly estimated as:

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

(Where  $P_{\text{osm}}$  is Plasma Osmolarity)

- Since Intracellular Osmolarity is the same as Extracellular Osmolarity under normal conditions, this also provides an estimate of Intracellular Osmolarity.)

### Clinical Laboratory Measurement:

- Plasma Osmolarity measured in Clinical Laboratory includes contributions from Glucose and Urea
- In healthy individuals contribution from Glucose and Urea is small
- Under certain Pathological conditions, concentrations of Glucose and Urea may increase,
- Thus the measured Plasma Osmolarity measured by Clinical laboratory can be calculated as:

$$P_{\text{osm}} (\text{measured}) = 2[\text{Na}]_{\text{p}} = [\text{glucose}]_{\text{p}} + [\text{BUN}]_{\text{p}}$$

- BUN = Blood Urea Nitrogen,
- Normal  $[\text{glucose}]_{\text{p}}$  is 60 – 100 mg/dl,
- Normal  $[\text{BUN}]_{\text{p}}$  is 10 – 20 mg/dl
- Glucose and BUN normally contribute about 5mOsm each (i.e., about 2% of the Plasma Osmolarity measured in the clinical lab)

### What is effective and ineffective Osmolarity?

#### Effective Osmolarity:

- Glucose,  $\text{Na}^+$  and Anions associated with  $\text{Na}^+$  have concentration gradients across the cell membrane and are therefore **Effective Osmoles** in the sense that they determine the distribution of water between ECF and ICF

#### Ineffective Osmolarity:

- Urea (BUN) crosses cell membranes just as easily as water, so it does not contribute to redistribution of water between ECF and ICF
- Urea is therefore called an **Ineffective Osmole**

- Effective Osmolarity is given as:

$$P_{\text{osm}} (\text{effective}) = 2[\text{Na}]_{\text{p}} + [\text{glucose}]_{\text{p}}$$

or,

$$P_{\text{osm}} (\text{effective}) = P_{\text{osm}} (\text{measured}) - [\text{BUN}]_{\text{p}}$$

### What is Osmolal Gap (OG)?

- ❑ **Osmolal gap** is the difference between Measured and Calculated Osmolality (Osmolarity)
- ❑ Osmolal gap occurred when the Clinically measured Osmolality (Osmolarity) is higher than the Calculated Osmolality
- ❑ Osmolal gap suggests the presence of an unmeasured osmotically active substance in the blood
- ❑ Knowledge of the serum concentration of Sodium ions, Glucose and Urea or blood urea nitrogen (BUN) allows calculation of the Serum Osmolality (Osmolarity) to a degree that compares quite well to measured Osmolality (Osmolarity)

### How is Osmolal gap (OG) calculated?

- ❑ To calculate the OG, serum determination of MO, Na<sup>+</sup>, Glucose and Urea are necessary
- ❑ Determination of MO and for CO should be performed on the same serum sample
- ❑ Difference between Measured Osmolality (MO) and Calculated Osmolality (CO) is known as the Osmolality Gap or Osmolal Gap (OG)

$$\text{Osmolality (Osmolarity) Gap (OG)} = \text{MO} - \text{CO}$$

### How is OG interpreted?

- ❑ A large positive OG can help identify the presence in Serum of substances such as Ethanol, Methanol, Isopropanol, Ethylene Glycol, and Acetone
- ❑ Proper interpretation of OG requires knowledge of **Anion Gap (AG)**, blood pH, and qualitative testing of the serum Ketone Bodies

$$\text{Anion Gap} = [\text{Na}^+] - \{[\text{HCO}_3^-] + [\text{Cl}^-]\}$$

### In Summary:

- ❑ Water is lost from the body as Urine and as obligatory “Insensible” losses from skin and lungs
- ❑ Na<sup>+</sup> ions may be lost from the body in prolonged vomiting, diarrhea and intestinal fistulae
- ❑ AVP regulates renal water loss and thus causes changes in the Osmolality of body fluid compartments
- ❑ Aldosterone regulates renal Na<sup>+</sup> ion loss and controls Na<sup>+</sup> content of the ECF
- ❑ Changes in Na<sup>+</sup> ion content of the ECF cause changes in volume of this compartment because of the combined actions of AVP and Aldosterone
- ❑ Hyponatraemia because of water retention is the commonest biochemical disturbance encountered in clinical practice



- In many patients the non-osmotic regulation of AVP overrides the osmotic regulatory mechanism and this results 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 the patient with gastrointestinal or renal fluid losses, which have caused sodium depletion
  - The low sodium concentration in serum occurs because water retention is stimulated by increased AVP secretion
- Patients with hyponatraemia because of sodium depletion show clinical signs of fluid loss such as Hypotension, such patients usually do not have Oedema

Fig. 2: Water tank model of body fluid compartments

Fig. 3: Effect of volume depletion and volume expansion on the water tank model of body compartments (a) Dehydration; (b) Over hydration

Fig. 2

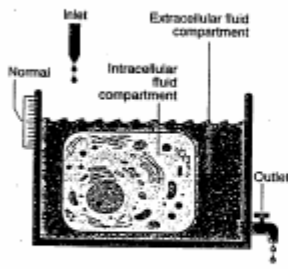


Fig. 2 Water tank model of body fluid compartments.

Fig. 3

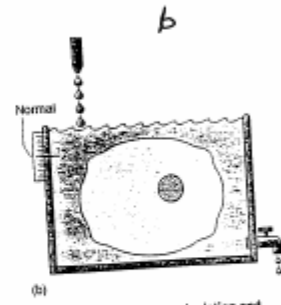
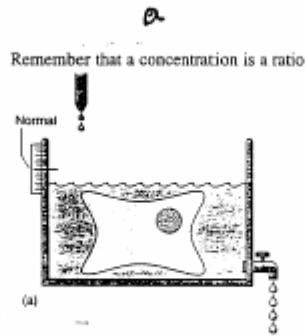


Fig. 3 The effect of volume depletion and volume expansion on the water tank model of body compartments.  
 (a) Dehydration: loss of fluid in ICF and ECF due to increased urinary losses.  
 (b) Overhydration: increased fluid in ICF and ECF due to increased intake.

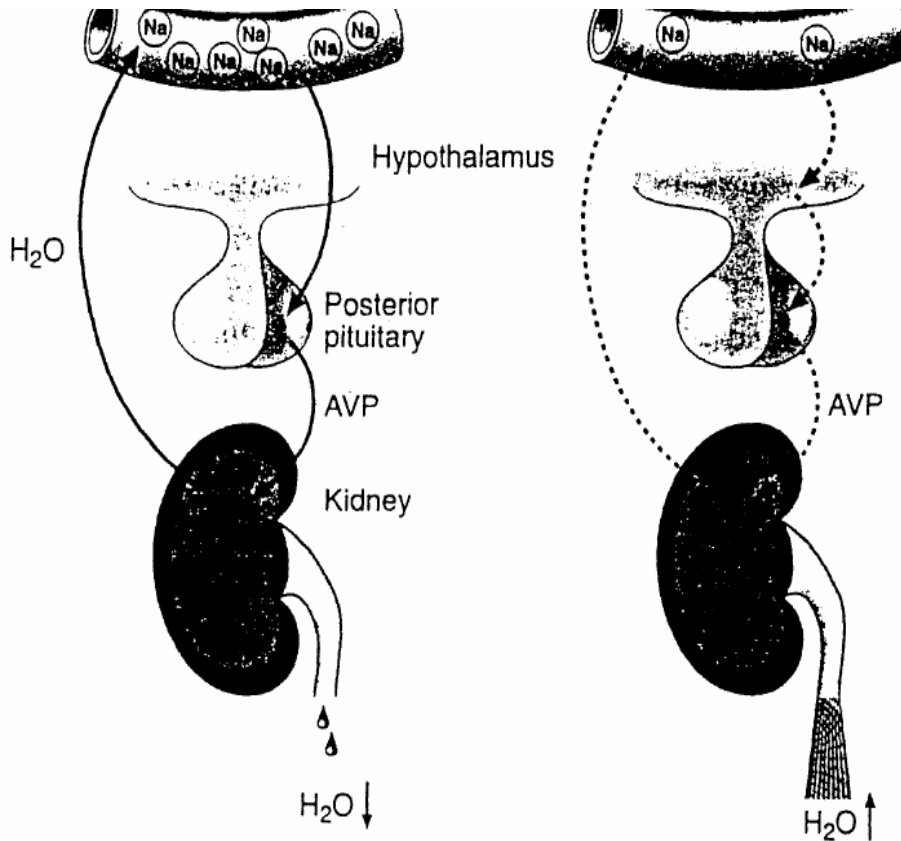


Fig. 4: Regulation of water balance by AVP and Osmolality

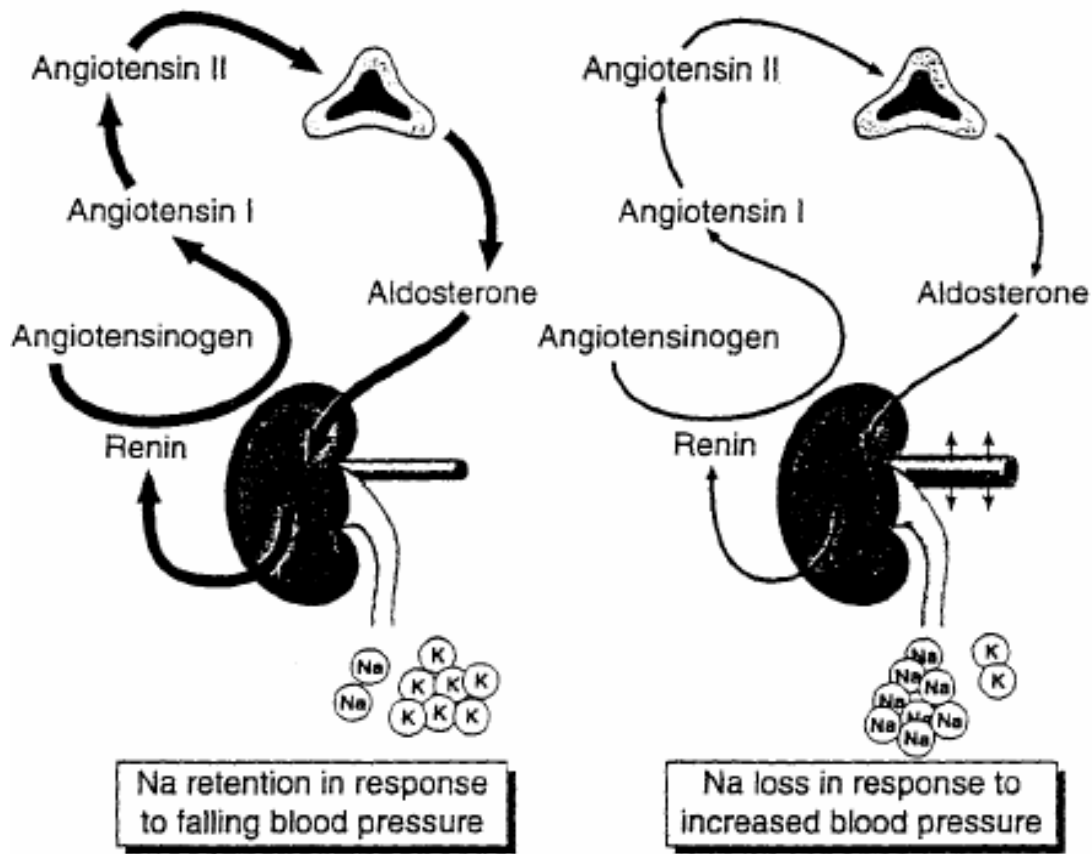
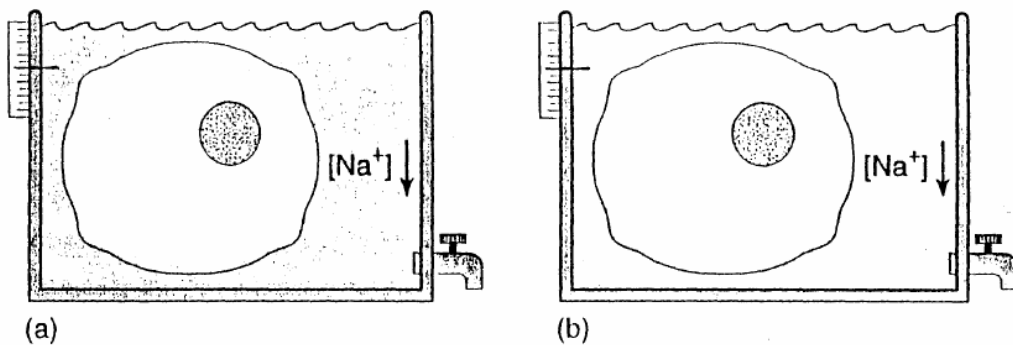
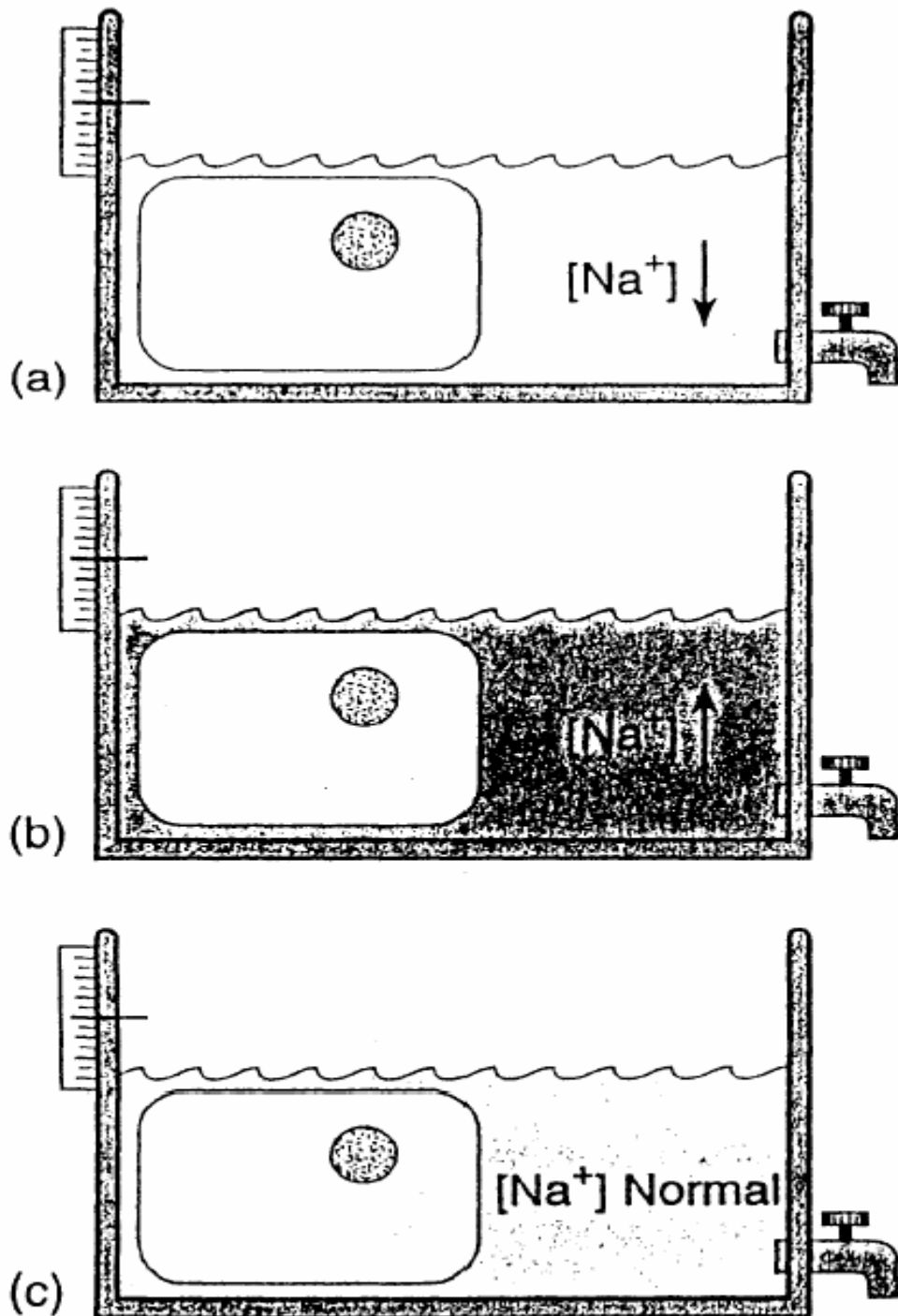


Fig.6. The regulation of sodium balance by aldosterone.

Fig. 7



Water tank models of hyponatraemia. (a) Water retention throughout ECF and ICF. (b) Sodium loss.



Water tank models showing that reduced ECF volume may be associated with reduced, increased or normal serum  $[Na^+]$ .