Regulation of fluid and electrolyte balance

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Abstract

The three fluid compartments of the body are interdependent. Their homeostasis relies on systems that regulate water balance and, as the principal extracellular solute, sodium balance. Maintenance of plasma volume is essential for adequate tissue perfusion. Regulation of plasma osmolality, which is determined primarily by the serum sodium concentration, is essential for the preservation of normal cell volume and function. The importance of osmoregulation is best illustrated by the consequences of a rapid fall or rise in serum osmolality, which can cause permanent neurological damage and death through shrinkage or swelling of cells. It is tempting to attribute control of plasma sodium concentration to sodium balance, but there is no direct relationship between plasma sodium and renal sodium excretion. Osmolality and volume are, therefore, regulated by separate mechanisms. It is important to recognize that osmoregulation occurs through changes in water balance, whereas volume regulation is principally determined by changes in sodium excretion.

Keywords Aldosterone; anti-diuretic hormone; atrial natriuretic peptide; baroreceptors; osmolality; renin–angiotensin system; sodium balance; water balance

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Learning objectives

After reading this article, you should be able to:

- recognize the role of water balance in regulation of serum sodium concentration and osmolality
- appreciate the concept of effective circulating volume
- understand the mechanisms regulating sodium excretion and, thereby, extracellular volume

Distribution of body water and sodium

To address the regulation of water and electrolyte balance, the processes which govern the distribution of body water must be considered. Body water constitutes approximately 60% of total body weight in adults (a higher proportion in infants and children).

Movement of water between compartments: osmotic pressure

The concept of osmotic pressure can be explained by considering two water-containing compartments, separated by a membrane that is permeable to water but not to solute. Random motion of water molecules results in movement across the membrane (**diffusion**). The presence of a solute on one side of the membrane decreases random movement on that side owing to intermolecular forces. There is, therefore, overall movement of water molecules into the solute-containing compartment (**osmosis**). This process will continue, thereby increasing the hydrostatic pressure within this compartment. When a steady state has been reached, the hydrostatic pressure within the solute-containing compartment opposing the osmotic movement of water into that compartment is known as the **osmotic pressure** of the solution.

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Osmotically active solutes: effective and ineffective osmoles

The osmotic pressure generated by a solute is proportional to the number of particles in solution, rather than the molecular weight or valency. A solute is able to generate an osmotic pressure across a membrane only if it is unable to cross that membrane.

Sodium and potassium are unable to equilibrate across cell membranes owing to the Na^+/K^+-adenosine triphosphatase (ATPase); therefore, they generate an osmotic pressure within the extracellular and intracellular compartments respectively. They are examples of **effective osmoles**.

Lipid-soluble molecules (e.g. urea) that can pass freely across cell membranes are unable to generate an osmotic pressure. Such molecules are known as **ineffective osmoles**.

Calculated and measured osmolality

In normal circumstances, plasma osmolality can be derived from the concentrations of the three principal solutes as follows:

$$\text{Plasmaosmolality} = 2 \times [Na^+] + [\text{glucose}] + [\text{urea}]$$

Sodium concentration is multiplied by a factor of 2 to account for anions.

Measured osmolality incorporates all solutes within the sample that are capable of generating an osmotic force.

A discrepancy between the calculated and measured osmolalities indicates the presence of a solute that is not routinely measured (e.g. ethanol) or an unusually low proportion of plasma water (e.g. lipaemic blood).

Effective osmolality

The osmolality of a solution is determined by the number of molecules of osmotically active solute contained in that solution. Sodium is the major extracellular cation. It is accompanied by anions, principally chloride and bicarbonate.

Urea is an ineffective osmole and glucose is present at a much lower concentration than sodium, except during severe hyperglycaemia. Therefore,

$$\text{Effective osmolality} = 2 \times [Na^+]$$

Fluid compartments

Body water is distributed between two principal compartments: intracellular and extracellular. Water is able to pass freely between these compartments and the distribution of water is therefore determined by osmotic pressure. The extracellular com-

partment is subdivided into the interstitial fluid and the intravascular compartment (plasma).

Each of the compartments contains a principal solute, which is confined largely to that compartment and therefore acts as the main osmotic agent. Potassium is the principal intracellular solute and sodium the principal extracellular solute, owing to the Na^+/K^+-ATPase in the cell membrane (Figure 1).

However, sodium is able to move freely across the capillary walls. Sodium is, therefore, not an effective osmole with respect to the distribution of water between the interstitial and intravascular compartments, which is determined by different factors.

Hydrostatic pressure within the leaky capillaries is opposed by the effect of the plasma proteins. Plasma proteins are too large to cross the capillary wall freely and act to retain water within the intravascular compartment. The force that they generate balances capillary hydrostatic pressure and is known as the **plasma oncotic pressure**.

Osmoregulation

Osmoregulation can be considered an essential mechanism to maintain cell volume. This is well illustrated by considering the consequences of an abrupt rise or an abrupt fall in plasma osmolality. Rapid onset of severe hyponatraemia causes water to move into cells, which swell. Within the confined space of the skull, uncontrolled cerebral oedema results in seizures, coma and death. Conversely, rapid development of severe hypernatraemia causes cells to shrink with potential for permanent neurological damage.

Although plasma osmolality is determined principally by plasma sodium concentration, osmolality is regulated by changes in water balance that bring about dilution or concentration of solute. It is not regulated by changes in sodium excretion.

The mechanism of osmoregulation involves osmoreceptors in the hypothalamus that control the release of anti-diuretic hormone (ADH) and stimulate thirst. Renal water retention, under the influence of ADH, and increased water intake lower the elevated osmolality towards normal.

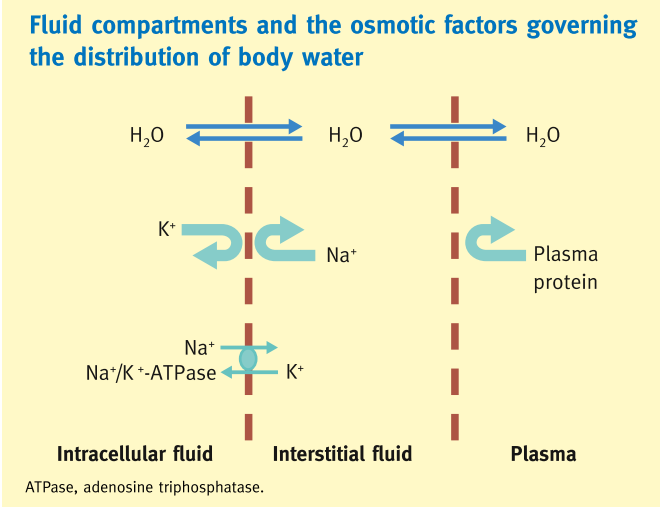

Figure 1

Volume regulation

In contrast, volume regulation is brought about largely through changes in sodium excretion. As the principal solute within the extracellular compartment, sodium balance is intimately related to body water content.

Volume regulation is an essential requirement to maintain perfusion of tissues. Although osmoregulation is managed by a single sensory arm, volume regulation is governed by multiple receptors reflecting the potential for variation in perfusion of different regions of the vasculature.

The differences between osmoregulation and volume regulation are emphasized by considering manoeuvres that would perturb the homeostasis of the three fluid compartments.

Consider infusion of hypertonic saline. Extracellular volume increases and, because sodium remains extracellular, the osmolality of the extracellular fluid increases. Osmoregulation results in water retention through the action of ADH, returning osmolality to normal but further expanding the extracellular volume.

It can be seen that there is no direct relationship between plasma sodium concentration (which is the principal determinant of osmolality) and plasma volume. Additional mechanisms are, therefore, needed to correct the volume excess, through increased excretion of sodium and water.

The differences between osmoregulation and volume regulation are listed in Table 1.

Anti-diuretic hormone

ADH is a nine-amino-acid peptide that increases the permeability of the renal collecting ducts to water. Water is thus reabsorbed without salt, producing a more concentrated urine. ADH is the principal regulator of so-called free water excretion, with urine osmolality ranging between extremes of approximately 50 mOsmol/kg and 1200 mOsmol/kg under the control of ADH.

ADH is produced in the supraoptic and paraventricular nuclei of the hypothalamus, and then migrates along the axons of these neurones into the posterior pituitary (Figure 2). The human form of ADH is known as arginine vasopressin (AVP), reflecting its pressor effect.

Control of anti-diuretic hormone release: osmoreceptors and volume receptors

ADH secretion is controlled by both hyperosmolality and hypovolaemia.[1] The hypovolaemic stimulus to ADH and thirst is the only effector mechanism common to both osmoregulation and volume regulation. Apart from this, osmolality and volume are regulated through entirely separate mechanisms.

Osmoreceptors

The osmoreceptors, located in the supraoptic nuclei of the hypothalamus, are stimulated by the presence of an osmotic gradient between their cytoplasm and the perfusing plasma, so that water transits out of or into the cells as serum osmolality rises or falls.

Because sodium is the major solute within the extracellular compartment, plasma sodium concentration is the principal osmotic factor controlling ADH secretion.