

## Chapter 4 / Capítulo 4

*Electrolyte and Internal Environment Imbalances in  
Emergencies (English Edition)*

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# Hyponatremia and Hypernatremia

## Hiponatremia e hipernatremia

Jorge A. Barrios Flores<sup>1</sup> , Dayci Vargas-Condori<sup>2</sup> , Luis Mariano Tecuatl-Gómez<sup>3</sup> 

<sup>1</sup>Seguro Social Universitario. Cochabamba, Bolivia.

<sup>2</sup>Hospital Clínico Viedma. Cochabamba, Bolivia.

<sup>3</sup>Instituto de Seguridad y Servicios Sociales de los Trabajadores del Estado (ISSSTE). Cabo San Lucas, Baja California Sur, México.

### Objectives:

- Understand the determinants of serum sodium concentration
- Describe the role of water in the genesis of hyponatremia and hypernatremia
- Identify cerebral volume alterations in the symptoms of dysnatremias
- Understand the mechanisms of hyponatremia and hypernatremia, as well as their approach and treatment

### INTRODUCTION

#### Determinants of serum sodium concentration.

The determinants of sodium concentration are exchangeable electrolytes ( $Na_i + K_i$ ) and total body water (TBW). The equation can be considered as:  $Plasma\ Na = (Na_i + K_i) / TBW$

Where the plasma concentration is directly proportional to the concentration of exchangeable electrolytes and inversely proportional to total body water.

PEARL:  $Na^+$  concentration increases with exchangeable electrolytes (i) and decreases with TBW.

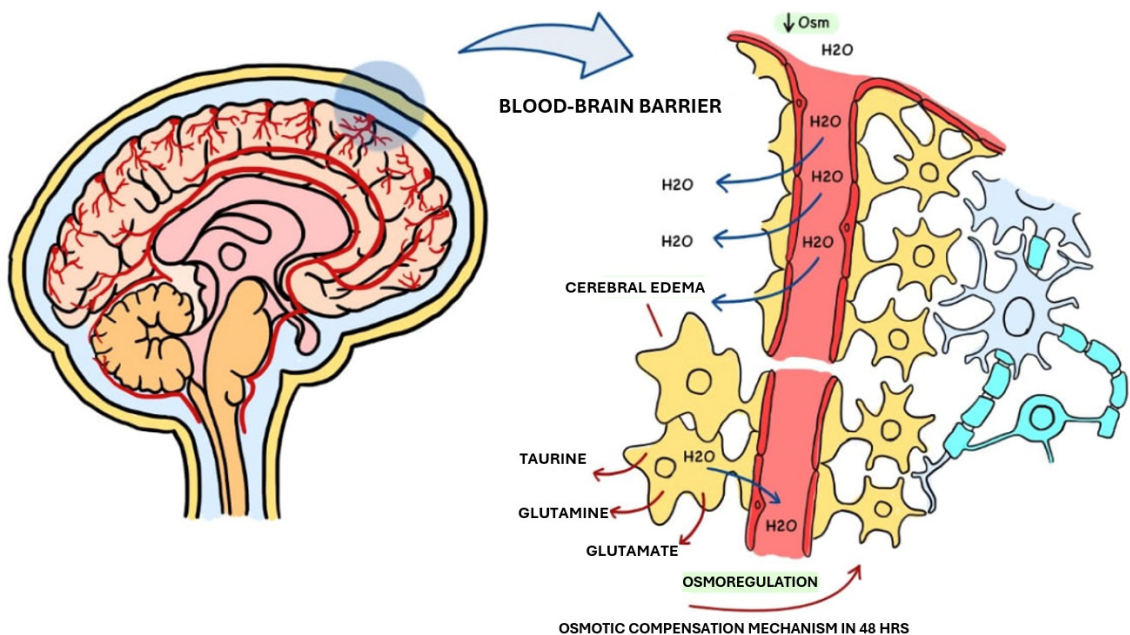


Figure 4.1. Effect of acute hypotonic state on the brain

### Clinical importance of osmoregulation

Water diffuses rapidly across most cell membranes; therefore, an acute decrease (within two hours) in sodium and osmolality in the extracellular fluid causes a shift of extracellular water into the brain by osmosis, producing cerebral edema (figure 4.1).

### Osmolytes and regulation of cell volume

The way the brain prevents this accumulation of water in its cells (cerebral edema) is through the production of solutes that are then lost, pulling water out of the cells along with them. These inorganic solutes are known as osmolytes, which include: the carbohydrate myo-inositol and the choline compounds, as well as, to a lesser extent, the amino acids glutamine, glutamate, and taurine.

### Implications for symptoms and treatment

In general, only acute hyponatremia and acute hypernatremia produce neurological symptoms (lethargy, seizures, coma). Chronic hyponatremias and hypernatremias usually do not produce symptoms unless they are very severe. Therefore, rapid correction of a chronic sodium disorder can cause water to move out of neuronal cells into the extracellular space and lead to osmotic demyelination syndrome, which may produce findings of central pontine myelinolysis, with severe and irreversible neurological damage characterized by paraparesis or quadriparesis, dysarthria (difficulty in speaking), dysphagia (difficulty in swallowing), and coma. Animal studies showed that increasing sodium in hyponatremia at a rate greater than 0,5 (mEq/L)/hour or more than 12 (mEq/L)/day can produce pontine myelinolysis. It was also identified that a decrease in sodium greater than 0,5 (mEq/L)/hour or more than 12 (mEq/L)/day in hypernatremia can produce cerebral edema (figure 4.2).

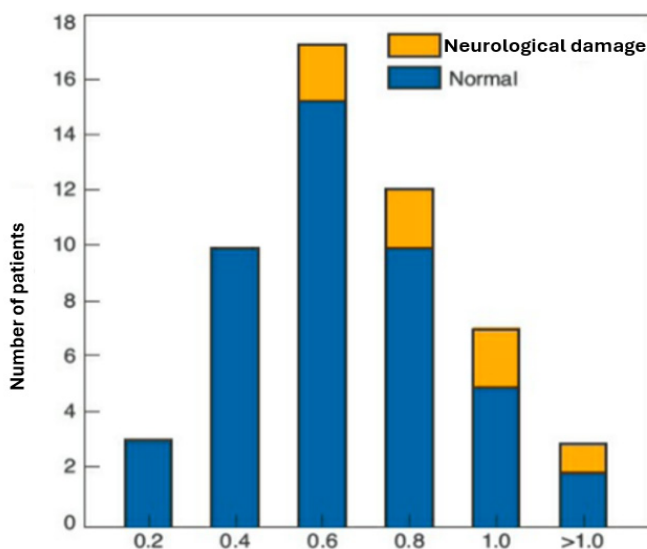


Figure 4.2. Sodium correction rate in (mEq/L)/h

### HYPONATREMIA

Hyponatremia is defined as a plasma sodium level below 135 mEq/L. Considering equation 1, hyponatremia occurs due to a decrease in exchangeable electrolytes (i) or an increase in water. The most common cause is an increase in total body water.

## Etiology

A deficit in water (H<sub>2</sub>O) excretion is frequently associated with *an inability to suppress ADH secretion*, which is mainly due to:

- a) A reduction in effective circulating volume.
- b) Syndrome of inappropriate ADH secretion (SIADH).
- c) Hormonal changes.
- d) Advanced renal failure.

**Table 4.1.** Main causes of hypoosmolar hyponatremia

|                                                                                                    |
|----------------------------------------------------------------------------------------------------|
| I. Conditions in which water excretion is impaired                                                 |
| A. Effective circulating volume depletion                                                          |
| 1. Gastrointestinal losses: vomiting, diarrhea, nasogastric catheter drainage, bleeding            |
| 2. Renal losses: diuretics, renal diseases with salt loss.                                         |
| 3. Cutaneous losses in which relatively dilute fluids are replaced with free water.                |
| 4. Congestive heart failure                                                                        |
| 5. Hepatic cirrhosis                                                                               |
| 6. Thiazide diuretics (which may partially act by inducing volume depletion)                       |
| B. Syndrome of Inappropriate Antidiuretic Hormone Secretion (SIADH)                                |
| 1. Virtually any neuropsychiatric condition or severe pain with or without narcotic administration |
| 2. Medications: most commonly antidepressants and anticonvulsants                                  |
| 3. Ectopic production by tumors: most commonly small cell lung carcinoma                           |
| 4. Post-surgical patient, a response mediated by pain afferents                                    |
| 5. Pulmonary diseases                                                                              |
| C. Advanced renal failure                                                                          |
| D. Hormonal changes                                                                                |
| 1. Hypothyroidism                                                                                  |
| 2. Cortisol deficiency                                                                             |
| 3. Pregnancy                                                                                       |
| II. Reset osmostat                                                                                 |

Source: Own elaboration

## Congestive heart failure

In heart failure, there are two mechanisms by which hyponatremia frequently develops.

First mechanisms is low cardiac output, which leads to an increase in angiotensin II, norepinephrine, and ADH, which cause water retention and renal vasoconstriction, further reducing water excretion.

And other mechanisms is increased thirst, induced by ADH, which raises total body water.

## Syndrome of Inappropriate ADH Secretion (SIADH)

This condition is due to an alteration in the hypothalamus or occurs ectopically in patients with tumor-induced disease, leading to elevated ADH secretion. This results in water retention and dilution of the extracellular fluid, causing consequent hyponatremia.

## Resetting of osmoreceptor.

In a very small group of patients with hyponatremia and SIADH, there is a phenomenon known as resetting of osmoreceptor, which means the osmoreceptors function again, but at lower sodium levels. As a result, patients will have suppression or limitation of ADH secretion, but at lower sodium concentrations (around 125 mEq/L).

## Diagnosis

The diagnosis is based on a physical examination that allows us to identify symptoms suggestive of hyponatremia (primarily neurological alterations). It is important to assess renal

function through creatinine levels and, if possible, request thyroid function tests and cortisol levels. Regarding the approach to patients with hyponatremia, the following should be assessed:

### ***Plasma osmolality***

Osmolality may be decreased in cases of true hyponatremia. It may be normal in pseudohyponatremia, when elements such as lipids or proteins reduce the aqueous fraction of plasma, leading to an artificially low measurement of serum sodium concentration. Osmolality is elevated in hyperglycemia or during mannitol infusion, which causes water to shift from the cells to the extracellular space, resulting in dilution and subsequent dilutional hyponatremia.

### ***Urinary osmolality***

This depends on ADH suppression, which will result in urine with decreased osmolality (less than 100 mOsm/kg). The presence of ADH will lead to urine with normal or elevated osmolality.

### ***Urinary sodium concentration***

In the two most common cases of true hyponatremia (volume depletion and SIADH), urinary sodium is distributed differently. In volume depletion, the body attempts to retain sodium aggressively in order to preserve volume, so urinary sodium will be low (<25 mEq/L). In SIADH, sodium depends on intake and is usually normal or high (>40 mEq/L).

## **Basic Principles of Treatment**

Considering equation 1 from this chapter, where sodium concentration is proportional to exchangeable electrolytes (i) and inversely proportional to total body water, the treatment of hyponatremia can involve either electrolyte (Na) administration or water restriction.

- Water restriction in patients with congestive heart failure, hepatic cirrhosis, or kidney disease.
- Volume replacement with isotonic solutions in patients with volume depletion.
- Water restriction in patients with primary polydipsia (SIADH).
- Replacement therapy with cortisol or thyroid hormones.
- There is no treatment to restore the osmostat.

## ***Sodium replacement***

Replacement depends on the presence of symptoms in the patient and/or the progression of the condition (acute or chronic).

- When the condition is acute (<48 hours) and symptomatic, sodium can be infused at an initial rate of 1,5-2 mEq/L until symptoms resolve.
- Afterward, sodium should be infused at a rate no greater than 0,5 mEq/L per hour to avoid complications from rapid correction (pontine myelinolysis).
- Hypertonic solutions can be used, such as 3 % NaCl solution, 7 % NaCl solution, etc. (see appendix for instructions on how to prepare these solutions).
- For more precise sodium replacement, the Adrogue-Madias formula is recommended (see appendix for details on how to use the formula).

## **HYPERNATREMIA**

Hypernatremia is defined as a plasma sodium concentration greater than 145 mEq/L, which is usually associated with hyperosmolality, since sodium is the main extracellular solute. The primary causes include water loss without adequate replacement, and to a lesser extent, the administration of hypertonic solutions.

### Defense mechanisms

The body responds to increased sodium through ADH (antidiuretic hormone) release and stimulation of thirst, which are key mechanisms to prevent the development of hypernatremia. If these mechanisms remain intact, the patient can maintain normonatremia even in severe conditions such as central diabetes insipidus (CDI) (figure 4.3).

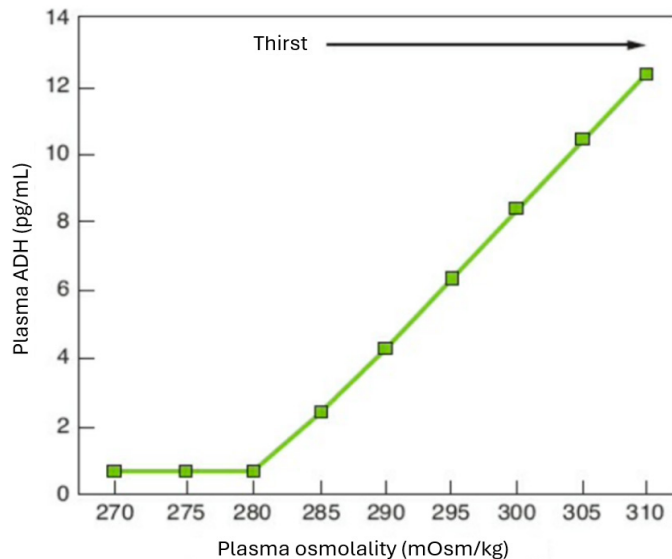


Figure 4.3. Relationship between osmolarity and ADH

### Etiology

The causes are divided into:

- Increased insensible water losses: fever, respiratory infections.
- Urinary water losses: CDI (central diabetes insipidus), NDI (nephrogenic diabetes insipidus), osmotic diuresis due to glucose.
- Gastrointestinal losses.
- Hypothalamic lesions (affecting the thirst center).
- Administration of hypertonic sodium or bicarbonate solutions.

Water loss is more significant when the lost fluid contains less sodium + potassium than plasma, which occurs in many cases of diarrhea and osmotic diuresis.

### Diagnosis

It is based on:

- Clinical history: presence of infections, diarrhea, vomiting, polyuria.
- Evaluation of the ADH-renal axis through urinary osmolality:
  - >500 mOsm/kg: extrarenal water loss or osmotic diuresis.
  - <300 mOsm/kg: indicates CDI or NDI.

The diagnosis can be confirmed with the administration of DDAVP (an ADH analog). A significant response (>50 % increase in urinary osmolality) suggests CDI.

### Treatment

- The goal is to correct hypernatremia slowly to prevent cerebral edema.

- Recommended reduction: no more than 10-12 mEq/L per day.
- Treatment includes the administration of free water, either orally or intravenously (5 % dextrose).
- Calculation of free water deficit: based on total body water and current sodium concentration.
- Treat the underlying cause (insulin for diabetes, DDAVP for CDI).

### **CONCEPT OF FREE WATER CLEARANCE**

The free water clearance formula ( $CH_2O$ ) is introduced as a useful tool to assess the kidney's ability to excrete solute-free water and to estimate water losses in states of hypernatremia. It is essential to consider only osmotically active solutes: sodium and potassium.

### **Polyuria**

Polyuria is defined as a urine output greater than 3 L/day. It originates from:

- Increased osmotic load to be excreted (glucose, mannitol).
- Alteration in ADH secretion or action.

The main mechanisms are:

- Osmotic diuresis: due to non-reabsorbable solutes.
- Water diuresis: due to alterations in ADH or its receptor.

### **Specific causes**

- Central Diabetes Insipidus (CDI): ↓ production of ADH.
- Nephrogenic Diabetes Insipidus (NDI): resistance to ADH.
- Primary Polydipsia: excessive water intake that suppresses ADH secretion.

### **Diagnosis**

It is performed through:

- Water restriction or administration of hypertonic saline solution to increase plasma osmolality.
- Evaluation of urinary response:
  - Primary polydipsia: normal increase in urinary osmolality.
  - CDI: increase with DDAVP.
  - NDI: no response to DDAVP.

### **Treatment**

- Primary polydipsia: no specific treatment, except for pharmacological causes (e.g., phenothiazines).
- CDI: treatment with DDAVP and drugs that enhance ADH action (chlorpropamide, carbamazepine).
- NDI:
  - Thiazides: paradoxically useful by inducing mild hypovolemia and increasing proximal reabsorption.
  - Amiloride: useful if the cause is lithium.
  - NSAIDs: increase ADH response by inhibiting prostaglandins.