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# Hyponatremia



## PROFILE

### Definition

Hyponatremia is defined as a plasma sodium ( $\text{Na}^+$ ) concentration  $< 140$  mEq/L in dogs and  $150$  mEq/L in cats.<sup>1</sup> Because plasma  $\text{Na}^+$  concentration is the main determinant of plasma osmolality ( $P_{\text{osm}}$ ), hyponatremia usually reflects hypoosmolality. Since the kidneys are highly efficient in excreting water, hypoosmolality almost always implies a defect in renal water excretion and excess of water in the body due to one of the following mechanisms:

- Impaired diluting ability in the loop of Henle and distal tubule (volume depletion, renal failure, diuretics)
- Increased collecting-tubule permeability due to the presence of antidiuretic hormone (ADH) (effective circulating volume depletion, inappropriate ADH secretion, pain, adrenal insufficiency, or hypothyroidism)

CONTINUES

ADH = antidiuretic hormone;  $\text{Na}^+$  = sodium;  $P_{\text{osm}}$  = plasma osmolality

**KEY WORDS**

**Na<sup>+</sup> concentration:** Reflects the content of sodium relative to the volume of water in the body, not total sodium content. Therefore, hyponatremic patients can have decreased, increased, or normal total sodium content.

**Na<sup>+</sup> content:** Reflects the total amount of sodium in extracellular fluid and is calculated by multiplying the concentration of sodium by the volume of extracellular fluid.

**Osmolality:** Concentration of osmotically active particles in a solution.

- Plasma osmolality (P<sub>osm</sub>) is the main determinant of water distribution in the body. Because water can move freely across almost all cell membranes, the osmolalities of intracellular and extracellular fluids are the same.

- Normal plasma osmolality ranges from 290 to 310 mOsm/kg in dogs and 290 to 330 mOsm/kg in cats.

$$P_{osm} = 2 \times Na^+ + \text{glucose}/18 + \text{BUN}/2.8$$

- The contributions of glucose and BUN to P<sub>osm</sub> are normally small, except in diabetes mellitus and renal failure. Urea can freely cross cell membranes; its contribution to P<sub>osm</sub> can be excluded:

$$\text{Effective } P_{osm} = \text{measured } P_{osm} - \text{BUN}/2.8$$

**Tonicity:** Osmotic pressure of a solution. It determines the ability of a solution to move across a membrane.

Na<sup>+</sup> expressed as mEq/L; glucose expressed as mg/dL; BUN expressed as mg/dL

**Signalment**

Hyponatremia is a common electrolyte disorder occurring in a broad spectrum of patients, from ones without clinical signs to the critically ill.

**Causes**

The principal causes of hyponatremia are:

- Disorders associated with impaired renal water excretion (more common):
  - Volume depletion
    - *Extrarenal losses:* Gastrointestinal disorders (vomiting, diarrhea); third-space disorders (pancreatitis, peritonitis)
    - *Renal losses:* Diuretic therapy (thiazide), osmotic diuresis (glucose, mannitol), advanced renal failure (decreased glomerular filtration rate)
    - *Edematous states:* Congestive heart failure, liver disease, nephrotic syndrome
  - ADH excess:
    - Inappropriate ADH secretion (SIADH)
    - Mineralocorticoid deficiency
    - Hypothyroidism
- Disorders associated with normal renal water excretion:
  - Excessive water intake (primary polydipsia)
  - Reset osmostat syndrome
  - Rapid infusion of hypotonic fluids
- Disorders associated with pseudohyponatremia or translocational hyponatremia:
  - Hyperlipidemia
  - Hyperproteinemia
  - Hyperglycemia

**Risk Factors**

There are currently no reports of risk factors for hyponatremia in dogs and cats, but serum Na<sup>+</sup> concentration should be measured in small animals with:

- Suspected hypoadrenocorticism
- Vomiting and diarrhea
- Diuretic use
- Effusive disorders
- Polyuria and polydipsia
- Abnormal mental status or behavior
- Seizures

**Pathophysiology: Why is there too much water?**

Body fluid balance depends largely on the interrelationship of salt and water. Although effective circulating volume is largely controlled by sodium balance, maintaining osmolality depends on regulation of water balance (Table 1).

- *Na<sup>+</sup> balance:* Several sensors in the body detect changes in extracellular fluid volume (which is largely determined by total sodium content).
- *Water balance:* Although extracellular fluid and intracellular fluid have different compositions, they must maintain the same tonicity. The balance is sensed and controlled by thirst and osmoregulation systems. Osmoreceptors of the hypothalamus and neurohypophysis are sensitive to alterations in plasma osmolality and hydrostatic pressure; they respond to plasma hypertonicity by increasing thirst and ADH secretion. When the osmolality is low, ADH secretion is suppressed and urine is diluted.

**Signs**

Depending on the severity of hyponatremia, patients may have no clinical signs or present with varying degrees of neurologic signs. Cerebral edema and water intoxication occur as serum sodium concentration decreases, and the osmotic gradient that develops makes water move into the brain. Typical neurologic signs include the following:

- Lethargy
- Irritability
- Nausea/vomiting
- Mental dullness or depression
- Stupor
- Seizures
- Coma

Clinical signs related to the underlying cause of the hyponatremia may also be present:

- Tachycardia
- Hypotension
- Prolonged capillary refill time
- Weakness
- Ascites
- Edema

**Table 1. Regulation of Body Fluid Balance**

	Water Balance	Na <sup>+</sup> Balance (Volume Regulation)
<b>Signal</b>	Plasma osmolality	Effective circulating volume
<b>Sensors</b>	Hypothalamic osmoreceptors	<ul style="list-style-type: none"> <li>• Baroreceptors of the aorta, carotid sinus, and afferent glomerular arteriole</li> <li>• Atrial distension</li> </ul>
<b>Effectors</b>	Antidiuretic hormone	<ul style="list-style-type: none"> <li>• Sympathetic nervous system</li> <li>• Renin-angiotensin aldosterone system</li> <li>• Atrial natriuretic peptide</li> <li>• Antidiuretic hormone</li> <li>• Pressure natriuresis</li> </ul>
<b>Response</b>	<ul style="list-style-type: none"> <li>• Water excretion (via antidiuretic hormone)</li> <li>• Water intake (via thirst)</li> </ul>	Na <sup>+</sup> excretion



**DIAGNOSIS**

**Definitive Diagnosis**

- Hyponatremia: Serum Na<sup>+</sup> concentration < 140 mEq/L in dogs or < 150 mEq/L in cats.
- Neurologic signs are not usually seen unless Na<sup>+</sup> concentrations are < 120 mEq/L in dogs or < 130 mEq/L in cats. However, the development of neurologic signs is also related to rapidity of onset of hyponatremia. In chronic disorders, the signs are more subtle and non-specific because the brain has had enough time to adapt to plasma hypotonicity.

**Laboratory Findings & Imaging**

- **Laboratory data** should ideally include plasma osmolality, Na<sup>+</sup>, potassium, chloride, bicarbonate, BUN, and glucose concentrations, and, where necessary, urine Na<sup>+</sup> concentration and osmolality and venous or arterial pH (see **Clinical Approach**).
- **MRI** (after rapid correction of hyponatremia and myelinolysis):<sup>2,3</sup> Extrapontine lesions are most common, especially lesions within the thalamus. The lesions are described as nonenhancing, symmetrical increased signal intensi-

ties on T2-weighted scans, which represent an increase in water density associated with inflammation, gliosis, edema, or necrosis. Central nervous system lesions may not always be visible on MRI early in the course of neurologic disease.

**Clinical Approach**

If the cause of hyponatremia is not readily apparent (also see **Diagnostic Tree: Hyponatremia**, page 55):

- **Evaluate blood sample** for lipemia and measure plasma protein concentration to rule out pseudohyponatremia. Lipemia and hyperproteinemia underestimate Na<sup>+</sup> concentration when flame photometry is used, but this does not happen with ion-selective electrode techniques. Plasma osmolality is normal because lipids and proteins contribute little to plasma osmolality.
- **Measure glucose concentration** to rule out translocational hyponatremia. The following formula can be used to correct sodium in the presence of hyperglycemia:

$$\text{Corrected Na}^+ = \text{Measured Na}^+ + 1.6 \left[ \frac{\text{Serum glucose} - 100}{100} \right]$$



ADH = antidiuretic hormone; BUN = blood urea nitrogen; MRI = magnetic resonance imaging; Na<sup>+</sup> = sodium; SIADH = syndrome of inappropriate antidiuretic hormone secretion

CONTINUES

**FIND MORE**

A case study addressing treatment for hyponatremia in a dog with lethargy, vomiting, and diarrhea can be viewed at

[cliniciansbrief.com](http://cliniciansbrief.com)

>>Go to Journal Extras on our homepage.



- **Measure or calculate  $P_{osm}$ , other electrolytes, and urea concentrations** with or without pH:
  - $P_{osm} < 290$  mOsm/kg confirms hypoosmolality. However, increased BUN may cause plasma osmolality to be normal or high while the effective osmolality is reduced.
  - Metabolic alkalosis and hypokalemia suggest vomiting or diuretic use.
  - Metabolic acidosis and hyperkalemia suggest Addison's disease or gastrointestinal disease (eg, trichuriasis) when renal function is normal.
- **Measure urine osmolality ( $U_{osm}$ )** to determine whether water excretion is normal or impaired. The normal response to hyponatremia is to suppress ADH secretion, resulting in maximally dilute urine ( $< 100$  mOsm/kg or urine specific gravity  $< 1.003$ ).
  - Hyponatremia with  $P_{osm}$  and  $U_{osm} < 100$  mOsm/kg (ADH suppression) suggests primary polydipsia.
- **Measure urine  $Na^+$  concentration ( $U_{na}$ )** to differentiate volume depletion and SIADH when urine osmolality is high.
  - $U_{na}$  should be  $< 20$  mEq/L with hypovolemia.
  - $U_{na}$  should be  $> 20$  mEq/L with Addison's disease, diuretic therapy, or SIADH. While SIADH is a common cause of hyponatremia in humans, it is rarely described in veterinary patients.
- **Perform a fecal examination** to rule out gastrointestinal parasitism.<sup>4</sup>
- **Consider an ACTH stimulation test** to rule out Addison's disease. Hypoadrenocorticism leads to urinary loss of sodium chloride, volume depletion, and ADH release. As many as 81% of dogs with hypoadrenocorticism are hyponatremic at presentation.<sup>5</sup>
- **Consider measurement of  $T_4$  and/or TSH.** Myxedema coma due to hypothyroidism may cause hyponatremia in people and dogs, possibly because of ADH release secondary to decreased cardiac output and decreased glomerular filtration rate (rare).<sup>6,7</sup>

**Tx TREATMENT**

**Inpatient or Outpatient**

- Patients with neurologic signs or severe hyponatremia should be treated in an intensive care unit.

- Volume-depleted patients require inpatient management with IV fluids.
- Normovolemic or edematous patients may be able to be managed as outpatients.

**Medical**

- Two basic goals of therapy for hyponatremia:
  - Treat underlying cause
  - Increase plasma  $Na^+$  concentration at a safe rate
- In general, hyponatremia is corrected by giving  $Na^+$  to patients who have extracellular fluid volume depletion and by restricting sodium in patients who are hyponatremic but normovolemic or edematous (eg, sodium-retaining states, such as congestive heart failure, cirrhosis, and nephrotic syndrome).

**Rate of Correction**

- Ideally, the rate of correction should be similar to that at which hyponatremia developed. For example, acute ( $< 24$ – $48$  hours' duration) hyponatremia with clinical signs should be treated aggressively to reverse cerebral edema. However, most patients develop hyponatremia over 2 or more days (chronic hyponatremia), a situation in which the brain has had time to adapt to hypoosmolality. Under these circumstances a conservative approach of no more than 0.5 mEq/L per hour or 10 mEq/L per day of sodium replacement is generally recommended to avoid rapid correction of sodium.<sup>1,2,6</sup>
- Rapid correction of chronic hyponatremia (generally  $\geq 15$  mEq Na/L per day) can lead to a neurologic disorder called demyelinating encephalopathy, or myelinolysis. The mechanism is not clear, but brain cells adapted to hyponatremia may be at particular risk. Clinical signs typically develop 3 to 4 days after correction of hyponatremia and are characterized by paraparesis or tetraparesis, dysphagia, coma, and seizures.<sup>1-3</sup>
- In correcting severe hyponatremia, formulas may be helpful, but serum  $Na^+$  concentrations should be measured frequently (eg, every 3–6 hours) and therapy adjusted accordingly.
- Conventional crystalloid solutions are generally recommended for correcting hypovolemic hyponatremic patients. **Table 2** provides the



**Table 2. Na<sup>+</sup> Content & Main Composition of Various Crystalloid Fluids**

Fluid	Na <sup>+</sup>	Cl	K	Ca	Mg	Dextrose (%)	Buffer	Osmolality
7.5% NaCl	1283	1283	-	-	-	-	-	2567
0.9% NaCl	154	154	-	-	-	-	-	308
Normosol-R (hospira.com)	140	98	5	-	3	-	27 acetate 23 gluconate	294
Lactated Ringer's solution	130	109	4	3	-	-	28 lactate	272
2.5% dextrose in 0.45% NaCl	77	77	-	-	-	2.5	-	280
0.45% NaCl	77	-	-	-	-	-	-	155
Normosol-M (hospira.com)	40	40	13	-	3	5	16 acetate	364
Dextrose 5% [D5W]	-	-	-	-	-	5	-	253

Ions & buffers are expressed as mEq/L; osmolality is expressed as mOsmol/L  
Ca = calcium; Cl = chloride; k = potassium; Mg = magnesium; Na<sup>+</sup> = sodium

main composition of several crystalloid fluids.

- The degree to which a given fluid will increase serum Na<sup>+</sup> can be estimated by using the following formula (infusate Na<sup>+</sup> = Na<sup>+</sup> concentration of the corrective fluid):

$$\Delta \text{ Serum Na}^+ =$$

$$\frac{\text{Infusate Na}^+ - \text{Serum Na}^+}{\text{TBW} + 1}$$

- The amount of sodium required (sodium deficit) can also be estimated by using the following formula:  
 $\Delta \text{ Na}^+ \text{ deficit} = \text{TBW} \times (\text{desired Na}^+ - \text{actual Na}^+)$
- Unfortunately, the above formulas are only estimates and do not account for the effect of concurrent potassium administration (which will increase serum Na<sup>+</sup> because of extracellular movement), the effect volume replacement has on ADH secretion, or ongoing fluid losses.
- In general, for most patients with chronic hyponatremia and hypovolemia, the initial fluid type and volume administered are based on the severity of hyponatremia, degree of volume depletion, estimated ongoing losses, and maintenance fluids; the goal is a Na<sup>+</sup> correction rate less than 0.5 mEq/kg per hour. At our institution, this usually results in the concurrent administration of maintenance (hypotonic) and replacement (relatively isotonic) crystalloid solutions (**Case Study** available

at cliniciansbrief.com). Therapy is then adjusted on the basis of serial serum Na<sup>+</sup> concentrations.



### IN GENERAL

#### Relative Cost

The cost of investigating and treating hyponatremia depends on the cause and severity. If the patient has no clinical signs and underlying disease is treatable, the treatment may be relatively inexpensive (\$\$-\$\$\$\$). However, if the patient is showing neurologic signs, has severe hyponatremia, or needs intensive care because of the underlying disease process, the cost will be much higher (\$\$\$\$\$).

#### Prognosis & Course

Outcome depends on the cause of hyponatremia and the presence of neurologic signs. Many patients without clinical signs have an excellent prognosis, whereas patients with acute severe hyponatremia that display neurologic signs (either before or during treatment) will have a prognosis from good to guarded.

See Aids & Resources, back page, for references and suggested reading.

#### Cost Key

- \$ = < \$100
- \$\$ = \$100-\$250
- \$\$\$ = \$250-\$500
- \$\$\$\$ = \$500-\$1000
- \$\$\$\$\$ = > \$1000

ACTH = adrenocorticotropic hormone; ADH = antidiuretic hormone; BUN = blood urea nitrogen; Na<sup>+</sup> = sodium; P<sub>osm</sub> = plasma osmolality; SIADH = syndrome of inappropriate antidiuretic hormone secretion; T4 = thyroxine; TBW = total body weight; TSH = thyroid-stimulating hormone; U<sub>na</sub> = urine concentration; U<sub>osm</sub> = urine osmolality