Hypernatremia

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Abstract: Salt toxicity can be fatal in dogs and cats. Whether toxicity occurs accidentally or iatrogenically, it is important to recognize the clinical signs of sodium toxicosis, which are mainly caused by hypernatremia and associated cerebral edema. Treatment involves prompt initiation of fluid therapy along with careful monitoring of neurologic status, serum and plasma electrolytes, and serum osmolarity. Salt was once recommended as an emetic for dogs and cats but has fallen out of favor because of the lethal complications that can arise from overzealous administration.

Table salt (sodium chloride) was once recommended in the human medical and veterinary communities as an emetic agent. Older literature and some current information sources (e.g., the Internet) include statements regarding the use of table salt to induce vomiting in dogs and cats. Table salt taken orally causes pharyngeal irritation, which can lead to emesis. However, salt ingestion does not consistently produce emesis, and multiple cases have been reported in the veterinary and human literature in which the use of table salt and salt water led to acute hypernatremia followed by sodium toxicosis and death. As a result, sodium chloride is no longer recommended as an emetic in animals or humans.

Sodium toxicosis can also occur with ingestion of homemade modeling dough, seawater, or sodium chloride–containing ice-melt products and in the hospital setting after administration of hypertonic saline solution or resuscitation with intravenous (IV) sodium bicarbonate. BOX 1 provides a quick reference for the amounts of sodium and chloride in various forms of salt. In dogs, a sodium chloride dose of 2 to 3 g/kg (87 to 130 mmol/kg) has been shown to cause signs of toxicosis, whereas a dose of 4 g/kg (174 mmol/kg) is lethal. Hypernatremia is defined as a serum sodium concentration greater than 155 mEq/L in dogs and greater than 162 mEq/L in cats. Sodium levels that exceed 170 mEq/L usually result in neurologic signs in animals with acute hypernatremia of less than 4 hours’ duration.

At a Glance

- Classification
- Pathophysiology
- Clinical Signs
- Diagnostic Evaluation
- Gross and Histologic Changes
- Treatment
- Gastrointestinal Tract Decontamination

BOX 1

Sodium and Chloride Content of Types of Salt

1 g of table salt has 400 mg of sodium and 600 mg of chloride.
1 tsp of table salt weighs a little more than 5 g (5000 mg) and contains a little more than 2000 mg of sodium and 3000 mg of chloride.
1 tbsp of table salt contains 17.85 g of sodium chloride.
The atomic weight of sodium is 23 and of chloride is 35.5.
1 mmol (1/1000 of a mole) of sodium equals 23 mg.
1 tsp of table salt has about 93.5 mmol of sodium.
Seawater contains ~350–500 mmol of sodium per L, or 8.05–11.5 g/L.

Salt = sodium chloride.
Hypernatremia

Classification

Hypernatremia can be classified as hypervolemic, euvolemic–isovolemic, or hypovolemic (TABLE 1).

Hypervolemic Hypernatremia

Salt intoxication increases the amount of sodium in the extracellular fluid space, causing a hyperosmolar state. As a result, the body moves water from the intracellular fluid space to the extracellular fluid space to restore osmotic equilibrium. This movement of fluid results in hypervolemia. The extracellular fluid compartment expands with the fluid shift, and in animals with a compromised cardiovascular system, the fluid can move into the interstitium of the lungs, leading to pulmonary edema. Other conditions (e.g., hyperaldosteronism, hyperadrenocorticism) can also cause hypervolemic hypernatremia.

Euvolemic–Isovolemic Hypernatremia

Euvolemic or isovolemic hypernatremia occurs when there is water loss without significant electrolyte loss. For example, there may be excessive water loss from the lungs or skin in hot, dry climates. Dehydration can also occur during febrile illness or due to inadequate water intake caused by central nervous system depression or lack of access to water. This form of hypernatremia is readily corrected by providing ample access to water and addressing defects in the thirst mechanism.

Hypovolemic Hypernatremia

Hypovolemic hypernatremia occurs with severe water loss (e.g., vomiting, diarrhea, use of loop diuretics, nonoliguric acute renal failure, chronic renal failure). In these situations, the animal is not able to replace large amounts of hypotonic fluid and loses normal body osmolality. Hypotension results from water and salt loss from the extracellular space, which causes contraction of extracellular fluid volume.

Pathophysiology

In a hypernatremic animal, water leaves the intracellular space to correct the osmotic difference between the intracellular and extracellular compartments. This results in cellular shrinkage and crenation. Due to fine vascular attachments to the calvarium, the brain is most vulnerable to shrinkage. Brain shrinkage can lead to subarachnoid and subcortical hemorrhages, vascular rupture with cerebral bleeding, subdural hematomas, venous thrombosis, infarction of the cerebral vessels, permanent neurologic damage, and death.

In cases of chronic hypernatremia, the brain promptly produces three major groups of organic osmolytes or idiogenic osmoles (amino acids [e.g., glutamine, glutamate, taurine], polyols [e.g., myoinositol], and methylamines [e.g., phosphocreatinine]) to counteract shrinkage of the brain cells and restore lost water. Production of idiogenic osmoles starts soon after the onset of hypernatremia. In a study of rabbits and rats, production of idiogenic osmoles began as early as 1 hour after the hypernatremic insult. In one rabbit

<table>
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<tr>
<th>TABLE 1</th>
<th>Classification of Salt Toxicity</th>
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<tr>
<td>Classification</td>
<td>Causes</td>
</tr>
<tr>
<td>Hypervolemic hypernatremia</td>
<td>Excessive salt intake, hypertonic saline administration, sodium bicarbonate administration, hyperaldosteronism (rare), hyperadrenocorticism (rare)</td>
</tr>
<tr>
<td>Euvolemic or isovolemic hypernatremia</td>
<td>Diabetes insipidus (central), nephrogenic causes, heatstroke, fever, burns, inadequate water intake (water not available), hypodipsia, general infirmity</td>
</tr>
<tr>
<td>Hypovolemic hypernatremia</td>
<td>Vomiting, diarrhea, osmotic diuresis (renal failure), diabetes mellitus, diuretic administration, third-space losses (intestinal obstruction), pancreatitis, peritonitis</td>
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</table>
population, the concentration of amino acids and idiogenic osmoles in the brain accounted for 42% to 49% of the total increase in brain osmolality 1 to 4 hours after the induction of hypernatremia. In another rabbit population in the same study, the higher levels of amino acids and idiogenic osmoles accounted for 71% of the total increase in brain osmolality after 1 week of hypernatremia. When osmolytes are present during chronic hypernatremia, free water must be reintroduced slowly to allow the brain cells to reequilibrate the water they contain. Introducing water too rapidly can cause brain cells to swell and lead to severe cerebral edema, convulsions, and death. The rate at which the idiogenic osmolyte levels in the brain return to normal varies depending on the osmolyte.

**Clinical Signs**

Signs of acute hypervolemic hypernatremia are related to central nervous system dysfunction caused by loss of water from the brain cells and brain shrinkage. The earliest clinical signs include lethargy, depression, and inappropriate vocalization. Signs progress to muscle rigidity, tremors, myoclonus, and generalized hyperreflexia. Seizures, coma, and death will follow if appropriate therapy is not instituted. Signs of chronic hypervolemic hypernatremia tend to be similar to those seen with acute disease, but they may be less dramatic due to the presence of idiogenic osmoles in the brain.

**Diagnostic Evaluation**

The initial evaluation in cases of suspected salt toxicity includes obtaining a thorough history from the owner (including environment and access to water), performing a physical examination, and conducting tests, including a complete blood count, a complete chemistry panel with electrolyte levels, and urinalysis. Patients with hypernatremia may have erythrocytes that appear crenated on peripheral blood smear assessment.

The following formula may be applied to calculations of plasma osmolality:

\[
\text{Plasma osmolality} = \frac{2(Na) + \text{BUN (mg/dL)} + \text{glucose (mg/dL)}}{2.8 + 18}
\]

\(Na = \text{sodium; BUN = blood urea nitrogen}\)

In this equation, conversion factors of 2.8 and 18 are used to convert urea and glucose, respectively, from mg/dL to mmol/L. BOX 2 gives a clinical example of calculation and use of plasma osmolality.

**Gross and Histologic Changes**

Cerebral and pulmonary edema can be seen on gross necropsy of animals that die of hypernatremia. Histopathologic changes in the central nervous system include intracranial hemorrhage, hematoma, thrombosis, infarction, and various degrees of edema. Vascular congestion, hemorrhage, and perivascular hemorrhage may also be evident in the brain, lungs, liver, and kidneys.

**Treatment**

The goal of treatment for hypervolemic hypernatremia is to bring sodium levels back into the normal range without causing adverse neuro-

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**Clinical Example: Calculations in Hypernatremia**

A 5-year-old spayed golden retriever weighing 77 lb (35 kg) presents with disorientation and vomiting after swimming in the ocean less than 4 hours previously. It is suspected that the dog may have ingested a substantial amount of salt water during this swim. The chemistry and electrolyte findings are:

- BUN: 14 mg/dL (normal: 7–26 mg/dL)
- Creatinine: 1 mg/dL (normal: 0.6–1.4 mg/dL)
- Glucose: 110 mg/dL (normal: 79–126 mg/dL)
- Sodium: 175 mmol/L (normal: 141–154 mmol/L)
- Potassium: 5 mmol/L (normal: 3.9–5.3 mmol/L)
- Chloride: 146 mmol/L (normal: 109–122 mmol/L)
- Calcium: 8 mg/dL (normal: 9.6–11.6 mg/dL)
- Osmolality: 361 mOsm/kg (normal: 292–308 mOsm/kg)

The appropriate fluid rate for therapy can be calculated as follows. In this example, D5W is used for treatment.

- **Change in Na⁺ concentration per liter of fluid (mEq/L):**
  \((0–175)/(35(kg) \times 0.6) + 1) = -7.95 \text{ mEq/L}

The rate of Na⁺ decrease chosen for this case is 1.0 mEq/L/hr (24 mEq/L/day).

- **Quantity of D5W needed in 1 day:** 24/7.95 = 3 L/day or 125 mL/hr

The rate of Na⁺ decrease will range from 0.5 to 2 mEq/L/hr depending on the chronicity of hypernatremia.
logic signs. If the animal is conscious and able to drink and swallow, oral water replacement is preferred; hypernatremia is rare in healthy animals with free access to fresh water. The volume and rate of free water replacement are similar to those for intravenous fluid administration. The total replacement volume should be divided into small amounts given fre-

**Case Report: Hypernatremia in a Miniature Schnauzer**

A 3-year-old castrated miniature schnauzer weighing 25 lb (11.3 kg) presented with a history of eating 8 oz of milk chocolate wrapped in aluminum foil. The owners administered salt until emesis was achieved. The dog received up to 8 tsp (47.6 g) of table salt (sodium chloride) orally. The lethal dose of sodium chloride for this dog is 45.5 g. Approximately 90 minutes after ingestion, the dog became lethargic and nonresponsive. It was transported to an emergency veterinary facility where it was noted to be cyanotic with weak pulses. Its heart rate was 37 beats/min; respiration, 20 breaths/min; capillary refill time, >3 sec; and rectal temperature, 102.2°F (39°C). There was some evidence of diarrhea around the perianal area. A complete blood cell count and electrolyte panels were obtained, showing the following changes:

- **WBC**: 15.20 × 10³/μL (normal: 6.0 × 10³/μL–17.0 × 10³/μL)
- **RBC**: 10.30 × 10⁶/μL (normal: 5.50 × 10⁶/μL–8.50 × 10⁶/μL)
- **Hemoglobin**: 23.2 g/dL (normal: 12.0–18.0 g/dL)
- **Hematocrit**: 76.4% (normal: 37.0%–55.0%)
- **Mean corpuscular volume (MCV)**: 74.3 fL (normal: 60.0–77.0 fL)
- **Mean cell hemoglobin (MCH)**: 22.6 pg (normal: 19.5–30.0 pg)
- **Mean cell hemoglobin concentration (MCHC)**: 30.4 g/dL (normal: 32.0–36.0 g/dL)
- **Platelets**: 297 × 10³/μL (normal: 200 × 10³/μL–500 × 10³/μL)
- **Neutrophils**: 14.5 × 10³/μL (normal: 3.0 × 10³/μL–11.4 × 10³/μL)
- **Lymphocytes**: 0.48 × 10³/μL (normal: 1.0 × 10³/μL–4.8 × 10³/μL)
- **Monocytes**: 0.10 × 10³/μL (normal: 0.15–1.35 × 10³/μL)
- **Eosinophils**: 0.010 × 10³/μL (normal: 0.0–0.75 × 10³/μL)
- **Basophils**: 0.06 × 10³/μL (normal: 0.0–0.1 × 10³/μL)
- **Sodium**: 175 mEq/L (normal: 141–154 mEq/L)
- **Potassium**: 3.5 mEq/L (normal: 3.9–5.3 mEq/L)
- **Ionized calcium**: 4.45 mg/dL (normal: 5–5.8 mg/dL)

Despite appropriate supportive care and therapy, the dog experienced cardiopulmonary arrest and died. Necropsy revealed severe, diffuse vascular congestion and perivascular hemorrhage with multifocal, mild-to-moderate axonal sheath dilation and axonal degeneration in the cerebrum and cerebellum (Figures 1 and 2). Multifocal endocardial and epicardial hemorrhages were also seen. There was multifocal necrosis and hemorrhage of the adrenal gland. Sodium levels in the brain were found to be 2000 ppm. Values greater than 2000 ppm are considered diagnostic for sodium toxicosis in animals.3

**FIGURE 1**

Perivascular hemorrhage, vascular congestion (blue arrow), axonal sheath dilation, and axonal degeneration (black arrow) in the cerebrum of the 3-year-old miniature schnauzer discussed in the case report. Hematoxylin–eosin (HE) stain, x100 objective.

**FIGURE 2**

Perivascular hemorrhage (arrows) in the lung of the 3-year-old miniature schnauzer. HE stain, x50 objective.

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WBC = white blood cell count; RBC = red blood cell count
Acute Hypervolemic Hypernatremia

It is very important to note that the treatment for acute hypervolemic hypernatremia (less than 2 to 4 hours since salt ingestion or administration) is different from that for chronic hypervolemic hypernatremia (more than 4 hours since salt ingestion or administration). If sodium ingestion is known to be acute, rapid correction of sodium levels improves the outcome. These patients have not had a chance to form idio genetic osmoles; therefore, a rapid decrease of peripheral osmolarity to normal will not result in fluid movement into the brain.11

In animals with no access to fresh water or with impaired thirst or swallowing mechanisms, IV fluids should be started immediately. Patients must be monitored carefully during the fluid therapy for any change in neurologic status. It is recommended that the serum or plasma sodium concentration be reduced at a rate of not more than 1 to 2 mEq/L/hr.11,14 Administration of 5% dextrose in water (D5W) solution combined with a loop diuretic (e.g., furosemide) facilitates the excretion of sodium. In addition to the water already present in the solution, D5W serves to replace free water when the glucose enters the cells and is metabolized into carbon dioxide and water.

Chronic Hypervolemic Hypernatremia

Patients with chronic hypervolemic hypernatremia may have a significant concentration of idio genetic osmoles in their brain that could promote cerebral edema if the sodium balance is corrected too quickly. Therefore, these patients should be treated more cautiously with a sodium correction rate of not more than 0.5 mEq/L/hr.8 The following formulas can be used to calculate the fluid rates for both acute and chronic conditions, using the selected infusate (TABLE 2). BOX 2 provides a clinical example.

A factor of 0.6 is used because water makes up 60% of the animal’s body weight.

A sampling catheter should be placed in a jugular or saphenous vein to allow fluid administration and more convenient access for repeated blood sampling. The plasma sodium level should be checked every 2 to 4 hours if the animal can tolerate multiple samplings.

Fluid correction is more complex in hypervolemic hypernatremic patients with pulmonary edema because of the increased fluid volume in the pulmonary interstitium. Treatment with water or hypotonic fluids will expand the extracellular compartment and worsen pulmonary edema. To balance the increase in extracellular fluid and decrease the sodium content, a loop diuretic (e.g., furosemide, 2 to 4 mg/kg three times a day for dogs and 1 to 4 mg/kg one to three times a day for cats) given orally, IV, or subcutaneously may be used in conjunction with IV fluid therapy.9 Fluid choices for hypervolemic hypernatremic patients are listed in TABLE 2.

**TABLE 2** Fluid Replacement Options for Hypervolemic Hypernatremia7

<table>
<thead>
<tr>
<th>Fluid Type</th>
<th>Sodium (mmol/L)</th>
<th>Osmolality (mOsm/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dextrose 5%</td>
<td>0</td>
<td>253</td>
</tr>
<tr>
<td>Sodium chloride 0.45%</td>
<td>77</td>
<td>155</td>
</tr>
<tr>
<td>Lactated Ringer's solution</td>
<td>130</td>
<td>272</td>
</tr>
<tr>
<td>Sodium chloride 0.9%</td>
<td>154</td>
<td>310</td>
</tr>
</tbody>
</table>

8Consider using if patient is clinically dehydrated or hypotensive.
Animals with heart failure or oliguric renal failure and hypernatremia may develop volume overload resulting in pulmonary edema and thus would benefit from the use of loop diuretics.10

Gastrointestinal Tract Decontamination

Due to the severe neurologic signs and mortality that can arise from sodium toxicosis, current literature no longer recommends using table salt as an emetic for gastrointestinal decontamination after toxin ingestion. Alternative decontaminants have been shown to more safely promote emesis in dogs and cats1 (Table 3). When gastrointestinal decontamination is necessary, practitioners must thoroughly evaluate the animal and substance ingested to choose the appropriate emetic. If activated charcoal products containing sorbitol are used during the gastrointestinal decontamination process, hydration status should be monitored closely, as sorbitol-containing products have been found to cause hypernatremia and dehydration in people.1

Conclusion

Sodium toxicosis in small animals, although rare, can lead to death if not treated promptly and appropriately. It is important to recognize the signs of hypernatremia and to obtain a detailed history from the owner to ensure timely initiation of therapy. Patients with acute hypervolemic hypernatremia should be distinguished from those with chronic hypervolemic hypernatremia because the treatment protocols are very different. Animals undergoing treatment to correct acute or chronic hypervolemic hypernatremia should have sodium levels and plasma osmolality checked every 2 hours and monitored closely during and after therapy. In toxicity cases that require an emetic for decontamination, the use of an emetic other than table salt is urged to prevent iatrogenic hypernatremia.

Table salt is no longer recommended as an emetic.

References

1. Salt intoxication causes
   a. hypervolemic hypernatremia.
   b. hypovolemic hypernatremia.
   c. hypovolemic hyponatremia.
   d. isovolemic hypernatremia.

2. Which statement best describes the fluid shift that occurs during an acute hypernatremic state in which the sodium concentration is increased in the extracellular fluid space?
   a. Water moves from the extracellular fluid space to the intracellular fluid space.
   b. Water moves from the intracellular fluid space to the extracellular fluid space.
   c. Water moves from the intercellular fluid space into the vascular space.
   d. Water does not shift in any direction, as sodium does not contribute to osmolality in animals.

3. What is the most effective route for fluid administration to correct hypernatremia in a conscious, alert animal?
   a. intraperitoneal
   b. intravenous
   c. oral
   d. subcutaneous

4. What is the most appropriate IV fluid type for replacing the free water deficit in an acutely hypernatremic animal?
   a. 4.5% sodium chloride
   b. D5W
   c. lactated Ringer’s solution
   d. buffered crystalloids

5. In animals that have pulmonary edema in conjunction with hypernatremia, which diuretic can aid in fluid and sodium diuresis?
   a. acetazolamide
   b. furosemide
   c. mannitol
   d. spironolactone

6. When treating acute hypernatremia with IV fluids, how quickly should the sodium levels decline?
   a. 0.5 to 1 mEq/L/hr
   b. 1 to 2 mEq/L/hr
   c. 2 to 3 mEq/L/hr
   d. 3 to 4 mEq/L/hr

7. What is the lethal dose (g/kg body weight) of ingested sodium chloride in dogs?
   a. 1 g/kg
   b. 2 g/kg
   c. 3 g/kg
   d. 4 g/kg

8. What is this animal’s plasma osmolality: sodium, 175 mmol/L; potassium, 5.2 mmol/L; chloride, 120 mmol/L; blood urea nitrogen, 24 mg/dL; glucose, 125 mg/dL; creatinine, 1.2 mg/dL?
   a. 129 mOsm/kg
   b. 320 mOsm/kg
   c. 366 mOsm/kg
   d. 510 mOsm/kg

9. Which two emetics are recommended for use in dogs?
   a. apomorphine and hydrogen peroxide
   b. apomorphine and xylazine
   c. hydrogen peroxide and metoclopramide
   d. hydrogen peroxide and dolasetron

10. All of the following are osmolytes except
    a. glutamate.
    b. glutamine.
    c. myo-inositol.
    d. water.