Hypernatremia in Dogs

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ABSTRACT: Hypernatremia is potentially life threatening and is caused by imbalances in water and sodium that occur from either water loss or sodium gain, often in the presence of inadequate water intake. The resultant hyperosmolarity, if acute or severe, can result in rapid shifts of water from the intracellular to extracellular space, causing intracranial hemorrhage and neurologic changes. Correction of hypernatremia through inappropriate fluid therapy can result in even more severe complications, ranging from cerebral edema to coma and death. This article reviews the pathophysiology, causes, classification, treatment, and prognosis of hypernatremia.

Hypernatremia is defined as an elevated sodium concentration in the blood. Although mild hypernatremia is often detected on serum chemistry panels, hypernatremia does not commonly warrant specific treatment. When marked hypernatremia is present, however, clinical signs can be severe and can result in death. The treatment of hypernatremia can be challenging, and success depends on an understanding of sodium and water balance.

NORMAL PHYSIOLOGY OF SODIUM HOMEOSTASIS

The total body sodium concentration is closely related to the volume of extracellular fluid in the body. Total body water is approximately two-thirds intracellular and one-third extracellular. One-quarter of the extracellular volume is intravascular (i.e., plasma), and the remaining three-quarters is interstitial.

Osmolality is defined as the number of particles per 1 kg of solution. Tonicity refers to the ability of those particles to induce water movement and can be thought of as effective osmolality. The osmolality of plasma can be calculated using the following formula:

\[
\text{Calculated plasma osmolality} = 2 \text{ Sodium ions (Na}^+) + \frac{(\text{Glucose} \div 18)}{1} + \frac{(\text{Blood urea nitrogen [BUN]} \div 2.8)}{1}
\]

BUN has the least effect on plasma osmolality because it is freely diffusible across cell membranes; thus it is an ineffective osmole. Glucose can freely cross the intravascular membrane but is impermeable to some cell membranes. The impact of glucose on plasma osmolality becomes more pronounced at higher glucose concentrations. Like glucose, sodium can cross freely between plasma and the interstitium. As indicated by the above equation, sodium is the most effective extracellular osmole. Hypernatremia results in hyperosmolality and hypertonicity. Hypernatremia in dogs is defined as a rise in the plasma sodium concentration to a value exceeding 155 mEq/L. Because of increased tonicity and because water freely diffuses across all membranes in response to hypertonicity, sodium induces water movement across cell membranes from an area of low osmolality to an area of high osmolality.
Plasma sodium concentration and thus plasma osmolality are reflections of water balance, which is controlled by thirst, arginine vasopressin (AVP, previously called antidiuretic hormone), and the kidneys. A disruption in water homeostasis is reflected by an increase or decrease in the plasma sodium concentration (e.g., hypernatremia occurring with water deficit).

The hypothalamus contains osmoreceptors and baroreceptors that detect and respond to plasma osmolality (normally 290 to 310 mOsm/kg in dogs) and blood pressure (BP), respectively.\(^1\) The osmoreceptors are extremely sensitive and can detect changes as little as 1% to 2% in osmolality.\(^2\) When hyperosmolar fluid bathes the hypothalamic osmoreceptors, water in the receptor diffuses into the surrounding interstitium, causing shrinkage and dehydration of the cell.\(^3,5\) This normally results in two responses: The first and most important is thirst stimulation. Thirst is the major defense against hypernatremia, which is rare in an alert, conscious animal with a normal thirst mechanism and access to water.\(^2,6,7\) Second, AVP is released from the posterior pituitary. AVP is produced by the supraoptic and paraventricular nuclei in the hypothalamus. It is then transported down the supraopticohypophyseal tract and is stored in the posterior pituitary until the hypothalamic osmoreceptors signal its release.\(^2,3\) Once released into the blood, AVP is delivered to the kidneys, where it binds to vasopressin (V\(_2\)) receptors on the epithelial cells of the renal collecting duct. This causes activation of the transmembrane protein G\(_s\), production of cAMP, and subsequent phosphorylation of serine residues of vesicles containing water channels (aquaporins).\(^8\) The vesicles then fuse to the luminal membrane, and aquaporin-2 water channels are inserted, allowing reabsorption of water, reduced volume of urine, and production of more concentrated urine.\(^8\)

Low-pressure baroreceptors in the atria, aortic body, carotid sinus, and pulmonary vasculature detect changes in circulating blood volume. When the vessel wall is stretched in response to an increase in volume, the receptors are activated, decreasing sympathetic tone and increasing release of atrial natriuretic peptide (ANP).\(^1,2,5\) Conversely, when receptors detect a decrease in volume, the sympathetic tone is increased and the release of ANP decreases.\(^1,2,5\)

The renin–angiotensin–aldosterone system is important in water balance and sodium excretion. Juxtaglomerular cells of the afferent arteriole in the glomeruli detect decreased renal perfusion and respond by releasing renin into the bloodstream, where renin enzymatically reacts with angiotensinogen, an \(\alpha_2\)-globulin produced by the liver, to release the inactive angiotensin I.\(^1,2,5\) In the lungs, angiotensin-converting enzyme then converts angiotensin I to the active form, angiotensin II, which is a potent pressor that causes peripheral vasoconstriction, thereby increasing BP. By direct action on the adrenal cortex, angiotensin II stimulates secretion of aldosterone, which acts in the distal renal tubules to promote sodium and bicarbonate reabsorption as well as potassium and hydrogen ion excretion.\(^2\) In addition, in hyperosmolar situations, angiotensin II can have direct effects on AVP-producing nuclei, causing AVP secretion.\(^5\)

Studies’ show that dogs have a protective natriuresis in response to having inadequate water during exercise.

Hypernatremia is rare in an alert, conscious animal with a normal thirst mechanism and access to water.
Hypernatremia in Dogs

Fluid, causing movement of water from the intracellular to extracellular space. The loss of volume occurs equally between the intracellular and extracellular spaces, resulting in minimal change in extracellular volume. Affected animals do not usually appear hypovolemic or even clinically dehydrated, despite marked hypernatremia. Pure water loss can result from central diabetes insipidus, nephrogenic diabetes insipidus, increased insensible fluid losses, or inadequate water intake (see box on this page).

Central Diabetes Insipidus

Central diabetes insipidus is characterized by a partial or complete deficiency of AVP, resulting in decreased ability or inability of the kidneys to conserve water and to concentrate the urine in response to increases in plasma osmolality. The water diuresis state (i.e., polyuria) causes increased plasma osmolality because fluid is lost in excess of solute. Increased osmolality stimulates thirst (i.e., polydipsia). Most dogs maintain their water balance because the thirst mechanism is intact. However, if water intake is inadequate, severe hyperosmolality and hypernatremia can result.

Central diabetes insipidus can be congenital, acquired, or idiopathic and most commonly results from pathology in the supraoptic or paraventricular nuclei in the hypothalamus or in the supraopticohypophyseal tract. However, the defect must be above the median eminence; transection of the tract below the median eminence or removal of the posterior pituitary has been shown to cause only transient central diabetes insipidus because the hormone can be released from the remaining stalk. Defects that have been found to result in central diabetes insipidus include neoplasia, trauma, pituitary malformation, cysts, and inflammation, although most cases are idiopathic. One report described central diabetes insipidus in two Afghan puppies from the same litter from a dam with polyuria and polydipsia, suggesting a possible hereditary form.

Nephrogenic Diabetes Insipidus

Nephrogenic diabetes insipidus occurs because of lack of or impaired renal tubular responsiveness to AVP. Primary nephrogenic diabetes insipidus occurs as a congenital defect in the nephron that impairs the responsiveness to normal or increased levels of AVP. This is a rare disorder, and only a few reports have appeared in the veterinary literature.

Secondary (i.e., acquired) nephrogenic diabetes insipidus is more common. The pathogenesis can be due to a defect in the binding of AVP to the V2 receptors in the collecting ducts, alterations in renal tubular cell function, or decreased tonicity of the renal medullary interstitium, causing osmotic diuresis. As was described with central diabetes insipidus, inability to concentrate urine, polyuria, and compensatory polydipsia result. Inadequate water intake can lead to hypernatremia.

Nephrogenic diabetes insipidus can occur secondary to various disorders, including infections, metabolic disease, and those that are drug induced. Escherichia coli endotoxins associated with pyometra or pyelonephritis...
compete with AVP for the binding of V₂ receptors. Pyelonephritis, hepatic disease, hypoadrenocorticism, and hyperthyroidism may decrease the renal medullary concentration gradient. Glucocorticoids associated with hypoadrenocorticism directly inhibit AVP release within the brain.

**Increased Insensible Fluid Losses**
Insensible fluid loss results from pure water loss through the lungs or skin. Fever, exposure to an elevated environmental temperature and resulting heatstroke, exercise, seizures, and respiratory infections can cause pure water loss and, ultimately, hypernatremia.

**Inadequate Water Intake**
The inability to drink because of either an altered state of consciousness or lack of access to water can result in hypernatremia. In addition, a defect in the thirst mechanism (primary hypodipsia) or an altered set-point in the osmoreceptors in the hypothalamus affecting the release of AVP (essential hypernatremia) can lead to inadequate water intake and hypernatremia.

**Primary hypodipsia** occurs when there is a defect in the thirst mechanism. Because thirst and drinking are the major mechanisms of water homeostasis, volume depletion and hypernatremia occur when the drive to replace lost body water is decreased or absent. Even in the presence of the normal release and action of AVP, insensible water loss and renal loss continue.

Primary hypodipsia is caused by a defect (e.g., due to neoplasia, trauma, inflammatory brain disease, hydrocephalus, congenital defects [e.g., dysplasia], idiopathic reasons) in the hypothalamus. There are published reports of young miniature schnauzers and a Dalmatian puppy with primary hypodipsia. Some of these animals had features of holoprosencephaly at necropsy: There was evidence of absent or smaller-than-normal prosencephalic structures, incomplete separation of normally paired forebrain structures, and/or hydrocephalus.

Primary hypodipsia can be differentiated from other causes of isovolemic hypernatremia by evaluation of urine osmolality. With primary hypodipsia, urine is concentrated appropriately through the release and actions of AVP. However, hypodipsia can occur in conjunction with central diabetes insipidus or essential hypernatremia, further confusing the diagnosis because, in these cases, the urine is dilute. Forced water intake, either orally (by combining water with food) or intravenously (by using 5% dex-
Essential hypernatremia occurs as a result of damage to the osmoreceptors in the hypothalamus, causing the osmoreceptors to recognize increases in plasma osmolality as normal.19,20 The osmoreceptors detect and respond to a higher osmolality than normal, stimulating AVP release and urine concentration when water is restricted. The hallmarks of this condition include hypodipsia, hypernatremia, and volume-mediated AVP release.

The hypothalamic baroreceptors of animals with essential hypernatremia respond to volume stimuli. To separate the effects of the osmoreceptors and the volume receptors in a dog with essential hypernatremia, both isotonic and hypertonic saline can be given intravenously, and the resulting urine tonicity can be monitored.17 Isotonic saline does not affect plasma osmolality but does stimulate volume receptors, thereby inhibiting AVP release and increasing urine production. Hypertonic saline increases both plasma osmolality and volume. A dog with essential hypernatremia produces a greater volume of urine after administration of hypertonic saline because it cannot release AVP and, therefore, cannot concentrate its urine, despite a rising plasma osmolality.

Essential hypernatremia can be diagnosed by observation of hypodipsia and low urine osmolality in the presence of hypernatremia.19,20 In contrast to primary adipsia or hypodipsia, essential hypernatremia does not respond to fluid loading.14,15,20 Features consistent with essential hypernatremia have been reported in a young Great Dane19 and an adult mixed-breed dog.6

Hypovolemic Hypernatremia
In hypovolemic hypernatremia, hypotonic fluid, rather than pure water, is lost. Both water and electrolytes are lost, although water is lost in excess of sodium.1–3,10 The result is reduced extracellular fluid volume with less stimulus for the intracellular fluid to equilibrate with the extracellular space.1,2 Thus a dehydrated and potentially hypovolemic condition may develop. Because both hypovolemia and hyperosmolality stimulate thirst and AVP release, some impairment of water intake has likely occurred. The patient often presents with clinical dehydration and tachycardia.2 This is the most common cause of hypernatremia and can be separated into renal and extrarenal causes.1

Most renal diseases, except for nephrogenic diabetes insipidus, result in hypotonic fluid loss.10 In animals with renal failure, there is inadequate delivery of tubular fluid to distal diluting sites in the nonfunctional nephrons, in which sodium chloride (NaCl) is normally removed without water.1 Loop diuretics have a similar mechanism in that they interfere with NaCl reabsorption in the ascending loop of Henle. This can result in increased NaCl excretion and osmotic diuresis in the remaining functioning nephrons.1,2 Similarly, when an excess of other nonreabsorbed solutes (e.g., glucose, mannitol, urea) is present in tubular fluid, they increase urine output and cause a dilutional decrease in urine sodium and other electrolytes.1,2 The urine then becomes hypotonic to the plasma.1,2 If the animal is unable to compensate with water intake, hypernatremia develops.

Extrarenal1,10 causes of hypotonic fluid loss include vomiting, diarrhea, and third-space losses (e.g., pancreatitis, peritonitis). Lactulose, sorbitol, and intestinal malabsorption syndromes can cause osmotic diarrhea, in which the fluid lost into the gastrointestinal (GI) tract is isosmotic to plasma. This becomes especially important when an animal is given lactulose for hepatic encephalopathy; an altered state of con-
sciousness might prevent adequate water intake, thereby exacerbating hypernatremia.\textsuperscript{2,3,10}

Animals with renal causes of hypovolemic hypernatremia often have low urine osmolality.\textsuperscript{21} With the use of diuretics or in patients with osmotic diuresis or sodium wasting, urine can be isotonic. If the cause of hypernatremia is extrarenal, urine is usually concentrated.\textsuperscript{2,21}

**Hypervolemic Hypernatremia**

Hypernatremia due to ingestion of excessive sodium or administration of sodium-containing substances is uncommon but can result in hypernatremia.\textsuperscript{1–3,10} The sodium is restricted to the extracellular space, causing hyperosmolality. The result is the movement of water from the intracellular space to the extracellular space, causing volume expansion. If signs of cardiac or renal disease are already present, the animal may develop signs of fluid overload, such as pulmonary edema.\textsuperscript{1–3,10}

Sodium phosphate–containing enemas, sodium bicarbonate, and hypertonic saline can cause hypervolemic hypernatremia.\textsuperscript{1–3,10} There have also been reports of excessive sodium ingestion by dogs resulting from ingestion of paintballs\textsuperscript{22} or homemade play-dough consisting of a salt–flour mixture\textsuperscript{23,24} (not to be confused with the commercially available product, Play-Doh, Hasbro). Although a dose of 4 g/kg of sodium may be lethal in dogs,\textsuperscript{25} a recent study\textsuperscript{23} found that serum sodium concentrations greater than 180 mEq/L consistently resulted in systemic signs, including vomiting, hyperthermia, and seizures. Primary hyperaldosteronism rarely causes hypernatremia, although an increase in total body sodium with normal plasma sodium concentrations is more common.\textsuperscript{4} Table 1\textsuperscript{26–28} lists sodium sources that may result in toxicosis.

**CLINICAL MANIFESTATIONS**

The brain is the major organ affected by hypernatremia.\textsuperscript{29} When a hyperosmolar state develops, water from brain cells moves down the osmotic gradient into the extracellular space. This results in brain parenchymal cell dehydration and an overall decrease in brain volume.\textsuperscript{30} The cerebral veins rupture as a result of pia mater blood vessel tearing, resulting in subarachnoid and intracerebral hemorrhage.\textsuperscript{29} At presentation, affected animals have evidence of neurologic disease. They can exhibit lethargy, ataxia, and weakness, which progress to seizures, coma, and death in severe cases.\textsuperscript{14–19,23,24} Clinical signs appear as the serum sodium concentration approaches 170 mEq/L.\textsuperscript{3,10}

The neurologic signs are related less to the magnitude of hypernatremia than to the acuteness of onset. Studies\textsuperscript{30,31} in rats have shown that, within hours of the development of hypernatremia, the brain begins to produce “idiogenic osmoles” to adapt to the hyperosmolar state. Idiogenic osmoles refer to electrolytes and other organic solutes (i.e., amino acids, inositol) that are retained by dehydrated brain cells, functioning to increase the intracellular osmolality and reequilibrating the brain volume.\textsuperscript{30,31} In rats, it can take 4 to 7 days for idiogenic osmoles to reach protective levels.\textsuperscript{31} When hypernatremia develops slowly, the brain has time to compensate, and neurologic signs are minimal.\textsuperscript{31} However, when
hypernatremia occurs acutely, more severe and potentially irreversible neurologic signs develop.

Other clinical manifestations of hypernatremia include GI signs such as anorexia, vomiting, and lethargy. NaCl is a gastric irritant, so these signs are often observed with sodium ingestion.23

**DIAGNOSIS**

The diagnosis of hypernatremia is based on a plasma sodium concentration greater than 155 mEq/L. Thorough physical and neurologic examinations should be performed. A detailed history should be obtained, with specific questions about the dog’s drinking and urinating habits (i.e., frequency and amount), the time period in which clinical signs developed, and exposure to sodium-containing substances. Other important aspects of the history include vomiting, diarrhea, or concurrent diseases; head trauma; or use of medications.

A minimum database including a complete blood count, serum chemistry profile, and urinalysis should be obtained to rule out underlying causes of hypernatremia, such as diabetes mellitus, hypercalcemia, hypokalemia, renal failure, or renal glycosuria.1 In addition to showing hypernatremia and hyperchloremia, blood work may reveal abnormalities attributable to dehydration, such as prerenal azotemia and hyperalbuminemia.14,16,19,23 Metabolic acidosis often occurs in conjunction with hypernatremia because of an associated increased anion gap and decreased tissue perfusion with concurrent lactic acidosis.5

The urine osmolality should be determined at presentation (Figures 1 and 2). If laboratory facilities that measure urine osmolality are not available, the value can be estimated by multiplying the last two digits of the urine specific gravity by 36. For example, a urine specific gravity of 1.010 would correlate with a urine osmolality
This method is not accurate when other osmoles, such as urea or glucose, are present in the urine. Normal dogs that are dehydrated usually have a urine osmolality greater than 1,100 mOsm/kg, whereas dogs that are unable to concentrate their urine have a urine osmolality less than 300 mOsm/kg. The amount of urine produced during hospitalization should be measured to monitor treatment progress as well as ongoing losses.

As discussed earlier, osmoregulation and response to volume can be assessed by administration of isotonic and hypertonic saline, differentiating essential hypernatremia from primary hypodipsia. Endocrine tests can be conducted to assess the function of the anterior pituitary; disease of the anterior pituitary may involve the posterior pituitary. Other diagnostics may include renal and liver function testing, urine culture and sensitivity testing, and imaging to identify a source of infection or neoplasia. When the patient is stable and all other causes of polyuria and polydipsia have been ruled out, either a vasopressin response test or water deprivation test can be conducted. These procedures are described in detail elsewhere.

**TREATMENT**

Definitive treatment of hypernatremia should occur if the plasma sodium concentration is greater than 170 mEq/L or clinical signs are present. Treatment objectives include reestablishing euvolemia, correcting metabolic acidosis (if severe), reducing plasma sodium concentrations, and addressing the underlying cause of disease (if possible). Treating underlying disease could include controlling GI fluid loss, managing fever, discontinuing administration of lactulose or diuretics, or addressing hypercalcemia or hypokalemia.

**Assessing Volume Status**

The volume status of the patient should initially be characterized based on the status of the extracellular fluid volume (Figures 1 and 2). Hypernatremic dogs assessed as clinically dehydrated are classified as hypovolemic hypernatremic, whereas those that are euhydrated are classified as isotonic hypernatremic. Hypervolemic hypernatremic patients can be hypertensive and often present with respiratory distress secondary to pulmonary edema.

**Hypovolemic Hypernatremia**

If the patient presents in a hypovolemic state, treatment should be directed toward restoring the intravascular volume with the use of an isotonic crystalloid (see box on page 158) and, if hypotension persists, colloids. The crystalloid dosage for hypovolemic shock in dogs is 70 to 90 ml/kg/hr. One-quarter to one-third of the shock dose should be given over 15 to 20 minutes, followed by reassessment of the patient’s vital signs, including mucous membrane color, capillary refill time, heart rate, BP, and pulse quality. Ideally, central venous pressure or arterial BP should be monitored. If poor perfusion persists despite crystalloid therapy, a colloid such as hetastarch or dextran can be administered; a bolus of 5 ml/kg should be given over 5 to 10 minutes, and the patient’s perfusion status should be...
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Figure 2. Approach to diagnosing the underlying cause of hypernatremia in hypovolemic dogs.

If this is still inadequate, the bolus can be repeated as needed until perfusion parameters improve. Dextran and, less frequently, hetastarch have been shown to cause defects in primary and secondary hemostasis when given at a rate greater than 20 ml/kg/day; caution should be observed if a higher dose is given. Electrolytes should be rechecked after resuscitation because crystalloids and colloids contain sodium and can alter the serum sodium concentration.

Metabolic Acidosis

Because sodium bicarbonate can worsen hyperosmolality, metabolic acidosis should be corrected in hypernatremic patients only when it is severe (<7.15). Tromethamine (THAM) is an alternative drug with buffering effects. One study compared the buffering capacities and side effects of equivalent doses of THAM and sodium bicarbonate in anesthetized dogs with metabolic acidosis and found that, unlike sodium bicarbonate, THAM does not cause transient hypernatremia. Other studies found that THAM caused a transient decrease in the plasma sodium concentration, raising concern regarding the speed of plasma sodium concentration correction and the possible complications.

Table 2. Sodium Concentrations of Various Infusates

<table>
<thead>
<tr>
<th>Infusate</th>
<th>Sodium Concentration (mEq/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>5% Dextrose in water</td>
<td>0</td>
</tr>
<tr>
<td>0.45% NaCl</td>
<td>77</td>
</tr>
<tr>
<td>2.5% Dextrose in 0.45% NaCl</td>
<td>77</td>
</tr>
<tr>
<td>Lactated Ringer’s solution</td>
<td>130</td>
</tr>
<tr>
<td>Plasmalyte A, Normosol R</td>
<td>140</td>
</tr>
<tr>
<td>0.9% NaCl</td>
<td>154</td>
</tr>
<tr>
<td>Hetastarch</td>
<td>154</td>
</tr>
<tr>
<td>Dextran</td>
<td>154</td>
</tr>
</tbody>
</table>

Isotonic Crystalloids That Can Be Used in Treating Hypovolemia

- 0.9% NaCl
- Lactated Ringer’s solution
- Plasmalyte A
- Normosol R
**Isovolemic Hypernatremia**

When the patient has been stabilized and hypovolemia corrected, or if the patient has been assessed as isovolemic at presentation, attention can be turned to correction of the water deficit and reduction of the plasma sodium concentration. Because of the presence of idiogenic osmoles, the water deficit should be replaced over 48 to 72 hours, and sodium levels should be corrected slowly (i.e., no faster than 0.5 to 1 mEq/L/hr) because hypernatremia developed over 24 hours or more. In the treatment of chronic hypernatremia, one practical guideline is to decrease the sodium level by no more than 8 to 12 mEq/L over any given 24-hour period.

Isotonic saline should not be used to correct isovolemic hypernatremia because the sodium concentration is not low enough to significantly alter the plasma sodium concentration (Table 2). Ideally, if the dog is drinking, water should be replaced orally or by nasogastric intubation. If the patient is unable to drink, intravenous fluids (0.45% NaCl or 5% dextrose in water) should be administered. Serum electrolytes and BP should be monitored every 2 to 4 hours during treatment, allowing adjustments to rate and fluid type. Because water and sodium balance is continuously changing during treatment, it is imperative to revise the fluid regimen often and according to need. Also, the conventional equations do not account for the sodium content in various fluid types and the impact this has on the patient’s plasma sodium concentration. The following equation considers these factors and estimates the effect that 1 L of infusate has on the patient’s plasma sodium concentration:

$$\Delta [Na]^p = \frac{([Na]_{inf} - [Na]^p)}{(Total\ body\ water + 1)}$$

**Example 1:** If a 10-kg dog presents in an isovolemic state with a plasma sodium concentration of 180 mEq/L, and the clinician decides to administer 5% dextrose in water intravenously (sodium concentration: 0 mEq/L), the following application can be used:

Total body water = 0.6 × Body weight (kg) = 0.6 × 10 kg = 6 kg

$$\Delta [Na]^p = \frac{([Na]_{inf} - [Na]^p)}{(Total\ body\ water + 1)} = \frac{(0 - 180)}{(6 + 1)} = \frac{-180}{7} = -25.7 \text{ mEq/L}$$

Thus 1 L of 5% dextrose in water decreases the plasma sodium by 25.7 mEq/L. If the goal is to decrease plasma sodium by 0.5 mEq/L/hr, the change in the sodium concentration will be −12 mEq/L/24 hr. Dividing −12 by −25.7 determines that 0.47 L (470 ml) of infusate is needed for 1 day of
fluid therapy. The 5% dextrose in water can be administered at 20 ml/hr.

**Example 2:** If, instead, 0.45% NaCl (sodium concentration: 77 mEq/L) is to be used for the same dog, the calculated rate of fluid administration will be different:

\[ \Delta [Na]_p = (\text{[Na]}_{\text{inf}} - \text{[Na]}_p) \div (\text{Total body water} + 1) = (77 - 180) \div (6 + 1) = -103 \div 7 = -14.7 \text{ mEq/L} \]

Thus 1 L of 0.45% NaCl decreases the plasma sodium concentration by 14.7 mEq/L. If the goal is to decrease the plasma sodium concentration by 0.5 mEq/L/hr or 12 mEq/L/day, 0.82 L (i.e., –12 ÷ –14.7) of 0.45% NaCl is required for the first day of fluid therapy.

The estimated ongoing losses should be replaced according to the type of loss that is occurring. If an animal with central diabetes insipidus continues to lose free water through polyuria, free water should be given orally or 5% dextrose in water parenterally. If hypotonic fluid is being lost by renal or extrarenal causes, hypotonic fluid should be given. In addition, the maintenance requirements should be calculated and replaced with isotonic crystalloids. The estimated ongoing losses and maintenance needs should be added to the fluid regimen.

**Hypervolemic Hypernatremia**

Therapy for patients with hypervolemic hypernatremia should be directed toward replacing water and electrolyte deficits and facilitating renal excretion of sodium. Because affected animals often vomit or are mentally depressed, this can be accomplished by administering intravenous fluid and intravenous diuretics. Free water deficit can be replaced as described for isovolemic hypernatremia: 5% dextrose in water has been recommended unless hypotension or dehydration occurs; in those cases, isotonic replacement fluids should be administered. A loop diuretic such as furosemide should be administered at 2 to 4 mg/kg IV q8h to induce natriuresis and minimize the risk for pulmonary and cerebral edema. When there has been an acute onset of hypernatremia, the prognosis can be improved by replacing the water deficit at a rate of 1 to 2 mEq/L/hr.

A recent study examining hypernatremia secondary to homemade play-dough ingestion found that emesis should be induced with either apomorphine or hydrogen peroxide if ingestion occurred within the previous 30 minutes. Administration of activated charcoal is not recommended, and access to water is essential. If plasma sodium concentrations increase despite treatment, a sodium source may be present in the stomach, and hypotonic intravenous fluids may be required.

**Essential Hypernatremia and Primary Hypodipsia**

In animals with essential hypernatremia or primary adipsia or hypodipsia, 5% dextrose in water can be given at a rate not exceeding 8 to 12 mEq/L/24 hr. When clinical signs have resolved, patients can be managed by adding the daily fluid requirements to their food.

**Complications**

If the patient’s neurologic condition deteriorates during the treatment of hypernatremia, cerebral edema should be suspected and treated using mannitol and furosemide for their osmotic and diuretic effects, respectively. Any diluting solution should be stopped for several hours to lessen the rate of decline of the plasma sodium concentration. Because administration of mannitol and furosemide may cause sodium and chloride wasting, electrolytes should be monitored closely.

**Prognosis**

The prognosis for patients with hypernatremia depends on the underlying cause, severity of hypernatremia and clinical signs at presentation, and response to fluid administration. Hypernatremia has a high mortality rate in humans, and mortality has been found to be associated with the initial plasma sodium concentration, severity of neurologic signs at presentation, and response to treatment. A recent study of 35 hypernatremic dogs and cats found a 42% mortality rate; another study in kittens with experimentally induced hypernatremia found a 30% mortality rate in the first 24 hours. One dog with diabetes insipidus and a plasma sodium concentration of 203 mEq/L was treated and survived. By understanding the pathophysiologic basis of this disorder and using this basis to guide appropriate treatment choices, clinicians can successfully manage severe hypernatremia.

**References**

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ARTICLE #2 CE TEST

This article qualifies for 2 contact hours of continuing education credit from the Auburn University College of Veterinary Medicine. Subscribers may purchase individual CE tests or sign up for our annual CE program. Those who wish to apply this credit to fulfill state relicensure requirements should consult their respective state authorities regarding the applicability of this program. CE subscribers can take CE tests online and get real-time scores at CompendiumVet.com.

I. Which is the most effective extracellular osmole?
   a. sodium     b. glucose     c. BUN     d. potassium

II. Which is considered the most important defense against the development of hypernatremia?
   a. AVP     b. thirst stimulation     c. ANP     d. the renin–angiotensin–aldosterone system

III. In animals with central diabetes insipidus, AVP release is _______; in animals with nephrogenic diabetes insipidus, AVP release is ________.
   a. increased; decreased     b. decreased; increased     c. decreased; decreased     d. increased; increased

IV. The hypernatremic condition in which there is an altered set-point of the osmoreceptors, although baroreceptor function is normal, is
   a. central diabetes insipidus.
   b. nephrogenic diabetes insipidus.
   c. primary hypodipsia.
   d. essential hypernatremia.
5. The major organ affected by hypernatremia is the
   a. heart. c. kidneys.
   b. liver. d. brain.

6. Hypotonic fluid loss by vomiting, diarrhea, and third-space accumulation of fluid can result in ____________ hypernatremia.
   a. isovolemic c. hypervolemic
   b. hypovolemic d. euvoolemic

7. If a 20-kg dog presents with a plasma sodium concentration of 180 mEq/L, what volume of 5% dextrose in water would you need to give over a 24-hour period to decrease the plasma sodium concentration by 0.5 mEq/L/hr?
   a. 2 L c. 870 ml
   b. 1.5 L d. 940 ml

8. If a 20-kg dog presents with a plasma sodium concentration of 180 mEq/L, what volume of 0.45% NaCl would you need to give over a 24-hour period to decrease the plasma sodium concentration by 0.5 mEq/L/hr?
   a. 2 L c. 870 ml
   b. 1.5 L d. 940 ml

9. A loop diuretic, such as furosemide, should be given to induce natriuresis in animals with ____________ hypernatremia.
   a. isovolemic c. hypervolemic
   b. hypovolemic d. euvoolemic

10. Which disease process should be suspected if the patient’s neurologic status deteriorates during the treatment of hypernatremia?
    a. cerebral edema
    b. kidney failure
    c. liver failure
    d. heart failure