



An In-Depth Look:

HYPERNATREMIA IN
CRITICALLY ILL CATS

Hypernatremia in Critically Ill Cats: Evaluation and Treatment*

Kristen Temo, DVM

Elke Rudloff, DVM, DACVECC

Marla Lichtenberger, DVM, DACVECC

Rebecca Kirby, DVM, DACVIM, DACVECC

Animal Emergency Center

Glendale, Wisconsin

ABSTRACT:

Hypernatremia can cause life-threatening complications in critically ill cats. Carefully monitoring neurologic status and serum electrolytes in these cats allows early recognition of hypernatremia and can prevent death. Successful therapeutic intervention depends on early recognition of an increased serum sodium concentration and implementation of the correct therapy.

It is vital to recognize trends in critically ill patients. Hypernatremia can arise as a life-threatening complication in many different disease processes and has been observed in critically ill cats. Careful initial evaluation and frequent reassessment of critically ill cats is vital to detect and treat sodium derangements.

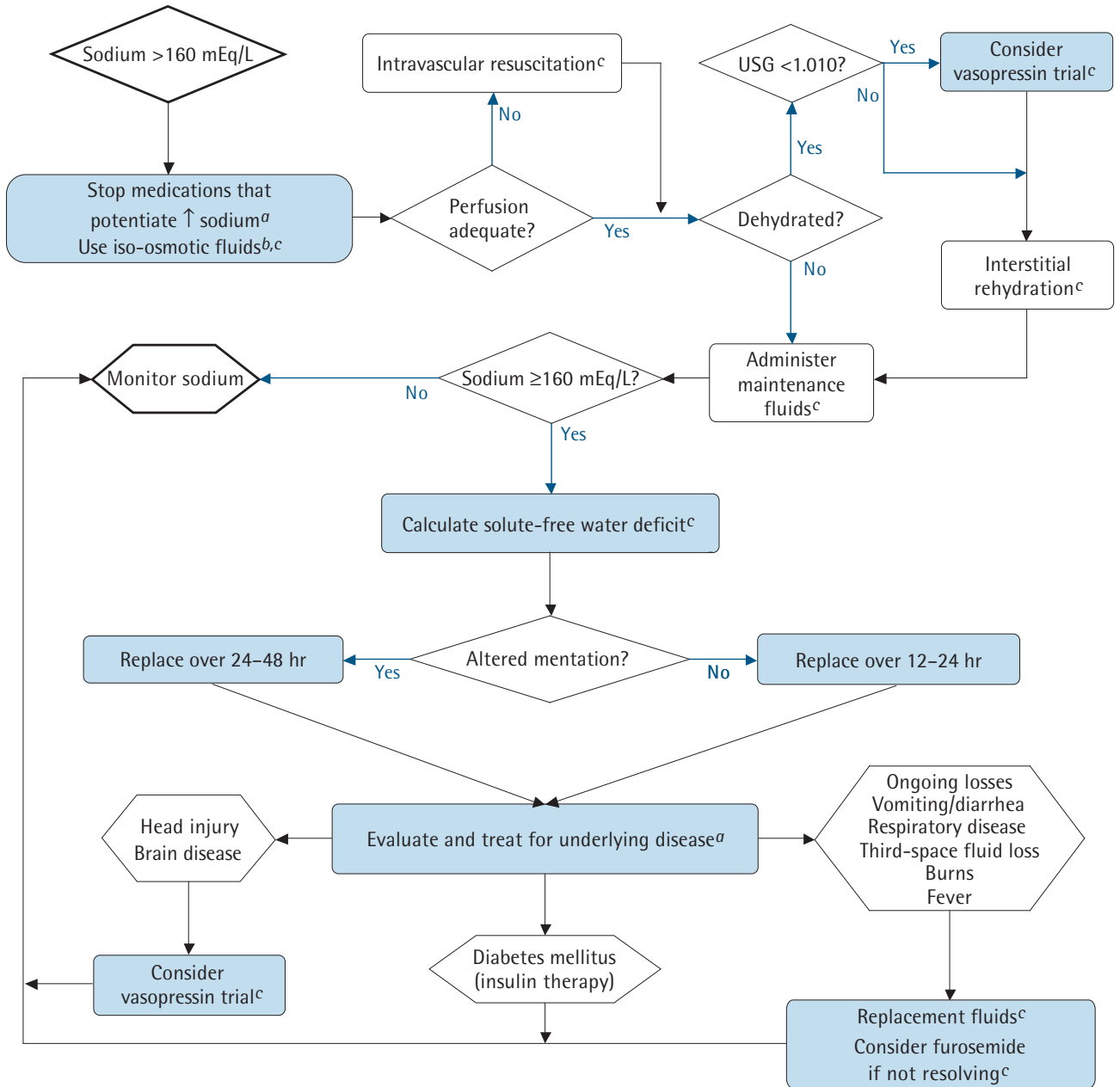
Acute hypernatremia requires immediate treatment. Successful therapeutic intervention depends on early recognition of an increased serum sodium concentration and administration of the correct therapy at the appropriate time and in the proper amount. Understanding normal sodium homeostasis, the mechanisms for alterations in sodium homeostasis in different diseases, and the reasons for resultant fluid shifts is essential for clinicians to formulate a therapeutic plan appropriate to the specific needs of each patient. The therapeutic approach to acute hypernatremia in cats should be individualized and can be determined after identifying the most likely underlying mechanism of the sodium and water disorder (see Figure 1 and Table 2).

EVALUATION

Hypernatremia may be evident on presenting blood work in critically ill cats or, more commonly, may appear during the course of therapy. History, physical examination, and initial laboratory evaluation can be used to detect underlying diseases or pathology that may lead to sodium or water imbalance. Carefully monitoring plasma electrolytes and

*A companion article on pathophysiology appears on p. 422.

Evaluation and Treatment of Hypernatremic Cats



^aSodium bicarbonate, hypertonic saline, mannitol, glucose. ^bSee Table 3, Figure 2. ^cSee Table 2.

Figure 1. Evaluating and treating hypernatremic cats requires immediate assessment of perfusion and commencement of resuscitation. USG is a vital diagnostic tool. Hypernatremic animals should have a high USG. If they do not, abnormal sodium regulatory mechanisms should be suspected.

Table 1. Correlating uOsm to USG (Human Values)

uOsm (mOsm/kg)	USG
800–1400	>1.030
300–800	1.010–1.023
<300	<1.010

urine specific gravity (USG) throughout hospitalization can lead to early intervention and a successful outcome.

A thorough history may prompt a careful investigation for hypernatremia. Owners may report the following in their pets: increased drinking

and/or urination suggestive of diabetes mellitus or chronic renal disease, altered mentation, head trauma, diarrhea, vomiting, altered respiration, chronic nasal discharge, and vulvar discharge. These signs may suggest loss of water into a third space (e.g., respiratory or gastrointestinal tract, uterus, peritoneal cavity) from the intravascular, interstitial, or intracellular space. Medications that may influence action or secretion of antidiuretic hormone (ADH) or osmotic agents (e.g., mannitol, glucose) should be promptly discontinued.

The most consistent physical examination findings suggestive of hypernatremia are dehydration and altered level of consciousness. When plasma sodium concentration increases rapidly and substantially (i.e., >165 mEq/L), signs of shock can include poor peripheral pulses, hypothermia, and prolonged capillary refill time. Carefully palpating the abdomen and examining the rectum may help detect fluid in the bowel or uterus, which suggests additional fluid losses that warrant aggressive volume replacement. Cats with evidence of brain pathology are at risk of developing hypernatremia and should have their electrolyte levels monitored closely.

The initial complete blood cell count, biochemistry profile, and urinalysis should be evaluated to detect underlying diseases (e.g., diabetes mellitus, renal

Administering isotonic sodium-containing fluids for extracellular volume replacement should not result in hypernatremia if normal sodium regulatory mechanisms are functioning.

disease, pyometra, pyelonephritis, acute gastroenteritis) that may be associated with polyuria, third spacing of fluid, persistent vomiting or diarrhea, osmotic diuresis, or gram-negative bacterial infections. Measuring the serum electrolyte level at presentation not only provides a baseline from which to monitor trends of change but can also reveal preexisting hypernatremia that can lead to serious neurologic consequences if fluid resuscitation is administered indiscriminately.

When hypernatremia persists despite volume replacement and rehydration, evaluation of urine osmolality (uOsm) and plasma osmolality (pOsm) may be required to determine the underlying cause.¹ Hypernatremia has been associated with elevated pOsm. When hypernatremia results from

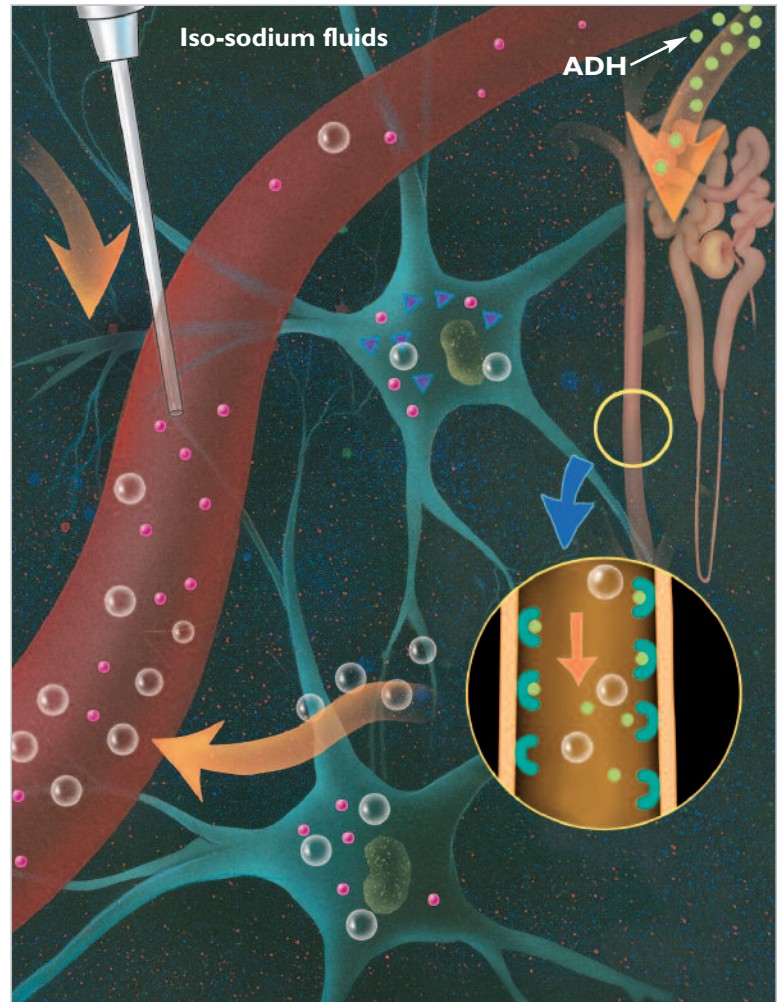


Figure 2. Goals of treating hypertremia. Intravascular volume can be maintained and significant fluid shifts avoided by treating patients with isosodium fluids. Administering ADH allows reabsorption from the kidneys and slows the decline in serum sodium. Brain cells eventually lose the need for idiogenic osmoles and return to normal. (Illustration by Barbara Harmon)

excessive sodium intake or water loss through third spacing of fluid or osmotic diuresis, increased uOsm is expected if ADH production and renal response to ADH are normal. The USG should reflect concentrated urine. Renal medullary washout that results from fluid therapy or underlying renal disease may prevent maximum urine concentration and should therefore be considered when evaluating USG.

pOsm and uOsm measurements are frequently not available in veterinary patients. In humans, uOsm can be loosely correlated to USG² (Table 1). This comparison can be made only if no osmotically active molecules such as glucose or mannitol are being excreted in the urine. In the absence of renal medullary washout, this correlation might prove beneficial in cats.

Cats that present with a normal electrolyte level and head trauma, brain dysfunction, diabetes mellitus, renal failure, gram-negative bacterial infec-

Table 2. Fluid Therapy Plan for Hypernatremia in Cats

Fluid Type	Dose	Serum Sodium (mEq/L)			Comments
		>170	160–170	<160	
RESUSCITATION OF POOR PERFUSION					
Hypotension Due to Hypovolemia with Normal Cardiac Function					
Isotonic crystalloids	10–15 ml/kg over 15 min	0.9% NaCl	0.9% NaCl	Plasmalyte-A Normosol-R	—
Synthetic colloids	5 ml/kg over 15 min	Hetastarch	Hetastarch	Hetastarch	If rectal temperature is <98°F, continue titration until systolic arterial pressure is >40 mm Hg, aggressive warming techniques, and maintenance crystalloid until rectal temperature is >98°F; if systolic arterial pressure is <90 mm Hg after rewarming, continue colloid titrations or consider vasopressor treatment.
Hypotension Due to Hypovolemia with Abnormal Cardiac Function					
Isotonic crystalloids	5 ml/kg over 15 min	Plasmalyte-A Normosol-R	Normosol-R Plasmalyte-A	Plasmalyte-A Normosol-R	Titrate up to 15 ml/kg until systolic arterial pressure is >60 mm Hg; if rectal temperature is <98°F, continue titration until systolic arterial pressure is >40 mm Hg, aggressive warming techniques, and maintenance crystalloid until rectal temperature is >98°F; treat underlying heart disease.
REHYDRATION					
Interstitial Volume Deficit^a					
Isotonic crystalloids	$L = \% \text{ dehydration} \times \text{kg}$	0.9% NaCl	0.9% NaCl	Plasmalyte-A Normosol-R	Administer over 4–8 hr for acute dehydration and 8–12 hr for chronic dehydration; add to the maintenance fluid dose.
Solute-Free Water Deficit^b					
Hypotonic fluids	$L = 0.6 \times \text{kg} \times ([\text{Na}^+ \div 140] - 1)$	2.5% dextrose in 0.45% NaCl ^{c,d}	5% dextrose in water	5% dextrose in water	Administer volume over 12–24 hr if mentation is normal; administer over 24–48 hr if mentation is abnormal; add to maintenance fluid dose. ^b
MAINTENANCE					
Isotonic crystalloids	2 ml/kg/hr + ml of ongoing losses	Plasmalyte-A ^e Normosol-R ^d Lactated Ringer's solution ^d	Plasmalyte-A Normosol-R Lactated Ringer's solution	Plasmalyte-A Normosol-R Lactated Ringer's solution	Begin treatment of underlying disease(s).
^a Replaced <i>after</i> perfusion deficits have been corrected.					
^b Replaced <i>after</i> perfusion and interstitial deficits have been corrected.					
^c May require a vasopressin trial if USG is <1.010 despite clinical dehydration: continuous IV infusion of aqueous vasopressin (0.036 U/kg/hr), titrated to obtain a urine output of approximately 1.4 ml/kg/hr or 0.5 U/kg IM or 1 to 2 drops of desmopressin nasal spray in the conjunctival sac q12h. ^{1,28}					
^d To prevent the consequences of rapid serum sodium reductions, 1 mol/L NaCl can be added to crystalloid and the rate adjusted q8h to keep the fluid input at 5–8.5 ml/kg/hr greater than urinary output.					
^e Consider administering furosemide (1–2 mg/kg q2–4h for two to three doses) to promote sodium excretion while replacing water deficit.					

tions, and/or gastroenteritis require vigilant monitoring for an increasing plasma sodium concentration throughout hospitalization. Hyponatremia that develops from metabolic causes has most commonly been related to insufficient volume resuscitation from using a fluid containing higher concentrations of sodium during continued, large, hypotonic fluid losses. When iatrogenic and metabolic causes of hyponatremia have been eliminated, an investigation for ADH deficiency must be conducted.

In critically ill cats, an elevated serum sodium concentration with a dilute USG warrants an investigation for diabetes insipidus (Figure 1). In humans, when hyponatremia (sodium concentration: >145 mEq/L) or elevated pOsm (>295 mOsm/L) occurs despite polyuria and urine hypoosmolality (uOsm: <200 mOsm/kg water), diabetes insipidus is suspected.^{3,4} Because ADH deficiency can manifest at any time after a head injury, serial testing of serum sodium concentration and uOsm or USG throughout hospitalization in a cat with a head injury can help recognize this life-threatening complication early. In humans with head trauma, laboratory evidence of central diabetes insipidus reportedly occurs between 10 and 240 hours after the initial traumatic event.^{5,6} However, in the four cats with head injury and hyponatremia that we have seen, hyponatremia occurred 2 to 13 days after the traumatic event. In one cat, the USG measured 1.023.

Water deprivation testing has been described as the classic diagnostic test for diabetes insipidus but has not been recommended in critically ill cats. Even under ideal circumstances, a specific diagnosis may not be obtained from water deprivation testing alone, and such tests can lead to life-threatening dehydration. In addition, chronic polyuria and medullary washout may prevent the kidneys from optimizing water reabsorption and urine concentration.⁵

Partial ADH impairment has been reported in humans, dogs, and cats.^{5,7} Urine-concentrating abilities in these patients may not exceed 300 mOsm/L during significant dehydration. Water deprivation testing is considered unnecessary in humans who have a lower uOsm than pOsm when pOsm is greater than 295 mOsm/L and serum sodium concentration is greater than 145 mEq/L.⁸ Finding low serum ADH levels in the presence of high pOsm and low uOsm provides a higher accuracy in diagnosing diabetes insipidus.⁵ However, ADH levels may not be readily available to most veterinary practitioners.

Administering exogenous ADH (vasopressin) can be both diagnostic and therapeutic (Table 2). Results of

Table 3. Sodium Concentrations of Crystalloids and Colloids

Fluid Type	Sodium Concentration (mEq/L)
Crystalloid	
5% dextrose in water	0
FreAmine (B. Braun)	35
Half-strength lactated Ringer's solution	65
2.5% dextrose in 0.45% NaCl	77
Lactated Ringer's solution	130
Plasmalyte-A	140
Normosol-R	140
0.9% NaCl	154
7.5% hypertonic saline	1,282
Colloid	
Oxyglobin (Biopure)	130
Dextran	154
Hetastarch	154

subcutaneously administering vasopressin have proven extremely variable in animals; thus IV aqueous or intranasal administration of vasopressin is preferred.⁷ In cats, vasopressin should be administered at 0.5 U/kg IM and USG and osmolality values obtained at 0, 30, and 60 minutes. Alternatively, oral tablets are available, as is intranasal desmopressin acetate (100 µg/ml administered in the conjunctival sac [1 to 2 drops, equaling about 1.5 to 4 µg bid for 5 days]). However, when clinical signs are severe and the level of hyponatremia is considered life threatening, IM or IV administration of vasopressin is preferred. If administering either of these drugs results in improved clinical signs, such as a 50% reduced water intake or increased uOsm or USG, a diagnosis of diabetes insipidus can be made.^{7,9,10}

TREATMENT

Figure 1 presents a general diagnostic and therapeutic approach to cats with hyponatremia. Although treating underlying problems (e.g., insulin therapy for diabetes mellitus, managing intracranial pressure or bleeding) is required to prevent or definitively resolve the pathology leading to hyponatremia, this discussion is directed only at treating sodium and water disorders in cats.

The goal of therapy is to slowly lower the serum sodium concentration while minimizing the rate of transcellular fluid shifts (Figure 2, page 438). Intracellular

osmolality increases in response to hypernatremia. Lowering the serum sodium concentration or osmolality too rapidly causes fluid to shift into the cells, with subsequent cellular swelling and death. In this case, neurologic signs may worsen with treatment efforts. If hypernatremia is diagnosed or anticipated, all drugs that can interfere with ADH production, release, or action as well as osmotic diuretics must be discontinued immediately. The treatment plan for hypernatremia gives priority to fluid therapy, with careful consideration given to the choice of fluid and rate of administration (Tables 2 and 3). The fluid therapy plan has two phases: resuscitation of hypovolemic hypernatremia and maintenance of euvoletic hypernatremia. When central diabetes insipidus has been determined to be the most likely cause of hypernatremia, administering exogenous ADH (vasopressin) may be a necessary part of the maintenance treatment plan for stabilization.

Resuscitation Phase

For hypovolemia during hypernatremia, the circulating plasma should be resuscitated using the least amount of fluid possible to correct volume and pressure deficits. Fluid selection depends on whether the fluid deficit is intravascular (due to poor perfusion), interstitial (due to dehydration), or both and whether cardiac dysfunction is contributing to hypotension. To avoid

cated in critically ill cats. It is important to repeat the examination during the fluid resuscitation process to detect volume overload.

Poor perfusion due to hypovolemia, with normal cardiac function, may benefit from low-volume infusion of high molecular weight synthetic colloids (e.g., hetastarch), titrated to effect, to help retain administered fluids within the intravascular space¹¹ (Table 2). Crystalloids with a relatively higher sodium concentration (e.g., 0.9% sodium chloride [NaCl]) should be administered to begin replacing interstitial volume deficits (Table 3). When cardiac failure is suspected to contribute significantly to hypotension, crystalloids containing a more conservative sodium concentration (e.g., lactated Ringer's solution, Plasmalyte-A, Normosol-R) should be used for resuscitation.

Maintenance Phase

Once perfusion and hydration have been restored, an electrolyte panel should be repeated; maintenance fluid selection should be based on these results. If serum sodium levels remain elevated (>160 mEq/L), the solute-free water deficit should be calculated⁴ (Table 2, Figure 1). When a patient has altered mentation, this volume should be replaced over 24 to 48 hours to slowly lower the serum sodium concentration (about 1 to 2 mEq/L/hr) and minimize transcellular fluid shifts.

Carefully monitoring a patient's neurologic status and serum electrolyte level may permit early recognition and prevention of life-threatening or fatal consequences.

rapid transcellular fluid shifts, using an isosodium fluid is recommended (i.e., the sodium concentration of the fluid administered should be similar to the serum sodium concentration; Table 2).

Poor perfusion in cats is characterized by weak or absent peripheral pulses, a slow or normal heart rate, hypothermia, depressed mentation, gray mucous membranes, prolonged capillary refill time, and low arterial blood pressure. Careful auscultation of the heart for a murmur, gallop, or arrhythmia and of the thorax for pulmonary edema or pleural fluid can help determine whether cardiac failure is contributing to hypotension. If no abnormalities are auscultated during the initial examination, thoracic radiographs should still be indi-

When a patient's mentation is normal, this volume may be replaced more rapidly (over 12 to 24 hours). Maintenance fluid volumes should be administered simultaneously using isotonic crystalloids, and the total volume of fluids administered should meet ongoing losses while preventing fluid overload.

The most common reason for mild to moderate hypernatremia during hospitalization is that the patient's water intake is failing to meet metabolic needs or correct ongoing losses. Hypernatremia can develop when sufficient water is not available and sodium is reabsorbed by the kidneys. This occurs more frequently when osmotic diuresis associated with diabetes mellitus or third spacing of fluid associated with gastroenteritis or peritonitis is

present. Cats with these conditions benefit from administering larger volumes of low-sodium crystalloids and replacing solute-free water as outlined in Table 2. Hetastarch administered at a maintenance rate can also help maintain intravascular volume despite ongoing crystalloid losses.

If a cat is isovolemic but has persistent hypertremia, administering low-dose furosemide (about 0.5 mg/kg IV) may stimulate renal sodium and water excretion. Renal volume loss can simultaneously be replaced using isotonic crystalloids with a lower sodium content (e.g., half-strength lactated Ringer's solution with 2.5% dextrose or 0.45% NaCl with 2.5% dextrose).

Symptomatic hypertremia associated with oliguric renal failure may require peritoneal dialysis for slow electrolyte equilibration. The dialysate should contain a sodium concentration similar to that of normal plasma. The technique for peritoneal dialysis in dogs and cats has been described elsewhere.¹²

Vasopressin Therapy

Cats with hypertremia that is not responsive to adjustments in fluid therapy might benefit from vasopressin administration (Figure 2). Hypertremia associated with head trauma or brain dysfunction may likely be due to abnormalities of ADH release and receptor responsiveness. In humans who are hypertremic and hemodynamically unstable, it has been recommended that a vasopressin trial be instituted immediately by continuous IV infusion of aqueous vasopressin (2.5 U/hr; 0.036 U/kg/hr [extrapolated for a 70-kg human]) titrated to obtain a urine output of approximately 100 ml/hr (1.4 ml/kg/hr [extrapolated for a 70-kg human]).¹³ This type of vasopressin administration has not been described in cats. Aqueous vasopressin administration in cats has been reported as 0.5 U/kg IM, or one to two drops of desmopressin acetate nasal spray in the conjunctival sac, q12h.^{7,10,14} Overdosing can result in water intoxication (hyponatremia) and reduced renal blood flow, with signs ranging from listlessness or depression to coma and seizures.

A protocol has been proposed for fluid therapy in humans with head injury to prevent the consequences of rapidly reduced serum sodium concentration¹⁵ (Figure 2). Twenty humans with head injury and hypoosmolar urine (suggestive of diabetes insipidus) were administered ADH intravenously and crystalloid infusion in which the sodium content was adjusted every 8 hours to match the patient's serum sodium concentration. If polyuria was observed (i.e., urine output >500 ml/hr or >7 ml/kg/hr), vasopressin (continuous IV infusion 0.02 U/hr or 0.003 U/kg/hr) was administered. The vasopressin dose was increased by 0.05 U/hr (or 0.007 U/kg/hr) until uOsm exceeded pOsm. This protocol has not been reported in treating critically ill hypertremic cats suspected of having diabetes insipidus. However, it warrants consideration when the serum sodium concentration rises with concurrent low Osm or USG.

MONITORING

Closely monitoring physical and biochemical parameters is essential to establish and maintain sodium and water balance in critically ill cats. Physical parameters that reflect perfusion and hydration should be assessed throughout hospitalization and fluid deficits replaced. Central venous pressure can be used to reflect central vascular volume. Deteriorating mentation and neurologic signs during therapy requires reassessment of fluid choice and rate of

administration, with adjustments made as indicated. Serum electrolyte levels and renal parameters reflect the progress made during therapy. Measuring water intake and urine output as well as uOsm and/or USG can reveal polyuria, polydipsia, and hyposthenuria associated with abnormal ADH mechanisms and excessive water loss, which require interventional therapy.

REFERENCES

1. Palevsky PM: Hypertremia. *Semin Nephrology* 18(1):20–30, 1998.
2. Rose BD, Post T: *Clinical Physiology of Acid–Base and Electrolyte Disorders*, ed 5. New York, McGraw-Hill, 2001.
3. Kern KB, Meislin HW: Diabetes insipidus: Occurrence after minor head trauma. *J Trauma* 24(1):69–72, 1984.
4. Geheb MA: Clinical approach to the hyperosmolar patient. *Crit Care Clin* 5:797–815, 1987.
5. Ober KP: Diabetes insipidus. *Crit Care Clin* 7(1):109–125, 1991.
6. Keren G, Barzilay Z, Schreiber M, et al: Diabetes insipidus indicating a dying brain. *Crit Care Med* 10:798–799, 1982.
7. Feldman EC, Nelson RW: *Canine and Feline Endocrinology and Reproduction*, ed 2. Philadelphia, WB Saunders, 1996.
8. Blevins LS, Wand GS: Diabetes insipidus. *Crit Care Med* 20(1):69–79, 1992.
9. Nichols R, Thompson L: Pituitary-hypothalamic disease, in Ettinger SJ, Feldman EC (eds): *Textbook of Veterinary Internal Medicine*. Philadelphia, WB Saunders, 1995, pp 1422–1436.
10. Plumb DC: *Veterinary Drug Handbook*. Ames, Iowa State University Press, 1999.
11. Rudloff E, Kirby R: The critical need for colloids: Maintaining fluid balance. *Compend Contin Educ Pract Vet* 19(6):705–718, 1997.
12. Garcia AM, Rudloff E, Kirby R: Peritoneal dialysis: Not just for renal failure. *Compend Contin Educ Pract Vet* 24(10):758–770, 2002.
13. Levitt MA, Fleischer AS, Meislin HW: Acute post-traumatic diabetes insipidus: Treatment with continuous intravenous vasopressin. *J Trauma* 24(4):532–535, 1984.
14. Kraus KH: The use of desmopressin in diagnosis and treatment of diabetes insipidus in cats. *Compend Contin Educ Pract Vet* (9)7:752–758, 1987.
15. Mizobata Y, Yokota J, Matsuoka T, et al: Volume supplementation with iso-sodium solution prevents hypertremia after head injury. *J Trauma* 50(5):871–877, 2001.

- c. nasal discharge and productive coughing.
- d. a prolonged capillary refill time.

2. History findings that should prompt a vigilant investigation for hypertremia include

- a. increased urination.
- b. recent head trauma.
- c. diarrhea or vomiting.
- d. all of the above

3. If initial electrolyte testing helps identify hypertremia in a critically ill cat, _____ should be tested next.

- a. plasma osmolality
- b. uOsm or USG
- c. water deprivation
- d. adrenocorticotropic stimulation

4. Which diagnostic tool is contraindicated in hypertremic animals?

- a. computed tomography
- b. an ADH response test
- c. uOsm or USG testing
- d. a water deprivation test

5. The preferred route(s) of vasopressin administration is(are)

- a. subcutaneous.
- b. intranasal.
- c. intravenous.
- d. b and c

6. Which phases are included in fluid therapy for hypertremic cats?

- a. resuscitation and maintenance
- b. maintenance and recovery
- c. maintenance and ADH administration
- d. resuscitation and recovery

7. In the resuscitation phase, the fluid should have a

- a. sodium content lower than that of the patient's plasma.
- b. sodium content higher than that of the patient's plasma.
- c. sodium content similar to that of the patient's plasma.
- d. high dextrose content.

8. The calculated water deficit should be administered

- a. over 4 hours.
- b. at variable times, depending on the duration of hypertremia and clinical signs in a patient.
- c. over 48 hours.
- d. over 24 hours.

ARTICLE #2 CE TEST



This article qualifies for 1.5 contact hours of continuing education credit from the Auburn University College of Veterinary Medicine. Subscribers who wish to apply this credit to fulfill state relicensure requirements should consult their respective state authorities regarding the applicability of this program. To participate, fill out the test form inserted at the end of this issue. To take CE tests online and get real-time scores, log on to www.VetLearn.com.

1. The most consistent physical examination finding suggestive of hypertremia is

- a. an altered level of consciousness and dehydration.
- b. abdominal pain.

9. Diabetes insipidus should be strongly suspected in a hypernatremic cat when the USG is

- a. greater than 1.040.
- b. less than 1.010.
- c. less than 1.040.
- d. greater than 1.010.

10. The treatment goal in acute hypernatremia is to

- a. reperfuse, rehydrate, and slowly lower the serum sodium level while minimizing transcellular fluid shifts.
- b. calculate the free water deficit and replace it immediately.
- c. decrease the serum sodium level as quickly as possible.
- d. maintain a high serum sodium level.