GET THE DETAILS
A thorough history is important in assessing hyponatremic patients as the details could impact the preferred treatment option.

INSIGHTS IN ELECTROLYTE DISORDERS

Evaluation and Management of the Hyponatremic Patient

***Audrey Cook**, BVM&S, DACVIM-SAIM, DECVIM-CA, DABVP (Feline), and **Justin Heinz**, DVM, DACVECC*
Texas A&M College of Veterinary Medicine & Biomedical Sciences

Hyponatremia is defined as a plasma or serum sodium concentration (i.e., [Na]) below the reference range and usually reflects the loss of sodium in excess of water. Healthy animals consuming adequate amounts of a balanced diet ingest about 4 times their daily sodium needs, and [Na] within the extracellular fluid is therefore easily maintained within a narrow range by hypothalamic osmoreceptors, acting through antidiuretic hormone (ADH), which permits the reclamation of water from filtrate in the renal collecting ducts and induces sensations of thirst.[1]

Decreases in extracellular fluid volume cause the release of renin from the juxtaglomerular apparatus and the subsequent secretion of aldosterone by the adrenal glands; this hormone promotes sodium and water reclamation in the distal convoluted tubules of the kidney. Concurrent activation of hypothalamic baroreceptors triggers the release of ADH, even if serum [Na] is falling below the desired range. In essence, maintenance of adequate extracellular fluid volume is prioritized over the maintenance of normal osmolality. This situation is commonly encountered in patients with renal or gastrointestinal compromise, in which substantial volumes of sodium-containing fluids are lost from the body and are replaced with ingested water.[2]

Less commonly, hyponatremia reflects the addition of water in excess of sodium; total body sodium may therefore remain unchanged. This situation reflects an inherent dysfunction of normal homeostatic or compensatory processes, such as the inappropriate secretion of ADH or congestive heart failure, respectively.[1,3]

Serum [Na] is also influenced by processes that impact serum osmolality, such as hyperglycemia. Under normal circumstances, blood glucose has a minor impact on this variable, but its effect becomes considerable as blood glucose rises, especially with acute onset increases.[1]

Mild, acute (i.e., ≤24 hours) hyponatremia is of little concern, but serum [Na] <130 mmol/L merits attention if the clinical history suggests chronicity. Because sodium is the primary determinant of serum osmolality, hyponatremia for >24 hours will alter intracellular events in an effort to maintain normal cell volume. The brain is particularly vulnerable to changes in serum osmolality, and rapid correction of hyponatremia therefore carries a substantial risk of irreversible osmotically induced neuronal damage.[4]

SubAtomicScope/shutterstock.com

CAUSES OF HYPONATREMIA

Loss of Sodium

Sodium loss through the gastrointestinal tract or kidneys is a common cause of hyponatremia.[5] Although vomitus and feces are usually hypotonic to plasma, with [Na] <100 mmol/L, hyponatremia is expected if these losses are replaced with only ingested water. It is important to remember that a patient's volume status is independent of [Na]; a puppy with parvovirus may therefore be significantly hyponatremic but hypovolemic or normovolemic depending on its ability to consume water orally. Third spacing of fluids can also result in hyponatremia, as the lost volume triggers sensations of thirst. Adequate oral salt intake can mitigate this effect; therefore, hyponatremia is more likely in anorexic patients.

Dogs with hypoadrenocorticism (Addison's disease) are unable to reclaim sodium from the filtrate in the distal portion of the nephron and are therefore routinely hyponatremic.[6] It has been suggested that this tendency is exacerbated by ADH secretion, as cortisol has an inhibitory effect on the release of this powerful hormone.[7] Patients with acute kidney injury may have impaired ability to reclaim filtered sodium and are also vulnerable to significant hyponatremia.

Addition of Water

Water intoxication is uncommon, but it can cause a rapid drop in [Na], resulting in cerebral edema. The few case reports in the literature primarily describe dogs gulping water while playing in ponds or lakes.[8] Water intoxication may also occur if a desmopressin trial is performed in a dog with psychogenic polydipsia.[9]

Various conditions associated with decreases in renal perfusion (e.g., congestive heart failure, cirrhosis, nephrotic syndrome) can trigger water retention through the activation of fluid-conserving mechanisms involving the renin-angiotensin-aldosterone system.[10] Affected animals are therefore concurrently hyponatremic and hypervolemic. Similar findings are noted in animals with the syndrome of inappropriate antidiuretic hormone secretion (SIADH). This is characterized by the inappropriate secretion of ADH and is associated with various underlying neurologic, traumatic, neoplastic, or inflammatory disorders.[11-13]

Iatrogenic

Poorly considered fluid therapy, primarily the administration of a nonreplacement fluid (e.g., 5% dextrose in water solution [D5W]) to a dehydrated patient, is a common cause of hyponatremia.[5] High-dose diuretic therapy may also result in clinically significant hyponatremia.

Spurious

Depending on the methodology used, reported serum [Na] can be affected by increases in lipids or proteins using the older flame photometry methodology. The newer ion-selective, patient-side devices are not affected by this issue.[1]

Dilutional

Significant hyperglycemia triggers a compensatory decrease in [Na]. The expected change can be calculated using this formula:[14]

$$Na_{corrected} = Na_{measured} + 1.6([Glucose_{measured} - Glucose_{normal}]/100)$$

The 1.6 factor should be increased to 2.6 with blood glucose levels exceeding 400 mg/dL.

CONSEQUENCES OF HYPONATREMIA

Patients with acute, severe hyponatremia from water intoxication are likely to present with vomiting and disorientation; these signs may quickly progress to seizures and death.[8] The pathology under such circumstances is cerebral edema.

Insidious hyponatremia is usually clinically silent. Changes in physiology within neuronal cells (loss of intracellular sodium and water) cause a decrease in intracellular osmotically active particles in order to prevent the ingress of water from the extracellular fluid. However, it takes approximately 48 hours to restore osmotic equilibrium; therefore, cells are vulnerable to shrinkage and damage if serum [Na] increases too quickly.[4]

Clinical signs from the subsequent osmotic demyelination syndrome (previously called central pontine myelinolysis) are usually somewhat delayed; patients may be appropriate for 1 day after correction of hyponatremia but then become mentally

inappropriate and neurologically compromised.[15] The prognosis for affected patients is guarded.

INITIAL PATIENT ASSESSMENT

It is essential to try to establish the cause of hyponatremia with a thorough patient history and careful review of other laboratory data. In most instances, the reason for hyponatremia is readily apparent (e.g., vomiting, diarrhea, acute kidney injury, hypoadrenocorticism). The history should also shed some light on the likely duration of hyponatremia; knowing this is important as it impacts treatment decisions. In a previously healthy patient with a per-acute 1-day history of profuse vomiting and diarrhea, a serum [Na] of 125 mmol/L is of little clinical significance. However, a similar serum [Na] in a patient with a >48-hour history of vague malaise must be carefully addressed.

Clinicians must also bear in mind that neurologic compromise may be either the cause (e.g., patients with SIADH) or the consequence (water intoxication) of hyponatremia or may reflect compromise due to an accompanying disease process, such as chronic liver disease. A patient in shock due to substantial crystalloid loss may also be neurologically abnormal.

See **FIGURE 1** for an algorithm showing evaluation of the hyponatremic patient.

TREATMENT OF HYPONATREMIA

If emergent fluid resuscitation is necessary, the fluid used should have [Na] within 10 mmol/L of the patient's serum [Na]. This is unlikely to cause a significant shift in the patient's [Na]. A suitable fluid can be created by adding an appropriate volume of dextrose 5% to a standard replacement fluid. The expected shift in [Na] following fluid administration can be estimated using the Adrogué-Madias formula (where K = potassium):[16]

Expected change in [Na] with 1 liter of fluids = (Fluid [Na + K] – Patient [Na])/(TBW + 1)

TBW = Total body water = Weight in kg × 0.6

Recommendations for addressing hyponatremia depend on both the etiology and status of the patient. In dogs with acute water intoxication, serum [Na] should be promptly raised to 125 mmol/L. This can be achieved with the administration of 2 mL/kg of 3% sodium chloride (NaCl) IV over 10 to 60 minutes; this is expected to increase [Na] by 2 mmol/L and can be repeated until the animal's status improves or [Na] is 4 to 6 mmol/L higher.[5] The total sodium increase over the first 24 hours should not exceed 10 to 12 mmol/L. If the rate of correction is determined to exceed the calculated rate, the threat of osmotic dysequilibrium can be circumvented by administering furosemide in order to promote natriuresis.[17]

In more stable patients, [Na] should be raised slowly; a maximum rate of 10 mmol/L/24 hr (<0.5 mmol/L/hr) is usually appropriate.[1] The patient's sodium deficit and time needed for its replacement must be determined:

Sodium deficit (mmol) = (Target [Na] – Patient [Na]) × TBW

Target [Na] = 150 mmol/L
TBW = weight (kg) × 0.6

Time to replace deficit (hr) = (Target [Na] – Patient [Na]) × 2.4 hr

In a euvolemic patient, this deficit can be addressed with 3% NaCl (513 mmol/L).

If the patient is also dehydrated, this can be simultaneously addressed using a standard buffered replacement fluid (e.g., lactated Ringer's solution, Normosol-R, Plasma-Lyte 148); this volume deficit should ideally be addressed over at least 12 hours. Because the sodium content of this fluid may be substantially higher than that of the patient, its impact on serum [Na] should be calculated using the Adrogué-Madias formula (see above), and the dose of 3% NaCl adjusted accordingly. Bear in mind that water taken in by mouth or used with the administration of other

It is essential to try to establish the cause of hyponatremia with a thorough patient history and careful review of other laboratory data.

medications will blunt the impact of fluid therapy, and it may be helpful to provide measured amounts of an oral rehydration solution rather than allowing unlimited access to water.

The [Na] of fluids given to meet maintenance needs must also be considered. True "maintenance" fluids contain approximately 40 mmol/L of sodium and are unlikely to increase the patient's [Na]. However, replacement fluids contain 3 to 4 times this amount and may have a significant effect, even when administered at a maintenance rate.

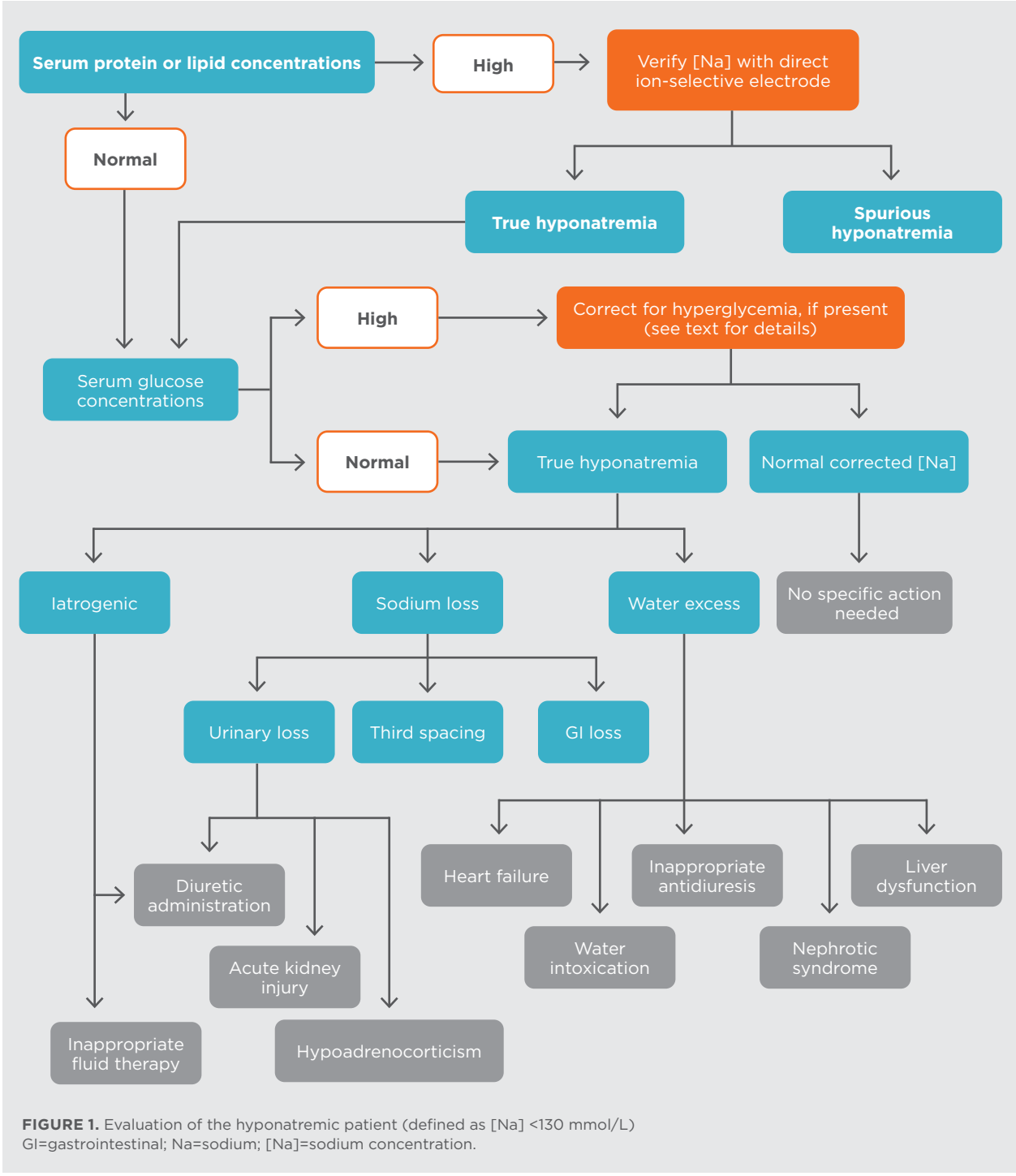


FIGURE 1. Evaluation of the hyponatremic patient (defined as [Na] <130 mmol/L)
GI=gastrointestinal; Na=sodium; [Na]=sodium concentration.

In patients with multiple needs (i.e., sodium deficit, volume deficit, maintenance fluid), it can be easier to decide how much volume to administer over a specified time period and then use the following calculation to determine the [Na] of the fluid administered:

Fluid [Na + K] = Patient [Na] + {TI × (TBW + Vol)}

TI = Target increase (mmol/L) in the patient's [Na] over a specified time period

Vol = Total volume of IV fluid (in liters) to be administered over the same time period

Although the calculations used to create a fluid plan provide a useful framework, they do not make allowances for the impact of factors such as body condition score and cannot allow for the fluid lost across the airway or via the urinary system. *In all instances, serum [Na] should be rechecked 2 to 4 hours after starting therapy, adjusted as necessary, and then assessed every 6 to 8 hours thereafter.*

See **FIGURE 2** for an algorithm of the management of the hyponatremic patient.

CASE SCENARIO

History

A 10-year-old spayed female miniature pinscher with a 7-day history of dyspnea and a poor appetite was evaluated at a primary care facility. On initial presentation, she weighed 6.2 kg. Radiographs revealed substantial pleural effusion, and 190 mL of chyle was removed from the thoracic cavity. Thoracentesis was

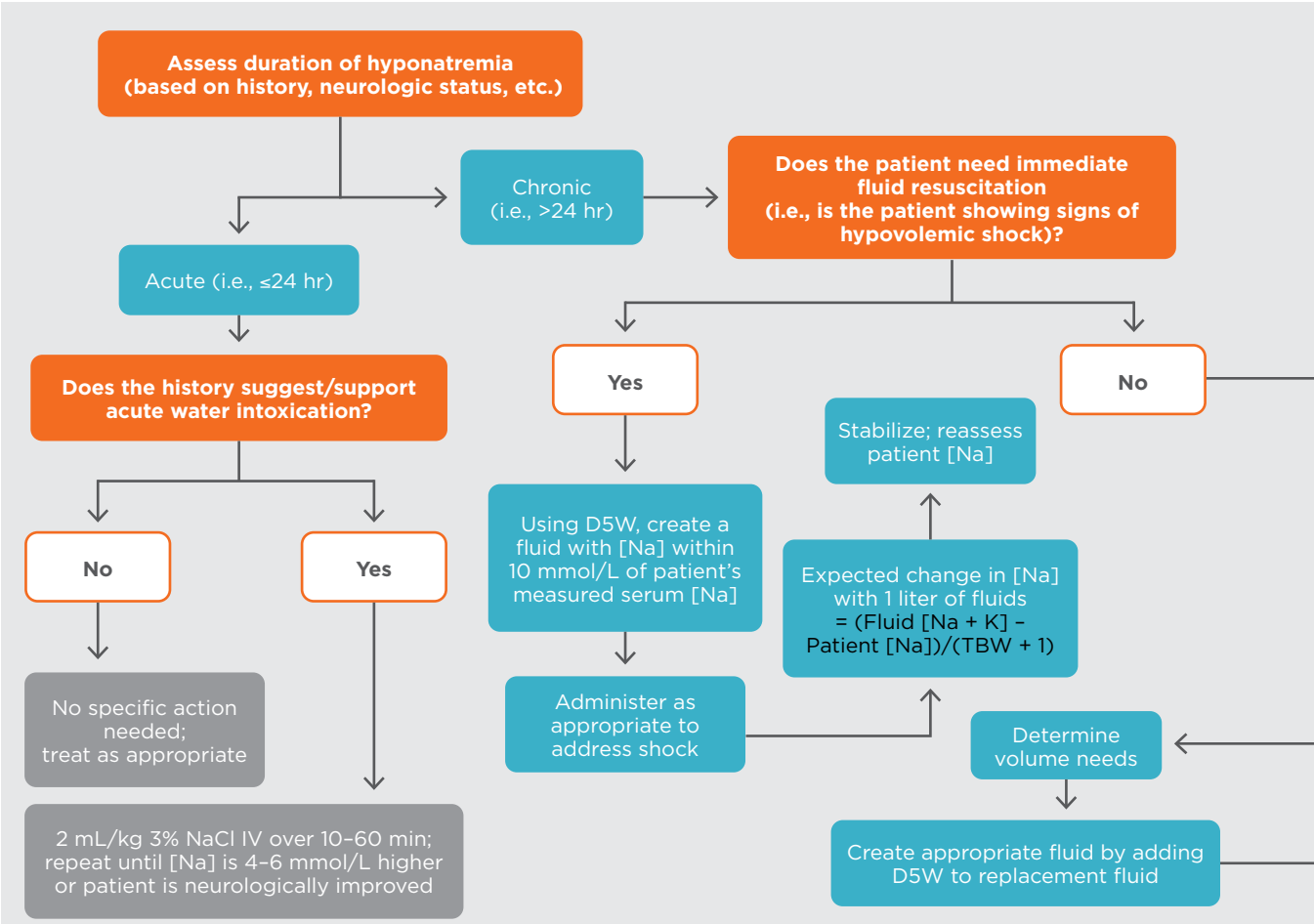


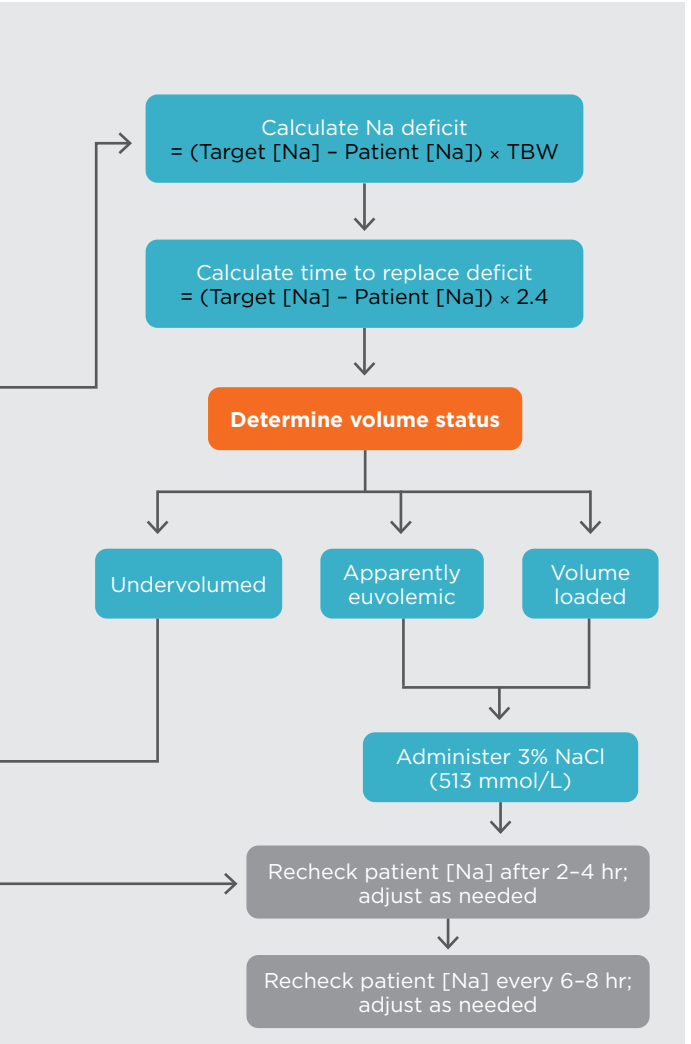
FIGURE 2. Management of the hyponatremic patient (defined as [Na] <130 mmol/L)
D5W=5% dextrose in water solution; K=potassium; Na=sodium; [Na]=sodium concentration; NaCl=sodium chloride; TBW=total body water.

repeated every 2 to 3 days for the next 3 weeks. The dog remained hyporexic throughout this time but was seen to drink water. On presentation at a referral center, the dog weighed 5.8 kg and was somewhat depressed; heart sounds were muffled and the respiratory rate was 48 breaths/min. Serum [Na] was 107 mmol/L (reference range, 144 to 155 mmol/L); potassium was 3.2 mmol/L (reference range, 3.5 to 5.1 mmol/L). Urine specific gravity was >1.04.

Assessment

Approximately 1500 mL of chyle was removed from this patient over a 3-week period. As the [Na] of this fluid matches that of the serum, this represents a substantial loss of sodium. The volume lost was replaced with ingested water, thereby slowly causing serum [Na] to decline. This trend was furthered by the lack of dietary intake. Based on this history, it can be reliably assumed that the serum [Na] has been <130 mmol/L for several days and must therefore be returned to the reference range very cautiously.

This patient's mentation and urine specific gravity were suggestive of mild dehydration (5%). This deficit should be replaced over 24 hours to reduce the risk of any sudden shifts in [Na].



Calculations

Target [Na]: 150 mmol/L

TBW: Weight in kg × 0.6 = 5.8 × 0.6 = 3.48 L

Sodium deficit: (Target [Na] – Patient [Na]) × TBW = (150 – 107) × 3.48 = 150 mmol

Time to replace deficit: (Target [Na] – Patient [Na]) × 2.4 = (150 – 107) × 2.4 = 103 hr

- **Note:** If the patient was volume replete and did not require any supplemental fluids, this could be replaced using 3% NaCl, as indicated below:
  - **Volume of 3% NaCl (513 mmol/L) needed to replace sodium deficit** = 150/513 = 0.292 L (292 mL)
  - **Rate of administration** = 292/103 = 2.8 mL/hr (OK to round up to 3 mL/hr)

Estimated dehydration: 5% = 290 mL

Time to replace deficit: 24 hr

Fluid rate to replace deficit: 12 mL/hr

Estimated maintenance fluid need: 13 mL/hr

For the first 24 hours:

Total volume/hr = 25 mL

Total volume in 24 hours = 600 mL (0.6 L)

Fluid [Na + K] = Patient [Na] + {TI × (TBW + Vol)} = 107 + {10 × (3.48 + 0.6)} = 107 + 40.8 = 147.8 (OK to round up to 148)

Patient K requirement = 30 mmol/L

Required Na content of fluid = 148 – 30 = 118 mmol/L

To create a suitable fluid:

Dilute a standard replacement fluid to achieve desired [Na].

Volume to be discarded and replaced with a sodium-free fluid = 1000 – {(Desired [Na] × 1000)/Fluid [Na]}

Plan:

Take 1 liter of lactated Ringer's solution (Na = 130 mmol/L; K = 4 mmol/L)

Volume to be discarded and replaced with a sodium-free fluid = 1000 – {(118 × 1000)/130} = 92 mL

Remove 92 mL and replace with sterile water or D5W.

Add 13 mL (26 mmol) of potassium chloride.

Rate: 25 mL/hr

■ **Note:** These calculations are designed to provide an appropriate starting point, but an individual patient's response may differ significantly from the calculated course. Frequent monitoring and adjustments are therefore necessary. **TVP**

Justin Heinz

Dr. Heinz obtained his DVM from Purdue University. He completed an internship at LSU and a residency in emergency and critical care at Texas A&M University. He is a diplomate of the American College of Emergency and Critical Care. After a year in private referral practice, Dr. Heinz joined the faculty at Texas A&M College of Veterinary Medicine. He is currently a clinical assistant professor and chief of the Emergency and Critical Care Service. His clinical interests include transfusion medicine, sepsis, acute kidney injury, and renal replacement therapies.

Audrey Cook

Dr. Cook is a graduate of the University of Edinburgh. She completed an internship at NCSU and a residency in internal medicine at UC Davis. She is a diplomate of the American and European Colleges of Veterinary Internal Medicine and is one of the few internists with additional board certification in Feline Practice. After a decade in private referral practice, Dr. Cook joined the faculty at Texas A&M College of Veterinary Medicine. She is currently professor and chief of the Internal Medicine Service. Her clinical interests include endocrinology, gastroenterology, and interventional radiology/endoscopy.

References

1. DiBartola SP. Disorders of sodium and water: hypernatremia and hyponatremia. In: *Fluid, Electrolyte, and Acid-Base Disorders in Small Animal Practice*. 4th ed. St. Louis, MO: Saunders Elsevier; 2011:45-75.
2. Ueda Y, Hopper K, Epstein SE. Incidence, severity and prognosis associated with hyponatremia in dogs and cats. *J Vet Intern Med*. 2015;29(3):801-807. doi: 10.1111/jvim.12581
3. Grant P, Ayuk J, Bouloux PM, et al. The diagnosis and management of inpatient hyponatraemia and SIADH. *Eur J Clin Invest*. 2015;45(8):888-894. doi: 10.1111/eci.12465
4. Wilson CS, Mongin AA. Cell volume control in healthy brain and neuropathologies. *Curr Top Membr*. 2018;81:385-455. doi: 10.1016/bs.ctm.2018.07.006
5. Burton AG, Hopper K. Hyponatremia in dogs and cats. *J Vet Emerg Crit Care (San Antonio)*. 2019;29(5):461-471. doi: 10.1111/vec.12881
6. Adler JA, Drobatz KJ, Hess RS. Abnormalities of serum electrolyte concentrations in dogs with hypoadrenocorticism. *J Vet Intern Med*. 2007;21(6):1168-1173. doi: 10.1892/06-270.1
7. Raff H. Glucocorticoid inhibition of neurohypophysial vasopressin secretion. *Am J Physiol*. 1987;252(4 pt 2):R635-R644. doi: 10.1152/ajpregu.1987.252.4.R635
8. Toll J, Barr SC, Hickford FH. Acute water intoxication in a dog. *J Vet Emerg Crit Care*. 1999;9(1):19-22. doi: 10.1111/j.1476-4431.1999.tb00135.x
9. Plickert HD, Pagitz M, Luckschander-Zeller N. Desmopressin acetate-induced water intoxication in a dog with psychogenic polydipsia. *Vet Rec Case Rep*. 2018;6(3):e000606. doi: 10.1136/vetreccr-2018-000606
10. Boswood A, Murphy A. The effect of heart disease, heart failure and diuresis on selected laboratory and electrocardiographic parameters in dogs. *J Vet Cardiol*. 2006;8(1):1-9. doi: 10.1016/j.jvc.2005.12.001
11. DeMonaco SM, Koch MW, Southard TL. Syndrome of inappropriate antidiuretic hormone secretion in a cat with a putative Rathke's cleft cyst. *J Feline Med Surg*. 2014;16(12):1010-1015. doi: 10.1177/1098612X14528192
12. Gójska-Zygner O, Bartosik J, Górski P, Zygner W. Hyponatraemia and syndrome of inappropriate antidiuretic hormone secretion in non-azotaemic dogs with babesiosis associated with decreased arterial blood pressure. *J Vet Res*. 2019;63(3):339-344. doi: 10.2478/jvetres-2019-0045
13. Shiel RE, Pinilla M, Mooney CT. Syndrome of inappropriate antidiuretic hormone secretion associated with congenital hydrocephalus in a dog. *JAAHA*. 2009;45(5):249-252. doi: 10.5326/0450249
14. Koenig A. Hyperglycemic hyperosmolar syndrome. In: *Small Animal Critical Care Medicine*. 2nd ed. St. Louis, MO: Elsevier; 2015:347-351.
15. O'Brien DP, Kroll RA, Johnson GC, et al. Myelinolysis after correction of hyponatremia in two dogs. *J Vet Intern Med*. 1994;8(1):40-48. doi: 10.1111/j.1939-1676.1994.tb03194.x
16. Adrogué HJ, Madias NE. Aiding fluid prescription for the dysnatremias. *Intensive Care Med*. 1997;23(3):309-316. doi: 10.1007/s001340050333
17. Merino PL. Osmotic disorders. In: Merino PL, ed. *Merino's The ICU Book*. 4th ed. Philadelphia, PA: Wolters Kluwer; 2014:667-668.