Electrolyte Disorders:
Which Fluid and Does It Really Matter?

Jennifer J Devey, DVM, Diplomate ACVECC
jenniferdevey@gmail.com

Important electrolytes in the body include sodium, chloride, potassium, magnesium, calcium and phosphorus. The list of diseases that can be associated with abnormalities of these electrolytes is lengthy and the reader is referred to other sources to discuss diagnosis and management of specific diseases. Electrolyte concentrations are reported on many blood tests that are routinely run in most veterinary practices; however, it is rare that these values fall into extremes. Normally these numbers, which are often taken at face value, in absolute terms, instead of being interpreted in light of the underlying disease, are only just out of the normal range. If the underlying reason for the electrolyte disturbance is known then the ideal choice of fluid should become apparent. If the fluid type is not available or not indicated for other reasons related to the patient's underlying disease then an understanding of electrolyte physiology will allow the clinician to monitor the patient for potential complications that might develop. Based on an understanding of electrolyte physiology and case examples, this lecture will discuss how to deal with electrolyte disorders that are life-threatening but more importantly to make the most appropriate fluid choices for a patient with only slightly abnormal sodium or chloride values.

Sodium

Sodium is primarily an extracellular anion with less than 10% being found intracellularly. An increase or decrease in the serum sodium concentration is almost always a reflection of an alteration in the water balance of the patient rather than an absolute increase or decrease in the amount of the total body sodium. This makes it extremely important to evaluate the patient's blood volume and hydration status whenever the serum sodium concentration is being assessed. It is essential to try and determine if the patient's blood volume is low, normal or high and whether or not the patient is dehydrated, normally hydrated or overhydrated. There are no specific measurements that can be made but physical exam parameters in particular, can provide a good estimation.

Water makes up approximately 60% of the weight of an adult animal of which two-thirds is intracellular and one third is extracellular. Three quarters of the extracellular water is in the interstitium and one quarter is in the intravascular space. The interstitial space is assessed by physical exam parameters such as mucous membranes and skin elasticity. Dehydration can be suspected based on the presence of dry mucous membranes, prolonged skin tenting, hyperalbuminemia and concentrated urine. Overhydration can be suspected based on parameters such as serous ocular or nasal discharge, gelatinous subcutaneous tissues and hyposthenuric urine.

Approximately 10% of the blood volume lives in the arteries, 20% in the capillaries and 70% in the veins. For this reason it is essential to evaluate the venous side of the circulation when evaluating the patient's volume status. Central venous pressure provides an estimation of central venous volume. If a central line is not present a subjective assessment can be made of central venous volume based on jugular venous distention. If the vein remains collapsed when the vein is occluded at the thoracic inlet then the patient is hypovolemic. A distended jugular vein may indicate hypervolemia but, similar to an increased central venous pressure, it may also indicate an obstruction to venous return to the heart such as occurs with pericardial tamponade, right-sided heart failure, pneumothorax or advanced liver disease. Delayed capillary refill and hypotension are often associated with hypovolemia. Blood pressure is a function of cardiac output as well as systemic vascular resistance so, although hypotension is usually associated with hypovolemia in small animals, it is not always the case. Hypervolemia is also associated with ascites, pleural effusion and pulmonary edema.

Normally when the plasma concentration of sodium decreases or increases it alters the osmolality of the blood, Hypernatremia triggers the thirst mechanism (adding free water) and antidiuretic hormone (vasopressin) release (decreasing water excretion in the kidney). The same osmoreceptors are triggered when other effective osmoles are added to the serum such as occurs with diabetes mellitus. Alterations in renal excretion of sodium in the

kidney are under the influence of aldosterone, atrial natriuretic factor as well as renal factors. These hormones become very important in diseases such as hypoadrenocorticism, dilated cardiomyopathy and acute hemorrhage.

It is important to attempt to classify the type of water disorder that exists when considering treatment. Hyponatremia can be classified based on hydration status or plasma osmolality and volume status. Hypoosmolar hyponatremia is the most commonly seen clinical entity. Hypoosmolar hyponatremia can be associated with gain of free water (hypervolemic hyponatremia), gain of hypotonic fluid (normovolemic hyponatremia) and salt loss (hypovolemic hyponatremia). Free water gain occurs with congestive heart failure, advanced liver disease and advanced renal disease. Hyponatremia in the sick diabetic patient is a combination of the osmolar effects of the hyperglycemia, and osmotic diuresis as well as third space losses. Normovolemic hyponatremia is rare but can occur with syndrome of inappropriate antidiuretic hormone secretion. Salt loss can occur with vomiting, diarrhea and third-spacing of fluids. Clinical signs related to the hyponatremia primarily relate to the central nervous system and are not normally evident until the sodium concentration is less than 125 mEq/L in the dog and 130 mEq/L in the cat. Signs include weakness, vomiting, diarrhea altered levels of consciousness and seizures. The presence of clinical signs depends on the severity of the hyponatremia and how rapidly the hyponatremia develops. Rapid onset hyponatremia leads to cerebral edema.

Hypernatremia can be present secondary to a free water deficit (normovolemic hypernatremia), hypotonic fluid loss (hypovolemic hypernatremia) or solute gain (hypervolemic hypernatremia). A free water deficit is caused by decreased water intake or diabetes insipidus. Hypotonic fluid occurs with vomiting and diarrhea, third-spacing of fluids, and renal loss from chronic renal failure, osmotic diuresis, drugs such as furosemide or postobstructive diuresis. Solute gain occurs with salt poisoning or infusion of hypertonic fluids. Clinical signs related to the hypernatremia primarily relate to the central nervous system and are not normally evident until the sodium concentration exceeds 170 mEq/L in the dog and 175 mEq/L in the cat. Signs vary depending on the severity of the hypernatremia and the rate of onset of the hypernatremia. Acutely the hyperosmolality causes movement of water out of the brain cells which can lead to hemorrhage from rupture of cerebral vessels if the rise is rapid and severe enough. With more chronic elevations idiogenic osmoles develop to maintain a normal water balance and clinical abnormalities may not be evident. Development of these idiogenic osmoles starts within a few hours but takes as long as 24 hours to fully compensate for elevation in the sodium. Clinically signs such as anorexia, lethargy, weakness, disorientation may be evident. If severe enough hypernatremia can cause seizures and death.

Care should be taken to assess the disease condition carefully prior to making an attempt to alter the sodium concentration. Minor alterations in sodium concentration will usually return to normal with treatment of the underlying condition. If the patient has a disease such as congestive heart failure it may be inappropriate to attempt to manipulate the sodium concentration other than through treating the congestive heart failure since this may lead to worse patient morbidity. When a decision is made to treat the sodium the concentration ideally should not change by more than 0.5 mEq/L/hr. Whenever sodium levels are being corrected blood or serum concentrations should be assessed very 2 to 4 hours depending on the patient's condition.

If the hyponatremia is mild then water restriction or hypertonic fluid may be the appropriate treatment. If the hyponatremia is more severe and the patient is hypovolemic an isotonic fluid may be indicated. If the patient is suspected to be chronically severely hyponatremic (sodium less than 135 mEq/l) then fluids should be adjusted to ensure the sodium levels do not rise faster than 0.5 mEq/l/hr to avoid central pontine myelinolysis. If the patient is normovolemic then furosemide will help prevent the sodium concentration from rising too rapidly if this becomes a concern.

If the patient is suspected to be chronically severely hypernatremic then hypotonic fluids may be indicated. Care should be taken to ensure the sodium levels do not drop faster than 0.5 mEq/L/hr to avoid causing cerebral edema. If the patient is comatose or seizing the sodium levels initially may need to increase at a rate of 1 to 2 mEq/L/hr until the patient's neurologic status stabilizes.

The free water deficit should be calculated by the following equation.

Na deficit (L) = TBW x serum $Na^+/146 - 1$ (dogs)
Na deficit (L) = TBW x serum $Na^+/156 - 1$ (cats)

Total body water (TBW) is calculated as 0.6 x the body weight in kg.

The volume of fluid to be administered is calculated as the sodium deficit in litres divided by the sodium concentration of the fluid being administered. Usually 5% dextrose in water is used to replace free water deficits but depending on the degree of hypernatremia a different fluid may be chosen. The number of hours the fluid should be administered over is calculated by subtracting 140 (150 in the cat) from the patient's sodium concentration and dividing by 0.5. The fluid rate is calculated by dividing the volume of fluid by the number of hours the fluid is to be administered over.

Chloride
Chloride is one of the most important anions in the body, representing approximately two-thirds of the anions in the blood. It is primarily extracellular. It is filtered by the glomerulus and reabsorbed in the renal tubules.

Fluids and drugs containing chloride such as 0.9% saline, hypertonic saline and potassium chloride can increase the chloride levels as can total parenteral nutrition. Chloride retention in the kidneys can occur secondary to renal failure, renal tubular acidosis, diabetes mellitus and chronic respiratory alkalosis. Loop diuretics and thiazide diuretics can cause an increased loss of chloride relative to sodium. Hypochloremia can occur with gastric vomiting and as an adaptive mechanism with chronic respiratory acidosis. Pseudohyperchloremia occurs when patients are being treated with potassium bromide. Most abnormalities of chloride are associated with acid-base abnormalities and clinical signs relate primarily to the acid-base disturbance rather than the alteration in the chloride. Hyperchloremia is typically associated with an acidosis and hypochloremia with an alkalosis. Because of this, it is essential to evaluate abnormal chloride levels in light of the acid-base status of the patient.

Chloride values must be corrected to take into account any changes in plasma free water before assessing whether or not the chloride concentration is low, normal or elevated. This is calculated by the following formula:

$$[Cl^-]_{corrected} = [Cl^-]_{measured} \times 146/[Na^+]_{measured}$$

The number of 146 is used in dogs under the assumption that 146 mEq/L is the mean sodium concentration in cats. The number 156 should be used in cats. This corrected value can have a significant impact on the choice of fluid therapy in certain conditions. For instance a ketoacidotic diabetic cat with a sodium of 140 mEq/L and a chloride of 118 mEq/L may become even more acidotic if 0.9% saline is infused. The corrected chloride in this situation is 131 mEq/L which is already a contributing factor to this cat's metabolic acidosis. There is a potential that this will only be worsen if 0.9% saline is infused.

Normal saline at 0.9% has a sodium concentration of 154 mmol/L which makes it hypertonic for most patients. The chloride is also 154 mmol/L which can lead to the development of a hyperchloremic metabolic acidosis. Due to its acidifying nature (pH of 5.4) it should generally be reserved for patients with gastric outflow obstructions, hypercalcemia and hypoadrenocorticism. It is important to note that electrolyte abnormalities are difficult to correct in patients with the first 2 conditions without administration of saline – usually in large volumes.

Potassium
Potassium is the major intracellular cation and 95% of the body's stores of potassium are maintained intracellularly. Potassium levels, along with sodium, play a key role in maintaining the resting membrane potential. If the patient is hyperkalemic then the membrane will be hyperpolarized making it impossible to develop an action potential. Hypokalemia also alters membrane excitability. The clinical manifestations of altered

potassium concentrations are similar, whether the potassium is low or high. Ultimately muscle weakness, especially involving the cardiac and skeletal muscles, will become apparent.

Potassium excretion is regulated primarily in the kidney, but to some extent in the colon, under the influence of aldosterone. Transcellular levels are primarily regulated by insulin, catecholamines, acid-base balance and the sodium-potassium-ATPase pump. Insulin drives potassium intracellularly along with glucose, and insulin also stimulates the sodium-potassium-ATPase pump directly, which also helps drive potassium intracellularly. When a patient becomes acidemic the body will shift hydrogen ions intracellularly in an attempt to maintain a more normal pH. For every 0.1 change in pH the potassium changes by 0.6 mEq/L. The hydrogen ions will be exchanged for potassium ions; therefore, hyperkalemia is expected with an acidosis and hypokalemia with an alkalosis. The finding of hypokalemia in the face of a significant metabolic acidosis should alert the clinician to the possibility of significant total body potassium depletion. If the patient has a metabolic alkalosis and a hypokalemia, the hypokalemia will actually tend to perpetuate the alkalosis via stimulation of increased bicarbonate resorption in the kidney.

In general terms hypokalemia can be caused by dilution, movement of potassium intracellularly, loss through the gastrointestinal tract and loss in the urine. Iatrogenic causes include fluid therapy, infusion of glucose or other hyperosmolar solutions, and the administration of loop and thiazide diuretics. Clinical signs rarely become apparent until the concentration decreases below 2.5 mEq/L. Clinical signs relate to weakness of the skeletal, cardiac and gastrointestinal muscles. Cervical ventroflexion occurs with significant hypokalemia, forelimb hypermetria and a broad-based stance have also been reported in cats. Hypokalemic polymyopathy has been reported in cats with chronic renal disease and poorly regulated diabetes mellitus. If the hypokalemia becomes severe enough respiratory paralysis and death will result.

Unfortunately there are no exact formulas for calculating the total body potassium depletion, nor the requirement for supplementation. Guidelines exist (see below) but the guidelines should always be modified based on how the patient is responding to therapy. A patient with hypokalemia and an osmotic diuresis will have a much higher requirement for potassium than one with normal urine output. It is recommended that the infusion rate not exceed 0.5 mEq/kg/hr; however, higher rates may be required in some patients. Rates as high as 1.5 mEq/Kg/hr can be used as long as the patient's heart rate and electrocardiogram are monitored continuously. Hypomagnesemia should be ruled out in patients with refractory hypokalemia.

Potassium (K^+) Supplementation Chart

Serum K^+	K^+/1000 ml
< 2 mEq/l	60 mEq
2.0-2.5	40
2.5-3.0	30
3.0-3.5	20

In general terms hyperkalemia can be caused by increased intake, movement of potassium extracellularly, and inadequate excretion in the kidneys secondary to renal or postrenal causes. Massive tissue damage such as occurs with severe crush injury as well as abrupt reperfusion such as can occur following a saddle thrombus can also cause severe hyperkalemia. Additional less common causes include severe thrombocytosis and severe leukocytosis (greater than 100,000 WBC). Iatrogenic causes include fluid therapy, the administration of spironolactone and angiotensin-converting enzyme inhibitors loop and thiazide diuretics. As with hypokalemia clinical signs relate to weakness of the skeletal, cardiac and gastrointestinal muscles. Cardiotoxic effects can become evident when the potassium concentration exceeds 7.5 mEq/L.

There are distinct electrocardiographic findings associated with hyperkalemia, although, the order with which they appear in the cat seems to be less consistent than with the dog. Also the electrocardiographic abnormalities

are less likely to be apparent in the acute hyperkalemia that exists in cats with lower urinary tract obstructions. The abnormalities (in the order they typically appear) include tall or peaked T waves, a prolonged PR interval, an absent P wave, a prolonged QRS complex, bradycardia, atrial standstill, sine wave complexes, ventricular fibrillation and complete standstill. By the time a sine wave is evident the patient is in imminent danger of dying.

Although dialysis can be used to decrease potassium concentration, it is not commonly used. The three primary treatments for a hyperkalemia that is significant enough to cause cardiotoxicity include infusion of insulin and dextrose, sodium bicarbonate and calcium gluconate. It is important to note that concurrent definitive treatment of the underlying condition is essential. Infusion of 0.5 to 1.5 ml/kg of 10% calcium gluconate has an immediate effect on the muscle because it decreases the membrane potential. Sodium bicarbonate given at a dose of 1 to 2 mEq/kg will cause an immediate transcellular shift of potassium, which once again decreases the resting membrane potential. Regular insulin can be injected at a dose of 0.5 U/kg IV which will drive the potassium intracellularly. The insulin injection should be followed by an injection of 2 g of 25% dextrose for every unit of insulin that was given to avoid iatrogenic hypoglycemia. It is likely that the infusion of dextrose alone should be sufficient to stimulate the release of endogenous insulin, which would cause the same effect. The insulin/dextrose treatment is an effective one but may require up to 20 minutes to achieve a peak effect.

References available on request.