Fluid Therapy for the Emergent Small Animal Patient
Crystalloids, Colloids, and Albumin Products

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KEYWORDS
- Intravenous fluids
- Crystalloids
- Colloids
- Albumin
- Volume resuscitation
- Dehydration

KEY POINTS
- Fluid therapy is essential in the treatment of emergent veterinary patients and includes crystalloid solutions, blood component therapy, concentrated albumin solutions, and synthetic colloids.
- Bolus intravenous (IV) fluid therapy can restore perfusion and stabilize critically ill and injured patients for further diagnostics and treatment.
- Synthetic colloids help maintain colloid osmotic pressure (COP) and improve blood pressure but should be used with caution in coagulopathic patients or those with cardiac disease.
- Concentrated albumin solutions may have a role in the treatment of critically ill veterinary patients with severe hypoalbuminemia (eg, septic peritonitis); further prospective, comparative studies are needed to fully elucidate the role of albumin solutions in dogs and cats.
- The pros and cons of the use of human serum albumin (HSA) and canine serum albumin (CSA) will be reviewed.

Water is essential for life. Without adequate fluid intake, normal body functioning becomes impaired and ultimately can lead to death. A fluid therapy plan should be considered for any small animal patient that has either inadequate fluid intake, excessive fluid loss, or both. A simplified approach to fluid therapy begins with an understanding of the composition of fluid and its distribution within the body. Next, consideration of electrolyte loss, acid-base disturbances, perfusion impairment, and loss of protein also becomes important when replenishing deficits by using various fluids that are commercially available to small animal practitioners.

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TOTAL BODY WATER AND FLUID COMPARTMENTS WITHIN THE BODY

A discussion of IV fluid administration is incomplete without an understanding of total body water (TBW) and fluid balance between the various compartments within the body. Approximately 60% of a healthy animal’s total body weight is water. This value can change slightly depending on age, lean body mass, degree of leanness or obesity, and gender. Total body water has been estimated as approximately 534 mL/kg to 660 mL/kg in healthy dogs and cats.1

Conceptually, the body can be divided into the intracellular and extracellular compartments. Fluid located within cells is known as intracellular fluid (ICF) and contributes approximately two-thirds (66%) to TBW. Extracellular fluid (ECF) is that located outside of cells and contributes approximately one-third (33%) to TBW; the ECF can be further subdivided into the intravascular and interstitial compartments. Fluid contained within blood vessels is intravascular fluid. The intravascular fluid contains plasma water, cellular components, proteins, and electrolytes. The interstitial extracellular compartment is the space located outside of the blood vessels. Intravascular fluid contributes only 8% to 10% of TBW, and interstitial fluid contributes 24% of TBW. A small amount of fluid is known as transcellular fluid and is located within the gastrointestinal tract, joints, cartilage, and cerebrospinal space.1 Total intravascular fluid volume has been estimated as 80 mL/kg to 90 mL/kg in dogs and cats. Of that, the fluid component, or intravascular plasma water volume, has been estimated as approximately 45 mL/kg to 50 mL/kg.1

GOALS OF FLUID THERAPY

Administration of IV fluids requires an understanding of the type of fluid lost, the presence of underlying disease processes, an animal’s hydration and intravascular volume status, acid-base and electrolyte derangements, an animal’s ability to retain fluid within the intravascular space, and determinants of resuscitation endpoints when treating dehydration or various forms of hypovolemia. An understanding of electrolyte and protein composition within the body is also essential to help maintain homeostasis and to use the variety of crystalloid fluids that are available to treat specific abnormalities. Thus, the goals of fluid therapy are to replenish interstitial, intracellular, and intravascular fluid deficits; to correct and maintain electrolyte and acid-base derangements; and to maintain normal TBW in the face of excessive loss or lack of adequate intake.

CRYSTALLOID FLUIDS

A crystalloid fluid contains water and various forms of electrolytes (including salt) or sugar crystals (Table 1).1,2 Some crystalloid fluids also contain buffers (eg, acetate, gluconate, and lactate) that are metabolized to bicarbonate to increase serum pH. Crystalloid fluids are categorized according to their osmolality relative to that of plasma. An isotonic crystalloid fluid has an osmolality similar to or equal to that of plasma and the extracellular compartment (eg, approximately 300 mOsm/L). Fluids with tonicity lower than that of the extracellular space are called hypotonic fluids (eg, 0.45% dextrose and 5% dextrose in water [D5W]) and can cause fluid influx into red blood cells (RBCs) and hemolysis.1,2 Fluids with tonicity greater than that of the ECF compartment (eg, >300 mOsm/L) are called hypertonic solutions (eg, 7.2% and 23.4% hypertonic saline) and can be used to expand intravascular fluid volume in a hypovolemic animal by pulling water from the interstitial into the intravascular space. It has been estimated that approximately 80% of an isotonic crystalloid fluid
<table>
<thead>
<tr>
<th>Fluid</th>
<th>Osmolarity</th>
<th>Buffer</th>
<th>Sodium</th>
<th>Chloride</th>
<th>Potassium</th>
<th>Calcium</th>
<th>Magnesium</th>
<th>Glucose</th>
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</thead>
<tbody>
<tr>
<td>Normosol-R</td>
<td>296</td>
<td>Acetate</td>
<td>140</td>
<td>98</td>
<td>5</td>
<td>0</td>
<td>3</td>
<td>0</td>
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<td></td>
<td></td>
<td>Gluconate 23</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PlasmaLyte-A</td>
<td>294</td>
<td>Acetate</td>
<td>140</td>
<td>98</td>
<td>5</td>
<td>0</td>
<td>3</td>
<td>0</td>
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<tr>
<td>0.9% Saline</td>
<td>308</td>
<td>0</td>
<td>154</td>
<td>154</td>
<td>0</td>
<td>0</td>
<td>0</td>
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<tr>
<td>LRS</td>
<td>272</td>
<td>Lactate</td>
<td>130</td>
<td>109</td>
<td>4</td>
<td>3</td>
<td>0</td>
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</tr>
<tr>
<td>D5W</td>
<td>252</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>50 g/L</td>
</tr>
<tr>
<td>0.45% NaCl + 2.5% dextrose</td>
<td>280</td>
<td>0</td>
<td>77</td>
<td>77</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>25 g/L</td>
</tr>
<tr>
<td>Normosol-M + 5% dextrose</td>
<td>364</td>
<td>Acetate 16</td>
<td>40</td>
<td>40</td>
<td>13</td>
<td>0</td>
<td>3</td>
<td>50 g/L</td>
</tr>
<tr>
<td>PlasmaLyte-M</td>
<td>363</td>
<td>Acetate</td>
<td>40</td>
<td>40</td>
<td>13</td>
<td>0</td>
<td>3</td>
<td>110</td>
</tr>
<tr>
<td>PlasmaLyte-56</td>
<td>110</td>
<td>Acetate</td>
<td>40</td>
<td>40</td>
<td>13</td>
<td>0</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
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<td>1026</td>
<td>0</td>
<td>513</td>
<td>513</td>
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<td>0</td>
<td>0</td>
<td>0</td>
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<tr>
<td>7% NaCl</td>
<td>2567</td>
<td>0</td>
<td>1283</td>
<td>1283</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>
administered IV leaves the intravascular compartment and move to the interstitial compartment within 1 hour of infusion.\textsuperscript{3}

Isotonic fluids have sodium concentrations similar to that of plasma and the ECF compartment.\textsuperscript{1,2,4} Water and sodium are intimately associated within the body’s fluid compartments. Wherever sodium goes, water must follow. For this reason, the concentration of sodium in a crystalloid fluid becomes important when selecting a particular fluid to treat a specific disease state. Other important components of isotonic crystalloid fluids to consider include the presence or absence of buffers or various electrolytes (calcium, magnesium, potassium, chloride, and so forth).

Fluids used to replace intravascular and interstitial volume deficit should contain 130 mEq/L to 154 mEq/L of sodium. Several solutions are used for replacement of fluid volume, electrolyte abnormalities, and correction of acid-base abnormalities, including Normosol-R, PlasmaLyte-A, normal (0.9\%) saline, and lactated Ringer solution (LRS) (also called Hartmann solution).

Maintenance crystalloid solutions contain lower concentrations of sodium and other compounds compared with the extracellular space\textsuperscript{1,2,4} and are used primarily to replace sensible fluid losses that can be measured and insensible fluid losses that can be estimated.\textsuperscript{3} An example of a maintenance isotonic crystalloid fluid is 0.45\% sodium with 2.5\% dextrose, PlasmaLyte-M, and PlasmaLyte 56. If such fluids are used as replacement solutions, a patient’s serum sodium can decrease and lead to a state of hyponatremia.

**HYPERTONIC SALINE**

Hypertonic sodium (eg, 7.2 and 23.4\% NaCl) contains the highest concentration of sodium (eg, 1283 mEq/L of sodium and approximately 4000 mEq/L). Infusion of hypertonic saline should only be considered in a hypovolemic patient with normal interstitial and intracellular hydration (ie, only lacking fluid within the intravascular space). Infusion of hypertonic saline increases intravascular sodium concentration, and the intravascular space has a higher osmolality compared with the interstitial and intracellular space. To maintain fluid equilibrium, water diffuses down a concentration gradient by osmosis, from an area of higher water concentration (lower osmolality). After infusion of hypertonic saline, water moves from the intracellular and interstitial space into the intravascular space and causes intravascular volume expansion at the expense of the interstitium. The effect is short-lived for 20 to 30 minutes unless the hypertonic saline is administered concurrently with a colloid to retain the fluid within the intravascular space.\textsuperscript{5,6} Hypertonic saline (23.4\%) can be diluted with a synthetic colloid at a ratio of 1 part hypertonic saline with 2.5 parts colloid, which creates a 7.5\% solution.\textsuperscript{7} Hypertonic saline in combination with a synthetic colloid (dogs: 5–10 mL/kg of the combination; cats: 2 mL/kg of the combination; total dose in either species should not exceed 1 mL/kg/min as a bolus)\textsuperscript{7} can also be used to initially treat hypovolemic shock, provided a patient is not clinically dehydrated.

After correction of intravascular hypovolemia, replacement crystalloid fluids must be administered after administration of hypertonic saline (with or without colloids) to replenish that fluid borrowed from the interstitial and intracellular compartments to rehydrate them. Potential complications of hypertonic saline administration include rapid respiratory rate, hypotension, bradycardia, and hypernatremia.\textsuperscript{1,7}

**SODIUM**

Sodium is the major extracellular cation (ie, positive charged molecule) in the body. Normal sodium concentrations are 140 mEq/L 150 mEq/L for dogs and 150 mEq/L for cats.
to 160 mEq/L for cats. The sodium content of most isotonic crystalloid fluids ranges from 130 mEq/L to 140 mEq/L. Normal (0.9%) saline is the isotonic crystalloid fluid with the highest sodium concentration (154 mEq/L) and is used as a replacement fluid. Fluids used to replace intravascular and interstitial volume deficit should contain 130 mEq/L to 154 mEq/L of sodium. In the realm of isotonic crystalloid fluids, LRS contains the lowest concentration of sodium (130 mEq/L) relative to plasma. Conditions that promote hyperaldosteronemia and sodium retention, such as congestive heart failure and hepatic failure, may benefit from infusion of lower concentrations of sodium.

Maintenance fluids can be used to replace daily ongoing sodium losses. Fluids, such as Plasmalyte-M and Plasmalyte 56, contain approximately 40 mEq/L sodium. If such fluids were used as replacement solutions, a patient’s serum sodium could be decreased and lead to a state of hyponatremia.

Rapid changes in serum sodium concentration can be detrimental, depending on the how quickly an animal’s sodium balance and serum sodium concentration become deranged. Diarrhea, heat-induced illness, hyperthermia, and lack of access to water can cause varying degrees of hypernatremia. Hypernatremia largely is characterized by a free water deficit, a deficit of fluid in excess of electrolytes. Ideally, serum sodium concentration should not be lowered by more than 15 mEq in a 24-hour period. Similarly, syndromes, such as hypoadrenocorticism, can cause decreases in serum sodium concentration. Overzealous administration of sodium-containing fluids, such as normal (0.9%) saline, can result in cerebral edema and central pontine myelinolysis.

CHLORIDE

Chloride is a major extracellular anion (ie, negative charged molecule). Chloride can be lost in vomitus caused by an upper gastrointestinal obstruction, from administration of diuretics (eg, furosemide) or from loss in diarrheic feces. The presence of a hypochloremic metabolic alkalosis is typically less common in veterinary medicine and is often characteristic of the causes discussed previously. Normal (0.9%) saline contains supraphysiologic concentrations of chloride (154 mEq/L) and is used as a chloride replacement fluid in cases of hypochloremia. Other isotonic crystalloid fluids contain varying concentrations of chloride (55–103 mEq/L). Although chloride is important, consideration of sodium and other electrolyte concentrations is more important when selecting a replacement fluid for a specific disease state.

POTASSIUM

Potassium is the major intracellular cation. Serum potassium can become elevated due to severe dehydration, hypoadrenocorticism, metabolic acidosis, diabetic ketoacidosis (DKA), renal failure, or obstructive uropathies. Most replacement and maintenance crystalloid fluids contain minimal supplementation of potassium (eg, 4 mEq/L of potassium in LRS) and typically need to be supplemented in the form of potassium chloride. In animals with hyperkalemia, it is ideal to avoid the administration of a potassium-containing fluid whenever possible; however, studies have shown that as long as the underlying disease mechanism is promptly treated, the small amount of potassium with replacement or maintenance fluids is rarely consequential. Administration of IV fluids alone dilutes serum potassium as intravascular fluid volume is replenished, even if the fluid contains small amounts of potassium. In animals with hypokalemia, potassium supplementation is commensurate with the degree of hypokalemia. It is advisable to not exceed administration of more than 0.5 mEq/kg/h of potassium IV.
MAGNESIUM

Magnesium is required for regulation and normal functioning of the sodium-potassium-ATPase pump. Some maintenance fluids (eg, PlasmaLyte and Normosol) contain trace amounts of magnesium. In general, most healthy patients do not require additional supplementation of magnesium. In animals with refractory hypokalemia (eg, DKA), animals with endocrine diseases predisposing them toward significant electrolyte changes (eg, DKA), or in critically ill patients, magnesium should be supplemented (eg, 0.75 mEq/kg/d or 0.375 mmol/kg/d) in addition to potassium, because both electrolytes follow similar physiologic paths within the body. Total body magnesium is a function of absorption and loss as well as redistribution throughout body compartments. Any physiologic condition that can cause a lack of intake and absorption, increased loss in diarrheic feces, renal tubular loss, or redistribution can cause hypomagnesemia. For example, in animals with DKA and whole-body magnesium depletion secondary to glucose/osmotic diuresis, administration of insulin and dextrose for treatment causes magnesium to rapidly shift to the intracellular space and result in a serum ionized hypomagnesemia. Although the crystalloid fluids contain small quantities of magnesium, the amount is insufficient to replenish a whole-body magnesium deficit in some populations of critically ill patients.

CALCIUM

Calcium is an important cation that is necessary for normal muscle conduction and coagulation. Calcium is present in small amounts in LRS (3 mEq/L) and typically does not need to be supplemented in healthy patients above this amount. In cases of puerperal tetany (eg, eclampsia), however, LRS may be the preferred fluid as adjunct therapy to those that do not contain calcium and to those that promote calcium excretion (0.9% NaCl). Additionally, the preemptive use of a calcium-containing fluid, such as LRS, may be beneficial in helping to prevent hypocalcemia during the postoperative period after surgical removal of the parathyroid gland.

Hypercalcemia can be seen due to a variety of causes. Administration of a calcium-containing fluid is contraindicated in hypercalcemic patients if other crystalloid fluids are available. Normal (0.9%) saline is the treatment of choice in cases of hypercalcemia not only because the fluid does not contain calcium but also because the higher sodium content (eg, 154 mEq/L) promotes calciuresis at the Na₂Ca exchanger.¹¹

BUFFERS

A buffer is a compound that is converted or metabolized in the body to bicarbonate to help maintain normal physiologic blood pH. The most common buffers found in IV fluids include lactate, acetate, and gluconate. Medical conditions that cause metabolic acidosis (lactic acidosis secondary to poor perfusion, DKA, uremia, ethylene glycol toxicosis, salicylate toxicosis, and so forth) should ideally be treated with a crystalloid fluid that contains a buffer. Certain medical conditions, however, may warrant the judicious use or the more appropriate use of certain buffers. In cases of hepatic dysfunction, the liver’s ability to convert lactate to bicarbonate may be diminished; therefore, LRS is contraindicated. Acetate and gluconate, commonly found in Normosol-R or PlasmaLyte, are buffers that are metabolized to bicarbonate in the liver and muscle tissue. Therefore, in patients with LSA or whose liver function is suboptimal, crystalloid fluids that contain acetate and gluconate may be preferable to lactate-containing solutions. Acetate, which has been reported to potential
hypotension with large, massive infusions (eg, dialysis), should ideally be avoided in patients requiring large, rapid boluses (eg, anesthetic-induced hypotension).

Normal (0.9%) saline contains no buffers and is known as an acidifying crystalloid fluid because it promotes excretion of bicarbonate by the renal tubules. In cases of a hypochloremic metabolic alkalosis, an acidifying solution, such as 0.9% saline without additional buffers, is preferred, to avoid administration of additional sources of bicarbonate and to replenish chloride ions lost in the vomitus.

**DEXTROSE**

Dextrose-containing fluids, such as D5W and 0.45% sodium chloride with 2.5% dextrose, are not common fluid choices in the dehydrated patients, and their use is typically limited to patients with severe hypernatremia, patients that cannot tolerate a large amount of sodium (eg, heart failure), or during treatment of conditions that cause hyperaldosteronism (hepatic failure, cardiac disease, and so forth). Dextrose-containing fluids are largely hypotonic compared with plasma; D5W is analogous to infusing a free water solution, once the dextrose is rapidly metabolized by the body. The remaining fluid redistributes within the intravascular, interstitial, and intracellular fluid compartments. Because free water alone is severely hypotonic (eg, 0 Osm/L) relative to plasma (eg, 300 Osm/L), infusion of free water causes rapid and severe hemolysis; hence, sterile water is not used. The addition of 5% dextrose (50 mg of dextrose/mL) makes the fluid isoosmolar and brings the tonicity of the fluid up to a safe acceptable range. The dextrose in these fluids is quickly metabolized but is insufficient to meet an animal’s daily metabolic caloric requirements.

**MAINTENANCE FLUID REQUIREMENTS**

Many estimates of the maintenance fluid requirements for healthy dogs and cats have been recommended. In general, the estimates have been extrapolated from those recommended for humans or have been suggested based on experiments performed on healthy dogs and cats. The most recent swing of the fluid pendulum has been based on data obtained from calorimetry analysis in which fluid requirements are extrapolated from an animal’s resting energy expenditure (REE) and lean body mass. An animal’s metabolic water requirements are equivalent to the number of basal calories required. During metabolism of 1 kcal of energy, 1 mL of water is consumed. By calculating the REE, or daily caloric requirements, a patient’s daily fluid requirements for metabolic purposes can be calculated by the following linear formula: 

\[ \text{REE} = m \text{L H}_2\text{O}^* = [(30 \times \text{body weight [kg]}) + 70], \]

where * denotes requirement for a 24-hour period.

This formula is accurate for animals greater than 2 kg and less than 100 kg. One caveat is that the REE is applicable to a healthy animal that is euvoletic, resting, and in a postprandial state. This formula denotes a starting point for dehydrated or hypovolemic animals or those with excessive fluid losses. Because some patients may become dehydrated when this formula is used, frequent evaluation of hydration status (body weight, evidence of hemodilution, urine specific gravity, and so forth) is essential during hospitalization. As a rule of thumb, 1 mL of water is equivalent to 1 g of body weight. Therefore, loss of 1 kg is equivalent to a loss of 1 L of water. Careful weighing of the animal on a regular basis allows clinicians to determine whether additional ongoing losses are occurring, allowing for accurate correction of interstitial and intracellular dehydration.
DEHYDRATION

Dehydration refers to the fluid deficit within the interstitial and intracellular fluid compartments. The extent of dehydration can be estimated based on subjective guidelines of skin turgor, mucous membrane dryness, and sunken appearance of the eyes within the orbit (Table 2). Once degree of dehydration is determined, the volume of fluid that must be administered to replace the fluid deficit can be calculated by the following formula:

\[
\text{Dehydration} \times \text{body weight in kg} \times 1000 = \text{milliliters fluid deficit}
\]

The fluid deficit then should be added to the animal’s maintenance fluid requirements and replaced over a 6-hour to 24-hour period, depending on a patient’s stability and ability to handle the volume administered. There is no absolute correct method of replacing an animal’s fluid deficit, as long as the deficit is considered in the calculation of the total amount of fluids that need to be administered to a dehydrated patient. Frequent weighing and calculation of urine, vomit, and diarrhea fluid output (again, knowing that 1 mL of fluid weighs 1 g) allow a clinician to determine whether a patient’s fluid deficit and maintenance needs are met or whether IV crystalloid dose needs to be adjusted.

HYPOVOLEMIA

Hypovolemia denotes loss of fluid from the intravascular space and is semantically different than dehydration. This fluid loss may be relative or absolute, meaning that in conditions of vasodilation (eg, sepsis or an anesthetized patient), there is a relative intravascular fluid deficit. Absolute intravascular fluid deficits occur as a result of fluid loss, such as that associated with hemorrhage or excessive ongoing losses (vomiting, diarrhea, renal loss, and so forth), where fluid efflux from the interstitial space to compensate for intravascular fluid loss has been depleted. Likewise, if an isoosmolar fluid is lost (eg, blood), there is no osmotic gradient drive to pull fluid from the interstitial space into the intravascular space. Clinical signs of hypovolemia are manifested as abnormalities of perfusion and include tachycardia, peripheral vasoconstriction with cool

<table>
<thead>
<tr>
<th>Estimated Degree of Dehydration</th>
<th>Clinical Signs</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;5%</td>
<td>History of vomiting or diarrhea or other fluid loss, normal mucous membranes, unable to detect &lt;5% on physical examination</td>
</tr>
<tr>
<td>5%</td>
<td>History of vomiting or diarrhea or other fluid loss, tachy or dry mucous membranes</td>
</tr>
<tr>
<td>7%</td>
<td>History of vomiting or diarrhea or other fluid loss, dry mucous membranes, increased skin tenting, tachycardia, normal pulse quality and arterial blood pressure</td>
</tr>
<tr>
<td>10%</td>
<td>History of vomiting or diarrhea or other fluid loss, dry mucous membranes, increased skin tenting, tachycardia, weak pulses, hypotension</td>
</tr>
<tr>
<td>12%</td>
<td>History of vomiting or diarrhea or other fluid loss, dry mucous membranes, sunken eyes, increased skin tenting, tachycardia or bradycardia, weak to absent pulses, hypotension, cold extremities, hypothermia</td>
</tr>
</tbody>
</table>
extremities, hypothermia, prolonged capillary refill time, hypotension, pallor, and mental dullness. When an animal presents in hypovolemic shock, the location of the fluid deficit, the presence of electrolyte abnormalities, and whether interstitial or intracellular dehydration is a component of a fluid deficit or if the deficit is associated with the intravascular space alone must be considered. With hypovolemia, rapid fluid replacement is imperative to improve perfusion parameters. Previously, recommendations for the treatment of hypovolemic shock (eg, shock volume) in dogs and cats have been reported as 90 mL/kg and 44 mL/kg, respectively,\textsuperscript{4,8,13,14} which represents the blood volume of a patient. Because administration of large volume of crystalloids can dilute coagulation factors, platelets, and RBCs, more recently, the use of smaller aliquots are recommended rather than replacing the whole blood volume at once Table 3.

Ideally, it is preferred to administer a one-fourth of the shock volume (eg, 20–30 mL/kg over 20 minutes) and reassess a patient’s perfusion parameters. If normalizing, then moving to maintenance fluid rates and performing diagnostics can be considered to assess and treat the primary cause of the problem. If a patient fails to respond (eg, perfusion parameters have still not normalized), additional aliquots (eg, one-fourth shock bolus) of crystalloid fluids should be readministered once or twice more; additional therapy may warrant the use of a colloid thereafter. Once stabilized, a continuous rate of infusion of fluids should be maintained, because 80% of a crystalloid fluid volume

### Table 3
Relative indications and relative contraindication for use of various isotonic, hypotonic, and hypertonic crystalloid fluids

<table>
<thead>
<tr>
<th>Fluid</th>
<th>Indications</th>
<th>Relative Contraindications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normosol-R</td>
<td>Replacement, metabolic acidosis, anorexia, vomiting, hypovolemic shock, diarrhea, renal failure</td>
<td>Hyperkalemia, metabolic alkalosis</td>
</tr>
<tr>
<td>PlasmaLyte-A</td>
<td>Replacement, metabolic acidosis, anorexia, vomiting, hypovolemic shock, diarrhea, renal failure</td>
<td>Hyperkalemia, metabolic alkalosis</td>
</tr>
<tr>
<td>0.9% NaCl</td>
<td>Replacement, hypovolemic shock, anorexia, vomiting, diarrhea, metabolic alkalosis, hyperkalemia, hypercalcemia acute hyponatremia, chronic hypernatremia, renal failure</td>
<td>Cardiac disease, liver disease, metabolic acidosis</td>
</tr>
<tr>
<td>LRS</td>
<td>Replacement, hypovolemic shock, vomiting, diarrhea, hypocalcemia, metabolic acidosis, renal failure</td>
<td>Hypercalcemia, hyperkalemia, lymphosarcoma, liver failure</td>
</tr>
<tr>
<td>D5W</td>
<td>Drug carrier, correction of hyponatremia and free water deficit, congestive heart failure</td>
<td>Does not provide sufficient calories to be used as a form of parenteral nutrition</td>
</tr>
<tr>
<td>0.45% NaCl + 2.5 dextrose</td>
<td>Maintenance, replacement of insensible losses, correction of free water deficit</td>
<td>Not to be used as a replacement fluid</td>
</tr>
<tr>
<td>Normosol-M</td>
<td>Replacement of insensible losses</td>
<td>Hyponatremia, not to be used as a replacement fluid</td>
</tr>
<tr>
<td>PlasmaLyte-M</td>
<td>Replacement of insensible losses</td>
<td>Hyponatremia, not to be used as a replacement fluid</td>
</tr>
<tr>
<td>3% NaCl</td>
<td>Intravascular volume expansion, hypovolemic shock</td>
<td>Interstitial dehydration, hyponatremia</td>
</tr>
<tr>
<td>7% NaCl</td>
<td>Intravascular volume expansion, hypovolemic shock</td>
<td>Interstitial dehydration, hyponatremia</td>
</tr>
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</table>
infused leaved the intravascular space within 1 hour of infusion, if not administered along with a colloid.3

**COLLOID OSMOTIC PRESSURE**

COP is the pressure exerted on membranes primarily due to the presence of albumin. Normal plasma COP in dogs and cats has been reported as 16.7 mm Hg to 28.9 mm Hg and 21 mm Hg to 34 mm Hg, respectively.15–17 Normal whole blood COP in dogs and cats has been reported as 17.9 mm Hg to 27.1 mm Hg and 21 mm Hg to 34 mm Hg, respectively.15,16 Starling’s law governs the movement of fluid between the intracellular and extracellular (intravascular and interstitial) space:

\[
J_v = K_f [(P_c - P_i) - \sigma (\pi_c - \pi_i)]
\]

where \(J_v\) is net fluid movement between compartments, \(K_f\) is filtration coefficient, \(P_c\) is capillary hydrostatic pressure, \(P_i\) is interstitial hydrostatic pressure, \(\sigma\) is reflection coefficient, \(\pi_c\) is COP, and \(\pi_i\) is interstitial osmotic pressure.

The filtration coefficient (\(K_f\)) is a measure of how well a tissue allows fluid to efflux and is a product of the surface area of the tissue and how permeable the capillary wall is to water (also referred to as hydraulic conductivity). The reflection coefficient (\(\sigma\)) is a measure of protein permeability in the membrane. If a membrane is completely impermeable to protein, then the osmotic forces are able to exert their full effect, making the reflection coefficient equal to 1.0. For example, the cerebrospinal fluid and the glomerular filtrate are impermeable to protein, and, therefore, the reflection coefficient for protein in these capillaries is close to 1. Proteins cross the walls of the hepatic sinusoids easily, so the reflection coefficient for protein in the sinusoids is low. The reflection coefficient in the pulmonary capillaries is approximately 0.5. Hydrostatic pressure (\(P\)) tends to force fluid out of the capillary, and the osmotic pressure (\(\pi\)) acts to pull inward, keeping fluid within the intravascular space.

**COLLOID SOLUTIONS**

Colloid solutions contain high molecular weight (MW) particles thereby increasing plasma COP and more efficiently holding fluid within the intravascular space. Colloids can be further classified as natural or synthetic. Natural colloid solutions include blood products (eg, plasma and whole blood) and concentrated albumin. Synthetic colloids include dextrans and hydroxyethyl starches (HESs).

**NATURAL COLLOIDS**

Blood products include whole blood, component therapy (eg, plasma), and concentrated albumin solutions. Packed RBCs (pRBCs) have a lower COP (eg, 5 mm Hg) and are not considered a true colloid compared with whole blood (eg, because the plasma proteins have been separated out of the solution). If an anemic patient is euolemic (eg, due to hemolysis of RBCs), pRBC transfusion is most appropriate, because the risk of hypervolemia can be avoided.

Plasma transfusions, with a COP of 20 mm Hg, are most appropriate in patients with coagulation abnormalities rather than hypoproteinemic patients. Although the COP of fresh frozen plasma or frozen plasma is comparable to normal plasma, the volume of plasma needed to significantly increase albumin by 1 mg/dL is large (eg, 45 mL/kg, IV) compared with the volume necessary to correct a coagulopathy (eg, 6–20 mL/kg, IV). This is usually cost prohibitive and increases the risk of fluid overload and triggering for future transfusion reactions.
Whole blood transfusions are indicated when both plasma and RBCs are required for transfusion. Whole blood also contains platelets; however, the number of platelets is not sufficient to support patients with severe thrombocytopenia. Also, platelet function within a unit of whole blood is negated once the unit has been refrigerated (Please see the article “Transfusion Medicine in Small Animals” elsewhere in this issue for more information). In patients with severe thrombocytopenia hemorrhaging into life-threatening tissue (eg, brain or lung), a whole blood transfusion or the use of lyophilized platelets may be indicated to attempt hemostasis.

Concentrated albumin solutions, including 25% HSA and CSA, have been used in critically ill canine and feline patients to help support blood pressure and to aid in the treatment of significant hypalbuminemia. Studies have been published assessing the utility of HSA in the treatment of critically ill, hypalbuminemic dogs and cats. These studies are descriptive and retrospective; at the time of this publication, there is no published prospective, comparative study on the use of HSA in veterinary medicine. Studies assessing the use of HSA in healthy dogs have been published, however, and have unmasked the occurrence of hypersensitivity reactions in some dogs, including immediate anaphylactoid reactions and delayed events, including urticaria, vasculitis, lethargy, and edema 1 week postinfusion. In addition, a study evaluating dogs that had received HSA revealed the presence of HSA autoantibodies in all dogs, increasing the risk for type III hypersensitivity reactions. In critically ill dogs and cats receiving HSA, there were few reported hypersensitivity reactions, which may be due to their immunoparalyzed state. In these studies, dogs and cats with higher serum albumin levels were more likely to survive compared with those with lower serum albumins. It is unknown if transfusing concentrated albumin solutions actually improves survival or if albumin is simply a marker of improved clinical outcome.

More recently, CSA has been produced and available through a national veterinary blood bank (Animal Blood Resources International, Dixon, California, and Stockbridge, Michigan; abrint.net). This may be a better, safer option with less risk for hypersensitivity reaction than with the human product. CSA is a lyophilized product and is currently sold in 5-g bottles at an estimated $125 per bottle. The published dose, based on company safety studies in healthy beagles, is 800 mg/kg to 844 mg/kg over 6 hours. (Animal Blood Resources International, package insert, lyophilized canine albumin; abrint.net) The use of CSA has been evaluated in a prospective, blinded, comparative study in dogs with septic peritonitis. This study showed that CSA was safe in this population of dogs and caused an initial increase in serum albumin that was significantly different than the untreated dogs. At the time of discharge or death, however, there was no significant difference in serum albumin levels between the 2 groups. Some limitations to the study included a small population (n = 14 total dogs) and dogs receiving CSA were only administered 1 dose (eg, after surgical intervention for septic peritonitis). It is unknown if multiple dosing, if indicated, would improve albumin levels for a longer period of time, providing a prolonged duration of effect. In addition, the study was not powered to assess outcome, so it is still not known if there is a survival benefit or decreased hospitalization when dogs with septic peritonitis are administered CSA.

Based on these studies, the use of HSA should be reserved for critically ill veterinary patients with a life-threateningly low albumin (eg, septic peritonitis). It should not be routinely used for patients with a low COP; rather, a safer synthetic colloid, such as an HES, can be used. If considering use of an albumin source (rather than a synthetic colloid), the alternative use of CSA over HSA seems a safer option for use in dogs; however, it is unclear if the use of concentrated albumin products decrease hospitalization time or improve survival compared with dogs with similar disease that do not
receive albumin products. A comparative, prospective veterinary study is required to more fully answer these questions.

SYNTHETIC COLLOIDS

Synthetic colloids, such as dextrans and HESs, are fluids that can be used to increase blood pressure and support COP. The HESs (eg, hetastarch, tetrastarch, and pentastarch) are most commonly used, because dextrans were found to induce renal disease in humans. In veterinary medicine, the use of synthetic colloids in the form of HES are most common, because they are readily available, inexpensive, and carry fewer potential side-effects compared with albumin.

HESs are esterified amylopectin-containing starches that remain in the intravascular space after administration due to its high MW. The differences between hetastarch, pentastarch, and tetrastarch are the average MW of the particles and the degree of substitution of glucose units on the starch particle with a hydroxyethyl group. Hetastarch (450 kDa) has the highest average MW, with pentastarch (260 kDa) and tetrastarch (130 kDa) having lower MWs. The MW of the product and the degree of substitution (hetastarch 0.5, pentastarch 0.45, and tetrastarch 0.4) determine the exerted COP of the fluid and the degradation time. The higher the substitution with hydroxyethyl groups, the longer the fluid persists in the intravascular space. Therefore, hetastarch lasts approximately 24 hours after administration, whereas pentastarch and tetrastarch lasts approximately 12 hours. Serum α-amylase degrades the HESs, and elimination occurs through the kidneys. When describing HES solutions, 3 numbers are used: the concentration of the HES solution, the MW, and the degree of substitution of hydroxyethyl groups/glucose unit.

Some key factors describing HES solutions include the following:

1. The concentration of HES solutions, commonly 6%, is iso-osmolar.
2. The higher the average MW of the HES solution, the longer the solution lasts, because larger molecules are more slowly degraded.
3. The degree of substitution of hydroxyethyl groups per glucose molecule is reported as a decimal percent. For example, hetastarch has a degree of substitution between 0.6 and 0.75, meaning that 60% to 75% of the glucose molecules contain a hydroxyethyl group at either the carbon-2 or carbon-6 position. The higher the degree of substitution, the longer the colloidal effects last, because the molecules are metabolized more slowly.

Side effects can also be seen with synthetic colloids and include influencing in vitro coagulation and increasing the potential for volume overload due to the efficacy of expanding intravascular volume. Coagulation abnormalities are more likely with the higher MW HES and at doses of greater than 20 mL/kg/d and include decreased circulating factor VIII and von Willebrand factor, platelet dysfunction, and decreased fibrin clot stabilization. Clinical manifestation of coagulation abnormalities secondary to the use of high MW HES has not been reported in the veterinary literature. Synthetic colloid administration may be safer and more effective than using concentrated albumin solutions for the treatment of low COP due to lower risk of immune reactions and increased effectiveness as a colloid due to its variation in size (eg, molecules larger than albumin may not leak through vessels).

SUMMARY

Fluid therapy is essential in the treatment of emergent veterinary patients and includes crystalloid solutions, blood component therapy, concentrated albumin solutions, and
synthetic colloids. Bolus IV fluid therapy can restore perfusion and stabilize critically ill and injured patients for further diagnostics and treatment. Synthetic colloids help to maintain COP and improve blood pressure but should be used with caution in coagulopathic patients or those with cardiac disease. Concentrated albumin solutions may have a role in the treatment of critically ill veterinary patients with severe hypoalbuminemia (eg, septic peritonitis); further prospective, comparative studies are needed to fully elucidate the role of albumin solutions in dogs and cats.

REFERENCES