Fluid and electrolyte therapy in the perioperative period continues to challenge veterinary clinicians, and no aspect of anesthesia is more important to recognize and manage. Patients are presented for anesthesia and surgical/diagnostic procedures in various states of physical condition and disease processes. Any significant fluid and electrolyte imbalances need to be identified, evaluated, and corrected prior to anesthesia. In addition, physiological changes are anticipated to occur during the perioperative period with the administration of drugs that provide chemical restraint and anesthesia. Most anesthetics decrease the force of myocardial contraction and relax blood vessels, leading to an increased vascular volume which results in a decrease in cardiac output and arterial blood pressure.

Not only do anesthetic agents have a significant effect on the cardiovascular stability of the patient, but the fluid balance and fluid requirements in many anesthetized surgical patients are altered. Especially in ill patients, these changes may be due to vasodilation; vasoconstriction; poor cardiac function; vascular leakage; changes in fluid composition; ongoing fluid losses due to hemorrhage, redistribution, and sequestration of fluids into traumatized tissue; and evaporation from respiratory and surgical sites. If significant, a decrease in intravascular volume can lead to poor perfusion and reduced oxygenation to the tissue capillary beds, resulting in a cellular energy deficit. As the integrity of the vessels is compromised, the changes in vascular tone result in maldistribution of fluid between the intravascular, interstitial, and intracellular compartments.
The goal of maintaining fluid balance in the perioperative period is to ensure perfusion and hydration to supply oxygen to the tissues. The successful outcome of the planned procedure depends on an integrated approach initiated during the evaluation of the patient preoperatively and carried through the postoperative period. For these reasons, knowledge of fluid therapy enhances the appropriate management of anesthetic cases.

**BODY FLUID AND ELECTROLYTE COMPOSITION**

**Body Water Distribution**

Water is the largest component in any species, and the overall percentage of body composition varies with age. Total body water at birth is greater than 75% of the body weight; as an animal matures, total body water is reduced to approximately 60% of the adult’s body weight.13,15 Thus, in a 20-kg adult dog, the total body water would be anticipated to equal about 12 L and is distributed into two functional compartments: the intracellular and extracellular spaces. The intracellular fluid volume increases slightly with age; in the mature animal, it is equal to about 40% of the body weight or 8 L in the above 20-kg patient. The volume of the extracellular fluid compartment decreases with maturation and comprises approximately 20% (or 4 L in a 20-kg patient) of the adult weight. The extracellular fluid volume is further divided into the interstitial space containing three quarters of the extracellular fluid (or 15% of the animal’s weight) and the intravascular space containing one quarter (or 5% of the body weight) of the extracellular fluid water.13,23 Total body water content is reduced in obese patients. Whether an administered fluid remains in the intravascular space or moves into the interstitial and intracellular space depends on two factors: fluid dynamics between the compartments and composition of the fluid.

**Dynamic Exchange of Water**

Most of the cell membranes of the body are permeable to water but not to most solutes. In the process of osmosis, the concentration of nonpermeative solutes is greater on one side of the membrane than on the other; thus, water passes through the membrane toward the side with the greater concentration of nonpermeative solutes.9 The net result is diffusion of water molecules across the membrane from the area of high water concentration to the side with the higher concentration of nonpermeative ions. The amount of pressure required to oppose this water movement across the membrane is called the “osmotic pressure” and is determined by the number of nonpermeative particles in the solution. The ability of the solutes to cause osmosis and osmotic pressure is measured in terms of osmoles or milliosmoles. An osmole is the
amount of substance that dissociates in the solution to form 1 mol of osmotically active particles. The osmotically active substances in body fluids include sodium, potassium, calcium, magnesium, chloride, bicarbonate, phosphates, sulfates, phosphocreatine, carnosine, amino acids, creatine, lactate, adenosine triphosphate, hexose monophosphate, glucose, protein, and urea. The osmolality of a solution is the concentration of osmotically active particles in the solution and is expressed as osmoles of solute per kilogram of solvent.

The capillary membrane consists of cells that rest on a basement membrane. The pores between the cells of the capillary membrane are larger than the pores in cell membranes, resulting in the capillary membrane being more permeable than most cell membranes. In addition, unlike most cell membranes, the capillary membrane is permeable to all of the ions in plasma, except for the plasma protein ions. The key factor that restrains fluid loss from the capillaries is the osmotic pressure of the plasma proteins and is called the “colloid osmotic pressure” or “oncotic pressure.” Protein molecules cause oncotic pressure only when they cannot pass through the capillary pores and are reflected instead of passing through the membrane. This reflection at the capillary pores maintains the plasma concentration of proteins at approximately three times that of the interstitial fluid. Electrostatic forces can also affect the movement of charged particles across membranes. If no difference in electrical charge exists across a permeable membrane, the system is in equilibrium. The oncotic pressure generated by plasma protein is greater than predicted on the basis of protein concentration alone. One reason for this behavior of albumin is its negative charge at the blood pH and the attraction and retention of cations (primarily sodium) in the vascular compartment. This is called the “Gibbs-Donnan effect.”

**Body Solutes Distribution**

Sodium is the major cation in the extracellular fluid. Water balance in the body is dependent on the strict regulation of the plasma sodium concentration and is maintained with hormones such as renin, aldosterone, and plasma atrial natriuretic peptide. Bicarbonate and chloride are the most abundant anions in the extracellular fluid. The primary intracellular cation is potassium, and magnesium is also present to a lesser degree. The intracellular concentration of potassium and the extracellular gradient for sodium are maintained by the active sodium-potassium adenosine triphosphatase pump, which shuttles sodium out of the cell and potassium into the cell. Proteins and phosphates are the primary intracellular anions. In a normal state, the force generated by sodium, chloride, and bicarbonate ions in the extracellular compartment is balanced by that generated by potassium, magnesium, and phosphate ions in the intracellular compartment.
Exchange of Water Between the Interstitium and Plasma

Any water or ion-containing fluid (crystalloid) administered into the vasculature can move across the capillary membrane. Water and solutes are continuously moving from the capillaries into the interstitium; however, not all the dose of a crystalloid administered intravenously passes into the interstitium. The relationship between hydrostatic pressure and oncotic pressure and the role of these forces in regulating fluid passage across the capillary membrane were described by Starling’s hypothesis:

$$\text{Fluid movement} = k[P_c + \pi_i] - (P_i + \pi_p) - Q_{\text{lymph}}$$

where $P_c$ is capillary hydrostatic pressure, $P_i$ is interstitial fluid hydrostatic pressure, $\pi_p$ is plasma protein oncotic pressure, $\pi_i$ is interstitial fluid oncotic pressure, $k$ is filtration constant for the capillary membrane, and $Q_{\text{lymph}}$ is lymph flow returning interstitial fluid and albumin back to the circulation. Fluid filtration occurs when the algebraic sum is positive, and absorption occurs when it is negative. Conditions that increase the movement of fluid from the intravascular space into the interstitium include intravascular volume overload, hypertension, and hypoalbuminemia, and these conditions can cause the hydrostatic pressure to exceed the oncotic pressure. Increased fluid movement could also result from an increase in capillary membrane pore size in cases of inflammation or vasculitis, where both colloid and fluid leak into the interstitium. The network of lymphatics in these situations is responsible for the uptake of the excess interstitial fluid and protein and for returning it to the intravascular compartment. The capacity of the lymphatics may be overwhelmed, resulting in interstitial edema. An increased oncotic pressure or decreased hydrostatic pressure favors reabsorption. If severe enough to cause hypovolemia, dehydration would increase oncotic pressure as hydrostatic pressure decreases.

If water is added to one compartment, it normally distributes evenly, and the amount of volume added to any given compartment is proportional to its fractional representation of total body water. Therefore, if 1 L of free water is administered to the intravascular space, a minimal increase in intravascular volume occurs due to equilibration. Only about 10% of the free water infused remains in the intravascular space after approximately 30 minutes postinfusion.8,19

INDICATIONS FOR FLUIDS

The indications for administration of parenteral fluids can be divided into maintenance and replacement requirements. The normal daily maintenance fluid and electrolyte requirements are based on both sensible and insensible fluid losses.3,16 Replacement fluids are used in an
attempt to maintain effective perfusion and oxygen delivery in situations in which an acute reduction in intravascular volume or an acute electrolyte and acid base disturbance results in poor perfusion and hypoxia. In anesthesia cases, administering fluids help to maintain vascular volume to counteract the effects of anesthetic drugs or a disease process and provides vascular access in the event that emergency drug therapy is required. In addition, administering fluids helps to normalize acid-base and electrolyte abnormalities and can be used for nutrition support.

COMPOSITION OF PARENTERAL SOLUTIONS

The composition of the fluid along with capillary dynamics determines how the administered fluid is distributed. The two major categories of administered fluids are crystalloids and colloids. Several types of parenteral fluids are available to treat specific conditions, and this topic is covered extensively elsewhere.16

Crystalloid Preparations

A crystalloid is an aqueous solution with small particles that are normally osmotically active in body fluids and can pass through the capillary membrane. Examples of crystalloids include normal saline, lactated Ringer’s solution, hypertonic saline, and 5% dextrose in water (Table 1). If the electrolyte composition of the prepared solution approximates that of extracellular fluid, the parenteral fluid is referred to as a “balanced” electrolyte solution. Electrolyte solutions are administered based on the concept that the patient controls whatever water and electrolytes are retained by intact regulatory mechanisms and not by the amount of water and electrolytes received. Parenteral fluids provide water, electrolytes, and, in some instances, alkalinizing agents or a source of calories, or both.

Movement of fluid across the cell membranes is determined by the tonicity of the fluid. The osmolality of the fluid in comparison to the intracellular osmolality is called the “tonicity” of the fluid. Regardless of their tonicity, crystalloid solutions equilibrate with the interstitial and intracellular compartments.

Isotonic Fluids

Fluids that have the same osmolality as the intracellular compartment cause no change in cell volume and are called “isotonic” fluids; they may be either crystalloid or colloid in origin. Lactated Ringer’s solution and normal saline are isotonic crystalloids. Plasma, whole blood, and synthetic colloids are isotonic colloids. Isotonic fluids cause no swelling or shrinkage of tissue cells and therefore expand only the
Table 1. COMPOSITION OF SELECTED CRYSTALLOID SOLUTIONS COMPARED TO PLASMA

<table>
<thead>
<tr>
<th></th>
<th>0.9% Saline</th>
<th>Lactated Ringer’s Solution</th>
<th>Normosol-R</th>
<th>7.5% Saline</th>
<th>5% Dextose</th>
<th>Plasma</th>
</tr>
</thead>
<tbody>
<tr>
<td>Na⁺ (mEq/L)</td>
<td>154</td>
<td>130</td>
<td>140</td>
<td>1283</td>
<td>—</td>
<td>145</td>
</tr>
<tr>
<td>K⁺ (mEq/L)</td>
<td>—</td>
<td>4</td>
<td>5</td>
<td>—</td>
<td>—</td>
<td>5</td>
</tr>
<tr>
<td>Ca²⁺ (mEq/L)</td>
<td>—</td>
<td>3</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>5</td>
</tr>
<tr>
<td>Mg²⁺ (mEq/L)</td>
<td>—</td>
<td>—</td>
<td>3</td>
<td>—</td>
<td>—</td>
<td>1.5</td>
</tr>
<tr>
<td>Cl⁻ (mEq/L)</td>
<td>154</td>
<td>109</td>
<td>98</td>
<td>1283</td>
<td>—</td>
<td>103</td>
</tr>
<tr>
<td>HCO₃⁻ (mEq/L)</td>
<td>—</td>
<td>28 (as lactate)</td>
<td>50 (acetate, 27)</td>
<td>—</td>
<td>—</td>
<td>27</td>
</tr>
<tr>
<td>HPO₄²⁻ (mmol/L)</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>2</td>
</tr>
<tr>
<td>Tonicity (mOsm/L)</td>
<td>Isotonic (308)</td>
<td>Isotonic (273)</td>
<td>Isotonic (273)</td>
<td>Hypertonic (2566)</td>
<td>Hypotonic (252)</td>
<td>Isotonic (290)</td>
</tr>
<tr>
<td>Glucose</td>
<td>5.4</td>
<td>6.7</td>
<td>7.4</td>
<td>—</td>
<td>4.0</td>
<td>7.5</td>
</tr>
<tr>
<td>pH</td>
<td>5.4</td>
<td>6.7</td>
<td>7.4</td>
<td>—</td>
<td>4.0</td>
<td>7.5</td>
</tr>
<tr>
<td>Colloid oncotic pressure (mm Hg)</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>20</td>
</tr>
</tbody>
</table>
extracellular space. Isotonic fluids can either replace or maintain the sodium and water composition of extracellular body fluids.

**Hypotonic Fluids**

Hypotonic fluids have an osmolality less than that of intracellular fluid. The crystalloid 5% dextrose in water is a hypotonic fluid, but as there is no sodium, it does not produce osmolality. The dextrose does provide osmotically active particles that make the fluid isotonic, but once the dextrose is metabolized, free water is left to be distributed into the intracellular and extracellular spaces. Thus, 5% dextrose in water is not used for volume resuscitation, intravascular maintenance, or interstitial volume replacement.

**Hypertonic Fluids**

Hypertonic fluids have significantly more osmotically active particles per unit of volume or weight compared to intracellular fluid and cause water movement from the interstitial and intracellular spaces into the intravascular space, thus increasing the interstitial sodium concentration and interstitial tonicity and causing intracellular dehydration. Once an equilibration is reached across the capillary membrane, the resultant intravascular hydrostatic pressure increase can push sodium and water back into the interstitial space. Hypertonic saline solutions of 5.0% and 7.5% have been used in the management of severe shock, particularly hemorrhagic shock, to provide hypovolemic resuscitation as well as possible benefits from mild positive inotropic effect and systemic and pulmonary vasodilation. Hypertonic saline rapidly increases preload for only approximately 30 minutes postinfusion. Estimated safe doses are 6 to 10 mL/kg with a maximum infusion rate of 1 mL/kg/min for a 5.0% solution and 4 to 8 mL/kg with a maximum infusion rate of 1 mL/kg/min for a 7.5% solution. More rapid infusion rates result in vagally mediated hypotension and bradycardia, bronchoconstriction, and rapid and shallow breathing. It is important that appropriate volumes of fluid or colloid be administered following hypertonic saline to maintain any improvement from its administration.

**Colloids**

Colloid solutions contain large particles that do not readily leave the intravascular space and attract and hold water in the vascular space, thereby expanding vascular volume and exerting osmotic pressure in a manner similar to that of plasma proteins. Natural colloids include plasma, albumin preparations, and whole blood. Artificial colloids include dextran, gelatin preparations, and hydroxyethyl starch (Table 2). The effectiveness of the artificial colloids is dependent on their physiochemical properties such as molecular weight, colloid content, and bio-
Table 2. COMPOSITION OF SELECTED COLLOID SOLUTIONS COMPARED TO PLASMA

<table>
<thead>
<tr>
<th></th>
<th>Whole Blood</th>
<th>6% Hetastarch</th>
<th>Dextran 40</th>
<th>Dextran 70</th>
<th>Frozen Plasma</th>
</tr>
</thead>
<tbody>
<tr>
<td>Na⁺ (mEq/L)</td>
<td>140</td>
<td>154</td>
<td>154</td>
<td>154</td>
<td>140</td>
</tr>
<tr>
<td>K⁺ (mEq/L)</td>
<td>4</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>4</td>
</tr>
<tr>
<td>Cl⁻ (mEq/L)</td>
<td>100</td>
<td>154</td>
<td>154</td>
<td>154</td>
<td>110</td>
</tr>
<tr>
<td>HCO₃⁻ (mEq/L)</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>HPO₄²⁻ (mmol/L)</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Tonicity (mOsm/L)</td>
<td>Isotonic (300)</td>
<td>Isotonic (310)</td>
<td>Isotonic (310)</td>
<td>Isotonic (310)</td>
<td>Isotonic (290)</td>
</tr>
<tr>
<td>Glucose</td>
<td>0-4 g/L</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>0-4 g/dL</td>
</tr>
<tr>
<td>pH</td>
<td>Variable</td>
<td>5.5</td>
<td>3.5-7.0</td>
<td>3.0-7.0</td>
<td>Variable</td>
</tr>
<tr>
<td>Colloid oncotic</td>
<td>20</td>
<td>32</td>
<td>40</td>
<td>Approximately 40</td>
<td>20</td>
</tr>
<tr>
<td>pressure (mmHg)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
The selection of a colloid for administration is based on its ability to expand intravascular volume and maintain oncotic pressure, thus maintaining perfusion pressures when crystalloids alone are inadequate. Synthetic colloids are more expensive than plasma but may be more readily available for intraoperative situations requiring colloids. Colloids are useful in patients that are hypovolemic and hypoproteinemic, traumatized and hypovolemic, hypovolemic with cerebral or pulmonary edema, or hypotensive and in shock. Colloids are also beneficial in patients with sepsis as well as in those with third-space losses such as ascites and or peripheral edema. Colloids often are used in combination with hypertonic saline to increase the duration of effect of the hypertonic saline and to reduce the volume of crystalloid needed to achieve and maintain adequate systemic arterial blood pressure and tissue perfusion.

**Synthetic Colloids**

Hetastarch is a synthetic polymer of amylopectin that has been hydroxylated and was developed for the treatment of hypovolemia. In animals, hetastarch has been used as a volume expander during shock and as a synthetic substitute in hypo-oncotic patients. Following a single dose of hetastarch, the mean colloid oncotic pressure was significantly higher than the mean colloid oncotic pressure prior to treatment. Intravenous administration of 1 L of hydroxyethyl starch expands the plasma volume by approximately 700 mL. The effect of a single dose of hetastarch on raising colloid oncotic pressure in dogs with hypoalbuminemia decreases significantly within 12 hours of administration; therefore, multiple doses are necessary to prolong the beneficial effects of hetastarch.17 The recommended dose of hetastarch in dogs is 10 to 40 mL/kg/d intravenously given in 5- to 10-mL/kg boluses until the end point of resuscitation is reached.22 The recommended dose for hetastarch in cats is 5 to 10 mL/kg/d but may be increased based on individual circumstances. The end point would be an improvement in perfusion, an increase in blood pressure, and a normalization of heart rate (Table 3). The goal would be to use the smallest volume of colloid possible to restore intravascular volume. In patients treated with synthetic colloids, the colloid oncotic pressure is increased without a significant change in refractometrical total solid readings; therefore, monitoring of synthetic colloids is best performed by direct measurement of colloid oncotic pressure or by observing resolution of the clinical signs of hypovolemia.2

Hetastarch molecules vary in size from 10,000 to 1,000,000 d, with the degree of substitution with hydroxyethyl groups important in the metabolism of the drug. The more substituted the parent molecule, the slower is the degradation process and longer is its persistence in the blood. There are three routes of elimination for hetastarch.17, 30 Seventy percent to 80% of elimination is via filtration through the glomeruli of the kidneys, with an initial rapid phase and a slower second phase; the rate is dependent on the size of the hetastarch molecule. Molecules less
than 59,000 d are filtered through the glomeruli in the rapid phase, and the larger molecules are slowly hydrolyzed by serum alpha amylase and then filtered through the glomeruli during the second slower phase. The degree of hydroxylation of the molecule delays the metabolism of hetastarch, thereby prolonging its excretion. The second route of elimination (20%-30%) is extravasation, uptake, and temporary storage of hetastarch molecules in the cells of the reticuloendothelial system of the liver, spleen, and lymph nodes. The hetastarch molecules are then thought to be catabolized by proteolytic enzymes in the reticuloendothelial cells. A third and minor route of elimination is through the gastrointestinal tract.

Dextrans are linear polysaccharide molecules synthesized by Leuconostoc mesenteroides (strain B12) growing in sucrose medium. The dextrans are hydrolyzed to dextrans 70 and 40. High-molecular-weight dextrans such as dextran 70 may increase intravascular sludging of red blood cells, which limits its use in cases of severe shock. Dextran 70 has an average molecular weight of 70,000 d and is prepared in a 6% solution in 0.9% sodium chloride. It contains 60 g/L of colloid and 154 mEq/L each of sodium and chloride, and it has an osmolality of 310 mOsm/kg. Dextran 70 is hyperoncotic compared to plasma and thus expands plasma volume. The infusion of 1 L of dextran 70 expands plasma volume by 800 mL; however, less than 30% of the infused dextran 70 is retained within the vascular compartment 4 to 6 hours postinfusion, thereby losing its initial volume-expanding effect.

Dextran 40 (molecular weight 40,000 d) in 0.9% sodium chloride contains 100 g/L of colloid, has an osmolality of 310 mOsm/kg, and is hyperoncotic to plasma. Administration of 1 L of 10% dextran 40 in 0.9% sodium chloride increases plasma volume by 1000 mL for approximately 2 to 6 hours. The shorter duration of dextran 40 is due to its lesser molecular weight, allowing more rapid removal from the intravascular space and renal excretion. Dextran 40 does not cause sludging of red blood cells and increases the partial pressure of oxygen in dogs with severe hemorrhagic shock. Anaphylactic reactions may occur with either
dextran 40 or 70, but the incidence is relatively low. Dextran reduces clotting levels by hemodilution, coating blood vessel walls and cellular elements, and impairs the elasticity and tensile strength of the fibrin clots. Dextran 70 impairs coagulation more than dextran 40. Hemostatic problems occur more readily in thrombocytopenic patients and in patients with renal disease because of uremic platelet dysfunction. The recommended dose of dextrans is 10 to 20 mL/kg/d in dogs and 5 to 10 mL/kg/d in cats.\(^6\)

Concentrated colloids are not considered to be hypertonic because they do not promote the movement of water out of the cells. If concentrated albumin is given intravascularly, water and sodium move from the interstitium into the vascular space as a result of the Gibbs-Donnan effect. The potentially reduced fluid volume in the interstitium is still isotonic and thus does not promote the shift of fluid from the intracellular space.

**Natural Colloids**

Plasma proteins play a predominant role in establishing plasma oncotic pressure and are responsible for maintaining vascular volume at the capillary level. Albumin (69,000 d) is the principal oncotic protein in blood, contributing about 75% of normal colloid oncotic pressure; globulins and fibrinogen contribute the remainder.\(^6\) Reductions in serum albumin concentrations to 15 g/L (1.5 g/dL) or in total serum protein levels to 35 g/L (3.5 g/dL) or lower result in a net water loss from the vascular compartment to the interstitial space. If untreated, vascular volume diminishes and interstitial edema occurs.

Plasma is harvested from whole blood and either used as fresh plasma for the treatment of coagulopathies or stored at \(-70^\circ\)C as fresh-frozen plasma.\(^{29}\) A blood administration set with an in-line filter (170–260 \(\mu\)) is used for intravenous administration of plasma. If the plasma of the donor is 30 to 35 g/L, the recipient should receive 28 to 33 mL/kg of plasma in order to administer 1 g/kg of albumin; alternatively, one may calculate the total protein deficit by multiplying the plasma protein deficit by the estimated plasma volume of the patient.\(^{29}\) One should be watchful of possible patient allergic reactions and take care not to volume overload the patient.

Natural colloids contain more than just oncotic proteins. Fresh whole blood also contains red blood cells, coagulation factors, platelets, white blood cells, and antithrombin. Severely anemic patients or patients with a significant decrease in their packed cell volume from normal are candidates for whole blood transfusion or the administration of packed red blood cells if plasma proteins are normal. Red blood cells provide hemoglobin for carrying oxygen to tissues. Considering the cardiopulmonary effects of most anesthetic agents, maintaining a hematocrit of at least 25% in the surgical patient helps to ensure that there is adequate oxygen delivery in the perioperative periods during excitement when increased oxygen demands occur. Transfusion reactions are more common with blood products containing red blood cells. Blood-typing and
crossmatching, collection, storage, administration of blood, and potential side effects associated with the infusion of whole blood have been extensively reported elsewhere.14

**ALTERNATIVES TO BLOOD TRANSFUSIONS: BLOOD SUBSTITUTES**

Transfusion of blood is currently the standard treatment for restoring tissue oxygen delivery following significant blood loss. Despite the technological and scientific advances in transfusion medicine, however, blood transfusion is both an expensive and time-consuming procedure. Crossmatching and blood-typing, collection, and storage procedures restrict the use of blood products in an emergency situation, especially in small veterinary practices dependent on a paucity of donors from client- or hospital-owned animals, thus limiting the availability of blood products for most practices.11 For these reasons, there is a clear role for an effective and safe blood substitute that is readily available in large quantities. Early in the twentieth century, anemic patients were treated with cell-free hemoglobin solutions. These experiments had multiple adverse effects such as hypertension, bradycardia, oliguria, and anaphylaxis due to unstable solutions. Contaminants like stromal phospholipids, endotoxin, and nonhemoglobin proteins were likely the causes of the early toxicities. Research and development of red blood cell substitutes intensified in the 1980s, primarily as a result of transmission of the acquired immunodeficiency syndrome by the blood-borne human immunodeficiency virus. This research led to the development of hemoglobin conjugated to synthetic materials such as dextrans, polyethylene glycol, and superoxide dismutase; hemoglobin encapsulated in liposomes; and synthetic hemes that bind or chelate oxygen. New problems arose with the use of cell-free hemoglobin such as the interaction of hemoglobin with nitric oxide and oxygen radicals and the effect of hemoglobin on the immune system.28

An ideal blood substitute should be nontoxic, free of pathogens, capable of transporting oxygen and carbon dioxide, have a long shelf life, and be available at a reasonable cost. Oxygen carriers should have characteristics similar to those of blood, including oxygen affinity, viscosity, plasma retention time, and colloid osmotic pressure.

A hemoglobin-based oxygen-carrying fluid derived from bovine hemoglobin (Oxyglobin; Biopure Corp., Cambridge, MA) has recently been approved by the United States Food and Drug Administration for the treatment of anemia in dogs. Oxyglobin is an ultrapurified polymerized bovine hemoglobin in a modified lactated Ringer’s solution. It contains 13 g/dL of hemoglobin and has an osmolality comparable to the blood’s osmolality of 300 mOsm/kg. Oxyglobin picks up and releases oxygen in a manner similar to that of red blood cells; however, the majority of the oxygen content of the blood is shifted to the plasma. The sterile oxyglobin solution has a pH of 7.8 and a P50 value of 35 mm Hg.
P50 is the partial pressure of oxygen when 50% of the hemoglobin is saturated. The P50 value of oxyglobin is modified to be higher than red blood cell hemoglobin so that the onloading and off-loading of oxygen occurs easier and facilitates delivery of oxygen to the tissue bed. Oxyglobin's affinity for oxygen is regulated by chloride, making the oxygen offloading immediate. The factor that drives the oxygen availability in stored blood is 2,3-diphosphoglycerate which may not exist in adequate quantities in patients with blood loss.

Oxyglobin is metabolized and eliminated via the reticuloendothelial system. Approximately 90% of the administered dose is eliminated from the body 5 to 7 days after the infusion. Less than 5% of oxyglobin existing as an unstabilized tetramer is cleared via the kidneys, resulting in transient hemoglobinuria.

Oxyglobin has a 2-year shelf life at room temperature. It requires no cross-matching or blood-typing prior to use because it contains no red cell membranes. Oxyglobin provides enhanced oxygen delivery by increasing the oxygen content of the plasma because of its low viscosity, therefore improving oxygen delivery without increasing cardiac work.

**Indications**

Oxyglobin is indicated for the treatment of anemia due to hemolysis, blood loss, or ineffective erythropoiesis. The improvement in arterial oxygen content following its administration has a duration of about 24 hours. Thus, oxyglobin acts as an oxygen-carrying bridge while the patient regenerates its red blood cells or until additional oxygen-carrying support in the form of blood is obtainable. The recommended dosage of oxyglobin in dogs is a one-time dose of 30 mL/kg administered intravenously at a rate of up to 10 mL/kg/h. The patient should be monitored closely for signs of circulatory overload by lung auscultation and by measuring central venous pressure and respiratory rate. Oxyglobin has been employed in an experimental model of feline hemorrhagic shock. Using 20 mL/kg of oxyglobin for resuscitation, the investigators found almost immediate increases in mean arterial pressure and central venous pressure when it was compared to resuscitation with autotransfused blood or 6% hydroxyethyl starch at the same volumes. This increase was thought to be related to nitric oxide scavenging. Oxyglobin restored oxygen delivery as effectively as autotransfused blood. Pulmonary edema was noted in cats receiving oxyglobin or autotransfused blood. This might have been a dose-related and or rate of delivery problem in cats.

**Special Considerations**

The presence of oxyglobin in serum may result in artifactual increases or decreases in some serum chemistry tests depending on the
Gastrointestinal insufficiency increases mL/kg/h, hemoglobin no post-infusion. Potentially expanding patients, transiently, dilution. Concentration of oxyglobin on the oxygen content of the blood. In anemic patients, if hypoxemia is not present, the limited number of red blood cells is still fully saturated. Treatment with oxyglobin results in volume expansion and thus a posttreatment decrease in hematocrit due to hemo-dilution. Hemoglobin and not hematocrit should be used to monitor the degree of anemia postinfusion. Instruments calculating hemoglobin concentration based on hematocrit are not accurate, because hematocrit no longer equals three times the hemoglobin concentration. Therefore, hemoglobin must be measured directly.

**Adverse Effects**

The most common side effects observed following oxyglobin administration are a transient discoloration from yellow to red of mucous membranes and sclera. This occurs because the hemoglobin solution can be seen in the capillary bed and should resolve 3 to 5 days post-infusion. Gastrointestinal side effects, including vomiting and diarrhea, may occur post-infusion. Circulatory overload may occur due to the plasma-expanding properties of oxyglobin. This may happen due to administration at an excessive rate or too much volume. Central venous pressure increases significantly within 2 to 7 hours of the onset of infusion and potentially can develop into pulmonary edema if steps are not taken to decrease or interrupt the infusion. When administered at less than 10 mL/kg/h, no complication of volume overload occurs in normovolemic dogs. In patients that are predisposed to pulmonary edema such as those patients that have preexisting cardiovascular disease or mitral insufficiency with congestion, one must be careful in administering not only oxyglobin but any fluid because of the possibility of pulmonary edema.

**FLUIDS AND HEMODYNAMIC CONTROL**

As stated, the goal in the perioperative period is to maintain perfusion to the tissues. Perfusion is a good indicator of intravascular volume, and hydration reflects the volume of the interstitial and intracellular space. Adequate perfusion is a result of intravascular volume, cardiac output, and vascular tone. Some of the parameters that reflect perfusion include the heart rate, pulse rate and quality, capillary refill time, and core-to-peripheral temperature differences. Normally, the baroreceptors
respond to an adequate volume and pressure by providing afferent neural input to balance the sympathetic neural activity to the heart and vessels, with the simultaneous vagal stimulation trying to downregulate the heart rate, thus providing a normal heart rate and preventing profound vasoconstriction in a normal animal with normal perfusion. In cases with a decrease in intravascular volume, cardiac output, or vascular tone, the tension in the vessel wall decreases, and the baroreceptors provide the increased neural input that coordinates an increase in central and peripheral sympathetic efferent neuronal output and suppresses vagal tone discharge, resulting in an increase in heart rate, contractility, and vasoconstriction. Because the response to poor perfusion is mediated by the vessel wall tone, the clinician must administer fluids that remain in the intravascular compartment to halt the baroreceptors' sympathetic response and return tissue perfusion to normal.

Hydration is the water content of the extravascular compartment, which is composed of the interstitial and intracellular compartments; therefore, a fluid deficit of these compartments is called "dehydration." Intracellular dehydration causes an increase in intracellular osmolality, and water moves from the interstitial space into the intracellular space, thus creating an increase in the interstitial osmolality. This results in water moving from the intravascular space to help restore the interstitial deficits. The resultant intravascular deficit, especially in patients with severe dehydration, leads to poor perfusion of the tissues. To replenish the fluid in the extravascular spaces in this situation, crystalloid fluids that are of the same tonicity as plasma are used. Replenishing the interstitial volume deficit is called "rehydration." If the dehydration is severe enough to cause poor perfusion, a combination of crystalloid and colloid should be selected to replenish both the interstitial and the intravascular compartments.

Fluids and Disease

The fluid dynamics described above change during many disease processes to increase the permeability of the capillaries and postcapillary venules. In the systemic inflammatory response syndrome resulting from parvoenteritis, septic shock, massive trauma, systemic neoplasia, heatstroke, and other conditions, the endothelial junctions in the capillary membranes may increase in size and number, resulting in a loss of albumin through the capillary wall because of a loss of the reflection coefficient. Depression of electrogenic pumps can lead to accumulation of sodium and water as well as to increased water accumulation of the intracellular and interstitial spaces which further damages the cell membrane. The resulting hypoalbuminemia leads to a decrease in plasma oncotic pressure and a loss of intravascular fluid, thus giving rise to a decrease in perfusion. Crystalloid fluids administered in such diseases with increased vascular permeability hasten the movement from the intravascular to the interstitial space. The goal in such a situation
would be to restore and maintain the patient's intravascular volume without overloading the interstitial space until the effects of the inflammatory processes have subsided. This goal would best be accomplished by using a combination of crystalloids and colloids.

Patients with systemic inflammatory response syndrome often have large amounts of fluid entering third spaces, for example, an actual or potential body cavity that does not participate in fluid exchange with the normal fluid compartments. Fluid leaks from the local interstitial and intravascular compartments because of hemorrhage or regional inflammation and increased vascular permeability. Fluid lost into the gastrointestinal tract, peritoneal cavity, and hematomas in trauma patients are examples of third-space fluid loss. Losses into third spaces add to the challenge of assessing the quantity of fluid required for restoration and maintenance of adequate perfusion and hydration. The combination of colloids and crystalloids helps to replace intravascular and interstitial deficits and minimizes ongoing fluid loss into third spaces.

**FLUID PLAN**

If the goal is to improve tissue perfusion, the clinician must decide on the type of fluid best suited for improving tissue perfusion with the fewest complications and side effects. The reasons why isotonic crystalloids should be considered for the replacement of interstitial volume have been stated; however, the infusion of crystalloids decreases intravascular oncotic pressure by diluting the concentration of the non-permeable protein anions. Therefore, the loss of osmotic gradient, the ability of water and solutes to pass through the membranes, and the increase in intravascular hydrostatic force cause the movement of the administered crystalloid into the interstitial space. Again, less than 10% of the volume of the isotonic crystalloid infused intravascularly remains there after 1 hour.\textsuperscript{6, 19}

Whole blood, plasma, and synthetic colloids are isotonic, but they primarily replace intravascular volume by drawing water into the intravascular compartment from the interstitial space and retaining it there, because the colloid molecules cannot pass through the capillary walls. Colloid administration results in little or no water movement from the intracellular space. If rapid expansion of plasma volume is needed, colloids are superior to crystalloids. It has been estimated that 3 to 12 times more volume of crystalloid may be needed to achieve the same increase in plasma volume. The time required to resuscitate a hypovolemic patient with crystalloids is reported to be twice that of colloids.

If the goal is to replenish the entire extracellular space, crystalloids are the fluids of choice; however, the amount of crystalloid fluid that remains in the vascular space in hypo-oncotic patients is even less than 10%. Therefore, treating hypo-oncotic patients with crystalloid solutions increases the risk for development of pulmonary and cerebral edema. Low plasma colloid oncotic pressure has been shown to be associated
with increased mortality in critically ill humans. Therefore, colloid solutions are being used to treat hypovolemia, especially in hypo-oncotic patients.

**SUMMARY**

A fluid therapy plan for a patient is developed prior to surgery and is designed to meet each patient's needs. The volume and type of fluid are dependent on the patient's physical status; the acid-base, fluid, and electrolyte status; the surgical procedure; and the expected losses occurring during the procedure. No one fluid regimen is ideal for all patients. All fluid regimens must be continually re-evaluated. A brief minor surgical procedure in a healthy surgical candidate requires little or no fluid administration. In cases of more extensive surgical procedures involving invasion of the abdomen or chest as well as in cases with trauma and major blood loss, much more volume and a specific balanced replacement fluid are required. Depending on the severity of the surgical case, administration rates of 5 to 15 mL/kg/h or greater of crystalloid may be required to maintain perfusion. These rates are merely guidelines, and resuscitation should continue until the desired end point is reached. Balanced replacement fluids may be used to replace blood loss at a ratio of 3:1 and are added to maintenance and replacement requirements. Blood loss of 20% to 25% of the calculated blood volume or hematocrit values less than 20% are indications for colloids or blood replacement at a ratio of 1:1. The optimal fluid therapy regimen for a patient may involve a combination of crystalloids as well as natural and synthetic colloids, using each type of fluid to obtain and maintain perfusion and oxygenation to the tissues.

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