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Fluid and electrolyte therapy in ruminants

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Why do ruminants need fluids and electrolytes?

Sick neonatal and adult ruminants frequently need fluid therapy to correct imbalances of acid-base, electrolyte, or water and to optimize tissue blood flow, provide nutrients (eg, parenteral nutrition), or treat shock. Acid-base and electrolyte abnormalities usually can be predicted on the basis of the suspected disease process; however, laboratory measurement is required to accurately quantify the magnitude of the derangement. Clinical signs can give clues to the presence of derangements in the absence of laboratory test results. Muscular weakness can result from changes in pH, K^+, and Na^+ or decreased Ca^{2+}. Depression and inappetence may be associated with changes in pH, K^+, and Na^+ or decreased Ca^{2+} and glucose, whereas excitement or mania may be due to decreased Ca^{2+} and Mg^{2+}. Altered hydration status (usually dehydration) can be estimated and quantified using eye position within orbit, extent of skin elasticity, and degree of mucous membrane moistness [1]. The effective circulating blood volume and cardiac output can be estimated and quantified by the clinical assessment of activity level, heart rate, mucous membrane color, capillary refill time, and temperature of the extremities (eg, ears and feet) [2].

Fluid therapy frequently is used to provide immediate and short-term nutrients, although a detailed discussion of parenteral and enteral nutrition is beyond the scope of this article. Enteral nutrition always should be preferred to parenteral nutrition, however, because it is more effective, physiologic, practical, and economic. Enteral nutrition (not parenteral nutrition) is the state-of-the-art treatment for critically ill ruminants.

In the treatment of shock, the first issue is to characterize the cause of shock as being attributable to a circuit or pump problem. There are three main types of circuit problems: (1) hypovolemic shock, as in hemorrhagic shock (iso-osmotic fluid loss) or dehydration (hypo-osmotic, iso-osmotic, or

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hyperosmotic fluid loss); (2) distributive shock, as in septic or endotoxemic shock with increased vascular permeability and pooling of blood in capacitance vessels, thereby creating fluid maldistribution and a "relative" iso-osmotic fluid loss; and (3) obstructive shock, as in thymic lymphosarcoma and traumatic reticulopericarditis, in which there is an obstruction to venous return [3] or cardiac diastolic filling, respectively, with no change in blood volume. There is only one type of shock due to a pump problem (heart failure): cardiogenic shock. Obviously, volume expansion is indicated in hypovolemic and distributive shock and not in obstructive and cardiogenic shock.

What fluids and electrolytes should be administered?

Based on the severity of the clinical signs and the relative probabilities of the differential diagnoses, a decision is made whether or not fluid and electrolyte therapy is needed. If indicated, treatment may be instituted immediately or delayed until laboratory test results are available. Fluids are categorized on the basis of their physical nature (crystalloid or colloid) and osmolarity (hypo-osmotic, iso-osmotic, or hyperosmotic) (Table 1). Iso-osmotic or slightly hypo-osmotic crystalloid solutions most commonly are administered parenterally, although under specific circumstances hyper-osmotic crystalloid solutions or iso-osmotic colloid solutions are preferred.

Crystalloid solutions

A crystalloid is a substance that forms a true solution and is capable of being crystallized. Examples of crystalloid solutions are Ringer's solution, lactated Ringer's solution, acetated Ringer's solution, 0.9% sodium chloride (NaCl), 7.2% NaCl (hypertonic saline), 1.3% sodium bicarbonate ($NaHCO_3$), 8% $NaHCO_3$, calcium gluconate, and 50% dextrose. NaCl is the classic crystalloid because table salt exists as a crystal but dissolves completely when placed in water. Because crystalloids dissolve completely in water, crystalloid solutions containing sodium distribute throughout the entire extracellular fluid space and are not confined to the intravascular space. Sodium-containing crystalloid solutions always are indicated in hypovolemia (a circuit problem) but are contraindicated in congestive heart failure (a pump problem) because they provide an additional sodium load, and animals with heart failure already have retained too much sodium. Sodium-containing crystalloid solutions also are contraindicated in the presence of severe hypoalbuminemia because sodium-containing crystalloids decrease plasma albumin concentration and oncotic pressure further, resulting in movement of fluid into the interstitial spaces and exacerbating tissue edema.

Crystalloid solutions are characterized in terms of the number of molecules (numerator) per volume of solution (denominator). The number of molecules is expressed in moles (abbreviated as mol), where one mole of compound is equivalent to the molecular weight of the compound in grams.

Table 1
Summary of effective SID and osmolarity of parenterally administered crystalloid solutions

Solution	Effective SID (mEq/L)	Osmolarity (mOsm/L)
Hyperosmotic solution (>312 mOsm/L)		
8.4% $NaHCO_3$	1000	2000
5.0% $NaHCO_3$	595	1190
10% NaH_2PO_4	145	1150
50% dextrose	0	2500
7.2% NaCl	0	2460
25% magnesium sulfate	0	2028
23% calcium borogluconate	0	1069
Iso-osmotic solutions (300–312 mOsm/L)		
Tromethamine	210	300
1.3% $NaHCO_3$	155	310
Carbicarb	75	300
McSherry's solution	54	312
Darrow's solution	53	312
Ringer's solution	0	309
0.9% NaCl	0	308
1.15% KCl	0	308
Hypo-osmotic solutions (<300 mOsm/L)		
Acetated Ringer's solution	27	294
Lactated Ringer's solution	<14	275
5% dextrose	0	250

The normal SID of ruminant plasma is approximately 40 mEq/L. Electrolyte solutions with an effective SID >40 mEq/L are therefore alkalinizing because they create a strong ion alkalosis. Electrolyte solutions with an effective SID = 0 are acidifying because they create a strong ion acidosis. Electrolyte solutions of intermediate SID may be alkalinizing or acidifying, depending on the change in plasma SID relative to the decrease in plasma protein concentration (which is alkalinizing).

Because ruminant body fluids are dilute, we express moles (mol) as millimoles (mmol = mol/1000) to facilitate readability. Chemical tables listing the molecular weight of compounds or elements are widely available, and the molecular weights of compounds commonly administered parenterally or orally to ruminants are provided in Table 2 (Appendix 1).

In veterinary and human medicine, crystalloid solutions are expressed more frequently in terms of the number of charged components (numerator) per volume of solution (denominator). The number of charged components is expressed in equivalents (abbreviated as Eq), where one equivalent is the number of each charged component that combines with or replaces one mole of hydrogen ion (this means that Eq is always a positive number). Because ruminant body fluids are dilute, we express equivalents (Eq) as milliequivalents (mEq = Eq/1000). To calculate the number of mEq from mmol, simply multiply the number of millimoles by the valence (charge), whereby:

$$\text{mEq/L} = (\text{mmol/L}) \times \text{valence}$$

For instance, 1 mmol of NaCl in solution provides 2 mEq: 1 mEq of Na^+ (1×1) and 1 mEq of Cl^- (1×1), assuming that NaCl acts as a strong electrolyte in water (ie, it completely dissociates into Na^+ and Cl^- in water). In comparison, 1 mmol of calcium chloride ($CaCl_2$) in solution provides 4 mEq: 2 mEq of Ca^{2+} (1×2) and 2 mEq of Cl^- (2×1), and 1 mmol of dextrose provides 0 mEq, because dextrose does not dissociate into charged components in water. To facilitate formulation of oral and parenteral solutions for treating sick ruminants, it is helpful to express each component in units of mEq/g of compound, whereby:

$$\begin{aligned} \text{mEq/g} &= (\text{mEq/mol})/(\text{mass in g per mol}) \\ &= (\text{mEq/mol})/(\text{molecular weight}) \end{aligned}$$

This information is included in Table 2 (Appendix 1).

The principal reason we define constituents of plasma in terms of mEq instead of mmol is because electroneutrality must be preserved at all times; the difference between the charge assigned to all strong cations (Na^+, K^+, Ca^{2+}, and Mg^{2+}) and strong anions (Cl^-, lactate, sulfate, ketoacids, non-esterified fatty acids, and so forth) in plasma is called the *strong-ion difference* (SID), and this factor independently and directly alters blood pH and therefore acid-base status [4–8]. The normal SID of ruminant plasma is approximately 40 mEq/L. Electrolyte solutions with an effective SID greater than 40 mEq/L are therefore alkalinizing because they create a strong-ion alkalosis (see Table 1). Electrolyte solutions with an effective SID equal to 0 are acidifying because they create a strong-ion acidosis. Electrolyte solutions of intermediate SID may be alkalinizing or acidifying, depending on the change in plasma SID relative to the decrease in plasma protein concentration (which is alkalinizing).

Iso-osmotic, hyperosmotic, and hypo-osmotic crystalloid solutions

The tonicity of the solution is an important clinical issue. Complete understanding of the tonicity concept requires differentiation of two terms, osmolality and osmolarity. *Osmolality* is the number of dissolved particles per kilogram of solution and is expressed as mOsm/kg of solution. The normal plasma osmolality in ruminants is approximately 285 mOsm/kg, and plasma osmolality is defended aggressively by increasing water intake (osmolality >285 mOsm/kg) or promoting free-water excretion (osmolality <285 mOsm/kg). The correct term in plasma and extracellular fluid is osmolality because this factor is measured in the laboratory; however, frequently the term osmolarity is used because 1 kg of plasma approximates 1 L of plasma and osmolarity can be calculated easily from the concentration of electrolytes in the fluid solution. *Osmolarity* is the number of particles per liter of solution and is expressed as mOsm/L of solution.

One kg (1 L) of plasma has two components, 70 g of protein and 930 g of plasma water. Accordingly, the osmolality of normal plasma (285 mOsm/

kg) is equivalent to a plasma water osmolarity of 306 mOsm/L ([285 mOsm/kg]/[0.93 L/kg]). Ringer's solution, 0.9% NaCl, and 1.3% $NaHCO_3$ therefore are considered iso-osmotic solutions because they distribute in plasma water and have calculated osmolarities of 309 mOsm/L, 308 mOsm/L, and 310 mOsm/L, respectively.

The normal plasma osmolarity for ruminants is 306 mOsm/L; we can define solutions empirically as being iso-osmolar (300–312 mOsm/L), hyperosmolar (>312 mOsm/L), and hypo-osmolar (<300 mOsm/L). Using this categorization, it is readily apparent that some routinely used crystalloid solutions are hypo-osmotic; in particular, lactated Ringer's solution (275 mOsm/L) is mildly hypo-osmotic, and 5% dextrose (250 mOsm/L) is moderately hypo-osmotic, although after glucose metabolism, 5% dextrose becomes a markedly hypo-osmotic solution. The mild hypo-osmolarity of lactated Ringer's solution rarely is acknowledged, even though ruminants receiving large volumes of lactated Ringer's solution frequently become mildly hyponatremic.

A thorough understanding of osmolarity is central to successful parenteral and oral fluid therapy in ruminants. Ruminant erythrocytes are resistant to increases in plasma osmolarity, whereas they are susceptible to mild decreases in osmolarity; this fact is the basis of the red blood cell fragility test whereby red blood cell suspensions are placed in solutions of decreasing osmolarity [9]. As the osmolarity of the solution decreases, water moves across the semipermeable red blood cell membrane into the erythrocyte, resulting in swelling of erythrocytes, fracture of the cell membrane, and hemolysis (Fig. 1) [9]. This occurrence is the reason that the rapid ingestion of large water volumes in neonatal [10] and adult ruminants [11] causes hemolysis and hemoglobinuria; the ingested water is absorbed rapidly across the forestomach and small intestine, decreasing plasma osmolarity and resulting in hemolysis. In contrast, increasing plasma osmolarity causes water to move out of erythrocytes, which are resistant to shrinking. As such, intravenous administration of hyperosmotic solutions does not cause hemolysis.

Because of hypo-osmolal–induced hemolysis, parenterally administered fluids should be iso-osmotic or hyperosmotic. Because ruminal and abomasal fluids are iso-osmotic [12] and there is a large surface area for water and electrolyte exchange across forestomach epithelium, the tonicity of orally administered fluids also must be considered when treating sick ruminants. The rapid oral administration of high volumes of hypo-osmotic solutions or water therefore should be discouraged.

Parenterally administered crystalloid solutions

It is easy to become transfixed by the minutia of fluid and electrolyte therapy. All too often we see clinicians in white laboratory coats running

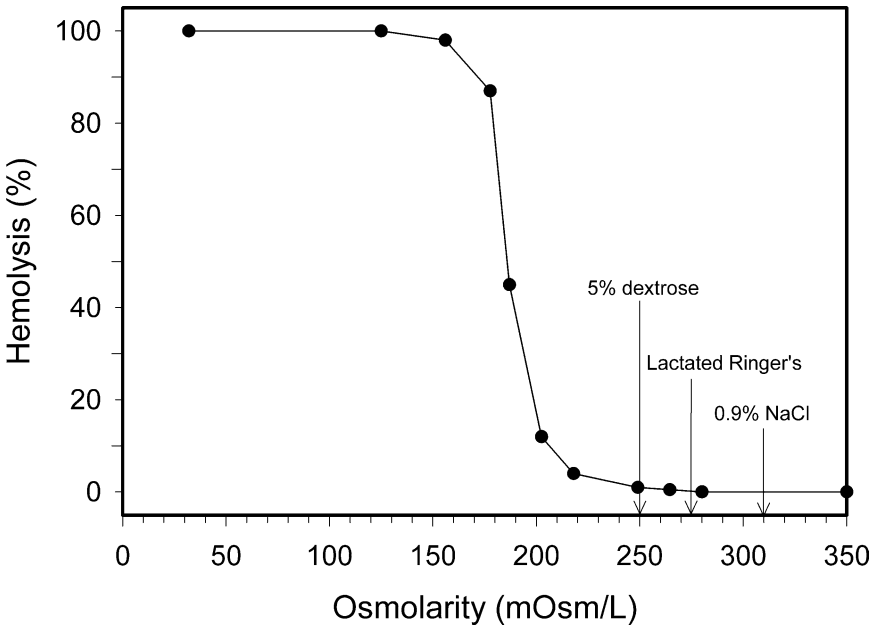

Fig. 1. Red blood cell fragility of bovine erythrocytes. Data are the mean values for cattle. Bovine red blood cells were placed in different concentrations of sodium chloride (NaCl) solution, and percent hemolysis was calculated by measuring the free hemoglobin concentration at different NaCl concentrations (different osmolarities). The figure clearly shows that the osmolarity of 5% dextrose is sufficiently low so that rapid intravenous administration may induce mild hemolysis. (*Data from* Binder JP, Mathois H. Die Osmotische resistenz der erythrozyten von kuhen. J Vet Med A 1986;33:89–92; Bianca W. Effects of dehydration, rehydration, and overhydration on the blood and urine of oxen. Br Vet J 1970;126:121–31.)

blood gas and serum biochemical analyses and calculating to the third decimal point the sodium, calcium, potassium, and bicarbonate deficits on the basis of insufficient information and incorrect assumptions while ignoring ongoing fluid and electrolyte losses that are difficult to quantify. A specific fluid formulation (''Clinician Cocktail'') then is administered, and the entire convoluted exercise is repeated in a few hours. When confronted with the temptation to formulate a ''Clinician Cocktail,'' it is valuable to remember two things: ''the dumbest kidney is smarter than the smartest clinician,'' and ''if the heart can pump and the kidney can filter, then administer an adequate volume of a balanced polyionic crystalloid solution.'' Because organic (structural) cardiac and renal diseases are rare and incompatible with a productive economic future in ruminants, it is appropriate to assume that the animal being treated has adequate cardiac and renal function if and when specific acid-base, electrolyte, and water derangements are corrected. Accordingly, parenteral fluid administration is simplified, and the need for repeated blood gas and serum biochemical analyses and frequent monitoring is obviated. Standard formulations of

hypo-osmotic, iso-osmotic, and hyperosmotic solutions used to treat ruminants are described in the following sections and in Appendix 2.

Hypo-osmotic crystalloid solutions

Lactated Ringer's solution

This solution frequently is abbreviated as LRS and is 275 mOsm/L. Lactated Ringer's solution is a balanced, polyionic, alkalinizing, iso-osmotic, crystalloid solution containing physiologic concentrations of Na^+, K^+, Ca^{2+}, Cl^-, and lactate ($CH_3CH(OH)COO^-$). Lactated Ringer's solution alkalinizes because lactate is metabolized predominantly to the bicarbonate ion, whereby:

$$CH_3CH(OH)COO^- + 3O_2 \Rightarrow 2CO_2 + 2H_2O + HCO_3^-$$

The lactate in lactated Ringer's solution is a racemic equimolar mixture of L-lactate and D-lactate; in healthy animals, L-lactate is metabolized rapidly. Ruminant tissues have negligible D-lactate dehydrogenase activity, however, leading to slow clearance of D-lactate primarily through the urinary system. DL-lactate solutions such as lactated Ringer's therefore have approximately half the alkalinizing ability of L-lactate solutions in ruminants. The effective SID of lactated Ringer's solution is less than 14 mEq/L because L-lactate also can be used in gluconeogenesis instead of bicarbonate production.

Lactated Ringer's solution is theoretically inferior to acetated Ringer's solution, because sick neonatal and adult ruminants may have increased blood lactate concentrations, and it is incongruous to add lactate in this situation. The rate of lactate metabolism to glucose is decreased by approximately 50% in severely dehydrated calves [13], resulting in delayed alkalinization after administration of lactated Ringer's solution. Despite these theoretic and real concerns, lactated Ringer's solution still is used routinely because of tradition and because commercially available formulations of acetated Ringer's solution contain gluconate, which, like D-lactate, is metabolized poorly by neonatal calves [14].

Acetated Ringer's solution

Acetated Ringer's solution is a balanced, polyionic, alkalinizing, hypo-osmotic, crystalloid solution and is 294 mOsm/L. Commercially available formulations of acetated Ringer's solution contain physiologic concentrations of Na^+, K^+, Mg^{2+}, Cl^-, acetate (CH_3COO^-), and gluconate ($CH_2(OH)\{CH(OH)\}_4COO^-$). All commercially available formulations in the United States (such as Plasma-Lyte A, Normosol-R, and Isolyte S) currently do not contain calcium but contain gluconate, which is problematic because calves (and presumably adult ruminants) slowly metabolize gluconate [14,15].

Acetated Ringer's solution alkalinizes because acetate (and gluconate in most species) is metabolized to the bicarbonate ion, whereby:

$$CH_3COO^- + 2O_2 \Rightarrow CO_2 + H_2O + HCO_3^-$$

$$CH_2(OH)\{CH(OH)\}_4COO^- + 5.5O_2 \Rightarrow 5CO_2 + 5H_2O + HCO_3^-$$

The strong-ion approach to acid-base balance states that acetated Ringer's solution is alkalinizing because it contains a metabolizable strong anion (acetate) that, when metabolized, increases the SID. Acetate provides an equivalent alkalinizing effect to L-lactate in neonatal calves, but it is metabolized more rapidly than L-lactate and therefore increases blood pH at a faster rate [14,16]. Because gluconate is metabolized slowly in calves [14], the administration of large volumes of gluconate-containing fluids maintains a strong-ion acidosis [4,6,7].

5% dextrose

This solution frequently is abbreviated as D5W and is 250 mOsm/L as administered, but plasma osmolarity decreases as the glucose is metabolized, leaving free water. Because 5% dextrose has no sodium to expand the extracellular volume and has much less energy content than 50% dextrose on a volume basis, the only application of 5% dextrose in ruminants is to provide free water. The solution has minimal usefulness in ruminants, as do variants such as 2.5% dextrose and 0.45% NaCl.

Iso-osmotic crystalloid solutions

Ringer's solution

Ringer's solution is a balanced, polyionic, nonalkalinizing, iso-osmotic, crystalloid solution that contains physiologic concentrations of Na^+, K^+, Ca^{2+}, and Cl^-. This solution is mildly acidifying because its effective SID equals 0 mEq/L [4–8]. Addition of a fluid with an SID of 0 mEq/L to plasma (normal SID $\approx$ 40 mEq/L) decreases plasma SID and therefore directly and independently decreases plasma pH [4–8], because a 1-mEq/L decrease in SID decreases plasma pH by 0.016 [7]. Ringer's solution is the standard intravenous fluid for adult ruminants because these animals tend to become alkalemic when inappetent [17].

Iso-osmotic sodium bicarbonate

Iso-osmotic sodium bicarbonate (1.3% $NaHCO_3$ solution) is an alkalinizing iso-osmotic crystalloid solution that is used to treat severe acidemia (indicated whenever blood pH $<$7.20 due to metabolic acidosis). This solution is alkalinizing because it buffers hydrogen ion

$$HCO_3^- + H^+ \Leftrightarrow CO_2 + H_2O$$

and because it increases SID (effective SID = 155 mEq/L). $NaHCO_3$ should not be used to treat severe respiratory acidosis because the additional carbon dioxide (CO_2) generated may worsen the respiratory acidosis.

Tromethamine

Tromethamine (Tham) [tris-hydroxymethyl aminomethane, $(CH_2OH)_3C\text{-}NH_2$, 300 mmol/L] is an iso-osmotic solution of an organic amine that is a safe and effective buffer [18]. After administration, 70% of the neutral compound $(CH_2OH)_3C\text{-}NH_2$ in tromethamine is protonated immediately to the strong cation $(CH_2OH)_3C\text{-}NH_3{}^+$ in plasma, with the net equation being

$$(CH_2OH)_3C\text{-}NH_2 + H^+ \Leftrightarrow (CH_2OH)_3C\text{-}NH_3^+$$

Tromethamine therefore provides an alternative alkalinizing agent to $NaHCO_3$. The remaining 30% of the administered tromethamine remains unprotonated and therefore can cross cell membranes and potentially buffer the intracellular compartment. Tromethamine also is known as THAM, Tris, tris buffer, trisamine, and Tromethane, and commercially available iso-osmotic formulations are available for intravenous administration with (Tham-E) or without (Tham) electrolytes; administration of tromethamine without electrolytes (Tham) leads to hyponatremia [18,19], and it would seem preferable to administer tromethamine in conjunction with electrolytes (Tham-E) [19]. There do not seem to be any reports of the intravenous administration of tromethamine to ruminants, and the solution does not currently seem to offer any important clinical advantages compared to $NaHCO_3$ in spontaneously breathing ruminants.

Carbicarb

Carbicarb was an experimental iso-osmotic buffer (300 mOsm/L) made from equimolar disodium carbonate and $NaHCO_3$; carbonate avoids generation of CO_2 when buffering acidemic blood [20,21].

$$CO_3^{2-} + H^+ \Leftrightarrow HCO_3^-$$

Carbicarb was suspected to decrease the incidence and magnitude of hypercapnea when rapid alkalinization was needed in animals with mixed metabolic and respiratory acidosis. Despite numerous studies comparing Carbicarb to $NaHCO_3$, the potential clinical advantages of Carbicarb have been demonstrated only in animals being ventilated or with extremely limited ventilatory ability. Carbicarb has been administered intravenously to diarrheic calves; however, these studies have failed to identify a clinically important advantage compared to conventional iso-osmotic $NaHCO_3$ administration [22,23]. There does not seem to be a compelling reason to prefer Carbicarb to iso-osmotic $NaHCO_3$ [24] when rapid alkalinization of conscious ruminants is required. Of interest is the observation that the manufacturer discontinued production of Carbicarb in the United States in 1997.

0.9% sodium chloride solution

Isotonic saline is an iso-osmotic solution that has little merit in the routine treatment of sick ruminants, principally because ruminants usually

develop hypocalcemia and hypokalemia when inappetent. The use of 0.9% NaCl should be confined to irrigation of surgical sites and wounds or as a vehicle for adding other electrolytes and dextrose. Like Ringer's solution, 0.9% NaCl is mildly acidifying because effective SID equals 0 mEq/L.

Darrow's solution

This iso-osmotic polyionic solution was formulated by Darrow in 1946 for use in human infants; the solution has been administered to calves [15,25]. Compared with other iso-osmotic polyionic solutions (see Appendix 2), Darrow's solution is hyponatremic, hyperkalemic, and hyperlactatemic and does not contain calcium or magnesium. As such, Darrow's solution is not recommended for administration to ruminants.

McSherry's balanced electrolyte solution

This iso-osmotic polyionic solution was formulated by McSherry and Grinyer in 1954 for intravenous and intraperitoneal administration to dehydrated diarrheic calves [26]. On theoretic grounds, this solution is an excellent parenteral fluid for resuscitating dehydrated diarrheic calves that deserves more frequent use. Unfortunately, commercial formulations are currently unavailable.

Hyperosmotic crystalloid solutions

50% dextrose

This solution is 2500 mOsm/L (approximately eight times normal osmolarity). The solution is administered commonly to ruminants with ketosis or hypoglycemia and produces a transient increase in cardiac contractility [27]. Some commercially available formulations in Europe contain an equimolar mix of dextrose and fructose, although the addition of fructose does not seem to produce a more sustained increase in plasma glucose concentration than that produced by glucose alone [28].

7.2% sodium chloride (hypertonic saline)

This solution is 2460 mOsm/L (approximately eight times normal osmolarity) and is used for the rapid resuscitation of ruminants. As discussed in a following section, hypertonic saline should be administered at 4 to 5 mL/kg intravenously for 4 to 5 minutes (1 mL/kg/min). Faster rates of administration lead to hemodynamic collapse due to vasodilation and decreased cardiac contractility, whereas slower rates of administration provide no advantages as compared to iso-osmotic crystalloid solutions. Like high-volume 0.9% NaCl, small-volume hypertonic saline consistently induces a mild strong-ion acidosis [29,30] because its effective SID is equal to 0 mEq/L [4,6,7]. In general, the decrease in pH after hypertonic saline administration is less than 0.08 pH units and rapidly dissipates with time [29]. The effect of hypertonic saline on acid-base balance is therefore clinically inconsequential.

8.4% sodium bicarbonate

This solution is 2000 mOsm/L (approximately seven times normal osmolarity). It is used for rapid alkalinization, particularly in the presence of severe acidemia (pH < 7.20). The solution osmolarity was selected because it provides 1 mEq of HCO_3^- per mL of solution, which facilitates calculation of the volume to be administered. The speed of intravenous administration of 8.4% $NaHCO_3$ should not exceed 1 mL/kg/min. There is one report of the intravenous administration of 8.4% $NaHCO_3$ to normovolumic calves with experimentally induced mixed respiratory and metabolic acidosis; the study found that rapid administration of $NaHCO_3$ (5 mL/kg, intravenously, for 5 minutes) rapidly corrected the metabolic acidosis, increased blood pH, and improved cardiovascular status without inducing paradoxic cerebrospinal fluid acidosis [31], suggesting that this treatment may be of value in treating dehydrated diarrheic calves. Efficacy studies in calves with naturally acquired diarrhea seem to be indicated.

5% sodium bicarbonate

This solution is 1190 mOsm/L (approximately four times normal osmolarity). This solution also is used for rapid alkalinization in the presence of severe acidemia (pH < 7.20). The speed of intravenous administration of 5.0% $NaHCO_3$ should not exceed 2 mL/kg/min.

23% calcium gluconate or calcium borogluconate

These solutions are 1069 mOsm/L (approximately 3.5 times normal osmolarity). Calcium borogluconate is the standard treatment for milk fever (hypocalcemia) in cattle. D-gluconate is an aldose sugar produced by oxidation of D-glucose and is the preferred salt for calcium-containing parenteral solutions because it does not cause tissue necrosis as severe as does $CaCl_2$. Calcium gluconate should not be added to $NaHCO_3$ solutions because a white precipitate ($CaCO_3$) forms immediately, which interferes with normal fluid administration. Likewise, calcium gluconate should not be administered with tetracycline antibiotics because a yellow precipitate forms.

Colloid solutions

A colloid is a substance that is too large to pass through a semipermeable membrane. Examples of colloid solutions administered to ruminants are whole blood, stroma-free hemoglobin, plasma, dextrans, hydroxyethyl starches, and gelatins. As a group, colloid solutions are excellent for sustained expansion of plasma volume, which is in marked contrast to the effect of crystalloid solutions. Colloid solutions are contraindicated in congestive heart failure because these animals have increased plasma volume. Colloid solutions also are contraindicated in the presence of oliguric or anuric renal failure because the sustained volume overload may lead to pulmonary edema.

Whole blood

Whole blood is the perfect balanced colloid-crystalloid solution, with great oxygen-carrying capacity. It has a short shelf life (<24 hours at 4°C) and is expensive to obtain, and administration runs the risk of disease transmission and allergic reactions, which are extremely rare in ruminants with the first blood transfusion. Excellent descriptions for collecting, storing, and administering blood are available elsewhere [32].

Stroma-free hemoglobin

Stroma-free hemoglobin is a blood substitute containing a purified hemoglobin glutamer-200 solution (13 g hemoglobin/dL) derived from cattle blood. The commercially available solution (Oyxglobin) has a 2-year shelf life at 20°C, an osmolarity of 300 mOsm/L, and an oncotic pressure of 43 mm Hg; the solution is therefore iso-osmotic but hyperoncotic. The hemoglobin solution is labeled for use in dogs (10–30 mL/kg intravenously, one treatment, at ≤10 mL/kg/h). Stroma-free hemoglobin solutions are excellent at increasing oxygen delivery and oxygen-carrying capacity while providing similar plasma volume expansion to dextrans and hydroxyethyl starches. The major theoretic concerns regarding administration of stroma-free hemoglobin solutions are potent vasoconstriction [33] and hemoglobinuric nephrosis. Some of the original experimental studies examining the effects of stroma-free hemoglobin administration were completed in sheep [34,35], although there do not seem to be any reports of its administration in a clinical situation. It is likely that the high cost of this product will minimize its administration to ruminants.

Plasma (fresh or frozen)

Plasma is an excellent balanced colloid-crystalloid solution. Compared with blood, plasma has a much longer shelf life (at least 1 year at −20°C) but is more expensive to obtain. Details for collecting, harvesting, storing, and administering plasma are available elsewhere [32], and bovine plasma is commercially available (Midwest Animal Blood Services, Stockbridge, Michigan; Immunodynamics, Perry, Iowa; Moregate BioTech, Bulumba, Queensland, Australia). Like blood, administration of plasma runs the risk of disease transmission and allergic reactions, although these risks are less than that with blood transfusion. Freeze-dried plasma obtained from blood donors or frozen plasma obtained from slaughterhouses has been administered to neonatal calves with diarrhea [25,36,37]; however, the plasma had a marked variability in the quality and level of bacterial contamination, leading to endotoxemia in some calves after treatment [36,37].

There seems to be only one report documenting the efficacy of plasma administered to neonatal calves with diarrhea, and these calves were probably colostrum-deprived. The 14-day survival rate in diarrheic calves

that received 600 to 800 mL of bovine plasma (5 g protein/dL) and electrolytes intravenously was 93% (37 of 40), which was significantly greater ($P = 0.0041$) than the survival rate of calves receiving intravenous electrolytes alone (54%, 7 of 13) [38]. Another study failed to identify a beneficial effect of blood transfusion in treating diarrheic calves [39]. Because blood is cheaper to obtain than plasma, whole-blood transfusions usually are administered when a neonatal ruminant needs plasma.

Dextran preparations (dextran 70)

Dextrans are high-molecular-weight glucose polymers obtained by the fermentation of sucrose by *Leuconostoc mesenteroides* and *Lactobacilli* spp; the fermentation metabolites then undergo acid hydrolysis and fractionation. The molecular weight of dextran therefore can be "selected," and two dextran products, dextran 70 (mean molecular weight = 70,000 g) and dextran 40 (mean molecular weight = 40,000 g) are commercially available. Because the molecular weight of dextran 70 is similar to albumin (molecular weight = 65,000 g), there is limited diffusion of dextran into the interstitial space, and dextran 70 therefore acts clinically as a plasma volume expander, in contrast to iso-osmotic crystalloid solutions that act as extracellular fluid volume expanders. Dextran 70 has been the most widely used dextran formulation in veterinary medicine and is therefore the recommended product for administration. Dextran 70 is supplied as a 6% concentration in 0.9% NaCl (Gentran 70); this concentration provides a hyperoncotic but approximately iso-osmotic solution. Reported administration rates of dextran 70 are 5 to 40 mL/kg/h, but it is safer to administer dextran 70 at less than or equal to 20 mL/kg/h. One milliliter of dextran 70 expands the plasma volume by 0.8 to 1.2 mL, but 50% of the administered dose is gone by 24 hours. Dextran administration runs the risk of exacerbating preexisting coagulopathies, although the clinical significance of dextran-induced prolongation of activated partial thromboplastin time (APTT) by decreasing factor VIII:C is probably minimal. The risk of coagulopathy is dependent on the administration rate, total dose administered (20 mL/kg is the maximal 24-hour dose in humans), and the molecular weight of dextran. The deleterious effects of dextrans usually are associated with large doses or prolonged administration [40].

The administration of dextran to dehydrated neonatal calves first was proposed by Watt in 1965 [38]. Dextran has been administered (in conjunction with hypertonic saline) to calves with naturally acquired [41] and experimentally induced diarrhea and dehydration [42,43] and to sheep with hemorrhagic shock [44,45]. Dextran 70 in isotonic saline also has been administered to calves with naturally acquired diarrhea and dehydration [46].

Hydroxyethyl starch preparations (hetastarch and pentastarch)

Two hydroxyethyl starch preparations are currently commercially available: hetastarch and pentastarch. Hetastarch is a high-molecular-weight

glucose polymer (mean molecular weight = 450,000 g) that is synthesized chemically from amylopectin, producing a highly branched glucose polymer with a structure similar to that of glycogen. Because the molecular weight of hetastarch is much greater than that of albumin, hetastarch decreases endothelial permeability by sealing separations of endothelial cells and ameliorates free radical injury during reperfusion of ischemic limbs [47]. Hetastarch is hydrolyzed in blood by α-amylase, and the addition of hydroxyethyl groups slows hydrolysis and therefore prolongs the duration of plasma volume expansion. Hetastarch is supplied as a 6% concentration in 0.9% NaCl (Hespan); this concentration provides a hyperoncotic but approximately iso-osmotic solution. Reported administration rates are 5 to 40 mL/kg/h, but like dextran 70, it is safer to administer hetastarch at less than or equal to 20 mL/kg/h. Like dextran 70, hetastarch administration also runs the risk of exacerbating preexisting coagulopathies. The risk of coagulopathy is dependent on the administration rate and total dose administered (20 mL/kg is the maximal 24-hour dose in humans).

Pentastarch has a mean molecular weight of 280,000 g and is available as a 10% solution (Pentaspan). Pentastarch has two important advantages when compared to hetastarch; it has less effect on exacerbating preexisting coagulopathies, and the rate of elimination is faster [48]. There do not seem to be any reports of the intravenous administration of hetastarch or pentastarch to ruminants.

Gelatins (modified bovine collagens)

A commercially available form of collagen (oxypolygelatin) is available for veterinary use. This formulation uses gelatin with a mean molecular weight of 30,000 g and is a 5.6% suspension in NaCl. Compared with dextrans and hydroxyethyl starches, gelatins have a shorter plasma half-life but seem to have less effect on coagulation [48]. In general, gelatins have not been evaluated as completely as dextrans and hydroxyethyl starches. There do not seem to be any reports of the intravenous administration of gelatins to ruminants.

Orally administered crystalloid solutions (oral electrolyte solutions)

Oral electrolyte solutions frequently are administered to dehydrated neonatal ruminants with diarrhea, and there is increasing interest in the administration of oral electrolyte solutions to adult ruminants. The formulation of the oral electrolyte solution should be different for neonatal and adult ruminants, because neonates frequently have acidemia, necessitating the inclusion of an alkalinizing agent [14,49], whereas alkalemia is more common in sick adult ruminants [15].

Neonatal ruminants

In neonatal calves, the ideal oral electrolyte solution should (1) supply sufficient sodium to facilitate normalization of extracellular fluid deficits; (2) provide two or more agents (such as glucose, acetate, propionate, or glycine) that facilitate intestinal absorption of sodium and water; (3) provide an alkalinizing agent (such as acetate, propionate, citrate, or bicarbonate) to treat the metabolic acidosis often present in dehydrated diarrheic calves; (4) not interfere with the clotting of milk; (5) provide sufficient energy, because these electrolyte solutions may be administered instead of milk or milk replacer for short periods; and (6) facilitate repair of damaged intestinal epithelium [49–55].

The optimal oral electrolyte solution should have a sodium concentration between 90 and 130 mmol/L; a potassium concentration between 10 and 20 mmol/L; a chloride concentration between 40 and 80 mmol/L; 40 to 80 mmol/L of metabolizable (nonbicarbonate) base, such as acetate or propionate; and glucose as an energy source [49]. Acetate or propionate is preferred to bicarbonate or citrate for treating dehydrated calves with mild metabolic acidosis because (1) acetate and propionate have similar alkalinizing ability to bicarbonate on an equimolar basis; (2) acetate and propionate are metabolized readily by peripheral tissues in calves and therefore provide a source of energy; (3) acetate and propionate stimulate sodium and water absorption in the calf small intestine; (4) acetate and propionate do not alkalinize the abomasum and intestine, whereas bicarbonate permits bacteria to proliferate in an alkalinized abomasum; and (5) acetate and propionate do not interfere with milk clotting, whereas bicarbonate or citrate inhibits clot formation in the abomasum [14,49,53–58].

Hyperosmotic oral electrolyte solutions provide greater nutritional support to dehydrated diarrheic calves than do iso-osmotic solutions [59,60]. When administered orally to neonatal calves without diarrhea, hyperosmotic solutions have no deleterious effects, particularly in relation to maintaining appropriate hydration status, intestinal osmolarity, serum glucose concentration, and intestinal flow rate [60]. The osmolality of the proximal small intestinal lumen in adult ruminants is approximately 415 mOsm/kg [12], and the osmolarity of the unstirred layer surrounding the villous tip in the mammalian small intestine is 600 to 700 mOsm/L [61]; both findings suggest that hyperosmotic solutions are physiologically more appropriate than iso-osmolar solutions in the proximal small intestine. Relative to iso-osmolar solutions, hyperosmotic solutions minimize the loss in body weight that occurs when healthy calves are deprived of milk [62].

An area of recent research interest is the inclusion of compounds that facilitate repair of damaged intestinal epithelium in neonatal calves with diarrhea. The most valuable treatment in this regard is to ensure a high nutritional plane; optimally, milk should be fed as soon as possible and in adequate volumes to diarrheic calves, with fresh milk being preferable to milk replacer. Glutamine-containing oral electrolyte solutions have been

investigated as an adjunct therapy; however, studies indicate that glutamine does not improve gut morphology in diarrheic calves [63].

The optimal oral electrolyte solution is hyperosmotic and uses acetate as the main alkalinizing agent. Unfortunately, only one such product (Hydralyte) is commercially available in the United States; this formulation contains the following: Na (85 mmol/L), potassium (30 mmol/L), Cl (45 mmol/L), acetate (60 mmol/L), citrate (10 mmol/L), glycine (16 mmol/L), and glucose (368 mmol/L), with a calculated osmolarity of 614 mOsm/L. Because the sodium and potassium concentrations in this solution are not ideal and the solution contains citrate, which interferes with milk clotting [54], an optimal oral electrolyte solution is not available in the United States. In contrast, numerous acetate-based solutions are available in Europe, and two are available in Canada.

Adult ruminants

Ruminants have evolved to adapt to a variety of environments. One of the major adaptations has been the development of a large water reservoir, the rumen, that enables the animal to go without water for days and then rapidly rehydrate without any negative effects [64]. The ruminal epithelium is capable of absorbing large volumes of water. The main force for water movement across the rumen wall is the gradient of osmolarity between ruminal fluid (which is normally iso-osmotic) and blood perfusing the ruminal epithelium [65]. Experimental studies in adult cattle indicate that a net flow of water from rumen to plasma occurs whenever plasma osmolality exceeds rumen osmolality by greater than or equal to 20 mOsm/kg; moreover, as rumen osmolality decreases, the rate of water movement from rumen into plasma increases [66], which means that to optimize free-water absorption, rumen osmolality should be markedly hypo-osmotic. In contrast, rumen osmolality should not be made hyperosmotic, because it will cause free water to move from the extracellular space into the rumen (worsening the dehydration), the main reason for dehydration in ruminants with grain overload. Interestingly, when rumen osmolality exceeds plasma osmolality by greater than or equal to 40 mOsm/L, the rumen epithelium becomes more permeable, even though it is not damaged morphologically [67].

To produce sustained expansion of the extracellular fluid space, both water and sodium must be absorbed. Acetic, propionic, and butyric acids are absorbed rapidly from the forestomach in their nonionized form and are absorbed more slowly in conjunction with a sodium ion in their ionized form. Sodium-coupled absorption of volatile fatty acids occurs at a rate inverse to their molecular weight. Large quantities of sodium are absorbed each day by adult ruminants [68]. Cattle produce up to 180 L of saliva per day, and saliva usually has a sodium concentration of 126 mEq/L [68]. Approximately half of the sodium secreted with saliva can be reabsorbed by the forestomach [68], primarily through active transport mechanisms [65].

This process is also responsible for the passive movement of water from the rumen into the extracellular space.

The oral administration of $NaHCO_3$ to adult ruminants (2.5 g of $NaHCO_3$/kg body weight, equivalent to 2 L of a 31% $NaHCO_3$ solution) causes a profound metabolic alkalosis (strong-ion alkalosis) [69]. Drenching of dairy cows with 700 mL of 40% $NaHCO_3$ or 46% Na-propionate solutions (both markedly hyperosmotic) increased blood pH to an equivalent degree [70]. Taken together, these studies demonstrate that oral administration of sodium salts with a high effective SID cause a metabolic alkalosis (strong-ion alkalosis) in adult ruminants, as they do in neonatal ruminants. Oral $NaHCO_3$ may be a useful treatment for grain overload.

The practitioner clinically can take advantage of the vast ruminal capacity for sodium and water absorption by administering hypo-osmotic oral electrolyte solutions to dehydrated adult ruminants. The optimal formulation of an oral rehydration solution for adult ruminants is unknown, but such a solution should contain Na^+, K^+, Ca^{2+}, magnesium, phosphate, and propionate to facilitate sodium absorption and provide an additional source of energy to the animal. Provided that the osmolality of the rumen contents remains hypo-osmotic to plasma, there will be a slow but sustained absorption of electrolytes and water in an oral electrolyte solution because of the reservoir function of the rumen. Formulation of a practical, effective, and inexpensive oral electrolyte solution for adult ruminants is currently the most important challenge in fluid and electrolyte therapy.

What route of administration should be used?

Fluids and electrolytes usually are administered orally or parenterally to ruminants. The oral route for fluid administration should be used whenever possible, because oral solutions are cheaper and faster to administer than intravenous fluids and do not need to be sterile or pyrogen-free. Oral administration creates a fluid and electrolyte reservoir in the forestomach and abomasum that provides sustained absorption of water and electrolytes. In neonatal ruminants, fluids administered by suckling induce closure of the esophageal groove and are deposited in the abomasum. In neonatal ruminants that are unable to suckle and in adult ruminants, esophageal intubation does not induce esophageal groove closure, and administered fluids are deposited directly into the rumen. Fluid passively flows into the abomasum after 400 mL has been intubated in calves 1 to 17 days of age and after 2 L in older calves (25–30 days of age [71]). The major disadvantage with oral fluid administration is that it slowly resuscitates, relative to intravenous fluid administration [43]. If rapid resuscitation is required, at least some fluid should be administered intravenously.

There are four routes for parenteral administration: (1) intravenous, (2) intraperitoneal, (3) subcutaneous, and (4) intraosseous. Crystalloid

solutions can be administered by way of all four routes; however, the contents must be known accurately, and ideally, the solution should be sterile and nonpyrogenic. Colloids can be administered by the intravenous and intraperitoneal routes. Iso-osmotic solutions can be administered by the intravenous, intraperitoneal, subcutaneous, and intraosseous routes, whereas hyperosmotic solutions should be administered only intravenously.

Intravenous administration of large volumes of iso-osmotic crystalloid solutions requires intravenous catheterization and periodic monitoring of the flow rate and fluid container. Excellent descriptions of the specific techniques for intravenous catheterization (jugular and auricular veins) and fluid delivery are available elsewhere [23,72–78]. It is often difficult to maintain a patent catheter and a constant flow rate using gravity-flow systems because of changes in position from recumbency to standing (thereby altering the hydrostatic pressure gradient) and because movement can lead to tangling of the fluid line. An additional problem in goats and occasionally sheep and calves is nibbling or suckling the fluid-administration line, with subsequent disruption. Catheter-related problems are identified easily and rectified in a veterinary hospital but usually go undetected and uncorrected when intravenous fluids are administered in on-farm situations [43].

The effectiveness of intraperitoneal fluid administration does not seem to have been evaluated in dehydrated neonatal or adult ruminants. Although intraperitoneal fluid administration has been used in dehydrated calves [26], the route is not recommended currently for neonatal calves because of altered peritoneal absorption in dehydrated calves [79] and the risk of peritoneal adhesions [25], although neither claim seems to have been substantiated. Plasma has been administered safely to neonatal calves through a catheter in the paralumbar fossa [80].

The effectiveness of subcutaneous fluid administration does not seem to have been evaluated in dehydrated neonatal or adult ruminants, despite reports of administration of 3 L of fluid in the lateral neck of adult cattle [72]. To facilitate absorption, hyaluronidase (150 U/L of solution) can be added to the solution [72,81], although the safety and efficacy of hyaluronidase does not seem to have been determined. Subcutaneously administered fluids are absorbed slowly for 6 to 8 hours in normovolumic dogs; absorption time is prolonged further in hypovolumic animals because of decreased cardiac output and blood flow to the periphery [81]. With the exception of calcium and magnesium solutions used to treat hypocalcemia and hypomagnesemia, fluids rarely are administered subcutaneously in ruminants because the absorption rate is suspected to be slow, although this supposition has not been substantiated in ruminants.

There do not seem to be any reports of intraosseous fluid administration in ruminants. It is unlikely that the intraosseous route is needed in ruminants, because of their large size and easy accessibility to veins for catheterization.

How much fluid should be administered?

Two aspects of fluid balance need to be considered when calculating the volume of fluid to be administered: (1) replacement of existing fluid deficits (need estimate of percent dehydration and distribution space for the administered fluid) and (2) provision for ongoing fluid losses. Both aspects only can be estimated, and because these estimates are imprecise, the volume required to normalize body fluids should be considered a rough guide and subject to modification.

The only experimentally determined guidelines to estimate hydration status are available for dairy calves [1], in which the best estimate of percent dehydration is obtained by multiplying eyeball recession into the orbit (in mm) by 1.7. This value provides an estimate of the whole body-water depletion, but in calf diarrhea, it is preferentially from the extracellular compartment. All other guidelines are empiric.

Adult lactating cows have a total body water of 60% of their body weight, comprising an intracellular fluid volume (30%) and an extracellular fluid volume (30%) of their body weight [82,83]. The extracellular fluid volume can be compartmentalized further into plasma volume (5%), interstitial volume (14%), and transcellular volume (11%) of their body weight [84,85]; the transcellular compartment contains water in the gut lumen, gut secretions (saliva, abomasum, bile), urinary tract, synovial fluid, and cerebrospinal fluid [86]. Ruminants have a much larger salivary secretion rate and gut volume than do monogastrics, which accounts for the much higher transcellular volume (11% of body weight) compared with that of monogastrics such as rats and dogs (3%–7% of body weight). The distribution space for iso-osmotic crystalloid solutions in adult ruminants therefore is assumed to be 30% of the body weight. In contrast, neonatal ruminants carry a greater percentage of their body weight in water, with total body water (73%), intracellular fluid volume (29%), extracellular fluid volume (44%), blood volume (10%), and a plasma volume (7%) of their body weight [87,88]. The distribution space for iso-osmotic crystalloid solutions in neonatal ruminants is approximately 50% of their body weight [14].

Large volumes of oral iso-osmotic electrolyte solutions can be administered safely to healthy neonatal calves because calves can consume 12% to 19% of their body weight in one feeding when fed ad libitum [89]. Such high intakes are not recommended, however, because these calves have tense abdomens and appear uncomfortable for some time after suckling high volumes [89]. Dehydrated adult cattle can drink 10% [90] or 15% [11] of their body weight in water in less than 10 minutes; however, these rates of ingestion are excessive and can lead to muscle trembling, weakness, hypothermia, and intravascular hemolysis [11].

To estimate ongoing fluid losses, practitioners need to know maintenance fluid requirements and the losses associated with the specific disease process.

Insensible water loss in the neonatal calf approximates 25 mL/kg/d [91], whereas an estimate for the adult sheep is 10 mL/kg/d [92].

How fast should fluid be administered?

The speed of administration is an important determinant of treatment success. If fluids are administered too slowly, then the animal dies because of the lack of effective treatment. If fluids are administered too quickly, then the animal dies because of treatment.

Aggressive intravenous fluid administration rates are 80 mL/kg body weight/h for iso-osmotic crystalloid solutions, 1 mL/kg body weight/min for hyperosmotic solutions such as hypertonic saline (7.2% NaCl), 0.5 mEq of K^+/kg body weight/h for iso-osmotic solutions of potassium, and 20 mL/kg body weight/h for colloidal solutions. These rapid rates of fluid administration usually are employed initially to rapidly resuscitate a critically ill patient; in animals that are not critically ill, it is preferable to correct the fluid and electrolyte deficit more slowly over 2 to 8 hours and then re-evaluate the patient. Studies with dehydrated calves indicate that 80 mL/kg body weight/h can be administered safely [43,93], whereas 40 mL/kg body weight/h may be the maximal fluid rate in adult ruminants [94]. The cycle of estimation, treatment, and reassessment is a useful clinical approach when administering fluids to critically ill ruminants [78].

During rapid intravenous fluid administration, the animal should be monitored for signs of fluid overload (principally pulmonary edema), which are manifest clinically in ruminants by tachypnea, increased depth of respiration, flared nostrils, chemosis, and rarely, a moist cough, and can be monitored by measuring jugular venous pressure.

Recommended fluid and electrolyte treatment protocols

Hypovolemia due to dehydration, endotoxemia, or hemorrhage

A number of studies have documented the cardiovascular and resuscitative effects of intravenous crystalloid and colloid solutions in ruminants. Studies have been published related to iso-osmotic crystalloid solutions [14–16,43,92,93,95–97] and colloids [41], whereas more studies have evaluated the effect of hyperosmotic crystalloid solutions with dextran 70 [42–45,97,98] and hyperosmotic crystalloid solutions without dextran 70 [30,99–108].

Large-volume iso-osmotic crystalloid solutions

The optimal parenteral fluid for dehydrated ruminants remains large-volume iso-osmotic crystalloid solutions. Crystalloid solutions provide a rapid but transient plasma volume expansion. For instance, when 4 L of

0.9% NaCl is administered intravenously to human patients, within 30 minutes, 1 L is intravascular and 3 L is in interstitial space [109], and within 2 hours much of the administered fluid has been eliminated from the extracellular compartment in the form of urine. The practitioner must administer 4 L of an iso-osmotic crystalloid solution to replace 1 L of plasma. This amount is consistent with the distribution of extracellular water in adult ruminants; the interstitial water is three times the plasma volume [84,85].

Commercially available products can be used for small ruminants; however, these products are cost-prohibitive when administered to severely dehydrated adult ruminants, as well as being inconvenient to store and transport. Many practitioners make their own intravenous solutions by adding electrolytes (as described in Appendices 1 and 2) to tap water, even though tap water is not sterile and may contain endotoxins [77,110]. Bacteria in tap water can be killed by autoclaving; however, this process does not remove endotoxins. Because the contents of tap water cannot be predicted, it is preferable to use sterile distilled water [78] if it can be purchased economically in convenient quantities. In the author's practice, commercial products are used for small ruminants, and tap water filtered through four filters with decreasing pore size down to 20 μm is mixed with electrolytes for administration to large ruminants. During fluid administration, adult ruminants are monitored for the presence of pyrogens in the fluid by measuring rectal temperature and looking for signs of shivering or clinical depression (droopy ears and head). These clinical signs of pyrogen administration are seen rarely, but if they are present, the intravenous fluid should be discarded and a new batch formulated.

Dehydrated or endotoxemic neonatal ruminants typically have a hyponatremic, hyperkalemic, metabolic acidosis. The current recommended treatment for moderately dehydrated neonatal ruminants (<8% body weight) is oral electrolyte administration alone, whereas intravenous fluid therapy is an absolute requirement for treating severely dehydrated neonatal ruminants (≥8% dehydrated). The cut-off value of 8% provides a useful clinical guide and corresponds to an eyeball recession of greater than or equal to 4 mm into the orbit [1]. Treatment of calves that had experimentally induced enterotoxigenic *Escherichia coli* diarrhea and were 8% dehydrated with intravenous fluids was universally successful, whereas treatment of similar calves with oral electrolyte solutions alone was always fatal [95].

Dehydrated or endotoxemic adult ruminants typically have a hypochloremic, hypokalemic, metabolic alkalosis [17]. The current recommended treatment for moderately dehydrated adult ruminants (<8% body weight) is oral electrolyte administration alone, whereas intravenous fluid therapy is required for treating severely dehydrated ruminants (≥8% dehydrated). The cut-off value of 8% is empiric but provides a useful clinical guide.

Acidemic neonatal and adult ruminants (blood pH <7.20) should be treated with intravenous iso-osmotic $NaHCO_3$ (1.3% solution). $NaHCO_3$

remains the alkalinizing agent of choice, despite continued interest in other alkalinizing solutions such as tromethamine and Carbicarb. Alkalemic ruminants (blood pH > 7.45) should received Ringer's solution; it is the acidifying agent of choice.

Small-volume hypertonic saline

The administration of large volumes of iso-osmotic crystalloid solutions may necessitate administering 40 to 60 L/d, which is impractical in an on-farm setting. Rapid administration of small-volume hypertonic saline (HS) solutions therefore offers an extremely attractive method for fluid resuscitation of dehydrated adult ruminants; however, with the exception of rapid resuscitation, HS provides an inferior treatment than conventional large-volume iso-osmotic crystalloid solutions. HS is clearly better than no treatment at all, however.

Studies have examined the effect of 7.2% HS in endotoxemic calves [100,101,103], diarrheic calves [111], dehydrated calves [103], normovolemic calves [107,112], endotoxemic cows [30,104–106], normovolemic cows [30,108], and sheep with hypochloremic, hypokalemic, or metabolic alkalosis [102] or hemorrhagic shock [44,99]. These studies have demonstrated the beneficial effects and safety of HS administered to cattle and sheep.

The beneficial hemodynamic effects of HS originally were attributed to four factors: (1) rapid plasma volume expansion (increased preload), (2) transient vasodilation (decreased afterload), (3) a vagally mediated reflex dependent on stimulation of pulmonary osmoreceptors, and (4) increased cardiac contractility [113]. The results of more recent studies, however, have demonstrated that the beneficial hemodynamic effect of HS is primarily due to rapid plasma volume expansion and transient decrease in afterload, and that HS actually decreases cardiac contractility and fails to activate a pulmonary reflex [27,113,114]. HS produces its resuscitative effects primarily by rapidly increasing plasma volume by "borrowing" free water from the intracellular space and gastrointestinal tract, thereby increasing cardiac output, mean arterial pressure, oxygen delivery, and glomerular filtration rate [113].

Although the resuscitative response to HS is not as sustained as that obtained from HS dextran, it is recommended that HS be used in adult ruminants because it is considerably cheaper. HS (2400 mOsm/L, 4–5 mL/kg, for 4–5 minutes, intravenously) can be administered safely to dehydrated or endotoxemic adult ruminants or ruminants with hemorrhagic shock. This method is equivalent to administering 2 L of HS to an adult cow through a 14-gauge needle in the jugular vein. Typically, this volume requires 8 to 10 minutes to be administered through a simplex; faster rates of administration can be obtained using a 60-mL syringe and extension tubing attached to the 14-gauge needle. Cattle should be provided with a supply of fresh water immediately after treatment (most drink 5–10 gallons for the next

10 minutes), and cattle not observed to drink within 5 minutes should have 5 gallons of water pumped into the rumen. It should be emphasized that HS should never be given alone without providing the animal with fresh water to drink or ororuminal administration of water. Treatment with HS can be repeated once in 24 hours if needed, but further additional treatments should not be contemplated without checking the serum sodium concentration.

HS solutions are commercially available but also can be formulated by adding 72 g of NaCl to 1 L of distilled water (see Appendix 2). Opened HS should be kept at room temperature if unused solutions, already opened, are not discarded.

Potential disadvantages of HS administration are hypokalemia, hypernatremia, and hyperosmolarity, particularly in patients with compromised renal function [115]. Hypokalemia results from rapid expansion of the extravascular space and a strong-ion effect resulting in extracellular potassium exchange for sodium [4–7]. A number of studies have reported a transient hypokalemia (decrease <0.8 mEq/L) after HS infusion [101–103,107]; however, hypokalemia-related cardiac arrhythmias have not been reported [113].

HS solutions (osmolarity, 2400 mOsm/L) should not be used in animals with chronic severe hyponatremia (solute loss in excess of water), because studies in rats with experimentally induced severe hyponatremia (plasma sodium concentration, 95 mEq/L) indicated that HS successfully resuscitated rats with acute hyponatremia (7 hours' duration) but induced 40% mortality in rats with longer periods of hyponatremia (>24 hours), with histologic evidence of central pontine myelinolysis [116]. The clinical relevance of this study for calves with dehydration and diarrhea remains uncertain, because mild hyponatremia usually is present in calves with diarrhea; plasma sodium concentrations less than 110 mEq/L are extremely rare [16,50,117]. HS solutions (osmolarity, 2400 mOsm/L) should not be used to treat hypernatremic, hyperosmolal, or hypovolemic (water loss in excess of solute) animals such as water-deprived cattle or calves fed inappropriately formulated oral electrolyte solutions; however, mildly HS solutions (osmolarity, 350 mOsm/L) are indicated. Rapid increases in serum sodium concentration have resulted in cerebral dysfunction and coma, particularly if the serum osmolarity increases acutely, greater than 350 mOsm/L [115]. Seizures in conscious animals after administration of 2400 mOsm/L of NaC1 for at least 1 minute have not been reported [118].

Small-volume hypertonic saline dextran

Experimental studies have examined the effect of HS dextran in dehydrated calves with diarrhea [42,43] and in sheep with hemorrhagic shock [44,45]. The addition of the colloid dextran 70 to HS (producing HS-dextran solution) prolongs the resuscitative effect [113]. The beneficial effects

of HS dextran have been attributed to a synergistic action of the hypertonic properties of NaCl and the hyperoncotic properties of dextran [119]. The hypertonic NaCl solution draws fluid from the intracellular space and gastrointestinal tract down a concentration gradient into the extracellular compartment. Water is believed to shift initially from red blood cells and endothelial cells, and then from the interstitial space and tissue cells [120]. Dextran maintains this mobilized fluid in the intravascular space by increasing colloidal oncotic pressure [119].

HS-dextran solution (2400 mOsm/L in 6% dextran 70, 4–5 mL/kg during 4–5 minutes, intravenously) can be administered safely to dehydrated or endotoxemic calves. This method is equivalent to administering 120 to 200 mL of HS dextran through an 18-gauge needle or temporary catheter in the jugular vein. Calves should be allowed immediately to suckle an isotonic oral electrolyte solution, and calves not willing to suckle within 5 minutes of administration of HS dextran should be intubated ororuminally. It should be emphasized that HS dextran should never be given alone without a "chaser" of isotonic oral electrolyte solution [42]. Treatment with HS dextran should not be repeated; calves that fail to respond to one intravenous treatment and isotonic oral electrolyte solutions should have their acid-base and serum electrolyte status determined and intravenous treatment administered as indicated by the results of laboratory analysis. It is also important to administer an iso-osmotic oral electrolyte solution instead of a hyperosmotic solution.

The HS-dextran solution is not commercially available, but it can be formulated easily from commercially available solutions of dextran 70. To make a 7.2% NaCl in 6% dextran 70 solution, take a 500-mL plastic bag containing 6% dextran 70 in 0.9% NaCl (such as Gentran 70). Remove the plunger from a sterile 60-mL syringe connected to a 16-gauge needle; place 31.6 g of NaCl into the syringe barrel and replace the plunger. Carefully draw 60 mL of dextran 70 solution into the syringe and dissolve the NaCl crystals in the syringe by gentle rocking. Then inject the dextran 70–NaCl solution back into the 500-mL plastic bag. This solution provides 500 mL of 7.2% NaCl in 6% dextran 70. The solution should be refrigerated and used within 3 months.

Hypocalcemia

Periparturient hypocalcemia (milk fever) remains an important cause of morbidity and mortality in dairy cows, and hypocalcemia is a common clinicopathologic finding in sick ruminants [17]. The administration of calcium should be a mandatory component of fluid and electrolyte administration to lactating ruminants.

Calcium should be administered by the intravenous, subcutaneous, or oral route. Calcium gluconate and calcium borogluconate are the preferred forms for intravenous and subcutaneous administration because $CaCl_2$

causes extensive necrosis and sloughs of tissue when administered perivascularly. Compared with calcium gluconate, calcium borogluconate has improved solubility and shelf life. Plasma-ionized calcium concentrations are increased to a greater extent following $CaCl_2$ treatment when high equimolar solutions of $CaCl_2$ and calcium gluconate are administered, leading to more cardiac arrhythmias during $CaCl_2$ administration [121,122]. As discussed previously, administration of large quantities of calcium gluconate or calcium borogluconate induces a mild strong-ion acidosis (metabolic acidosis) because ruminants do not metabolize gluconate (and presumably borogluconate) [14,123]. A typical treatment to an adult lactating dairy cow with periparturient hypocalcemia is 500 mL of 23% calcium borogluconate by slow intravenous injection with cardiac auscultation, which provides 10.7 g of calcium. Although the calculated calcium deficit in a recumbent periparturient dairy cow is 4 g of calcium, practitioners should provide additional calcium to overcome the continued loss of calcium in milk [124]. A field study comparing the effectiveness of different doses of calcium for treating periparturient milk fever determined that 9 g of calcium was superior to 6 g [125]. A good rule of thumb for administering 23% calcium borogluconate solutions (2.14 g of calcium/100 mL) to cows with periparturient hypocalcemia is therefore to administer 1 mL/kg body weight.

The normal cardiac response to calcium administration is an increase in the strength of cardiac contraction and a slowing of the heart rate. Intravenous administration is continued until the first arrhythmia is detected (a bradyarrhythmia, such as a prolonged pause); the rate of intravenous administration then is slowed until a second arrhythmia is detected, at which time intravenous administration is discontinued and the remainder of the solution is placed subcutaneously over the lateral thorax. This treatment method titrates the calcium dose required for each animal. Auscultation of the heart is an absolute requirement during treatment; visual monitoring of the jugular pulse at the base of the neck does not allow the early detection of bradyarrhythmias, making it more likely that the cow will receive a toxic and possibly lethal dose of calcium. The maximum safe rate of calcium administration in cattle is 0.07 mEq of Ca^{2+}/kg body weight/min [126], which is equivalent to 0.065 mL of 23% calcium borogluconate/kg body weight/min. For a 500-kg normocalcemic dairy cow, this rate corresponds to a maximum safe rate of administration of 33 mL/min. Typical rates of administration through a 14-gauge needle are 50 mL/min; this rate of administration is safe for cows with hypocalcemia, provided that cardiac auscultation is performed during administration.

Subcutaneous administration of calcium solutions has been practiced for many years. To facilitate absorption, it is preferable to administer no more than 125 mL at a site, although this supposition (and volume) do not seem to have been verified. A 14-gauge needle is placed subcutaneously over the lateral thorax, 125 mL is administered, the needle is redirected, and another

125 mL is administered. The process then is repeated on the other side of the cow. Although the effectiveness of subcutaneous administration of calcium has been documented in healthy normal cows [124], there do not seem to be any reports documenting the rapidity by which subcutaneous calcium is absorbed by cows with periparturient hypocalcemia. Subcutaneous administration of calcium gluconate is not recommended in recumbent cows because poor peripheral blood flow is suspected to lead to slow absorption from the subcutaneous site. $CaCl_2$ is not recommended for subcutaneous administration because of extensive tissue damage; the addition of dextrose to the administered calcium also is not recommended because it increases the tonicity of the solution and propensity for bacterial infection and abscessation. Rectal calcium administration is not recommended because it causes severe mucosal injury and tenesmus but does not increase plasma concentrations of calcium [127].

Oral administration of calcium also has been practiced for many years, usually by ororuminal intubation of calcium borogluconate solutions designed for parenteral administration. During the past decade, there has been increased interest in improving the efficacy of oral calcium formulations. The results of a number of studies indicate that oral calcium salts are effective at increasing plasma calcium concentration; orally administered calcium is absorbed by a dose-dependent passive diffusion process across ruminal epithelium and a dose-independent calcium-binding protein mechanism in the small intestine that is modulated by vitamin D [128]. Passive diffusion across the ruminal epithelium occurs when the calcium concentration is greater than 1.5 mmol/L [129] but is substantial when the calcium concentration in rumen fluid is greater than 6 mmol/L [130], which is approximately five times the normal value in plasma. Rapid correction of hypocalcemia by oral calcium administration must use passive ruminal diffusion, because small intestinal absorption is too slow to be of clinical value [124].

Two calcium formulations currently are recommended for oral administration to ruminants: $CaCl_2$ and calcium propionate. Most commercially available products, however, contain 50 g of $CaCl_2$. $CaCl_2$ has the advantage of low cost and low volume (because of its high solubility), but $CaCl_2$ can damage the pharynx and esophagus in ruminants severely, causing reduced swallowing ability; it can lead to necrosis of the forestomach and abomasum when administered in high doses; and it can lead to aspiration pneumonia when administered as a drench. Calcium propionate has the advantage of being less irritating while providing a gluconeogenic substrate (propionate) but the disadvantages of higher volumes and cost. The effectiveness of ororuminal administration of higher-volume calcium propionate solutions has been evaluated [131]. Oral calcium solutions should be administered only to cattle that have normal swallowing ability, precluding their administration to animals with advanced clinical signs of hypocalcemia. Higher plasma calcium concentrations are obtained more

quickly when calcium solutions are drenched after administration of vasopressin to induce esophageal groove closure, or when the calcium solution is administered as a drench instead of ororuminal intubation [128].

Calcium solutions are suspected to be associated with a higher likelihood of aspiration pneumonia than calcium gels (with a consistency similar to toothpaste), although this supposition does not seem to have been verified. Only two studies have examined the safety of $CaCl_2$ gels and emulsions; oral administration of 880 g of $CaCl_2$ in a gel over 24 hours caused diarrhea and severe injury to the reticular groove, omasum, and abomasum of adult cattle (suggesting induction of esophageal groove closure), whereas oral administration of 576 g of $CaCl_2$ in a soybean emulsion caused only minor irritation [132]. In a second study, oral administration of 592 g of $CaCl_2$ in a gel over 24 hours caused diarrhea and severe injury to the forestomach of adult cattle, whereas oral administration of 604 g of $CaCl_2$ diluted in a soybean emulsion caused only minor irritation [133]. Commercially available formulations of calcium gels contain 50 g of $CaCl_2$ and increase plasma calcium concentrations within 30 to 60 minutes and for at least 6 hours. Retreatment at 12-hour intervals (if needed) therefore seems indicated and provides 100 g of $CaCl_2$ and 37 g of calcium over 24 hours, but more aggressive treatment protocols are not recommended.

Hypomagnesemia

Magnesium usually is administered parenterally only when a ruminant exhibits clinical signs of hypomagnesemia. Treatment of hypomagnesemia is more dangerous (to the animal and the clinician) and less satisfying than treatment of periparturient hypocalcemia; the response to treatment is much slower in hypomagnesemia, presumably because magnesium concentrations must be normalized in cerebrospinal fluid, which turns over at approximately 1% per minute.

Treatment of hypomagnesemia historically has used 25% epsom salt solution (magnesium sulfate heptahydrate; $MgSO_4 \cdot 6H_2O$); this solution concentration was selected because it provided approximately 1 mmol of magnesium per liter. It should be noted that 25% epsom salt solution is markedly hyperosmotic (2028 mOsm/L). A typical treatment to an adult cow has been slow intravenous administration (for at least 5 minutes) of 100 mL of the 25% epsom salt solution, which provides 2.5 g of magnesium (0.025 g of magnesium/mL of solution). More recently, hypomagnesemia has been treated using commercially available combined calcium, magnesium, and phosphorous solutions; 500 mL of these solutions typically contains 1.6 to 2.7 g of magnesium in the form of a borogluconate, chloride, or hypophosphite salt (as noted in a following section, the phosphorous in hypophosphite salt form is unavailable to ruminants and therefore worthless). Although the calculated extracellular deficit in a cow with hypomagnesemia is 2 g of magnesium, the practitioner should provide

additional magnesium to correct presumed intracellular deficiencies and to overcome the anticipated urinary loss of magnesium [124]. Combined calcium and magnesium solutions are preferred for intravenous administration to 25% epsom salt solution because ruminants with hypomagnesemia frequently have hypocalcemia, and hypercalcemia provides some protection against the toxic effects of hypermagnesemia. Administration of solutions containing magnesium as the only cation increases the risk of developing cardiac and respiratory failure during treatment [134]. The maximum safe rate of administration of magnesium in cattle is 0.08 mEq of Mg^{2+}/kg body weight/min [126], which is equivalent to 0.04 mL 25% epsom salts/kg body weight/min. For a 500-kg beef cow with hypomagnesemia, this rate corresponds to a maximum safe rate of administration of 20 mL/min.

Magnesium-containing solutions (such as 25% epsom salt solution) also can be administered subcutaneously, although this method frequently leads to necrosis of the skin, particularly when 50% epsom salt solution is administered. Only combined calcium-and-magnesium solutions should be administered subcutaneously.

The oral bioavailability of magnesium is low and much lower than that of calcium. Oral administration of magnesium is not recommended for the treatment of hypomagnesemia, but it is essential for the prevention of hypomagnesemia. Magnesium absorption from the rumen is facilitated by volatile fatty acids but decreased by potassium and the ammonium ion [135]. Rectal administration may be the only practical and safe method for treating a convulsing hypomagnesemic beef cow. After evacuating the rectal contents, an enema containing 60 g of epsom salt (magnesium sulfate heptahydrate) or magnesium chloride in 200 mL of water can be placed in the descending colon (not the rectum) and the tail held down for 5 minutes; this solution increases plasma magnesium concentrations within 10 minutes. Enema solutions can be evacuated prematurely, however, eliminating the chance for therapeutic success, and some degree of colonic mucosal injury is expected because of the high osmolarity of 30% solutions (approximately 2400 mOsm/L). The safety of this treatment protocol does not seem to have been evaluated, although a 50 mL enema of a 30% $MgCl_2 \cdot 6H_2O$ solution rapidly and effectively increased serum magnesium concentration in 7- to 10-week-old calves and relieved clinical signs of hypomagnesemia [136].

Oral administration of magnesium hydroxide and magnesium oxide excessively alkalinizes the rumen and can create a severe metabolic alkalosis (strong-ion alkalosis), because absorption of magnesium leads to hypermagnesemia [137,138] and increased plasma SID. Because oral administration of $NaHCO_3$ causes expansion of the plasma volume and creates a metabolic alkalosis (strong-ion alkalosis) without hypermagnesemia [69,70], it is likely that oral $NaHCO_3$ is a more effective treatment for grain overload in ruminants than oral magnesium hydroxide or magnesium oxide, although this presumption remains to be verified.

Hypophosphatemia

Hypophosphatemia has long been considered a cause of muscle weakness and recumbency in ruminants, although unequivocal documentation of this effect is not available. Many inappetent and weak cows have marginal hypophosphatemia, however, and clinically appear to benefit from normalization of their plasma concentration of phosphate. As such, it currently is recommended that ruminants with marked hypophosphatemia and signs of illness should be treated with phosphorus-containing solutions.

Almost all commercially available intravenous solutions for treating hypophosphatemia use phosphite (PO_2^{2-}) or hypophosphite (PO_3^{3-}) salts as the source of phosphorus because these salts are soluble, even in the presence of calcium and magnesium [139]. Seminal work by Goff and his colleagues [139] clearly has demonstrated that phosphorus in phosphite and hypophosphite is unavailable to ruminants, meaning that most ''phosphate''-containing solutions have no efficacy in treating hypophosphatemia. Instead, the monobasic monophosphate form of sodium phosphate (NaH_2PO_4) should be administered. The pH of the solution should be mildly acidic (pH = 5.8) to maintain phosphate solubility in cold weather but is not needed in warm, ambient temperatures [124]. A recommended treatment to an adult lactating dairy cow with severe hypophosphatemia is 300 mL of 10% NaH_2PO_4 (monohydrate) solution by slow intravenous injection, which provides 7 g of phosphate and increases plasma phosphate concentrations for at least 6 hours. Although the calculated phosphorus deficit in a dairy cow is 4.8 g of phosphate, the practitioner should provide additional phosphorus to correct presumed intracellular deficiencies and the continued loss of phosphorus in saliva [124]. Human enema formulations that contain a mixture of monobasic sodium phosphate monohydrate and dibasic sodium phosphate heptahydrate in a buffered solution (Unflavored Phospho-Soda, available over the counter) also have been administered to cattle with hypophosphatemia [124]. This human enema solution is extremely hyperosmotic (calculated osmolarity of 8970 mOsm/L) and therefore must be diluted with at least 4 mL of water for every 1 mL of enema solution (decreasing the osmolarity to 1794 mOsm/L, which is similar to 10% NaH_2PO_4 monohydrate solution). Obviously, intravenous administration of 10% NaH_2PO_4 (monohydrate) solution is preferable to the intravenous administration of a diluted human enema solution. A major drawback with intravenous administration of phosphate solutions is that they should not be administered within 2 hours of intravenous calcium administration, because of concerns that calcium-phosphate precipitates may be formed in the plasma of cattle with treatment-induced hypercalcemia and hyperphosphatemia [124].

Hypophosphatemia is treated more safely by administration of oral phosphate, and this method is preferred for administration in ruminants with rumen motility. Oral administration also results in a more prolonged

increase in plasma phosphorus concentration. The recommended dose is 200 g of feed-grade monosodium phosphate (it contains 50 g of phosphate) administered in gelatin boluses, drench, or by ororuminal intubation [139]. Phosphorus in other feed-grade minerals (such as bone meal or dicalcium phosphate) is poorly available and not recommended for the treatment of hypophosphatemia [124].

Hypokalemia

Hypokalemia occurs commonly in inappetent adult ruminants [15], particularly in lactating dairy cows because of the loss of potassium in the milk [140], and severe hypokalemia (serum $[K^+] < 2.2$ mEq/L) causes muscular weakness and recumbency [118,141,142]. Similar to calcium, oral administration of potassium is a mandatory component of fluid and electrolyte administration to lactating dairy cows.

Potassium should be administered intravenously or orally. The intravenous route is used only for the initial treatment of recumbent ruminants with severe hypokalemia and rumen atony, because it is much more dangerous and expensive than oral treatment. The most aggressive intravenous treatment protocol is an iso-osmotic solution of potassium chloride (KCl) (1.15% KCl), which should be administered at less than 3.2 mL/kg/h, equivalent to a maximal delivery rate of 0.5 mEq of K^+/kg/h. Higher rates of potassium administration run the risk of inducing hemodynamically important arrhythmias, including ventricular premature complexes that can lead to ventricular fibrillation and death. A less-aggressive intravenous treatment is an iso-osmotic equimolar mixture of NaCl (0.45% NaCl) and KCl (0.58% KCl), and the least aggressive intravenous treatment is the addition of 10 mmol of KCl/L of Ringer's solution, which increases the solution osmolarity to 329 mOsm/L. Clinical experience with oral administration of KCl markedly has decreased the number of adult ruminants treated with intravenous KCl.

Oral potassium administration is the method of choice for treating hypokalemia. Practitioners routinely treat inappetent adult cattle with 30 to 60 g of feed-grade KCl twice at a 12-hour interval, with the KCl placed in gelatin boluses. Adult cattle with severe hypokalemia (<2.5 mEq/L) should be treated initially with 120 g of KCl, followed by two 60-g KCl treatments at 8-hour intervals, for a total 24-hour treatment of 240 g of KCl. Higher doses have been administered to dairy cows but are accompanied by diarrhea [118], and oral administration of 0.58 g of KCl/kg body weight was toxic in 6-month-old Holstein calves, manifest by excessive salivation, muscular tremors of the legs, excitability, and a peak plasma $[K^+]$ of 9.0 mEq/L [143]. Extrapolating this toxic dose in normokalemic calves to hypokalemic 600-kg cows suggests that a daily dose of 240 g of KCl approaches the upper limit of safety. The recommended doses are empiric but are effective in rapidly increasing serum $[K^+]$ and $[Cl^-]$.

Hyperkalemia

Hyperkalemia traditionally has been treated by intravenous administration of $NaHCO_3$, glucose, insulin, and sometimes calcium. HS is just as effective as hyperosmotic $NaHCO_3$ in decreasing hyperkalemia and hyperkalemia-associated bradyarrhythmias [144]. The electrocardiographic effects of hyperkalemia are exacerbated by the presence of hyponatremia, acidemia, and hypocalcemia [145]. Intravenous administration of HS (1670 mOsm/L) to human patients with hyperkalemia and hypovolemia rapidly reversed electrocardiographic abnormalities of hyperkalemia and decreased the concentration of potassium in the serum, probably because of intracellular movement of potassium, extracellular volume expansion [145], and the strong-ion effect of increasing the serum concentration of a strong cation. Similar electrocardiographic changes are observed when HS is administered to dehydrated calves with hyperkalemic-induced bradyarrhythmias [113].

The long-held myth regarding the need to administer glucose and insulin to "drive" potassium into the cells during hyperkalemia needs to be re-evaluated. The administration of high glucose concentrations to hyperkalemic, dehydrated calves decreases serum potassium concentration probably because it also increases serum sodium concentration [16], and hypernatremia induces hypokalemia through a strong-ion effect. The focus of treatment in hyperkalemia should be correction of acidemia and plasma volume expansion and increasing the serum sodium concentration. Glucose and insulin are not needed to correct hyperkalemia.

Hypoglycemia

The maintenance requirement for a dairy cow is 60 g of glucose/h, whereas 120 g of glucose/h is required for high-producing dairy cows. Administration of one 500-mL bottle of 50% dextrose (which contains 250 g dextrose) every 4 to 6 hours therefore provides the maintenance glucose requirements and is a useful treatment for severe ketosis or hepatic lipidosis. During treatment, urine and blood glucose concentrations should be monitored to ensure that the rate of glucose administration is appropriate. In calves aged 5 to 8 weeks, the plasma glucose threshold for glycosuria was approximately 180 mg/dL (9.0 mmol/L), and administration rates greater than 0.06 g of dextrose/kg body weight/min were deleterious [146].

Summary

Five important questions always must be asked and answered regarding fluid and electrolyte therapy in ruminants: (1) Is therapy needed? (2) What type of therapy? (3) What route of administration? (4) How much should be administered? and (5) How fast should the solution be administered?

Food animal veterinarians routinely should carry the following commercially available crystalloid solutions and have the knowledge of how to use the products appropriately: Ringer's solution, 1.3% $NaHCO_3$, acetated Ringer's solution, HS (7.2% NaCl), 8% $NaHCO_3$, 23% calcium gluconate, calcium-magnesium solutions, and 50% dextrose. Ruminants with a blood pH less than 7.20 should be treated intravenously with 1.3% or 8.0% $NaHCO_3$, and those animals with a blood pH greater than 7.45 should be treated intravenously with Ringer's solution. Oral electrolyte solutions or intravenous acetated Ringer's solution should be administered to ruminants with a blood pH greater than 7.20 but less than 7.45, and acetated Ringer's solution is preferred to lactated Ringer's solution. HS solution should be administered whenever rapid resuscitation is required.

Oral administration of electrolyte solutions is underused in neonatal and adult ruminants. The optimal solution for oral administration to neonatal ruminants has a sodium concentration between 90 and 130 mmol/L; a potassium concentration between 10 and 20 mmol/L; a chloride concentration between 40 and 80 mmol/L; 40 to 80 mmol/L of metabolizable (nonbicarbonate) base, such as acetate or propionate; and glucose as an energy source. The optimal formulation for adult ruminants is unknown, but such a solution should contain sodium, potassium, calcium, magnesium, phosphate, and propionate to facilitate sodium absorption and to provide an additional source of energy to the animal.

Acidemia is treated best by intravenous or oral administration of $NaHCO_3$. Alkalemia is treated best by intravenous administration of Ringer's solution and oral administration of chloride-rich electrolytes such as KCl; the latter provides a physiologically more appropriate treatment than oral administration of vinegar or acetic acid solutions. Hypocalcemia is treated best by administering intravenous calcium borogluconate solutions or oral $CaCl_2$ gels. Hypomagnesemia is treated best by intravenous or subcutaneous administration of combined calcium and magnesium solutions. Hypophosphatemia is treated best by oral administration of feed-grade monosodium phosphate. Hypokalemia is treated best by oral administration of feed-grade KCl; hyperkalemia is treated best by intravenous administration of 8.0% $NaHCO_3$ or HS. The major challenges in treating fluid and electrolyte disorders in ruminants are making treatment protocols more practical and less expensive and formulating an optimal electrolyte solution for oral administration to adult ruminants.

Appendix 1

Table 2
Calculation of milliequivalents and milliosmoles for compounds commonly administered to ruminants

		When in solution			
Chemical formula	Molecular weight (g)	Eq/mol	Total mEq (mEq/g)	Osm/mol	Osmolality (mOsm/g)
NaCl (sodium chloride)	58.4	2	34.2	2	34.2
KCl (potassium chloride)	74.6	2	26.8	2	26.8
$CaCl_2 \cdot 2H_2O$ (calcium chloride dihydrate)	147.0	4	27.2	3	20.4
$MgCl_2 \cdot 6H_2O$ (magnesium chloride hexahydrate)	203.3	4	19.7	3	14.8
$NaHCO_3$ (sodium bicarbonate)	84.0	2	23.8	2	23.8
Na L-lactate $(CH_3\text{-}(CHOH)\text{-}COO^-)Na$	112.1	2	17.8	2	17.8
Na-acetate $(CH_3\text{-}COO^-)Na^+$	82.0	2	24.4	2	24.4
Na D-gluconate $(CH_2OH\text{-}(CHOH)_4\text{-}COO^-)Na^+$ = D-gluconic acid sodium	218.1	2	9.2	2	9.2
Ca D-gluconate $(CH_2OH\text{-}(CHOH)_4\text{-}COO^-)_2Ca^{2+}$ = D-gluconic acid calcium	430.4	4	9.3	2	4.6
$MgSO_4 \cdot 7H_2O$ (magnesium sulfate heptahydrate, Epsom slats)	246.5	4	16.2	2	8.1
$NaH_2PO_4 \cdot H_2O$ (sodium phosphate, monobasic, monohydrate)	138.0	2.8	20.3	2	14.5
Glucose $(C_6H_{12}O_6) \cdot H_2O$ = dextrose monohydrate	198.2	0	0	1	5.0

Appendix 2. Hypo-osmotic, iso-osmotic, and hyperosmotic crystalloid solutions administered to ruminants

Hypo-osmotic solutions (<300 mOsm/L)

1. Lactated Ringer's solution (synthesized Hartmann's solution, 275 mOsm/L calculated). Commercially available. Solution can also be formulated by adding 4.4 ml of sodium lactate as a syrup (70% solution) to 996 ml of water containing the other electrolytes and mixing well.

NaCl	6.0 g/L	Na^+	130 mEq/L
KCl	0.30 g/L	K^+	4 mEq/L
$CaCl_2$-dihydrate	0.17 g/L	Ca^{2+}	3 mEq/L
Sodium lactate	3.1 g/L	Cl^-	109 mE/q/L
		Lactate	28 mEq/L

2. Acetated Ringer's solution (294 mOsm/L calculated). Commercially available.

NaCl	5.3 g/L	Na^+	140 mEq/L
KCl	0.38 g/L	K^+	5 mEq/L
$MgCl_2 \cdot 6H_20$	0.23 g/L	Mg^{2+}	3 mEq/L
Sodium acetate	2.2 g/L	Cl^-	98 mEq/L
Sodium gluconate	5.0/L	Acetate	27 mEq/L
		Gluconate	23 mEq/L

3. Isotonic Dextrose (5% solution, 250 mOsm/L calculated). Commercially available.

D-glucose monohydrate	50 g/L	Glucose	0 mEq/L

Iso-osmotic solutions (300–312 mOsm/L)

1. Isotonic saline (0.9% solution, 308 mOsm/L calculated). Commercially available.

NaCl	9.0 g/L	Na^+	154 mEq/L
		Cl^-	154 mEq/L

2. Ringer's solution (309 mOsm/L calculated). Commercially available.

NaCl	8.6 g/L	Na^+	147 mEq/L
KCl	0.30 g/L	K^+	4 mEq/L
$CaCl_2$-dihydrate	0.30 g/L	Ca^{2+}	4 mEq/L
		Cl^-	155 mEq/L

3. Darrow's solution (312 mOsm/L calculated). Not commercially available.

NaCl	4.0 g/L	Na^+	121 mEq/L
KCl	2.61 g/L	K^+	35 mEq/L
Sodium lactate	5.9 g/L	Cl^-	103 mEq/L
		Lactate	53 mEq/L

4. McSherry's solution (312 mOsm/L calculated). Not commercially available.

NaCl	5.0 g/L	Na^+	140 mEq/L
KCl	0.75 g/L	K^+	10 mEq/L
$CaCl_2$ = dihydrate	0.37 g/L	Ca^{2+}	5 mEq/L
$MgCl_2 \cdot 6H_2O$	0.3 g/L	Mg^{2+}	3 mEq/L
Sodium acetate	4.4 g/L	Cl^-	103 mEq/L
		Acetate	54 mEq/L

5. Isotonic sodium bicarbonate (1.3% solution, 310 mOsm/L calculated). Commercially available.

$NaHCO_3$	13.0 g/L	Na^+	155 mEq/L
		HCO_3^-	155 mEq/L

6. Isotonic KCl (1.15% solution, 308 mOsm/L calculated). Not commercially available.

KCl	11.5 g/L	K^+	154 mEq/L
		Cl^-	154 mEq/L

Hyperosmotic solutions (>312 mOsm/L)

1. Hypertonic saline (7.2% solution, 2460 mOsm/L calculated). Commercially available.

NaCl	72 g/L	Na^+	1230 mEq/L
		Cl^-	1230 mEq/L

2. Hypertonic sodium bicarbonate (8.4% solution, 2000 mOsm/L calculated). This solution provides 1 mEq/ml of HCO_3^-. Commercially available.

$NaHCO_3$	84 g/L	Na^+	1000 mEq/L
		HCO_3^-	1000 mEq/L

3. Hypertonic sodium bicarbonate (5% solution, 1190 mOsm/L calculated). Commercially available.

$NaHCO_3$	50 g/L	Na^+	595 mEq/L
		HCO_3^-	595 mEq/L

4. Hyperosmotic dextrose (50% solution, 2500 mOsm/L calculated). Commercially available.

D-glucose monohydrate	500 g/L	Glucose	0 mEq/L

5. Calcium gluconate (23% solution as calcium borogluconate, 1069 mOsm/L calculated). Commercially available.

Calcium borogluconate	230 g/L	Ca^{2+}	1069 mEq/L
		Gluconate	1069 mEq/L

6. Magnesium sulfate (25% solution, 2028 mOsm/L calculated). Not commercially available.

$MgSO_4 \cdot 7H_2O$	250 g/L	Mg^{2+}	2028 mEq/L
		SO_4^{2-}	2028 mEq/L

7. Monosodium phosphate (10% solution, 1450 mOsm/L calculated). Not commercially available.

$NaH_2PO_4 \cdot H_2O$	100 g/L	Na^+	725 mEq/L
		HPO_4^{2-}	580 mEq/L
		$H_2PO_4^-$	145 mEq/L

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