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Disturbances of Free Water, Electrolytes, Acid-Base Balance, and Oncotic Pressure

5

There are many diseases of farm animals in which there are disturbances of body fluids (free water), electrolytes, and acid-base balance. A disturbance of body water balance in which more fluid is lost from the body than is absorbed results in reduction in circulating blood volume and in **dehydration** of the tissues. In contrast, the rapid ingestion of large quantities of water can lead to overhydration (**water intoxication**).

Electrolyte imbalances occur commonly as a result of loss of electrolytes, shifts of certain electrolytes, or relative changes in concentrations caused by loss of water. Common electrolyte imbalances include hyponatremia, hypokalemia, hyperkalemia, hypocalcemia, hypochloremia, and hypophosphatemia.

Acid-base imbalances, either **acidemia** or **alkalemia**, occur as a result of the addition of acid and depletion of alkali reserve, or the loss of acid with a relative increase in alkali reserve.

Decreased **oncotic pressure** is caused by hypoalbuminemia or hypoproteinemia and results from severe gastrointestinal disease, renal glomerular disease, peritonitis, pleuritis, extensive burns, hepatic failure, chronic malnutrition, and severe starvation (increased loss of plasma protein, decreased production of plasma protein, or third spacing of plasma protein). The most common clinical sign of decreased oncotic pressure is generalized edema. Increased oncotic pressure occurs less frequently, and the most common cause is decreased free water from dehydration.

Under most conditions, disturbances of free water, electrolyte, acid-base balance, and oncotic pressure occur simultaneously, in varying degrees, depending on the initial cause. Each major abnormality will be described separately here with an emphasis on etiology, pathogenesis, clinical pathology, and treatment. However, it is important to remember that actual disease states in animals in which treatments with fluids and electrolytes are contemplated are rarely caused by single abnormalities. In most cases it is a combination of dehydration together with an electrolyte deficit, and often without a disturbance of the acid-base balance, that necessitates treatment.

Dehydration

ETIOLOGY

There are two major causes of dehydration (decrease in free water):

- Inadequate water intake
- Excessive fluid loss

Deprivation of water, a lack of thirst caused by toxemia, and the inability to drink water as in esophageal obstruction are examples of dehydration from inadequate water intake. The most common cause of dehydration is when excessive fluid is lost. Diarrhea is the most common reason for excessive fluid loss, although vomiting, polyuria, and loss of fluid from extensive skin wounds or by copious sweating may be important in sporadic cases. Severe dehydration also occurs in acute carbohydrate engorgement in ruminants, acute intestinal obstruction and diffuse peritonitis in all species, and in dilatation and volvulus of the abomasum. In most forms of dehydration (deprivation of drinking water being an exception), the serious loss, and the one that needs correction, is not the fluid but the electrolytes (Fig. 5-1).

The ability to survive for long periods without water in hot climates represents a form of animal adaptation that is of some importance. This adaptation has been examined in camels and in Merino sheep. In the latter, the ability to survive in dry, arid conditions depends on a number of factors, including the insulating ability of the fleece, the ability to carry water reserves in the rumen and extracellular fluid space, the ability to adjust electrolyte concentrations in several fluid locations, the ability of the kidney to conserve water, and the ability to maintain the circulation with a lower plasma volume. Dehydrated mammals in hot environments can save water by reducing the rate of panting and sweating and regulating body temperature above hydrated levels. Sweating is a significant avenue of evaporative heat loss in goats when they are hydrated and when exposed to high ambient temperatures above 40°C.

Observations of drinking behavior of cattle transported to the abattoir indicate that those animals that had been sold in livestock markets before arrival at the abattoir are thirstier and more tired than cattle sent directly from farms. This indicates inadequate water intake and dehydration.

PATHOGENESIS

Two factors are involved in the pathogenesis of dehydration:

- Depression of tissue water content with resulting interference in tissue metabolism
- Reduction in the free water content of blood

The initial response to negative water balance is the withdrawal of fluid from the tissues and the maintenance of normal blood volume. The fluid is drained primarily from the intracellular and interstitial fluid spaces. Essential organs, including the CNS, heart, and skeleton, contribute little and the major loss occurs from connective tissue, muscle, and skin. The loss of fluid from the interstitial and intracellular spaces results in loss of skin elasticity, dryness of the skin and mucosa, and a reduction and retraction of the eyeball (enophthalmia) caused by reduction in the volume of the postorbital fat deposits. In the goat, total body water may be reduced as much as 44% before death occurs.

The secondary response to continued negative water balance is a reduction in the fluid content of the blood causing a reduction in circulating blood volume (**volume depletion**) and an increase in the concentration of the blood (**hemoconcentration**). Because of the hemoconcentration, there is an increase in the viscosity of the blood, which impedes blood flow and may exacerbate peripheral circulatory failure. The loss in circulating blood volume also contributes to the mental depression of dehydrated animals, which is

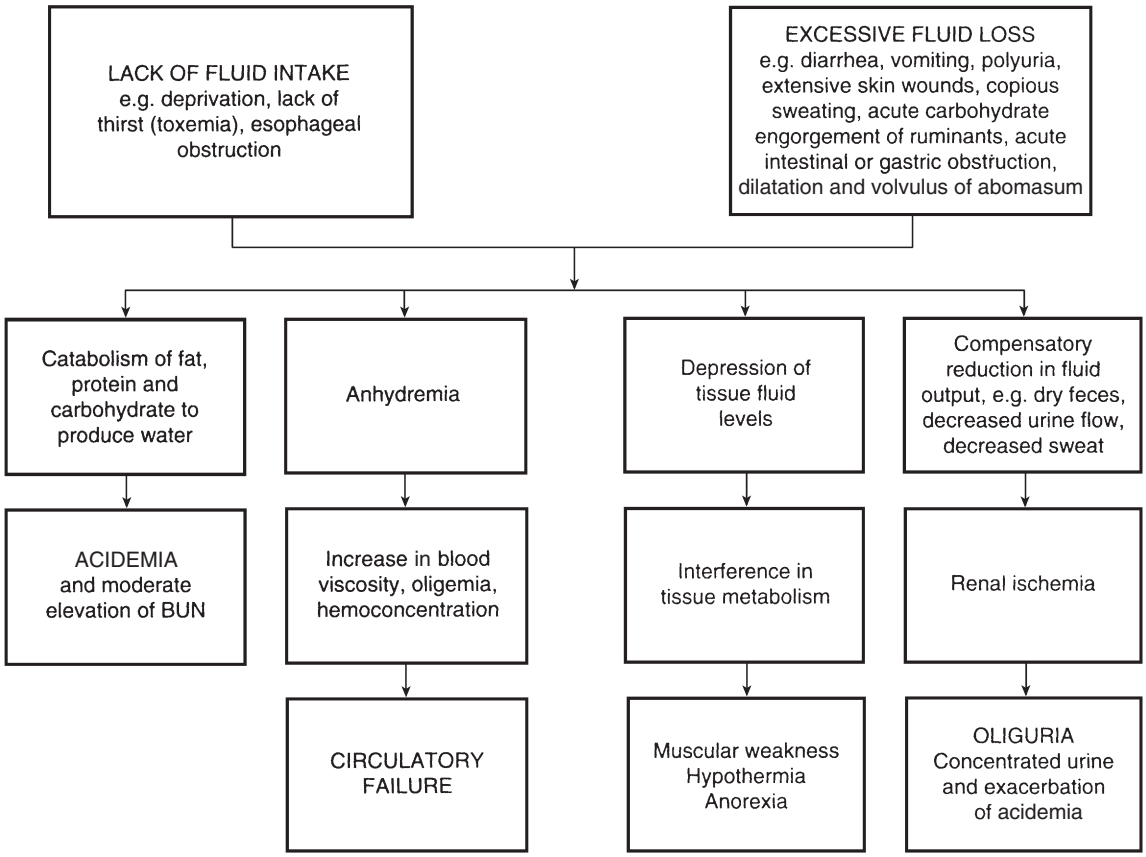


Fig. 5-1 Etiology and pathogenesis of dehydration.

also caused by varying degrees of acidemia and toxemia depending on the cause of the dehydration. In deprivation of water and electrolytes or in deprivation of water alone or inability to consume water in an otherwise normal animal (e.g., esophageal obstruction), the dehydration is minimal because the kidney compensates effectively by decreasing urine output and increasing urine osmolality. In addition, water is preserved by reduced fecal output and increased absorption, which results in dehydration of the contents of the rumen and large intestine, which in turn results in dry, scant feces.

In calves with acute diarrhea there is increased fecal output of water compared with normal calves, but the total water losses are not much greater than in normal calves. In the diarrheic calf the kidney compensates very effectively for fecal water loss, and the plasma volume can be maintained if there is an adequate oral fluid intake. Urine excretion decreases, the urine becomes progressively more concentrated, and the renal insufficiency may accentuate preexisting acidemia and electrolyte imbalance, hence, the importance of restoring renal blood flow and renal function. The newborn calf is able to concentrate urine at almost the same level as the adult. This illustrates the importance of oral fluid and electrolyte intake during diarrhea to compensate for continuous losses. However, it is possible for metabolic acidosis to occur in diarrheic calves and goat kids that are not dehydrated.

Goats are more sensitive to water deprivation during pregnancy and lactation than during anestrus. Water deprivation for 30 hours causes a marked increase in the plasma osmolality and plasma sodium concentration in pregnant and lactating goats, which drink more than goats in anestrus.

The dehydration in horses used for endurance rides is hypotonic, in which both sodium and water are lost through sweating. This may account for the lack of thirst in some dehydrated horses with exhaustion syndrome. Weight losses of 10 to 15 kg/h may occur in horses exercising in high environmental temperatures exceeding 32°C (89°F), and a horse weighing 450 kg can lose 45 L of fluid in a 3-hour ride.

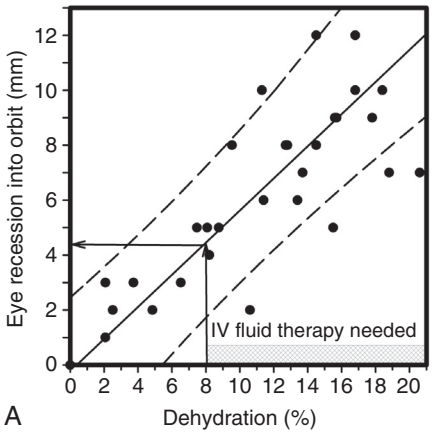
Dehydration exerts important effects on tissue metabolism. There is an increase in the breakdown of fat, then carbohydrate, and finally protein to produce water of metabolism. The increased endogenous metabolism under relatively anaerobic conditions results in the formation of acid metabolites and the development of metabolic acidosis. Urine formation decreases because of the restriction of renal blood flow and this, together with the increased endogenous metabolism, causes a moderate increase in plasma concentration of urea nitrogen. The body temperature may increase slightly initially (as in dehydration hyperthermia) because of insufficient fluid to maintain the loss of heat by evaporation. The onset of sweating in steers after exposure to high environmental temperatures has been shown to be delayed by dehydration.

Dehydration may cause death, especially in acute intestinal obstruction, vomiting, and diarrhea, but it is chiefly a contributory cause of death when combined with other systemic states, such as acidosis, electrolyte imbalances, toxemia, and septicemia.

CLINICAL FINDINGS

The first and most important clinical finding in dehydration is **dryness** and **wrinkling of the skin**, which gives the body and face a shrunken appearance. The eyes recede into the sockets, and the skin subsides slowly after being picked up into a fold. The dehydration is usually much more marked if water and electrolyte losses have been occurring over a period of several days. Peracute and acute losses may not be obvious clinically because major loss will have occurred from the intravascular compartment and only minor shifts have occurred from the interstitial spaces. Sunken eyes and inelastic skin are not remarkable clinical findings of dehydration in the horse.

The best indicator of hydration status in dairy calves has been demonstrated to be the **degree of recession of the eye into the orbit**.



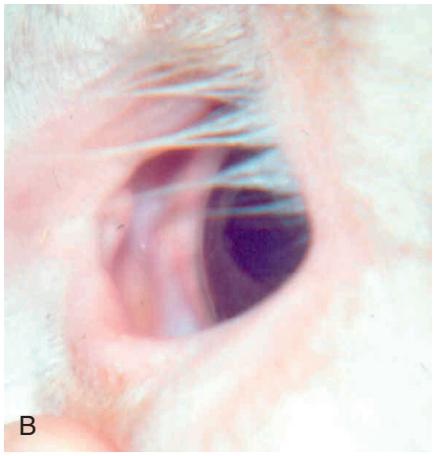


Fig. 5-2 **A,** Association between eye recession into the orbit and dehydration as a percent of body weight in milk-fed calves with experimentally induced diarrhea and dehydration. The filled circles in the left panel are individual data points, the solid line is the linear regression line, and the dashed lines are the 95% confidence interval for prediction. Intravenous fluid is recommended when dehydration is estimated at 8% or more of body weight, equivalent to an eye recession into the orbit of 4 mm or more. **B,** The calf has an 8-mm eye recession into the orbit, equivalent to being 14% dehydrated. (Reprinted with permission from Constable PD et al. *J Am Vet Med Assoc* 1998;212(7):991-996.)

Hydration status is assessed by gently rolling the lower eyelid out to its normal position and estimating the distance of eye recession in millimeters. This distance is multiplied by 1.7 to provide an estimate of the degree of dehydration as a percentage of euhydrated body weight (BW; Fig. 5-2). The second best indicator of hydration status in calves is the elasticity of the skin of the neck and lateral thorax, which are assessed by pinching the skin between the fingers, rotating the skin fold 90°, and noting the time required after release of the skin fold for the skin fold to disappear (normally <2 s). The elasticity of the skin fold on the upper or lower eyelid is a poor indicator of hydration status in calves and is not recommended. The best method for assessing hydration status in adult cattle and other large animals has not been determined, but it is likely that eye recession and skin tent duration in the neck region provide the most accurate and sensitive methods for estimating hydration status. The presence or absence of mucous membrane moistness may provide a sensitive indication of dehydration in dairy calves, but it was not useful as a predictor of hydration status in Brahman-cross calves housed in a hot environment.[1] Hydration status may also be more difficult to clinically evaluate in sheep.[2]

In diarrheic calves, the severity of dehydration, hypothermia, and metabolic acidosis are associated with the degree of mental depression. The combined effects of acidemia and dehydration also contribute to hypothermia.

Loss of BW occurs rapidly in dehydration, and muscular weakness and inappetence or anorexia is common. In horses deprived of water for 72 hours there is a mean BW loss of about 15%, and 95% of the animals have a urine specific gravity of 1.042, a urine osmolality of 1310 mOsm/kg, and a urine osmolality/serum osmolality ratio of 4:14. Prerenal azotemia also develops.

The degree of thirst present will depend on the presence or absence of other diseases causing an inflammatory response or endotoxemia. In primary water deprivation, dehydrated animals are very thirsty when offered water. In dehydration secondary to enteritis associated with severe inflammation, acidemia, and electrolyte imbalance there may be no desire to drink. Horses that become dehydrated in endurance rides may refuse to drink, and the administration of water by oral intubation and enemas may be necessary. In cattle on pasture and deprived of water for up to 9 days and then given access to water, there will be staggering, falling, convulsions, and some death—signs similar to salt poisoning in pigs. Experimental restriction of the water intake in lactating dairy cattle for up to 4 days may reduce milk yield by 75% and decrease BW by 14%. A 10% reduction in water intake causes a drop in milk production that may be difficult to detect. Behavioral changes are obvious: cows spend considerable time licking the water bowls. In cold climates, cattle are often forced to eat snow as a source of water. The snow must be soft enough so that it can be scooped up by the cattle and 3 to 5 days are necessary for the animals to adjust to the absence of water and become dependent on snow. During this time there is some loss of BW. Lactating ewes relying on snow as a source of free water reduce their total water turnover by approximately 35%.

CLINICAL PATHOLOGY

Dehydration is characterized by an increase in the packed cell volume (PCV) and total serum protein concentration, although the latter response may be modified by the presence of severe enteritis, peritonitis, or proteinuria.

Water Intoxication

SYNOPSIS

Etiology Rapid ingestion of large quantities of water

Epidemiology Access to water by thirsty calves, or calves that have been marginally deprived of water for some time

Clinical findings Dark red urine, weakness, and depression

Clinical pathology Hemoglobinuria, hemoglobinemia, hypoosmolality, hyponatremia, and hypochloremia

Necropsy findings Hemoglobinuria and renal cortical necrosis

Diagnostic confirmation Epidemiologic, presence of hyponatremia and hypochloremia; rule out other causes of intravascular hemolysis

Treatment Time, possibly intravenous hypertonic saline but usually too late to be effective

The rapid ingestion of large amounts of water by young calves with normal serum sodium concentrations may result in intravascular hemolysis, hemoglobinemia, and hemoglobinuria. In contrast, water ingestion in hypernatremic animals may result in cerebral edema, but it does not produce hemoglobinuria. The cerebral edema syndrome is described in sodium chloride poisoning. Water intoxication (acute overhydration) is described here.

ETIOLOGY

The ingestion of excessive quantities of water when animals are very thirsty may result in overhydration, which is also called water intoxication. The primary cause of acute overhydration is a rapid decrease in the osmolality of the small intestinal contents, which are normally isotonic to plasma. Such a rapid decrease in luminal osmolality occurs within 5 minutes of water ingestion because thirsty calves close their esophageal groove when drinking. This results in a large volume of water in the abomasum, which is subsequently emptied into the duodenum. Free water rapidly moves from the small intestinal lumen into the intravascular compartment because of the large surface area for absorption in the small intestine and development of an osmotic gradient between the small intestinal lumen and intestinal capillary bed. The end result is a rapid decrease in plasma osmolality and expansion and rupture of erythrocytes, leading to intravascular hemolysis, hemoglobinemia, hemoglobinuria, hyponatremia, hypochloremia, and a decrease in plasma protein concentration from preingestion.

EPIDEMIOLOGY

The syndrome has been reported from several countries but is uncommon. Calves 2 to 4 months of age are most commonly affected, but the disease is also recorded in adult cattle, sheep, and pygmy goats. Water intoxication occurs in calves in normal husbandry systems when animals that have had limited access to water are suddenly given free access. Commonly water intoxication occurs when calves previously fed a milk-replacer diet but no other fluid, or weaned calves that have been on a starter diet but limited water, are turned out to pasture or to yards where water is freely available. Calves that are not fed supplementary salt or that have lost salt as a result of severe exercise or high environmental temperatures may be at higher risk, but the syndrome also occurs where salt has not been restricted. The majority of calves show clinical signs within minutes to hours of access to water.

The condition has been reproduced in calves by gavage with water at 12% of BW.

CLINICAL FINDINGS

Hemoglobinuria as a result of intravascular hemolysis is prominent, and there may be a moderate to severe hemolytic anemia. Dark red urine is passed shortly following access to water. Additional signs include tachycardia and hypothermia if the temperature of the water ingested is below body temperature. Affected animals are usually depressed and weak. (Fig. 5-3)

CLINICAL PATHOLOGY

Hemoglobinuria and hemoglobinemia are evident and there is hypoosmolality, hyponatremia, and hypochloremia. Serum total protein and albumin concentration may be decreased, but are usually within the normal range, because animals are usually mildly dehydrated and thirsty before ingesting large volumes of water.

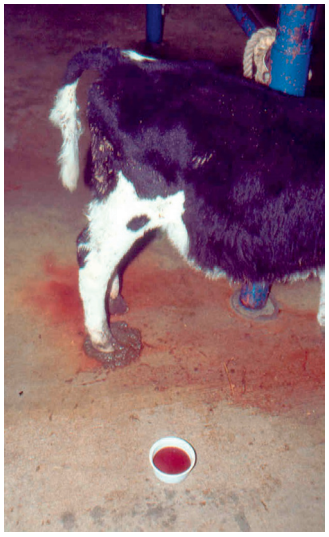


Fig. 5-3 Hemoglobinuria in a Holstein–Friesian heifer calf that had not been provided free access to water. The calf voluntarily drank 5 L in 5 minutes and voided red-tinged urine (on floor and in white container) 30 minutes later.

Postmortem Findings

Marked pallor of the carcass and renal cortical necrosis caused by hemoglobinemic nephrosis may be evident histologically.

DIFFERENTIAL DIAGNOSIS

- Other causes of intravascular hemolysis and hemoglobinuria

TREATMENT

Treatment of affected animals is usually not attempted because hypoosmotic lysis has already occurred when clinical signs have manifested, and serum osmolality is usually gradually increasing as the distal convoluted tubules eliminate excessive free water. Hypertonic saline (7.2% NaCl, 5 mL/kg BW over 5 minutes intravenously) is usually administered to correct the hyponatremia and hypochloremia, but treatment is not necessary in mild cases. Case fatality is low, and hemoglobinuria persists for only a few hours.

CONTROL

Water intoxication is not common and can be avoided by preventing thirsty animals from having unlimited access to water. Calves should have free access to water as soon as they are born.

FURTHER READING

Angelos SM, van Metre DC. Treatment of sodium balance disorders: water intoxication and salt toxicity. *Vet Clin North Am Food Anim Pract.* 1999;15:609-618.

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1. Fordyce G, et al. *Aust Vet J.* 2015;93:214.
2. Combs MDA, et al. *Aust Vet J.* 2014;92:107.

Electrolyte Imbalances

Most electrolyte imbalances are caused by a net loss of electrolytes associated with diseases of the alimentary tract. Sweating, excessive salivation and vomiting, and exudation from burns also result in electrolyte losses, but are of minor importance in farm animals, with the exception of sweating in the horse and dysphagia in ruminants. The electrolytes of major concern are sodium, chloride, potassium, calcium, phosphorus, and magnesium. Losses of bicarbonate are presented later.

HYPONATREMIA

Sodium is the most abundant ion in the extracellular fluid and is chiefly responsible for the maintenance of osmotic pressure of the extracellular fluid. The most common cause of hyponatremia is increased loss of sodium through the intestinal tract in enteropathies (Fig. 5-4). This is particularly marked in the horse with acute diarrhea and to a moderate extent in calves with acute diarrhea. The sodium is lost at the expense of the extracellular fluid. In calves with acute diarrhea caused by enterotoxigenic *Escherichia coli* the sodium concentration of the intestinal fluid secreted in response to the enterotoxin is similar to that of plasma, and hyponatremia usually occurs (**hypotonic dehydration**). Animals affected with diarrhea of several days' duration continue to lose large quantities of sodium, and the hyponatremia may become severe. Hyponatremia can become severe when sodium-free water or 5% dextrose are used as the only fluid therapy in animals already hyponatremic. Hyponatremia can also occur in animals with proximal tubular dysfunction.

Hyponatremia causes an increase in the renal excretion of water in an attempt to maintain normal osmotic pressure, which results in a decrease in the extracellular fluid space, leading to a decreased circulating blood volume, hypotension, peripheral circulatory failure, and ultimately renal failure. Muscular weakness, hypothermia, and marked dehydration are common findings.

Isotonic dehydration occurs when there is a parallel loss of sodium and water. **Hypertonic dehydration**, which is uncommon, occurs when there is a loss or deprivation of water with minor losses or deprivation of sodium. Hypertonic dehydration can occur in animals that are unable to consume water because of an esophageal obstruction. The dehydration in isotonic and hypertonic dehydration is mild compared with the marked clinical dehydration that can occur in hypotonic dehydration accompanied by marked loss of water and concentration of the extracellular space (Fig. 5-5).

There are no clinical signs that are characteristic of hyponatremia. There is usually dehydration, muscular weakness, and mental depression, which occur with other disturbances of both water and electrolytes and with acid-base imbalance. Similarly, there are no clinical signs that are characteristic of hypochloremia. However, hyponatremia affects the osmotic pressure of the extracellular fluid, and hypochloremia promotes the reabsorption of bicarbonate and further development of alkalosis. Polyuria and polydipsia occur in cattle with dietary sodium chloride deficiency.

Hypotonic hyponatremia results in **cerebral edema** caused by water entry to the brain; however, if hyponatremia is slow to develop, solutes can leave brain tissue at a sufficiently fast enough rate to mitigate the development of cerebral edema. Clinical neurologic sequelae of hyponatremia are primarily determined by the speed of onset of

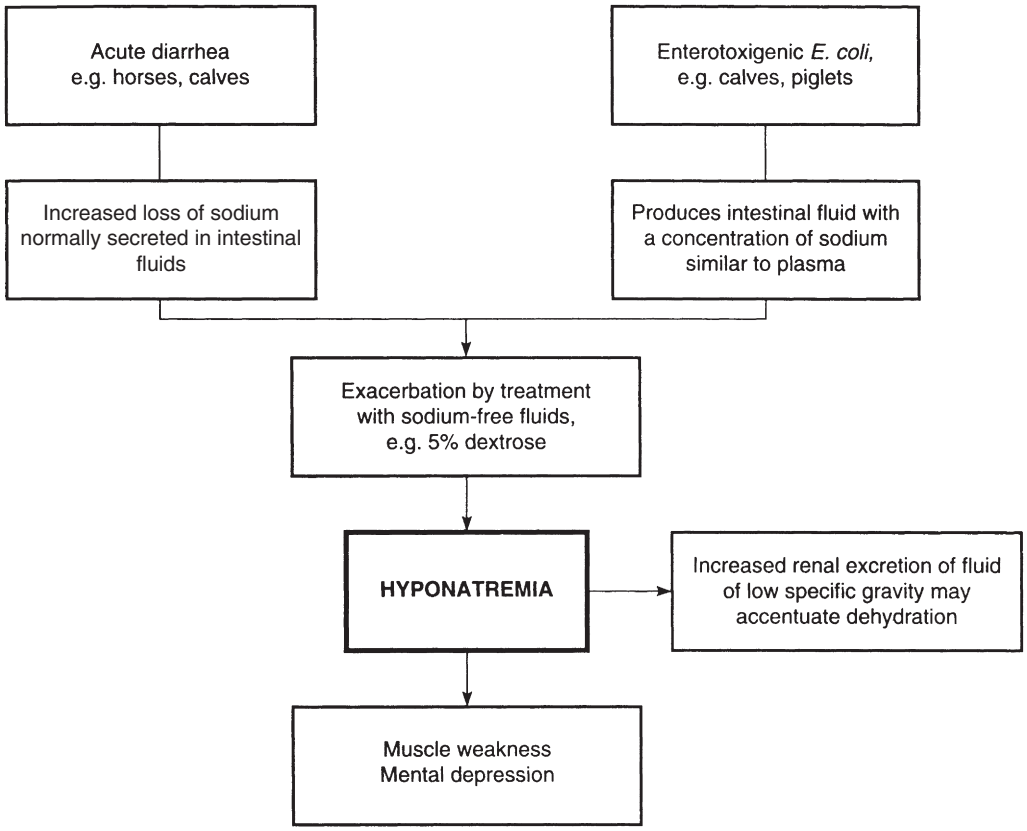

Fig. 5-4 Etiology and pathogenesis of hyponatremia.

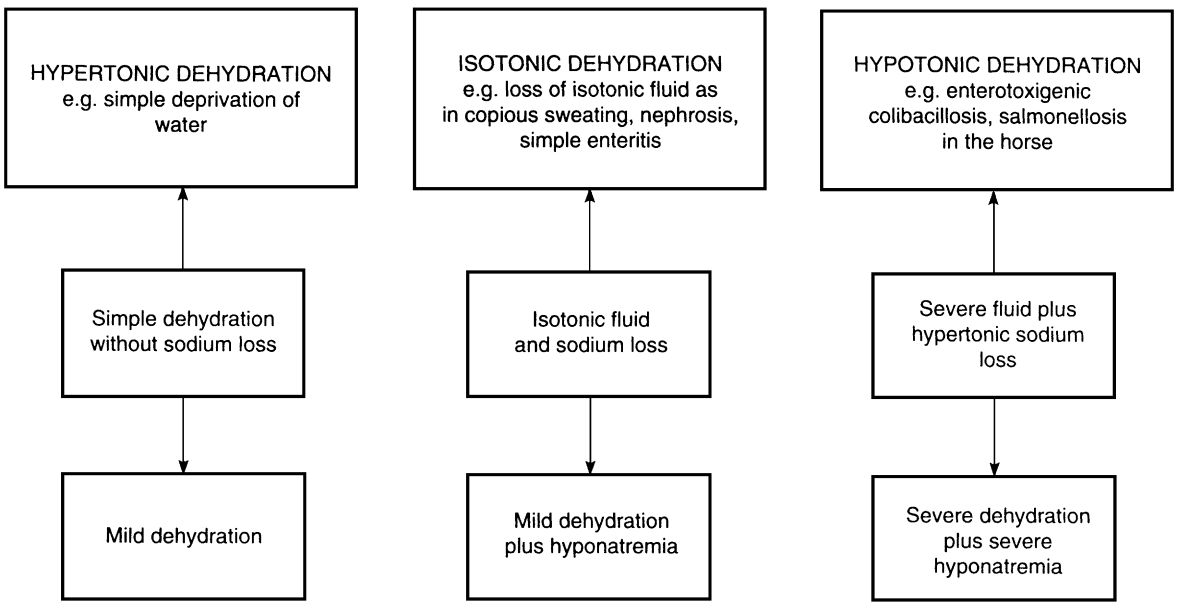

Fig. 5-5 Types of dehydration.

hyponatremia and the rapidity by which marked hyponatremia (serum sodium concentration <120 mEq/L) is corrected. Too rapid correction of chronic hyponatremia (defined as hyponatremia >48 hours) should be avoided because of the potential for **demyelination of pontine and extrapontine neurons** that can produce severe neurologic deficits. These deficits are not well described in agricultural animals, but in humans, rapid correction of chronic hyponatremia has been associated with improvement of neurologic abnormalities within 1 to 2 days, followed by the development of progressive ataxia, dysphagia, myoclonus, spastic tetraparesis, and death within 2 to 5 days. Current recommendations are to increase serum sodium concentration by 8 mEq/L/day in large animals with chronic hyponatremia. This is clinically managed by infusing 1 L of a mixture of 7.2, 5.0, and 0.9% NaCl solutions

(all commercially available), which are assumed to distribute 100% within the extracellular space.[1] To estimate the effect of 1 L of the NaCl infusate on serum sodium concentration ([Na]), the following formula is applied:

$$\begin{aligned} &Change\ in\ serum\,[Na] \\ &\quad = (infusate\,[Na] - serum\,[Na])/ \\ &\quad\ (total\ body\ water + 1) \end{aligned}$$

where total body water is estimated in liters from the BW in kilograms using a standard formula of 60% BW for adult animals. With a targeted increase of 8 mEq/L over 24 hours and an infusion volume of 1 L, this equation can be rearranged to calculate the required infusate [Na] in mEq/L to be administered intravenously over 24 hours in 1 L of fluid:

$$\begin{aligned} Infusate\,[Na] = 8 \times (0.6 \times \{BW\ in\ kg\} + 1) \\ - serum\,[Na]. \end{aligned}$$

HYPERNATREMIA

Hypernatremia is most commonly caused by water restriction or mixing errors in neonatal animals, particularly in milk-replacer solutions or oral electrolyte formulations administered to neonatal calves with diarrhea as part of the treatment of dehydration. Hypernatremia appears to be increasing in North America in dairy calves fed milk replacer because milk-replacer formulations are increasingly dependent on whey from cheese manufacture, and whey has a high sodium concentration. Less common causes of hypernatremia include high-salinity water.[2] Hypernatremia occurs transiently after hypertonic saline (7.2% NaCl) administration, but serum sodium concentrations never exceed 170 mEq/L and may occasionally exceed 160 mEq/L for a few minutes. Transient episodes of mild hypernatremia caused by intravenous hypertonic saline administration are not thought to have any clinical consequences.

Clinically relevant hypernatremia occurs when serum sodium concentrations exceed 160 mEq/L, with significant mortality occurring whenever serum sodium concentrations exceed 180 to 190 mEq/L before treatment is instituted. The clinical signs of hypernatremia are nonspecific and include weakness, depression, inappetence, abnormal posture, recumbency, apparent blindness, and muscle twitching, particularly of the facial muscles (Fig. 5-6). Some animals may convulse shortly before death. Cerebral depression is caused by inhibition of neuronal cell glycolysis. Less severely affected animals may exhibit a mania for water. Hypernatremia has been associated with persistent hyperglycemia in New World camelids, in which it has been assumed that hyperglycemia-induced diuresis has resulted in excessive free water loss with inadequate water intake.

Correction of hypernatremia is challenging because too rapid a rate of correction can result in cerebral edema and brain herniation through the foramen magnum, particularly in animals with chronic hypernatremia. Treatment of hypernatremia focuses on identifying and removing the underlying cause (such as incorrectly mixed milk replacer) and slowly reducing the serum sodium concentration, with a reduction of serum [Na] of 0.5 to 1.0 mEq/L/h being a goal (10 mEq/L decrease per day representing an ideal goal). The preferred method for decreasing serum [Na] concentration is by oral administration of sodium containing electrolytes. The first equation presented earlier can be applied to the use of intravenous fluids for correction of hypernatremia.

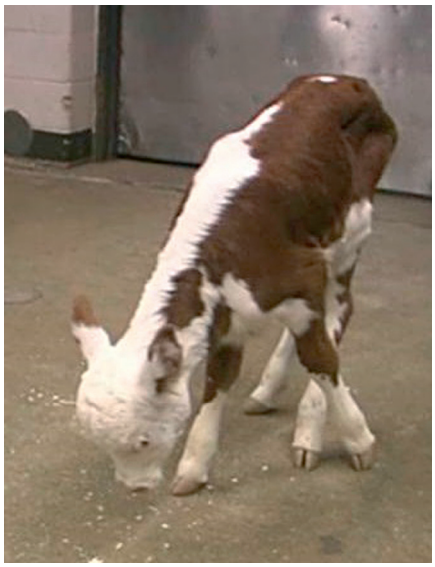

Fig. 5-6 Calf with neurologic signs of hypernatremia, including abnormal mentation and posture and fasciculation of facial muscles. (From Byers SR, Lear AS, Van Metre DC: Sodium balance and the dysnatremias, *Vet Clin Food Anim* 2014;30:333-350).

HYPOCHLOREMIA

Hypochloremia occurs as a result of an increase in the net loss of the electrolyte in the intestinal tract in acute intestinal obstruction, dilatation and impaction, and volvulus of the abomasum and in enteritis (Fig. 5-7). Normally a large amount of chloride is secreted in the abomasum by the mucosal cells in exchange for bicarbonate, which moves into the plasma. The hydrogen, chloride, and potassium ions secreted in gastric juice are normally absorbed by the small intestine. Failure of abomasal emptying and obstruction of the proximal part of the small intestine will result in the sequestration of large quantities of chloride, hydrogen, and potassium ions, which leads to a **hypochloremic hypokalemic metabolic alkalosis**. A severe hypochloremia can be experimentally produced in calves by feeding them a low-chloride diet and daily removal of abomasal contents. Clinical findings include anorexia, weight loss, lethargy, mild polydipsia, and polyuria. A marked metabolic alkalosis occurs resulting in hypokalemia, hyponatremia, azotemia, and death.

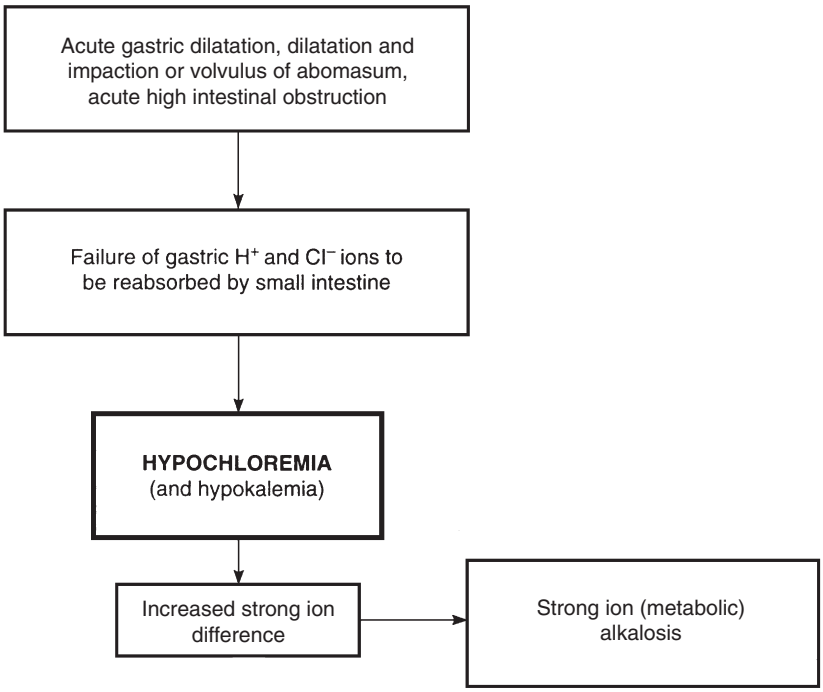

Fig. 5-7 Etiology and pathogenesis of hypochloremia.

HYPOKALEMIA

Hypokalemia may occur as a result of decreased dietary intake, increased renal excretion, abomasal stasis, intestinal obstruction and enteritis, and repeated administration of corticosteroids with mineralocorticoid activity (Fig. 5-8). The prolonged use of potassium-free solutions in fluid therapy for diarrheic animals may result in excessive renal excretion of potassium and hypokalemia. Calves with neonatal diarrhea can have marked depletion of their body potassium stores, particularly when a marked acidemia and metabolic acidosis is present, and the calves have had a low milk intake and a long history of diarrhea.[3] Alkalosis may result in an exchange of potassium ions for hydrogen ions in the renal tubular fluid, resulting in hypokalemia. Hypokalemia can cause muscle weakness, prolonged unexplained recumbency, inability to hold up the head, anorexia, muscular tremors and, if severe enough, coma. The treatment of ketosis in lactating dairy cows with multiple dosages of isoflupredone, a glucocorticoid with some mineralocorticoid activity, can cause hypokalemia and recumbency, with a high case fatality rate.

Hypokalemia (defined as serum or plasma potassium concentration <3.9 mEq/L) is common in lactating dairy cows with left displaced abomasum (LDA), right displaced abomasum (RDA), abomasal volvulus (AV), abomasal impaction, clinical mastitis, dystocia, retained placenta, and hepatic lipidosis.[4] The high prevalence of hypokalemia in sick lactating dairy cows is most likely caused by a combination of decreased dry matter intake; alkalemia from sequestration of chloride in the gastrointestinal tract in cattle with LDA, RDA, AV, or decreased abomasal emptying rate; hyperinsulinemia secondary to hyperglycemia;[5,6] the obligatory loss of potassium in milk (1.4 g of potassium per liter of milk); sympathetic nervous system activation; aldosterone release in response to hypovolemia and the need for sodium retention; and decreased whole-body potassium stores caused by the relatively low muscle mass in dairy cows. Whole-body depletion of potassium may be present in healthy dairy cattle immediately after calving, based on the results of potassium balance studies, studies documenting decreased skeletal muscle potassium content at calving, and decreased urine potassium concentrations immediately after calving. A low serum potassium concentration was a significant predictor of nonsurvival in cattle undergoing surgical correction of LDA or treatment of hepatic lipidosis.[4]

Metabolic alkalosis and hypokalemia in cattle are often accompanied by muscular weakness and **paradoxical aciduria**. Hypokalemia causes muscle weakness by lowering the resting potential of membranes, resulting in decreased excitability of neuromuscular tissue. Thus the differential diagnosis of the animal with muscle weakness should always include hypokalemia.

Hypokalemia and alkalemia also are often directly related because of the renal response to either. Hypokalemia from true body deficits of potassium will cause decreased intracellular concentration of this ion. The intracellular deficit of potassium and excess of hydrogen will cause hydrogen secretion into the urine when distal sodium reabsorption is required. This situation exists in alkalemia and metabolic alkalosis, in which sodium bicarbonate reabsorption in the proximal nephron is decreased because of the excess of plasma bicarbonate. Distal nephron avidity for sodium is increased to protect extracellular fluid volume, and the increased distal sodium reabsorption is at the expense of hydrogen secretion, although it is contrary to the need of acid retention in the presence of alkalosis. In other words, the kidney prioritizes maintenance of plasma volume above that of acid-base balance, presumably because respiratory compensation can usually keep blood pH within the normal physiologic range. Because electroneutrality of extracellular fluid must be maintained by

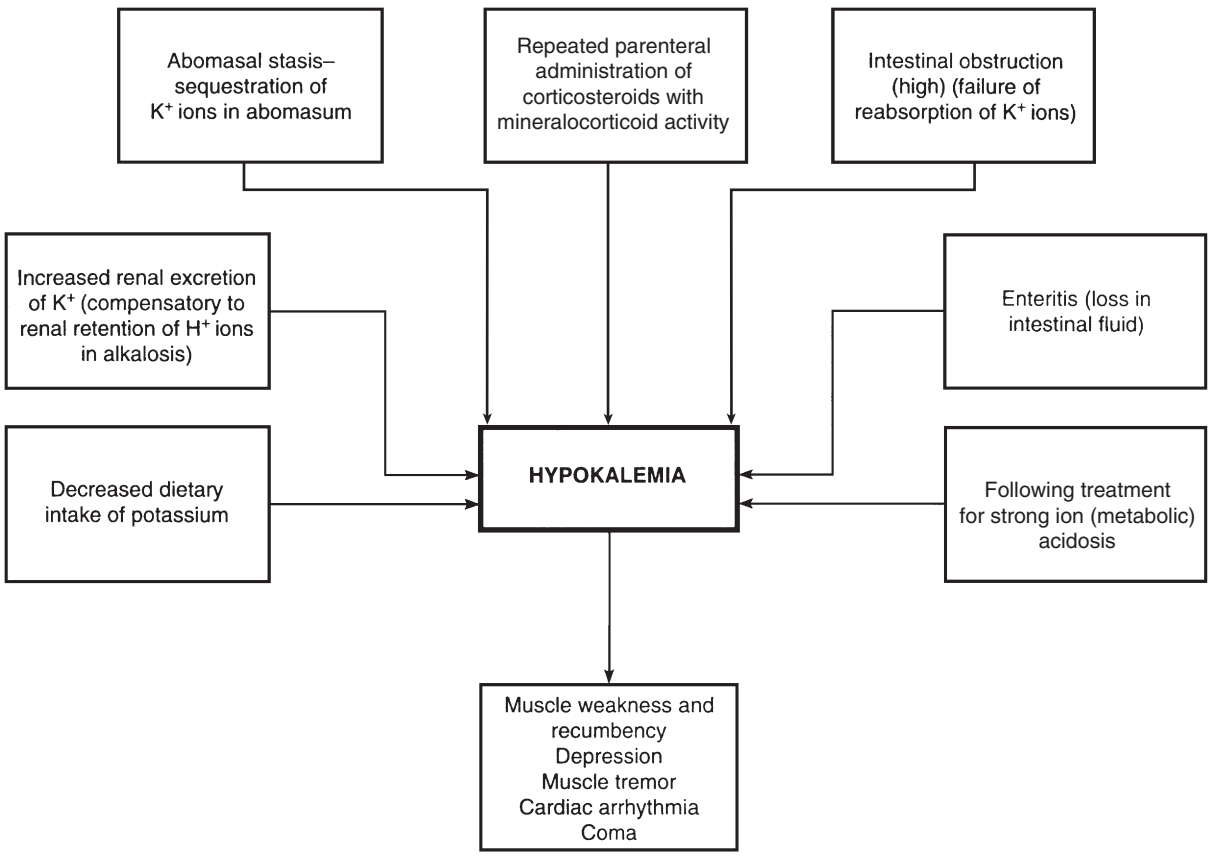

Fig. 5-8 Etiology and pathogenesis of hypokalemia.

reabsorbing an equivalent charge of cations and anions, the reabsorption rates of chloride and bicarbonate in the kidneys are inversely proportional to each other. Thus with excess trapping of chloride in the abomasum, the kidneys will compensate for the resulting hypochloremia by increasing bicarbonate reabsorption, which may proceed until metabolic alkalosis and alkalemia develop.

Because potassium is the major intracellular cation, the measurement of plasma or serum potassium is not a reliable indication of whole-body potassium status. Extremely low plasma or serum concentrations or high concentrations are usually indicative of a potassium imbalance often associated with other electrolyte and acid-base imbalances. In alkalemia, for example, potassium leaves the extracellular space and becomes concentrated in the cells. This may result in low serum potassium concentrations when there might not be potassium depletion of the body. Conversely, in severe acidemia and metabolic acidosis of calves with acute diarrhea, the potassium leaves the cells and moves into the extracellular fluid. This results in hyperkalemia in some cases in which the body potassium is normal or even decreased. When changes occur in the concentration of intracellular and extracellular potassium, the ratio of intracellular to extracellular potassium may decrease by as much as 30% to 50%, which results in a decrease in the resting membrane potential. This is thought to be the explanation for the effects of hypokalemia and hyperkalemia on muscle function.

The potassium concentration of red blood cells does not appear to provide a more accurate indicator of whole-body potassium deficit in horses and ruminants than the actual plasma or serum concentration.[4] There is marked cow-to-cow variability in the erythrocyte potassium concentration (7–70 mmol/L) and sodium concentration (15–87 mmol/L) of healthy cattle that has a genetic basis with no breed influence. Moreover, no relationship between plasma and erythrocyte potassium concentrations could be identified in a study of 180 cows. Milk potassium concentration is theoretically more sensitive than serum or plasma potassium concentration in detecting whole-body potassium depletion in individual cows because milk potassium concentration is constant for an individual cow over a short time period. However, milk potassium concentration changes during lactation, being 42 mmol/L in early lactation, 40 mmol/L in midlactation, and 27 mmol/L in late lactation, with a mean bulk milk tank potassium concentration of 37 mmol/L. Milk potassium concentration also increases in quarters with clinical or subclinical mastitis. As a consequence of these two factors, there is marked individual variation in milk potassium concentration in healthy cattle, with variations of up to 50% occurring among cows. The large cow-to-cow variability in milk potassium concentration makes it difficult to identify a suitable cut point that accurately predicts whole-body potassium depletion in sick lactating dairy cows.[4] However, monitoring milk potassium concentration in individual cows without clinical or subclinical mastitis may have clinical utility as a monitoring tool to gauge the response to therapy with KCl.

Skeletal muscle potassium content provides the most sensitive and specific method for assessing whole-body potassium status.[4,7] Skeletal muscle is considered the best tissue to sample because it contains approximately 75% of the whole-body stores of potassium. A standardized muscle should be obtained for analysis in cattle because differences in potassium content of greater than 15% are present in individual animals, and this muscle-to-muscle variation is greater than that produced by breed.[7]

The treatment of hypochloremic, hypokalemic alkalosis requires correction of extracellular fluid volume and sodium and chloride deficits with 0.9% NaCl infusions and oral KCl. The provision of adequate chloride ion allows sodium to be reabsorbed without bicarbonate. Increased proximal reabsorption of sodium will decrease distal acid secretion because less sodium is presented to the distal nephron. As less bicarbonate is reabsorbed and less acid secreted, the metabolic alkalosis is resolved. Specially formulated solutions containing potassium are necessary in cases of severe hypokalemia and small-intestinal obstruction.

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 isotonic solution of 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 BW per hour. 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 isotonic 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 will increase the solution osmolarity to 329 mOsm/L. Clinical experience with oral administration of KCl has markedly decreased the number of adult ruminants treated with intravenous KCl.

Oral potassium administration is the method of choice for treating lactating dairy cattle with hypokalemia. The absorption efficiency of potassium on a typical lactating dairy cow diet ranges from 74% to 88%, with potassium absorbed in the forestomach and small intestine and forestomach absorption predominating. Rumen fluid in cattle usually has a potassium concentration of 24 to 85 mEq/L, and rumen fluid potassium concentration and potassium absorption are strongly and linearly dependent on potassium intake. This indicates that increasing rumen potassium concentration by the oral administration of KCl will directly lead to increased potassium absorption. Oral administration of KCl therefore provides the optimal salt formulation for treating cattle with hypokalemia because potassium is needed in cattle with whole-body potassium depletion, and chloride is needed in cattle with alkalemia and pH-induced compartmental shift of potassium to the intracellular space.[7]

Current treatment recommendations are to administer 120 g of feed grade KCl orally twice at a 12-hour interval to inappetent dairy cattle with hypokalemia, providing a total 24-hour dose of 240 g of KCl; this dose is equivalent to a daily KCl dose of 0.4 g/kg BW for a 600-kg dairy cow.[4,7] Daily oral doses of KCl exceeding 0.4 g/kg BW are not currently recommended, except in cattle with profound hypokalemia, because they have the potential to result in diarrhea, excessive salivation, muscular tremors of the legs, labored breathing, convulsions, and death.[4,7] Oral administration of 0.58 g of KCl/kg BW was toxic in 6-month-old Holstein calves, manifested by excessive salivation, muscular tremors of the legs and excitability, and a peak plasma potassium concentration of 9.0 mEq/L. Extrapolating this toxic dose in normokalemic calves to hypokalemic 600-kg cows suggests that a daily dose of 240 g KCl approaches the upper limit of safety.

Hypokalemia also occurs following treatment of the horse affected with metabolic acidosis and hyponatremia, and probably reflects whole-body potassium depletion. Horses used for endurance rides may be affected by hypokalemia, hypocalcemia, and alkalosis caused by loss of electrolytes during the competition. Synchronous diaphragmatic flutter also occurs, which may be the result of the electrolyte imbalance (particularly hypocalcemia) causing hyperirritability of the phrenic nerve. Inappetent horses often have whole-body potassium depletion and would benefit from supplementary dietary potassium (25–50 g/day KCl).

HYPERKALEMIA

Hyperkalemia is not as common in farm animals as hypokalemia, and is most common in severe metabolic acidosis and acidemia. The classic description for the development of hyperkalemia in metabolic acidosis involves a purported redistribution of potassium from the intracellular space to the extracellular space because a large

proportion of the excess hydrogen ions are buffered intracellularly. Thus potassium is supposedly exchanged with hydrogen ions across the cell membrane to maintain electroneutrality. Although widely accepted, this purported mechanism has never had a sound physicochemical basis because a decrease in plasma pH from 7.4 to 7.0 (equivalent to an increase in plasma hydrogen ion activity from 40 to 100 nEq/L) would decrease plasma [K] from 7.0 to 6.99994 mEq/L on the basis of electrochemical exchange of cations. Not only is such a decrease physiologically irrelevant, but the decrease is undetectable using current laboratory equipment.[8] An attractive hypothesis for the development of hyperkalemia in acidemic animals is that the low intracellular pH slows Na-K-ATPase activity causing potassium ions to leak down a concentration gradient from the intracellular to the extracellular space; however, there is no experimental data indicating that Na-K-ATPase activity is directly influenced by pH within the physiologic range. Low intracellular pH does exert a marked effect on phosphofructokinase activity in the glycolytic pathway; with Na-K-ATPase activity dependent on ATP availability, decreased phosphofructokinase activity presents a potential pathway for acidemia-induced hyperkalemia. Hampered insulin-dependent cellular potassium uptake in states of acidemia presents a second potential mechanism for the association between hyperkalemia and acidemia; mild declines in blood pH can induce insulin resistance. Because insulin triggers a transcellular shift of glucose and potassium, tissue resistance to insulin has the potential to contribute to hyperkalemia. A third potential mechanism for acidemia-induced hyperkalemia is activation of a cell membrane potassium channel called TREK-1 by low intracellular pH, resulting in potassium efflux from the cell.[8] An interesting recent finding is that hyperkalemia is much less common in neonatal calves with acidemia caused by hyper D-lactatemia than in calves with acidemia and plasma D-lactate concentrations within the reference interval.[9]

Hyperkalemia is potentially more life-threatening than hypokalemia. Hyperkalemia (when over 7–8 mmol/L) has a profound effect on cardiac function. There is usually marked bradycardia and arrhythmia, and sudden cardiac arrest may occur. Electrocardiogram (ECG) changes in experimentally induced hyperkalemia in the horse have been described. The changes include four successive stages as hyperkalemia increased. There was a widening and lowering of amplitude followed by inversion and disappearance of the P wave; an increase in the amplitude of the T wave; an increase in the QRS interval, with some irregularity in the ventricular rate; and periods of cardiac arrest that became terminal or were followed by ventricular fibrillation. The minimum plasma potassium concentration required to induce ECG changes was 6 to 7 mmol/L, and severe cardiotoxic effects occurred at levels between 8 and 11 mmol/L. The effects of hyperkalemia on the ECG are exacerbated by the presence of hyponatremia, which is common in neonatal calves with diarrhea.

Hyperkalemia has traditionally been treated by intravenous administration of sodium bicarbonate, glucose, insulin, and sometimes calcium. Because hyperkalemia is most strongly associated with a decreased glomerular filtration rate, the primary treatment goal in hyperkalemia is to reestablish normal renal blood flow and rate of urine formation by the administration of sodium-containing fluids,[9] particularly sodium containing fluids that also produce rapid alkalinization, such as 1.3% sodium bicarbonate.[10] Hypertonic saline has been shown to be just as effective as hypertonic sodium bicarbonate in decreasing hyperkalemia and hyperkalemia-associated bradyarrhythmias as a result of sodium-induced intracellular movement of potassium, extracellular volume expansion, and the strong ion effect of increasing the serum concentration of a strong cation.[8] Calcium counteracts the effect of hyperkalemia on the resting membrane potential by increasing the threshold potential to a higher value, returning an appropriate difference between resting and threshold potentials. Calcium can be administered intravenously at 0.2 to 0.4 mL of a 23% calcium gluconate solution/kg BW. In summary, the focus of treatment in hyperkalemia should be optimizing renal blood flow and glomerular filtration rate by plasma volume expansion, correction of acidemia, and increasing the serum sodium concentration. Glucose and insulin are not routinely needed to correct hyperkalemia, but can be administered to animals not responding to reestablishment of a normal rate of urine production and correction of acidemia.

Hyperkalemic periodic paralysis occurs in heavily muscled Quarter Horses. Affected horses become weak, may stand base-wide, and are reluctant to move. Sweating commonly occurs and generalized muscle fasciculations are apparent. Affected horses remain bright and alert but may yawn and do not eat or drink. Some horses become recumbent and may appear to be in a state of flaccidity. Attacks may occur in a rest period following exercise or at random. During the episode the serum potassium concentration is elevated by up to twofold and returns to normal values when the animal recovers. Treatment consists of sodium bicarbonate, hypertonic saline, or 5% dextrose given intravenously, possibly with insulin.

HYPOCALCEMIA

The calcium fractions in plasma are in equilibrium and exist in three forms: free (43% of total); bound to proteins in a salt-type manner (49%); and complexed to other compounds in plasma such as bicarbonate, lactate, citrate, sulfate, and phosphate (8%). The ionized (free) calcium fraction is the biologically active form of calcium and therefore is the preferred method of calcium measurement. The ionized calcium concentration ($c\mathrm{Ca}^{2+}$) in bovine plasma is primarily dependent on the total calcium concentration, with total protein concentration explaining 85% of the variation in $c\mathrm{Ca}^{2+}$. Ionized calcium concentration is dependent to a lesser extent on pH, the plasma concentration of albumin (and therefore total protein), lactate, and chloride, and the temperature and ionic strength.

Ionized calcium concentration should be measured on an anaerobically collected blood sample, and should be reported as the measured $c\mathrm{Ca}^{2+}$ at the actual pH of the patient. Correction of the measured ionized calcium concentration to a pH of 7.40 is routinely applied in experimental studies to assist in the interpretation of measured values relative to a reference range. This should only be done in samples that were not anaerobically collected and where there is loss of carbon dioxide from the sample (such as in a vacutainer tube). In this case a pH-corrected $c\mathrm{Ca}^{2+}$ is used only to correct for CO_2 loss. The formula most commonly used for pH correction of $c\mathrm{Ca}^{2+}$ in ruminant and equine plasma is $c\mathrm{Ca}^{2+}\text{corrected} = c\mathrm{Ca}^{2+} \times 10^{(-0.24 \times \{7.40 - \mathrm{pH}\})}$. Small differences in the measured value for $c\mathrm{Ca}^{2+}$ exist, depending on whether the blood sample is anaerobically collected using sodium heparin or calcium-balanced heparin.

Hypocalcemia or milk fever may occur in recently calved mature dairy cows that have been inappetent or anorexic for a few days. Hypocalcemia can be caused by a reduction in dry matter intake because of illness or it may be the earliest stages of hypocalcemic parturient paresis. The clinical findings include anorexia; mild tachycardia with a reduction in the intensity of the heart sounds and occasionally an arrhythmia; a decrease in the frequency and amplitude of rumen contractions or complete ruminal stasis; and a decrease or complete absence of feces, which may last from 6 to 36 hours if untreated.

Hypocalcemia cases often mimic intestinal obstruction and create problems in the differential diagnosis. Affected cattle may not exhibit any evidence of muscular weakness, and the detection of the hypocalcemic state can be elusive. The total serum calcium concentrations range from 1.5 to 2.0 mmol/L and the response to intravenous therapy is usually good, although recovery may require several hours before the appetite returns to normal and feces are passed.

Calcium can 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. A typical treatment for an adult lactating dairy cow with periparturient hypocalcemia is 500 mL of 23% calcium borogluconate by slow intravenous injection with cardiac auscultation; this provides 10.7 g of calcium. Although the calculated calcium deficit in a recumbent periparturient dairy cow is 4 g, additional calcium should be provided to overcome the continued loss of calcium in milk. 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. A good rule of thumb for administering 23% calcium borogluconate solutions (2.14 g calcium/100 mL) to cows with periparturient hypocalcemia is therefore to administer 1 mL/kg BW. There do not appear to be any clinically important advantages to slow administration of the solution over 6 hours, compared with over 15 min.

The normal cardiac response to **intravenous 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 is then 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 individually 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 BW per minute, which is equivalent to 0.065 mL 23% calcium borogluconate per kilogram BW per minute. For a 500-kg normocalcemic dairy cow, this 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 cardiac auscultation is performed during administration. Intravenous administration of calcium gluconate or calcium chloride to horses increased serum calcium concentrations by approximately 35% and resulted in hypomagnesemia, hypokalemia, and hyperphosphatemia, induced diuresis, and increased excretion of calcium, magnesium, potassium, sodium, phosphate, and chloride.[11]

Subcutaneous administration of calcium solutions has been practiced for many years as part of the treatment of hypocalcemic cattle. To facilitate calcium absorption, it is preferable to administer no more than 125 mL at a site. A 14-gauge needle is placed subcutaneously over the lateral thorax, 125 mL is administered, and the needle is redirected and another 125 mL is administered. The process is then repeated on the other side of the cow. The effectiveness of subcutaneous administration of calcium has been documented in healthy normal cows, and subcutaneous calcium injections appear to be absorbed by cows with periparturient hypocalcemia at a fast enough rate to be clinically effective. Subcutaneous administration of calcium gluconate in recumbent cows can therefore be expected to have some efficacy in improving plasma calcium concentrations; such treatment can be administered by producers until a veterinarian can arrive to administer intravenous calcium gluconate. Calcium chloride is not recommended for subcutaneous administration because of extensive tissue damage; the addition of dextrose to the administered calcium is also not recommended because it increases the tonicity of the solution and propensity for bacterial infection and development of abscesses. Rectal calcium administration is not recommended because it causes severe mucosal injury and tenesmus and does not increase plasma concentrations of calcium.

Oral administration of calcium has also been practiced for many years, usually by ororuminal intubation of calcium borogluconate solutions designed for parenteral administration. Over 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. Rapid correction of hypocalcemia by oral calcium administration is predominantly by passive ruminal diffusion because small intestinal absorption is too slow to be of clinical value.

Two calcium formulations are currently recommended for oral administration to ruminants, $CaCl_2$ and calcium propionate, but most commercially available products contain 50 g of $CaCl_2$. Calcium lactate does not appear to be absorbed in appreciable quantities when administered orally to cows in a large volume of water (20 L) followed immediately by oral administration of sodium phosphate; this result may have been caused by formation of calcium-phosphate complexes in the rumen.[12] Calcium chloride has the advantage of low cost and low volume (because of its high solubility), but $CaCl_2$ can severely damage the pharynx and esophagus in ruminants with reduced swallowing ability, can lead to necrosis of the forestomach and abomasum when administered in high doses, and can lead to aspiration pneumonia when administered as a drench. Calcium propionate has the advantage that it is less irritating than $CaCl_2$ while providing a gluconeogenic substrate (propionate), but the disadvantages of calcium propionate are higher volumes and cost. Oral calcium solutions should only be administered 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. Calcium solutions are suspected to have a higher likelihood of aspiration pneumonia than calcium gels (with a consistency similar to toothpaste), although this supposition does not appear to have been verified. 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 appears to be indicated and provides 100 g of $CaCl_2$ and 37 g of calcium over 24 hours, but more aggressive treatment protocols are not recommended.

HYPOPHOSPATEMIA

Hypophosphatemia occurs in cattle under conditions similar to those of hypocalcemia. A decrease in feed intake or alimentary tract stasis will result in a decrease in serum inorganic phosphate concentration. Acute recumbency in lactating dairy cattle may be associated with marginal phosphorus deficiency, although a cause-and-effect relationship between hypophosphatemia and recumbency has not been established. However, many inappetent and weak cows have marginal hypophosphatemia and clinically appear to benefit from normalization of their plasma concentration of phosphate. As such, it is currently 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 very soluble, even in the presence of calcium and

magnesium. However, the phosphorus in phosphite and hypophosphite is unavailable to mammals, meaning that the vast majority of "phosphate"-containing solutions are not efficacious in treating hypophosphatemia.[13] 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 this is not needed when solutions are stored in warm ambient temperatures. 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; this provides 7 g of phosphate (2.3 g of inorganic phosphate), and increases plasma phosphate concentrations for at least 6 hours. Human enema formulations that contain a mixture of monobasic sodium phosphate monohydrate and dibasic sodium phosphate heptahydrate in a buffered solution have also been administered intravenously to cattle with hypophosphatemia but are not recommended. This human enema solution is extremely hypertonic and must be diluted before administration. 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. This has traditionally been evaluated by calculating the **calcium-phosphorus product**, in which metastatic calcification may occur if the product of serum calcium concentration and serum phosphate concentration (both in mg/dL) exceeds 70.

Hypophosphatemia is more safely treated by administration of **oral monosodium phosphate**, and this is the preferred method of administration in ruminants with rumen motility. Oral administration also results in a more prolonged increase in plasma phosphorus concentration. Recommended dose is 200 to 350 g of feed grade monosodium phosphate ($NaH_2PO_4.2H_2O$, contains 50–70 g of phosphate) administered in gelatin boluses, drench, or by ororuminal intubation.[12] Phosphorus in other feed grade minerals (such as bone meal or dicalcium phosphate) is poorly available and is not recommended for the treatment of hypophosphatemia.

HYPOMAGNESEMIA

Magnesium is usually administered parenterally only when a ruminant exhibits clinical signs of hypomagnesemia. Treatment of hypomagnesemia is more dangerous (to the animal and 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 (CSF), which turns over at approximately 1% per minute.

Treatment of hypomagnesemia has historically used 25% Epsom salts solution (magnesium sulfate heptahydrate; $MgSO_4.6H_2O$); this solution concentration was selected because it provided approximately 1 mmol of magnesium per liter. It should be noted that 25% Epsom salts solution is markedly hypertonic (2028 mOsm/L). A typical treatment for an adult cow has been slow intravenous administration (over at least 5 min) of 100 mL of the 25% Epsom salts solution, which provides 2.5 g of magnesium (25 mg of magnesium per mL of solution). More recently, hypomagnesemia has been treated using commercially available combined calcium and magnesium solutions; 500 mL of these solutions typically contain 1.6 to 2.7 g of magnesium in the form of a borogluconate, chloride, or hypophosphite salt. Although the calculated extracellular deficit in a cow with hypomagnesemia is 2 g of magnesium, additional magnesium should be provided to correct presumed intracellular deficiencies and to overcome the anticipated urinary loss of magnesium. Combined calcium and magnesium solutions are preferred for intravenous administration to 25% Epsom salts solution because ruminants with hypomagnesemia frequently have hypocalcemia, and hypercalcemia provides some protection against the toxic effects of hypermagnesemia. Moreover, administration of solutions containing magnesium as the only cation increases the risk of developing cardiac and respiratory failure during treatment. The maximum safe rate of administration of magnesium in cattle is 0.08 mEq Mg^{2+}/kg of BW per minute, which is equivalent to 0.04 mL 25% Epsom salts per kilogram of BW per minute. For a 500-kg beef cow with hypomagnesemia, this corresponds to a maximum safe rate of administration of 20 mL/min.

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

The oral bioavailability of magnesium is low and much lower than that of calcium. Accordingly, oral administration of magnesium is not recommended for the treatment of hypomagnesemia, but 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.

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 salts (magnesium sulfate heptahydrate) or magnesium chloride in 200 mL of water can be placed in the descending colon (and not the rectum) and the tail held down for 5 minutes; this increases plasma magnesium concentrations within 10 minutes. However, enema solutions can be prematurely evacuated, 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 appear to have been evaluated, although a 50-mL enema of a 30% $MgCl_2.6H_2O$ solution rapidly and effectively increased serum magnesium concentration in 7- to 10-week-old calves and relieved clinical signs of hypomagnesemia.

Oral administration of magnesium hydroxide and magnesium oxide excessively alkalinizes the rumen and can create a severe metabolic alkalosis (strong ion alkalosis), as absorption of magnesium leads to hypermagnesemia and increased plasma strong ion difference (SID). Because oral administration of sodium bicarbonate causes expansion of the plasma volume and creates a metabolic alkalosis (strong ion alkalosis) without hypermagnesemia, it is likely that oral sodium bicarbonate is a more effective treatment for grain overload in ruminants.

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Acid-Base Imbalance

The pH of mammsalian blood is maintained within the normal range of 7.35 to 7.45 by its buffer systems, of which hemoglobin (Hb) is the most important, because it has the greatest buffering capacity. However, because the

blood Hb concentration is regulated on the basis of oxygen delivery instead of acid-base balance, rapid changes in Hb concentration occur only with marked changes in hydration status or splenic contraction associated with exercise, and the bicarbonate system is an open buffering system via carbon dioxide loss through the respiratory system. The **bicarbonate system** has traditionally been considered to be the most important buffer. Other buffers in blood are plasma proteins and phosphate. The addition of relatively large amounts of acid or alkali to the blood is necessary before its buffering capacity is exhausted and its pH changed. Changes from normal acid-base balance toward alkalemia or acidemia are common in sick animals and make a significant contribution to the observed clinical signs.

The traditional approach for assessing acid-base balance focuses on how plasma carbon dioxide tension (PCO_2), plasma bicarbonate concentration ($[HCO_3^-]$), the negative logarithm of the apparent dissociation constant (pK_1') for plasma carbonic acid (H_2CO_3), and the solubility of CO_2 in plasma (S) interact to determine plasma pH. This relationship is most often expressed as the **Henderson–Hasselbalch equation**: $pH = pK_1' + \log([HCO_3^-]/S \times PCO_2)$. The evaluation of acid-base balance using the Henderson–Hasselbalch equation has historically used pH as an overall measure of acid-base status, PCO_2 as an independent measure of the respiratory component of acid-base balance, and extracellular base excess and actual HCO_3^- concentration or standard HCO_3^- as a measure of the nonrespiratory (also called metabolic) component of acid-base balance.

When using the traditional Henderson–Hasselbalch approach, **four primary** acid-base **disturbances** can be distinguished: **respiratory acidosis** (increased PCO_2), **respiratory alkalosis** (decreased PCO_2), **metabolic acidosis** (decreased extracellular base excess or actual HCO_3^- concentration), and **metabolic alkalosis** (increased extracellular base excess or actual HCO_3^- concentration). The anion gap (AG) is easily calculated from the results of serum biochemical analysis and is used to determine whether unmeasured anions (UAs) are present. The Henderson–Hasselbalch equation has a long history of use and remains widely and routinely used in the clinical management of acid-base disorders. These advantages should not be overlooked. The principal disadvantage of the Henderson–Hasselbalch equation is that it is more descriptive than mechanistic, decreasing the value of the approach in explaining the cause of acid-base changes during disease. This is because the Henderson–Hasselbalch equation fails to distinguish among the effects of independent and dependent variables on plasma pH.

Actual plasma HCO_3^- concentration in units of mmol/L is not measured but calculated using the Henderson–Hasselbalch equation and measured values for pH and PCO_2:

$$[HCO_3^-] = S \times PCO_2 \times 10^{(pH - pK1')}$$

The values for pK_1' and S at 37°C are 6.105 and 0.0307 per mm Hg, respectively, for normal mammalian blood. The equation at 37°C is

$$[HCO_3^-] = 0.0307 \times PCO_2 \times 10^{(pH - 6.105)}$$

Because actual HCO_3^- concentration is calculated from pH and PCO_2, it can never provide an independent measure of the nonrespiratory component of an acid-base disturbance. A primary decrease in PCO_2 (respiratory alkalosis) at normal pH always is accompanied by a decrease in plasma HCO_3^- concentration (which would be interpreted as a metabolic acidosis). Likewise, a primary increase in PCO_2 (respiratory acidosis) at normal pH always produces an increase in plasma HCO_3^- concentration (which would be interpreted as a metabolic alkalosis). In both cases, the actual HCO_3^- concentration is dependent on the pH and PCO_2, providing no additional information as to the cause of the acid-base imbalance other than that obtained by knowledge of the pH and PCO_2. It is therefore illogical to use the actual HCO_3^- concentration to define the nonrespiratory (metabolic) component of an acid-base disturbance.

The current use of actual HCO_3^- concentration in the evaluation of acid-base status results from Van Slyke's work in 1924, in which pH and total CO_2 (which is highly correlated with actual $[HCO_3^-]$) could be measured more accurately than PCO_2. This led to the graphical depiction of the curvilinear HCO_3^-–pH relationship, the so-called Davenport diagram, to represent acid-base disturbances (Fig. 5-9). With the later development of accurate and practical laboratory methods in the 1950s to measure PCO_2, acid-base derangements were graphically depicted as approximately linear $\log(PCO_2)$–pH relationships. This development led directly to the **base excess** concept.

The normal range of plasma bicarbonate in large animals is 24 to 30 mmol/L (this should be compared with the normal range in humans, which is 22–24 mmol/L). In mild metabolic acidosis the bicarbonate concentration is in the range of 20 to 24 mmol/L, moderate metabolic acidosis is 14 to 18 mmol/L, and in severe cases the values are below 10 mmol/L and carry a grave

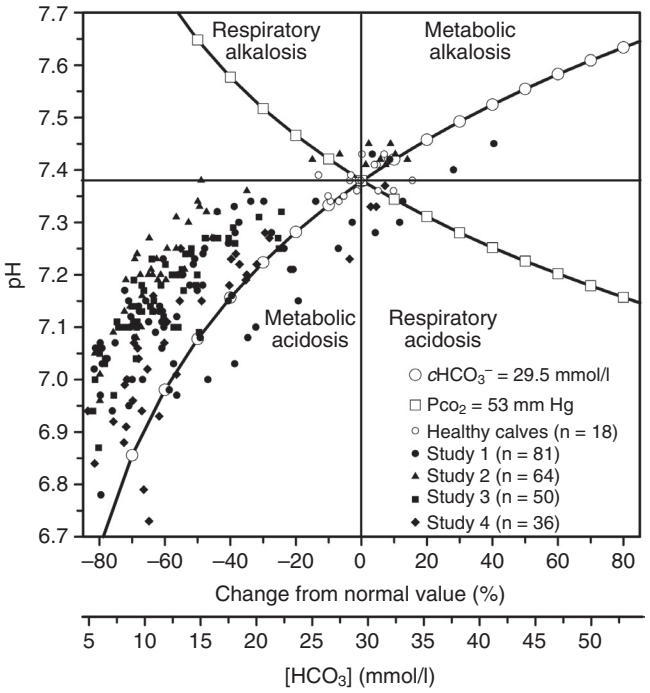

Fig. 5-9 Spider plot revealing the association between changes in two variables of the Henderson–Hasselbalch equation, plasma bicarbonate concentration ($cHCO_3^-$) and carbon dioxide tension (PCO_2), on venous blood pH in 231 sick calves, most of which had diarrhea. The spider plot was obtained by systematically varying one input variable ($cHCO_3^-$ or PCO_2) while holding the remaining input variables at their reference values for calf venous plasma. Reference values for the two input variables for calf plasma were 29.5 mmol/L for $cHCO_3^-$ (large open circles) and 53 mm Hg for PCO_2 (open squares). The solid vertical and horizontal lines indicate that venous blood pH = 7.38 when $cHCO_3^-$ and PCO_2 are at their reference values. Note that the individual data points are displaced from the predicted pH–$cHCO_3^-$ relationship. This displacement indicates that changes in plasma $cHCO_3^-$ do not account for all of the changes in blood pH in sick calves. (Reproduced with permission from Constable PD, *Vet Clin North Am Food Anim Pract* 2014;30:295-316.)

prognosis. The levels of P_{CO_2}, P_{O_2}, plasma bicarbonate, and blood pH can be used to determine the degree of compensation, if any, that has taken place. In metabolic acidosis there may be a compensatory decrease in P_{CO_2} caused by hyperventilation; in metabolic alkalosis there may be an increase in P_{CO_2} caused by hypoventilation. In respiratory acidosis caused by severe pneumonia the arterial P_{O_2} will be markedly decreased.

The **base excess** value directly expresses the amount (usually expressed in units of mEq/L) of strong base (or acid) added per liter of blood or plasma, when the normal mean base excess value is arbitrarily fixed at zero. As such, the base excess is defined as the amount of strong acid (such as HCl) needed to titrate the pH of 100% oxygenated human blood to 7.40 at 37°C and at a P_{CO_2} of 40 mm Hg. By definition, the normal base excess value for humans is 0 mEq/L (range is −2 to +2 mEq/L), and a base excess of more than +2 mEq/L indicates metabolic alkalosis, whereas a value of less than −2 mEq/L (negative base excess value or base deficit) reflects metabolic acidosis. The **normal range of base excess** in large animals is 0 to 6 mEq/L.

Mathematical formulas and nomograms are available to calculate base excess from measured pH, P_{CO_2}, and blood Hb concentration. Base excess is usually expressed as BE_{ECF} (also called **standard base excess** or **in vivo base excess**). Extracellular base excess is the preferred measurement because this formulation provides the best clinical estimate of the required mmol/L of HCO_3^- required to correct metabolic acidosis and because it assumes a fixed Hb concentration of 5 g/dL. Clearly, the BE_{ECF} value will be incorrect when applied to animals with anemia or polycythemia; however, the error introduced by this approximation is small and usually clinically insignificant.

Most blood gas analyzers calculate base excess in units of mEq/L using Siggaard–Andersen's empirical equation derived from his nomogram with Hb concentration [Hb] and actual HCO_3^- concentrations in mmol/L:

$$BE_{blood} = (1 - 0.023 \times [Hb]) \times ([HCO_3^-] - 24.4) + (7.7 + 2.3 \times [Hb]) \times (pH - 7.40),$$

which is equivalent to the following expression when [Hb] = 3.1 mmol/L = 5 g/dL:

$$BE_{ECF} = 0.93 \times ([actual\ HCO_3^-] - 24.4) + 14.83 \times (pH - 7.40)$$

The calculated BE_{ECF} value assumes normal serum protein concentration (7.2 g/dL) providing an inaccurate estimate of the magnitude of a metabolic acidosis or alkalosis in domestic animals with hypoproteinemia or hyperproteinemia. The ability of BE_{ECF} and actual HCO_3^- concentration to accurately characterize the metabolic component of acid-base status has been controversial for many years, although BE_{ECF} has advantages compared with actual HCO_3^- concentration. The major advantages of the base excess approach are that BE_{ECF} is theoretically related to SID and is independent of respiratory activity. On this basis, when using the traditional Henderson–Hasselbalch approach to acid-base balance, the recommended approach is to use pH as an overall index of acid-base status, P_{CO_2} as an index of the respiratory component, and standard (in vivo) base excess as an index of the nonrespiratory (metabolic) component (Fig. 5-10).

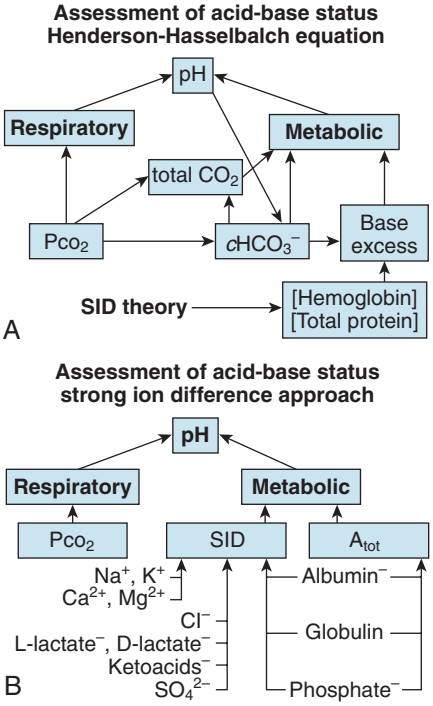

Fig. 5-10 Evaluation of acid-base balance using the traditional Henderson–Hasselbalch equation **(A)** and strong ion difference (SID) theory **(B)**. The Henderson–Hasselbalch equation posits that blood pH is dependent on the respiratory system, as assessed by the partial pressure of carbon dioxide (P_{CO_2}), and metabolism, as assessed by the bicarbonate concentration ($cHCO_3^-$) or base excess. **A,** It highlights one of the fundamental flaws with using the Henderson–Hasselbalch equation in that blood pH cannot be dependent on $cHCO_3^-$ because bicarbonate concentration is calculated from blood pH and P_{CO_2}. **B,** For comparison, this conveys that the strong ion approach to acid-base balance posits that blood pH is dependent on the respiratory system, assessed by P_{CO_2}, and on metabolism, assessed by the SID and concentration of nonvolatile buffers (A_{tot}, such as albumin, globulin, and phosphate) in plasma. (Reproduced with permission from Constable PD: Clinical assessment of acid-base status: Strong ion difference theory, *Vet Clin North Am Food Anim Pract* 1999;15:447-71).

The **strong ion approach** to acid-base balance provides a revolutionary method to assess acid-base balance, which is becoming more widely adopted. In particular, the strong ion model is thought to provide a more accurate assessment of acid-base status than the traditional Henderson–Hasselbalch approach and can identify complex mixed acid-base disorders.[1,2,3,4] This strong ion approach differs in three important areas from the traditional bicarbonate-centered application of the Henderson–Hasselbalch equation: (1) acid-base balance is examined using a systems approach, (2) a clear conceptual distinction is made between dependent variables (such as pH and $[HCO_3^-]$) and the independent variables, and (3) the effects of protein concentration on acid-base balance are considered.

The strong ion approach reduces the chemical reactions in plasma to that of simple ions in solution. This assumption can be made because the quantitatively important plasma cations (Na^+, K^+, Ca^{2+}, and Mg^{2+}) and anions (Cl^-, HCO_3^-, protein, lactate, sulfate, and ketoacids) bind each other in a saltlike manner. Plasma ions (such as Cu^{2+}, Fe^{2+}, Fe^{3+}, Zn^{2+}, Co^{2+}, and Mn^{2+}) that enter into oxidation–reduction reactions, complex ion interactions, and precipitation reactions are not categorized as simple ions but are assumed to be quantitatively unimportant in determining plasma pH, primarily because their plasma concentrations are low.

Simple ions in plasma can be differentiated into two main types, nonbuffer ions (strong ions or strong electrolytes) and buffer ions. Strong ions are fully dissociated at physiologic pH and therefore exert no buffering effect. Strong ions do, however, exert an electrical effect because the sum of completely dissociated cations does not equal the sum of completely dissociated anions. Stewart termed this difference the SID. Because strong ions do not participate in chemical reactions in plasma at physiologic pH, they act as a collective positive unit of charge.

In contrast to strong ions, **buffer ions** are derived from plasma weak acids and bases that are not fully dissociated at physiologic pH. The conventional dissociation reaction for a weak acid (HA), conjugate base (A^-) pair is

$$HA \rightleftharpoons H^+ + A^-$$

and, at equilibrium, an apparent weak acid dissociation constant (Ka) can be calculated adopting the accepted convention regarding hydrated solutes as $K\text{a} = [H^+][A^-]/[HA]$. For a weak acid to act as an effective buffer, its pKa (defined as the negative logarithm of the weak acid dissociation constant Ka) lies within the range of pH ± 1.5.

Conceptually, the buffer ions can be subdivided into volatile buffer ions (HCO_3^-) and nonvolatile buffer ions (non-HCO_3^-). Bicarbonate is considered separately because this buffer system is an open system in arterial plasma; rapid changes in carbon dioxide

tension and hence arterial plasma HCO_3^- concentration can be readily induced through alterations in respiratory activity. In contrast, the non-HCO_3^- buffer system is a closed system containing a fixed quantity of buffer. Another important physiologic distinction between these two buffer systems is that an open buffer system such as HCO_3^- can be effective beyond the limits of pH = p*K*a ± 1.5. Finally, it should be appreciated that HCO_3^- is a homogeneous buffer ion, whereas the nonvolatile buffer ion (A^-) represents a diverse and heterogeneous group of plasma buffers (albumin, globulin, and phosphate) that is being modeled as a single buffer. Another assumption in Stewart's strong ion model is that HA and A^- do not take part in plasma reactions that result in the net destruction or creation of HA or A^-. This is because when HA dissociates it ceases to be HA (therefore decreasing plasma [HA]) and becomes A^- (therefore increasing plasma [A^-]). The sum of [HA] and [A^-] (called A_{TOT}) therefore remains constant through conservation of mass:

$$[A_{TOT}]=[HA]+[A^-]$$

In summary, the strong ion approach assumes that plasma ions act as either strong ions, volatile buffer ions (HCO_3^-), or nonvolatile buffer ions (A^-). Plasma therefore contains three types of charged entity: SID, HCO_3^-, and A^-. The requirement for electroneutrality dictates that at all times the SID equals the sum of bicarbonate buffer ion activity (HCO_3^-) and nonvolatile buffer ion activity (A^-), such that SID − HCO_3 − A^- = 0. This equation obviously assumes that all ionized entities in plasma can be classified as either a strong ion (SID), a volatile buffer ion (HCO_3^-), or a nonvolatile buffer ion (A^-; see Fig. 5-9).

An equation **relating plasma pH to three independent variables (P_{CO_2}, SID, and A_{TOT})** and three constants (K_a, K_1, and *S*) has been developed based on these assumptions. The most important factors that determine plasma pH are P_{CO_2}, SID, and the concentrations of individual nonvolatile plasma buffers (albumin, globulins, and phosphate). A change in any one of these variables will produce a direct and predictable change in plasma pH. Using the strong ion approach, six **primary acid-base disturbances can be distinguished** (Fig. 5-11) instead of the four primary acid-base disturbances (respiratory acidosis, respiratory alkalosis, metabolic acidosis, and metabolic alkalosis) differentiated when using the traditional Henderson–Hasselbalch approach. The strong ion approach indicates that acidemia results from an increase in P_{CO_2} and nonvolatile buffer concentration, or from a decrease in SID. Alkalemia results from a decrease in P_{CO_2} and nonvolatile buffer concentration, or from an increase in SID. The unmeasured strong anion concentration is quantified by calculating the strong ion gap (SIG).

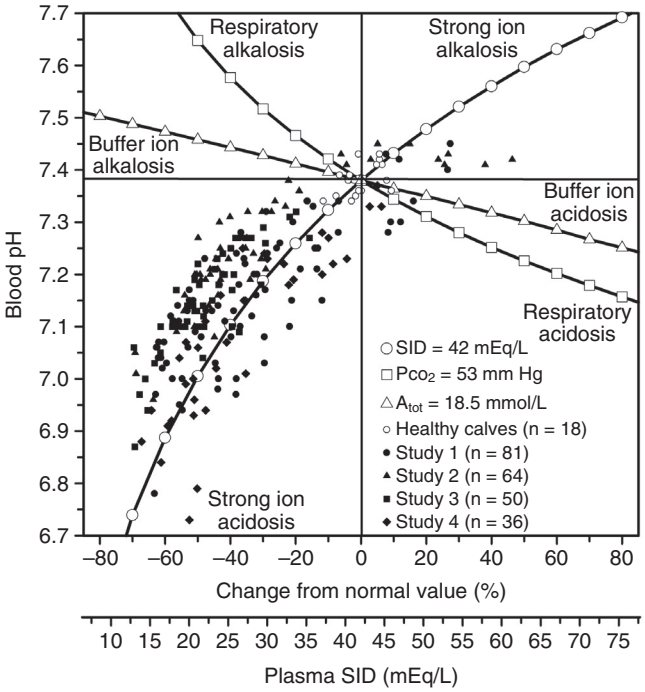

Fig. 5-11 Spider plot revealing the association among changes in three independent variables of the simplified strong ion equation, strong ion difference (SID, open circles), carbon dioxide tension (P_{CO_2}, open squares), and the plasma concentration of nonvolatile buffers (A_{tot}, open triangles), on venous blood pH in 231 sick calves, most of which had diarrhea. The spider plot was obtained by systematically varying one input variable (SID, P_{CO_2}, or A_{tot}) while holding the remaining input variables at their reference values for calf venous plasma (42 mEq/L for SID), 53 mm Hg for P_{CO_2}, and 18.5 mmol/L for A_{tot}. The solid vertical and horizontal lines indicate that venous blood pH = 7.38 when SID, P_{CO_2}, and A_{tot} are at their reference values. Note that the individual data points are located more centrally around the predicted pH–SID relationship than for the pH–cHCO_3^- relationship identified in Figure 5.9. This is because changes in plasma protein concentration (and therefore A_{tot}) caused by changes in hydration status account for some of the change in blood pH. The plot also indicates the six primary acid-base disturbances (respiratory, strong ion, or nonvolatile buffer ion acidosis and alkalosis) and the relative effect of each disturbance on blood pH in the neonatal calf. Note that changes in SID have the greatest relative effect on blood pH. (Adapted from Constable PD, Stämpfli HR, Navetat H, et al.: Use of a quantitative strong ion approach to determine the mechanism for acid-base abnormalities in sick calves with or without diarrhea. *J Vet Intern Med* 2005;19:581-9. IN Constable PD: Acid-Base Assessment When and How to Apply the Henderson-Hasselbalch Equation and Strong Ion Different theory, *Vet Clin Food Anim*. 2014;30:295-316.)

ACIDEMIA

ETIOLOGY

The traditional Henderson–Hasselbalch approach to acid-base balance indicates that general causes of nonrespiratory **(metabolic) acidosis** can be divided into three categories on the basis of pathogenesis (Fig. 5-12):

- Excessive loss of base (bicarbonate)
- Accumulation of endogenous or exogenous acid
- Combination of both of these processes

For comparison, the strong ion approach indicates that general causes of nonrespiratory (metabolic) acidosis can be divided into **two categories: strong ion acidosis** caused by a decrease in strong cation concentration (hyponatremia) or increase in strong anion concentration (hyperchloremia, hyper L-lactatemia, hyper D-lactatemia, and ketoacidosis), and **nonvolatile buffer ion acidosis** caused by an increase in albumin, globulin, and phosphate concentration.

Some common specific causes include acute diarrhea in newborn animals, acute enteritis in adult cattle and horses, and carbohydrate engorgement in ruminants and horses. Metabolic acidosis without dehydration, which is probably caused by hyper D-lactatemia, has been described in neonatal goat kids and neonatal calves.[4] Respiratory acidosis also occurs when there is retention of carbon dioxide in the blood as a result of interference with normal respiratory exchange. Thus pneumonia, severe pulmonary emphysema, depression of the respiratory center, and left-sided heart failure may all be accompanied by respiratory acidosis. Metabolic acidosis occurs in the newborn at the time of parturition if this is prolonged and difficult. It is also common in shock with peripheral circulatory failure and anaerobic oxidation. A decrease in renal excretion of

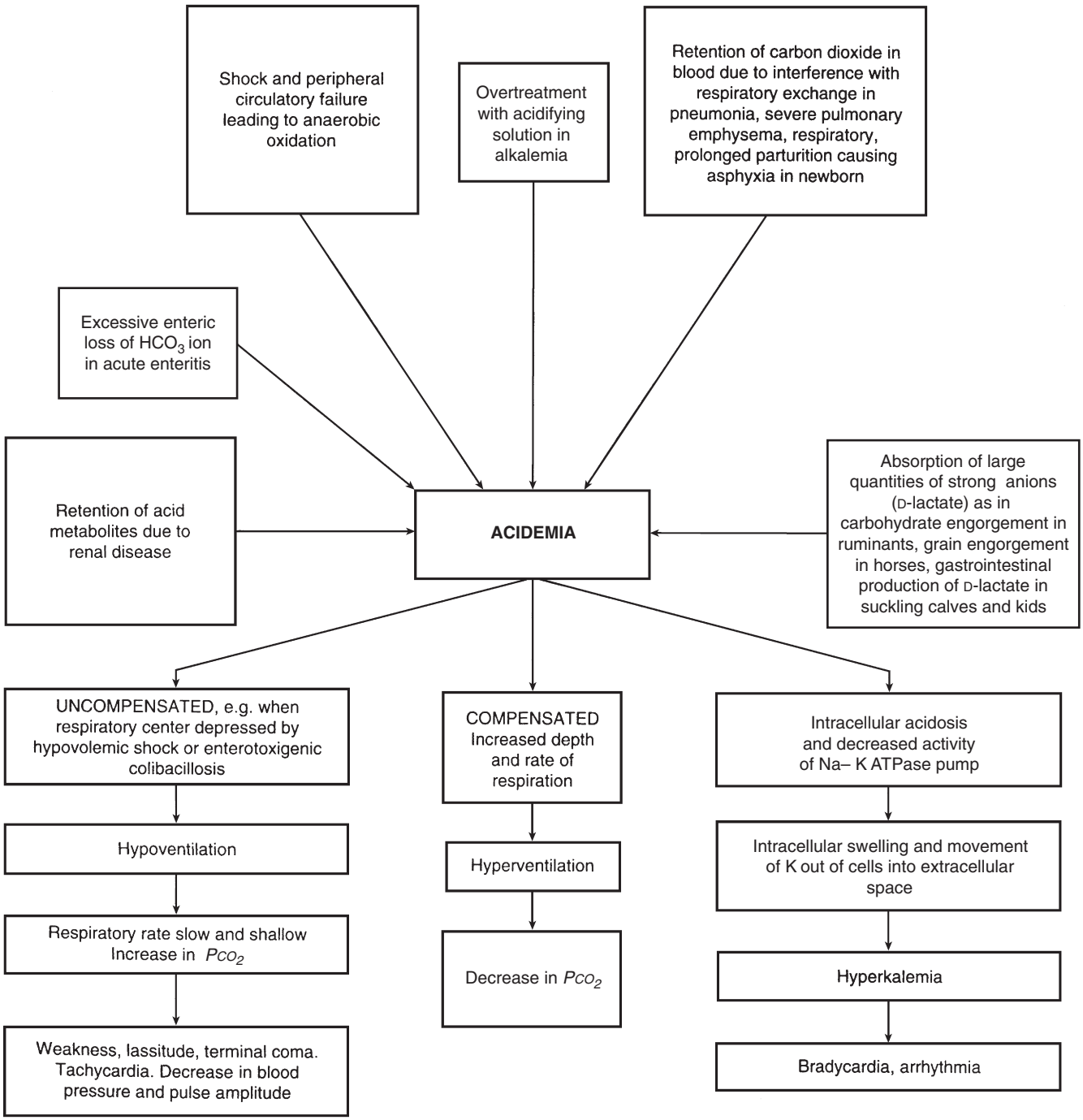

Fig. 5-12 Etiology and pathogenesis of acidemia.

acid in renal insufficiency or renal failure also contributes to a metabolic acidosis. The administration of excessive quantities of acidifying solutions for the treatment of metabolic alkalosis also may cause acidosis. Acute intestinal obstruction in the horse is commonly accompanied by metabolic acidosis, whereas in adult ruminants it is accompanied by alkalosis, at least initially.

PATHOGENESIS

The traditional Henderson–Hasselbalch approach indicates that metabolic acidosis is characterized by a low arterial blood pH and a low plasma bicarbonate concentration, following the loss of bicarbonate or the addition of hydrogen ions. Extracellular and intracellular buffering and respiratory compensation minimize the change in pH until the kidney can excrete sufficient hydrogen ions to correct the acid-base imbalance. Generally, the body will tolerate a pH range of 7.0 to 7.6, although survival has been reported at pH values beyond these limits for short periods, particularly in neonatal animals with diarrhea.

Acidemia generally depresses cardiac contractility and cardiac output in the denervated heart. In the intact animal, however, activation of the sympathetic nervous system in response to acidemia causes increased cardiac contractility, increased heart rate, and increased cardiac output. In acidemia, the myocardial response to catecholamines is not depressed until the blood pH is below 7.0 to 7.1. The increased carbon dioxide tension of the blood and depletion of bicarbonate causes an increase in the depth and then the rate of respiration by stimulation of the

respiratory center (**Kussmaul breathing**). However, when hypovolemic shock is severe enough, there is often depressed respiratory function, resulting in the additional accumulation of hydrogen ions; thus the acidemia is accentuated.

Acidemia causes varying degrees of depression of the central nervous system (CNS) and muscular weakness. Central nervous abnormalities may develop in neonatal foals that develop severe respiratory compromise, resulting in hypoxemia and hypercapnia, because of the reduced ability of the CSF to buffer acid-base changes. Carbon dioxide concentration within the CNS may have an effect on respiratory rate, neurotransmitter activity, CNS activity, cerebral blood flow, and cerebral extracellular fluid volume. If the blood–CSF and brain–CSF interfaces in the neonate are immature and unable to adequately compensate for vascular changes in CO_2, the hypercapnia may contribute to the CNS abnormalities that are often seen in sick newborn foals. The increased cerebral blood flow may be associated with cerebral edema, resulting in the depression of cerebral activity observed in these same foals.

The increased urinary excretion of acids in acidosis also causes polyuria, which may be sufficiently severe to cause dehydration or accentuate concomitant dehydration. Urine pH is also likely to be decreased in herbivores; however, aciduria may not always be present because of concurrent electrolyte and free water abnormalities.

CLINICAL FINDINGS

The major clinical manifestation of metabolic acidosis is mental depression and varying degrees of muscular weakness, depending on the mechanism for acidemia. Newborn calves, lambs, and goat kids with profound acidemia and metabolic acidosis are depressed, weak, and reluctant to suck. In severe acidemia, affected animals may be in lateral recumbency and appear to be in a state of coma. The depth and rate of respirations may be increased because of the increased P_{CO_2}. Respiratory compensation is normally evident when the bicarbonate level is diminished to 50% of normal. Calves affected with severe acidemia and dehydration caused by acute diarrhea may be unable to compensate because of depressed respiratory function. Their respiratory rate will be much slower and the depth of respiration much more shallow than normal. There is usually tachycardia, which becomes worse as the acidosis becomes more severe, and the amplitude of the pulse and blood pressure both decrease. A concomitant hyperkalemia will cause bradycardia, heart block, sudden collapse, and rapid death. This is particularly evident when animals with acidosis and hyperkalemia are transported and handled for treatment. The increased muscular activity appears to accentuate the abnormalities, and sudden death is not uncommon. Weakness, lassitude, and terminal coma are frequent observations. An interesting recent observation is that experimentally induced acute acidemia and metabolic acidosis (jugular venous blood pH 6.96; base excess −22 mEq/L) in healthy neonatal calves, following intravenous administration of 4 L of a mixture of HCl and NaCl solutions, produced no clinically detectable abnormalities.[5] This finding suggests acidemia must be chronic to produce clinically apparent abnormalities, or that most of the clinical abnormalities observed in acidemic patients are caused by their disease process and concurrent electrolyte and energetic abnormalities.

A syndrome of metabolic acidosis with minimal signs of dehydration or diarrhea has been described in calves from 1 to 4 weeks of age.[4] Affected calves are depressed, weak, and ataxic, and the suck and menace reflexes may be weak or absent. Some calves appear comatose. Similar clinical presentations have also occurred in lambs and goat kids with no apparent history of previous diarrhea.[6-8] The abnormal laboratory findings include a reduced venous blood pH, P_{CO_2} and bicarbonate ion concentration, marked hyper D-lactatemia, elevated blood urea nitrogen, increased AG, and a neutrophilic leukocytosis with a left shift. Many of the clinical signs appear to be primarily the consequence of hyper D-lactatemia. The intravenous administration of 2.5 to 4.5 L of isotonic (1.3%) sodium bicarbonate solution, the amount depending on the severity of the condition, is necessary to return the neonatal calf to health.

ALKALEMIA

ETIOLOGY AND PATHOGENESIS

Alkalemia is caused by an increased absorption of alkali, excessive loss of acid, or a deficit of carbon dioxide (Fig. 5-13). Abomasal atony caused by dilatation, impaction, or torsion of the abomasum is one of the most common causes of alkalemia in cattle. There is continuous secretion of hydrochloric acid and potassium into the abomasum, with failure of evacuation of the abomasal contents into the duodenum for absorption. Sequestration of hydrochloric acid and potassium occurs in the abomasum, along with reflux into the rumen, all of which results in a hypochloremic, hypokalemic alkalosis. In metabolic alkalosis, potassium will shift from the extracellular to the intracellular space, resulting in a hypokalemia when there may not be depletion of total body potassium. In cattle with metabolic alkalosis there is a paradoxical aciduria, which is not well understood but may be caused by severe electrolyte depletion placing limits on the kidney to regulate acid-base balance. Paradoxical aciduria must be differentiated from postparturient aciduria, which has been reported to occur in dairy cows.

Metabolic alkalosis has been recorded in cows with severe coliform mastitis, but the pathogenesis is unknown.

CLINICAL FINDINGS

The clinical findings of alkalosis are not characteristic enough to be recognized reliably. Alkalosis results in slow, shallow respirations in an attempt to preserve carbon dioxide. Muscular tremors and tetany with tonic and clonic convulsions may occur in extreme alkalemia (pH > 7.60) because of marked pH changes and possibly depression of the ionized fraction of serum calcium. Hyperpnea and dyspnea may also occur in the terminal stages.

Oncotic Pressure and Edema

ETIOLOGY

Decreased plasma oncotic pressure caused by hypoalbuminemia or hypoproteinemia is the most common cause of generalized symmetric edema. However, edema can also result from three other causes: **increased hydrostatic pressure** in capillaries and veins caused by chronic (congestive) heart failure or obstruction to venous return; **increased capillary permeability** in endotoxemia, part of the allergic response, vasculitis, and damage to the vascular endothelium; or **obstruction to lymphatic flow**.

Decreased Plasma Oncotic Pressure

Decreased total protein concentration in plasma, and particularly decreased plasma albumin concentration, will result in symmetric ventral edema. Hypoalbuminemia is more important than hypoglobulinemia in inducing edema formation because albumin provides the largest contribution to plasma oncotic pressure. Hypoalbuminemia can result from **increased loss** (caused by blood-sucking parasites or across the gastrointestinal tract, kidneys, or into a large third space such as the pleural or peritoneal cavities), **decreased production** (as in chronic hepatic failure), or **decreased intake**:

- Chronic blood loss, especially in heavy infestations with blood-sucking parasites such as *Strongylus* spp. in the horse; *Fasciola* spp. in ruminants; *Haemonchus* spp. in ruminants of all ages, especially goats; and *Bunostomum* spp. in calves
- Protein-losing gastroenteropathies as in Johne's disease and amyloidosis in adult cattle and right dorsal colitis in horses; proliferative enteropathy in foals caused by *Lawsonia intracellularis;* heavy infestation with nematode parasites in ruminants, particularly *Ostertagia* spp. in young cattle and cyathostomiasis in horses
- Glomerulonephropathies, such as amyloidosis in adult cattle and inherited

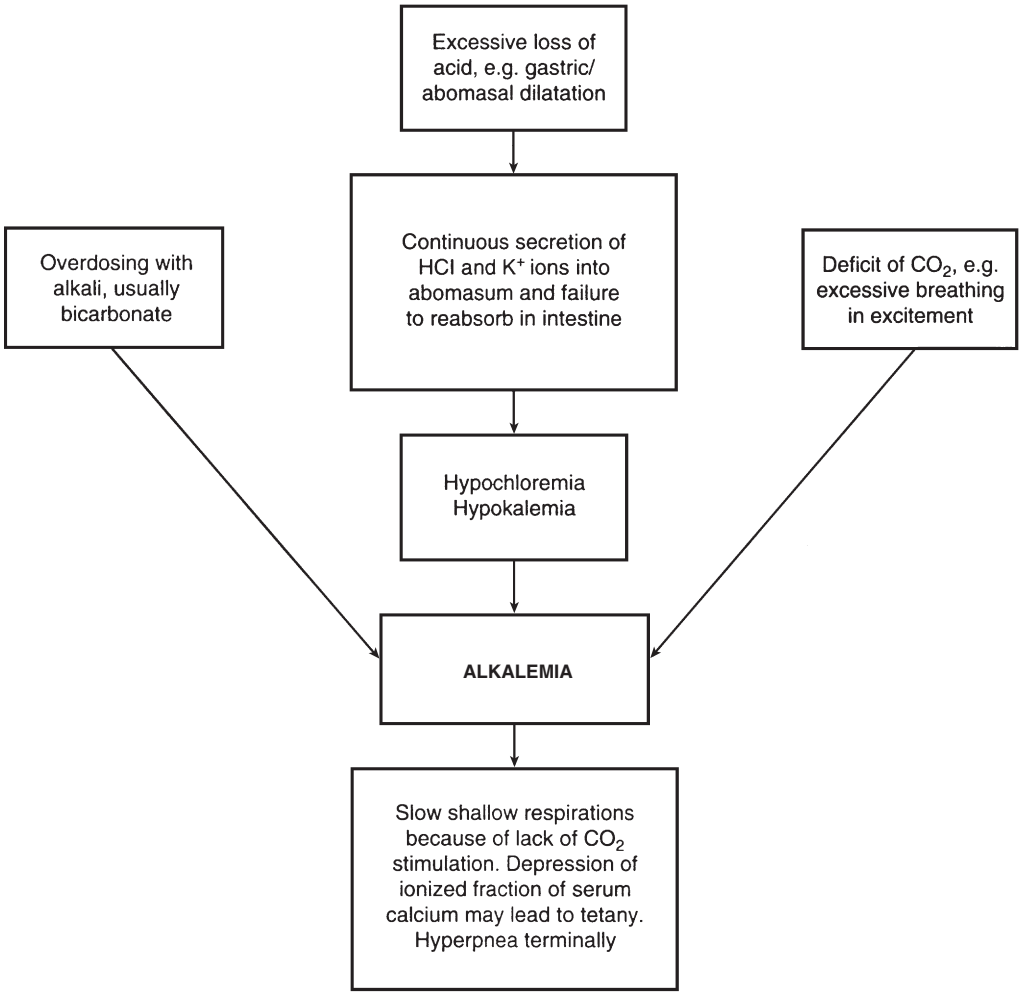

Fig. 5-13 Etiology and pathogenesis of alkalemia.

glomerulonephritis in Finnish Landrace lambs
- Chronic liver damage causing failure of plasma protein synthesis (rare and terminal in large animals)
- Terminally in prolonged malnutrition with low dietary protein intakes, e.g., ruminants at range in drought time

Increased Hydrostatic Pressure

Increased hydrostatic pressure can be caused by the following:
- Symmetric ventral edema in chronic (congestive) heart failure and symmetric pulmonary edema in acute heart failure
- Generalized edema in enzootic calcinosis of cattle
- Local symmetric ventral edema in udder edema in late pregnancy from compression of veins and lymphatics by the developing mammary gland (and possibly the enlarging fetus and uterus), causing mammary or ventral edema in cows (particularly heifers), mares, and occasionally ewes. Sodium and potassium intakes and cation–anion differences in the diet contribute to the severity of udder edema. Edema resolves 5 to 10 days following parturition.
- Local edema by compressive lesions on veins (as in thymic lymphosarcoma with compression of the cranial vena cava) draining other anatomic locations
- Local edema in portal hypertension caused by hepatic fibrosis causing ascites (rare in large animals)

Increased Capillary Permeability

Increased capillary permeability can be caused by the following:
- Endotoxemia
- Allergic edema as in urticaria and angioneurotic edema caused by local liberation of vasodilators
- Toxic damage to vascular endothelium or vasculitis such as in anthrax, gas gangrene, and malignant edema in ruminants; edema disease of pigs; mulberry heart disease in pigs; equine viral arteritis, equine infectious anemia, and purpura hemorrhagica in horses; and heartwater (cowdriosis) in ruminants

Obstruction to Lymphatic Flow

- Part of the edema caused by tumors or inflammatory swellings is lymphatic obstruction. Extensive fluid loss also originates from granulomatous lesions on serous surfaces. Ascites or hydrothorax may result.
- Congenital in inherited lymphatic obstruction edema of Ayrshire and Hereford calves
- Sporadic lymphangitis (big leg) of horses
- Edema of the lower limbs of horses immobilized because of injury or illness

PATHOGENESIS

Edema is the excessive accumulation of fluid in the interstitial space of tissue caused by a disturbance in the mechanism of fluid interchange among capillaries, the interstitial space, and the lymphatic vessels. At the arteriolar end of the capillaries the hydrostatic pressure of the blood is sufficient to overcome its oncotic pressure, and fluid tends to pass into the interstitial space. At the venous end of the capillaries the position is reversed

and fluid tends to return to the vascular system. The pressure differences are not great, but there is a large area for exchange, and a small increase in hydrostatic pressure or a small decrease in oncotic pressure leads to failure of the fluid to return to the capillaries.

Increased fluid passage into the interstitial space can also occur where there is increased vascular permeability caused by vascular damage. Under these circumstances, fluid accumulates in the interstitial space when the fluid flux across the endothelium is greater than the ability of the lymphatic system to drain it. Alternatively, capillary hydrostatic pressure, oncotic pressure, and vascular permeability might be normal, but fluid and vascular permeability can accumulate in the interstitial space when lymphatic drainage is occluded.

Edema of the lower limbs of immobilized horses (*filling*) is usually ascribed to poor lymphatic or venous return caused by inactivity of the *foot pump*. Lower limb edema in horses may also be related to changes in the hematocrit and plasma protein concentration in the distal limb vasculature as a result of inactivity.

CLINICAL FINDINGS

Accumulation of edematous transudate in subcutaneous tissues is referred to as **anasarca**, in the peritoneal cavity as **ascites**, in the pleural cavities as **hydrothorax,** and in the pericardial sac as **hydropericardium**. Anasarca in large animals is usually confined to the ventral wall of the abdomen and thorax, the brisket and, if the animal is grazing, the intermandibular space because of the large hydrostatic pressure gradient between the submandibular space and heart. Intermandibular edema may be less evident in animals housed because they do not have to lower their heads to feed. Edema of the limbs is uncommon in cattle, sheep, and pigs but is quite common in horses when the venous return is obstructed or there is a lack of muscular movement. Hydrothorax is not common with generalized edema and is usually an indication of an obstructive intrathoracic lesion. Local edema of the head in the horse is a common lesion in African horse sickness and purpura hemorrhagica.

Edematous swellings are **soft**, **painless,** and **cool to the touch** and **pit on pressure**. In ascites there is distension of the abdomen and the fluid can be detected by a fluid thrill on tactile percussion, fluid sounds on succussion, and by paracentesis. A level top line of fluid may be detectable by any of these means. In the pleural cavities and pericardial sac the clinical signs produced by the fluid accumulation include restriction of cardiac movements, embarrassment of respiration, and collapse of the ventral parts of the lungs. The heart sounds and respiratory sounds are muffled, and the presence of fluid may be ascertained by percussion and thoracocentesis or pericardiocentesis.

More localized edemas cause more localized signs: pulmonary edema is accompanied by respiratory distress and in some cases by an outpouring of froth from the nose; cerebral edema is manifested by severe nervous signs of altered mentation. A not uncommon entity is a large edematous plaque around the umbilicus in yearling horses. The plaque develops rapidly, causes no apparent illness, and subsides spontaneously after about 7 days. Thrombophlebitis is a common cause of localized edema, particularly of the head in horses and cattle with thrombophlebitis of both jugular veins. Head edema usually occurs in affected animals only when there is rapid and complete occlusion of both jugular veins by thrombophlebitis; a slower rate of jugular vein occlusion permits development of collateral veins for venous drainage of the head.

CLINICAL PATHOLOGY

Cytologic examination of a sample of fluid reveals an absence of inflammatory cells in which edema is the result of decreased plasma oncotic pressure (hypoalbuminemia), increased hydrostatic pressure, and increased vascular permeability or obstruction to lymphatic flow. Thoracocentesis or abdominocentesis is useful to differentiate the causes of fluid accumulation, in conjunction with measurement of serum albumin concentration and mean central venous pressure.

Examinations should always be directed toward determining the mechanism for hypoalbuminemia; in particular, the renal and gastrointestinal systems and liver are examined for evidence of disease and altered function. Generally, the serum albumin concentration is usually less than 15 g/L in animals with generalized edema caused by decreased plasma oncotic pressure. Generalized edema should always be expected whenever serum albumin concentration is less than 10 g/L.

NECROPSY FINDINGS

The nature of the accumulation of fluid in most cases is obvious on gross postmortem examination, but the determination of the cause of the disease that has resulted in hypoalbuminemia may require further histologic and cultural examination. Necropsy findings for the specific diseases in which edema is a feature are given in later chapters.

DIFFERENTIAL DIAGNOSIS

- Rupture of urethra or bladder for differentiation of ascites
- Peritonitis or pleuritis for accumulation of fluid in abdominal or pleural cavities
- Cellulitis for local edema

TREATMENT

The treatment of edema should be aimed at correcting the cause, whether it is decreased plasma oncotic pressure, increased hydrostatic pressure, increased endothelial permeability, or obstruction to lymphatic drainage. Hypoalbuminemia may require the administration of colloids such as plasma or Dextran 70, although this is only a short-term measure and is expensive. Chronic (congestive) heart failure may need to be treated with digoxin and thrombophlebitis of the jugular veins may need specific treatment (see Chapter 10). Parasitic gastroenteritis requires administration of the appropriate anthelmintic, obstructive edema requires removal of the physical cause, and increased permeability edema requires resolution of the cause of endothelial damage.

Ancillary nonspecific measures include restriction of the amount of salt in the diet and the use of diuretics. Diuretics may relieve the effects of pressure temporarily, but the primary cause needs to be addressed for a satisfactory outcome. Aspiration of edema fluid is rarely successful and is not routinely recommended but usually provides temporary relief because the fluid rapidly accumulates.

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Naturally Occurring Combined Abnormalities of Free Water, Electrolyte, Acid-Base Balance, and Oncotic Pressure

These abnormalities are seldom primary and are usually secondary to a serious disease state such as abomasal volvulus, rumen overload, or acute intestinal obstruction—diseases that are in themselves life-threatening. Fluid and electrolyte abnormalities are also life-threatening and simple correction of the primary abnormality, for example, removal of a large section of a horse's small intestine, is valueless unless the dehydration,

hyponatremia, and acidosis are also corrected. The variation that can occur in these naturally occurring errors of fluid, electrolyte, and acid-base balance is what makes their diagnosis and treatment so difficult. If it were possible to have instant clinicopathologic advice on what the abnormalities were and how they were progressing as determined by constant laboratory monitoring, there would be little clinical challenge. The increased availability of point-of-care devices have made real-time clinicopathologic values rapidly available; however, economics may preclude use of such equipment. It is therefore necessary to have an understanding of the basic physiology and pathology of these diseases to be able to predict, by clinical examination and examination of the history, the likely deficiencies and imbalances and their degrees of severity.

In the preceding paragraphs the individual abnormalities of fluid and electrolyte homeostasis were described. In most naturally occurring diseases, the abnormalities are complex. For example, the probable events in a case of acute diarrhea are set out diagrammatically in Fig. 5-14. It is important

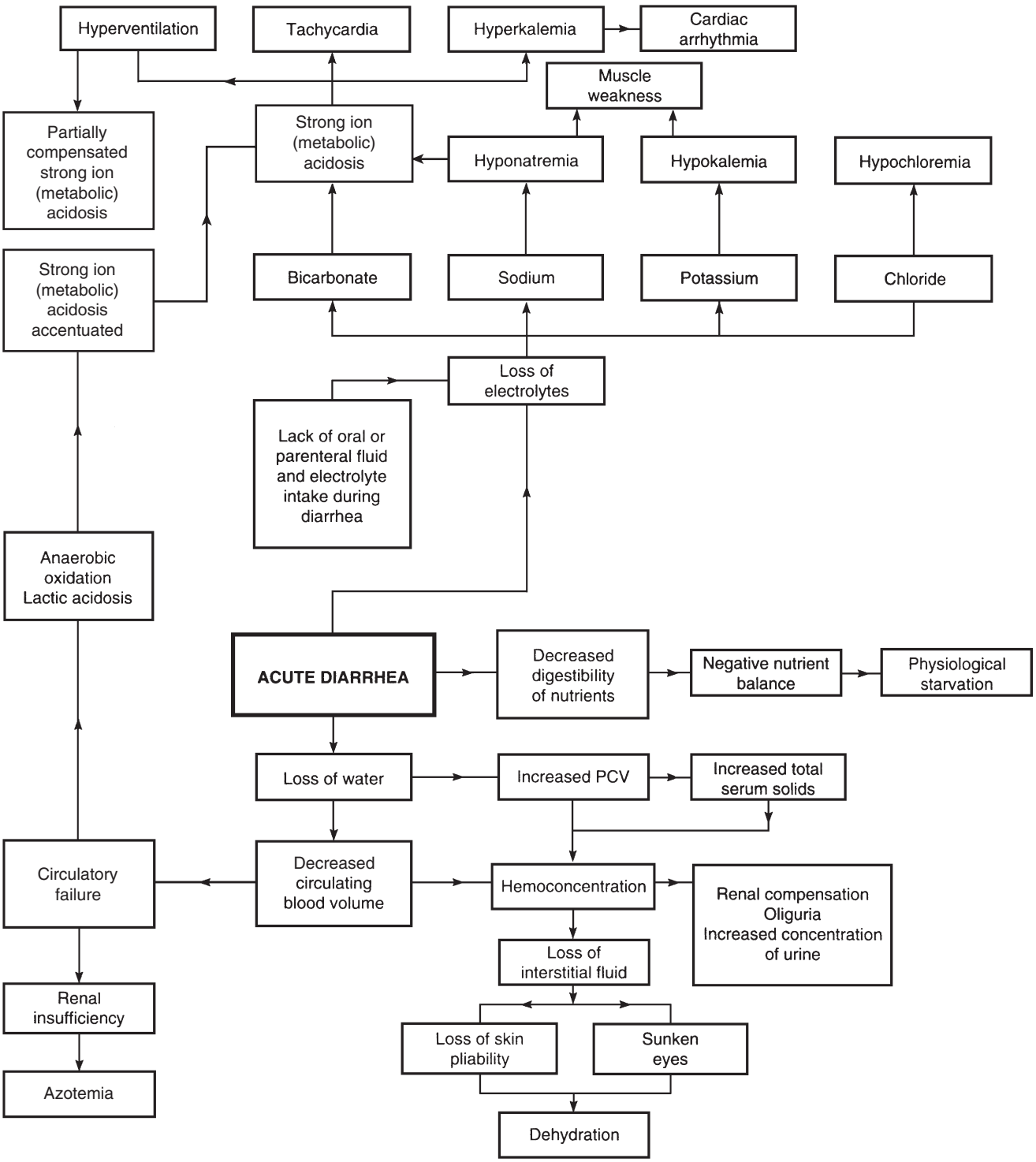

Fig. 5-14 The interrelationships among the changes in body water, electrolytes, and acid-base balance that can occur in diarrhea.

to remember that the variation in fluid and electrolyte imbalance is **dynamic** as a result of the compensatory changes occurring in various organs, especially the respiratory and circulatory systems and the kidneys. It is this volatility that makes clinicopathologic monitoring so important. Some generalizations on the dynamics of fluid and electrolyte status are as follows:

- Total body water and electrolytes are maintained at a homeostatic level by the buffering system of the blood, the lungs, and the kidneys.
- In disturbances of body water and electrolytes, the changes that occur are also dynamic, and there is constant reaction by the homeostatic mechanism to restore the water and electrolyte relationship to normal.
- With some exceptions, it is unusual to find an uncompensated alkalemia or acidemia. A partial compensation in the opposite direction of the primary acid-base imbalance is usually in progress, and it is important to determine the nature of the primary disturbance for the selection of rational therapy. A useful rule of thumb is that the primary disturbance (acidosis and alkalosis) is indicated by whether the blood pH is increased (alkalosis) or decreased (acidosis) relative to the mean value for the species examined.
- Often, the nature of the primary disturbance can be determined from a consideration of the history and the clinical findings.
- Dehydration caused by deprivation of water and electrolytes (lack of water or inability to drink) is mild and animals may appear only mildly dehydrated even after several days of water deprivation. The feces are hard and dry, the rumen contents are firm and dry, and urine volume is considerably decreased.
- With the exception of clinical dehydration, the clinical findings of electrolyte and acid-base imbalances are not characteristic.
- Without laboratory evaluation, the nature and degree of electrolyte and acid-base imbalance must be assumed and estimated based on the history of the affected animal and the changes that are most likely to have occurred.

NATURE OF THE DISEASE AND HISTORY

The **history of the case**, the **length of time** the animal has been affected, and the **tentative diagnosis** will provide a clinical assessment of the possible nature and degree of electrolyte and acid-base imbalance. Animals affected with acute diarrhea caused by infectious enteritis are likely to be in a state of metabolic acidosis and hyponatremia. In intestinal obstruction of the horse, there are varying degrees of dehydration and metabolic acidosis. Obstruction of the upper intestinal tract, or abomasal stasis, is characterized by varying degrees of dehydration and metabolic alkalosis with hypochloremia and hypokalemia. Chronic renal disease is characterized by hyponatremia and hypochloremia. Chronic inappetence in herbivores is characterized by hypokalemia, particularly in lactating ruminants. A combination of the clinical assessment and the available laboratory evaluation will allow the clinician to make the most rational approach to treatment.

The information on the duration of illness must be accurate or it will be misleading. The sequence of clinical findings in the history may indicate the trend in severity. Animals that have had a profuse watery diarrhea for 18 to 24 hours may be severely acidemic. Acute intestinal obstruction in cattle is not as severe as in the horse. Acute gastric or intestinal rupture in the horse or in cattle is usually rapidly fatal. Acidosis in grain overload in cattle may be fatal in 24 to 48 hours; acidosis in the horse with grain overload may be much more rapidly fatal because electrolyte disturbances are more severe in the horse.

CLINICAL FINDINGS

Dehydration is usually obvious clinically and determination of the PCV and serum or plasma total protein concentration will improve the assessment and provide values for daily comparison of response to treatment.

A normal rectal **temperature** is not a good prognostic guide, but a subnormal temperature suggests a worsening situation.

A gradually progressive **tachycardia** indicates that the patient is deteriorating. Generally, in the horse, a heart rate up to 60 beats/min suggests a minor lesion (but not always), a heart rate of 60 to 80 beats/min is in the danger area, 80 to 100 beats/min is serious, and more than 100 beats/min is commonly premortal (except in intestinal tympany that may be relieved).

A **cold clammy skin** that remains tented for more than 30 seconds suggests severe dehydration. **Cyanosis of the oral mucous membranes and a capillary refill time of more than 4 seconds** suggests a poor prognosis, as does rapid respiration (three to four times normal) with intermittent hyperpnea and apnea.

Muscular tremors and leg buckling are grave signs in the horse and are commonly followed by collapse and death. The inability of any dehydrated animal to stand (other reasons being eliminated) is ominous. **Severe depression** and dullness are commonly observed in acute conditions, and coma is usually terminal.

Metabolic acidosis is characterized by varying degrees of mental depression, decreased or absent suckle in neonatal animals, weakness, and ataxia. Some of the depression and weakness will be caused by dehydration, acidemia, or hyper D-lactatemia, although interestingly, acute and profound acidemia (jugular venous blood pH 6.96) in neonatal calves was not associated with depression or muscular weakness.[1] This is in contrast to the results of other studies in calves with more chronic and profound acidemia that profound acidemia is associated with decreased suckle and other clinical signs.[2,3] In newborn animals with metabolic acidosis associated with diarrhea, a failure to suck and the lack of a suck reflex are common.[4,5] Hyper D-lactatemia should be suspected in neonatal calves with a slowed or absent palpebral reflex, and profound acidemia and metabolic acidosis should be suspected in neonatal calves that stand unsteadily or have an inability to stand or have a delayed or absent reaction to acoustic, optical, or painful stimuli such as venipuncture.[4] Hyper D-lactatemia should also be suspected in neonatal lambs and goat kids with decreased or absent suckle that appear somnolent with varying degrees of ataxia.[6-8]

CLINICAL PATHOLOGY

Some representative laboratory values in examples of body water and electrolyte disturbances are given in Table 5-1.

Packed Cell Volume and Total Serum Protein or Plasma Protein

The PCV and the **total serum protein** or **plasma protein concentration** (historically called **total solids**) will indicate the severity of water loss. Anemic animals and those affected with diseases causing hypoproteinemia may provide misleading values. Neonatal animals often provide misleading values because of the variability of PCV in newborn animals and large differences in the transfer of colostral immunoglobulins.

The normal range depends on the age and species of animal, previous excitement, and the presence of anemia or hypoproteinemia. A PCV of 30% to 40% is considered normal; between 40% and 50%, fluid therapy may or may not be necessary; between 50% and 60%, fluids are necessary for recovery; and above 60% intensive fluid therapy is necessary and the prognosis is unfavorable. A total serum protein concentration of 6.0 to 7.5 g/dL is usually considered normal, at 8 to 10 g/dL fluids are needed and the prognosis is favorable, and above 10 g/dL the prognosis is unfavorable.

Total CO_2

A useful screening test for acid-base status in animals without evidence of respiratory disease is the total CO_2. Total CO_2 is defined as the amount of total carbon dioxide in plasma that can be liberated with a strong acid, and it can be calculated from the results of routine blood gas analysis as total $CO_2 = [HCO_3^-] + \text{dissolved } CO_2 + [H_2CO_3]$. The $[HCO_3^-]$ is calculated using the

Table 5-1 Representative laboratory values (mean ± sd) in body water and electrolyte disturbances

Clinical pathology	Acute diarrhea in horse	Acute diarrhea in calf	Metabolic alkalosis caused by abomasal dilatation impaction/ volvulus in cattle	Acute intestinal obstruction in horse	Acute carbohydrate engorgement in ruminants
Packed cell volume (%)	60 ± 7	45.3 ± 7.0	42 ± 6	64 ± 5	45 ± 6
Total serum solids (g/dL)	10 ± 2	8.6 ± 1.5	8.2 ± 1.5	11.5 ± 1.5	8.5 ± 1.8
Blood pH (venous)	7.10 ± 0.15	7.08 ± 0.12	7.49 ± 0.15	7.15 ± 0.04	7.10 ± 0.05
Plasma bicarbonate (mmol/L)	12 ± 3	13.7 ± 4.2	35.4 ± 5.7	18 ± 6	12.5 ± 3.5
Partial pressure of carbon dioxide (mm Hg)	45 ± 8	46.8 ± 6.4	46.4 ± 7.5	48 ± 6	40 ± 6
Serum sodium (mmol/L)	126 ± 3	138 ± 9.4	138.5 ± 5.4	135 ± 5	132 ± 4
Serum chloride (mmol/L)	99 ± 3	101.4 ± 7.5	88.6 ± 12.8	98 ± 4	93 ± 3
Serum potassium (mmol/L)	3.0 ± 1.2	7.4 ± 1.6	3.4 ± 0.6	3.8 ± 0.6	5.0 ± 2.5
Blood urea nitrogen (mg/dL)	60 ± 30	50.1 ± 30.5	40 ± 15	65 ± 35	55 ± 25

Henderson–Hasselbalch equation and the dissolved CO_2 is equal to $S \times PCO_2$, whereas $[H_2CO_3]$ is negligible.

Many automatic serum biochemical analyzers directly measure total CO_2 (instead of calculating its value from the results of blood gas analysis), but for total CO_2 measurement it is important that blood collection tubes are completely filled before serum is harvested: failure to completely fill the blood tubes promotes escape of CO_2 from serum into the partial vacuum above, resulting in measured total CO_2 values that underestimate true serum total CO_2. It is also important that large partially evacuated tubes are used to collect the blood sample; this is because the air to blood sample ratio is higher in small tubes (3 mL or less in sample volume), leading to lower measured values for total CO_2 even with complete filling of the tube. As a consequence, total CO_2 is most accurately measured when partially evacuated tubes of 4- to 10-mL sample volume are used,[9] and samples are stored at 4°C.[10] Because changes in total CO_2 reflect changes in actual bicarbonate concentration, total CO_2 can never provide an independent measure of the nonrespiratory component of an acid-base disturbance. Total CO_2 does, however, provide a useful screening test for the presence of acid-base disturbances in domestic animals without clinical evidence of respiratory disease. In the absence of respiratory disease, a decrease in total CO_2 indicates a metabolic acidosis, whereas an increase in total CO_2 indicates metabolic alkalosis. Total CO_2 has historically been measured using the Harleco apparatus, although this methodology is no longer used because of the wide availability of point-of-care analyzers for blood gas and pH assessment.

Blood Gas and pH Analysis

Blood collected anaerobically into a glass syringe and stored in iced water represents the reference method for blood gas and pH analysis, but glass syringes are no longer used clinically because of their cost, fragility, and inability to be sterilized. Polypropylene syringes have replaced glass syringes for blood gas and pH analysis; however, clinicians should be aware that small differences exist in blood pH and gas measurements when syringes from different manufacturers are used.[11]

The method used for collection of an anaerobically collected blood sample for blood gas and pH analysis differs depending on whether the clinical interest is on the **respiratory system** (which requires collection of an **arterial blood sample**) or **metabolic status** (usually best evaluated using a blood sample from a large vein such as the **jugular vein**). Because respiratory disease that is clinically relevant can usually be detected during the physical examination of large animals,[12] most blood samples collected for blood gas and pH analysis are collected from the jugular vein.

If the primary clinical interest is an acid-base assessment of a large animal, then a jugular venous blood sample should be anaerobically obtained in a 3-mL polypropylene syringe that has been previously coated internally with sodium heparin (by drawing sodium heparin into the syringe barrel and then expelling all heparin from the syringe into the barrel before blood collection). Three milliliters of air should then be drawn into the syringe and forcibly expelled; this process is repeated three times. Evacuating the syringe in this manner ensures that minimal heparin is retained to dilute the blood sample, but a sufficient quantity is still present to prevent coagulation. Alternatively, commercially available polypropylene syringes that contain lyophilized lithium heparin can be used, but these syringes are considerably more expensive than standard polypropylene syringes.[13] Air bubbles should be immediately removed from the blood in the syringe after collection by holding the syringe vertically and tapping the syringe forcefully with a finger so that bubbles are dislodged and float upward. Once all visible bubbles are removed, a small amount of blood is expelled with the syringe still held vertically so that the syringe hub and needle lumen no longer contain air bubbles. A cork is then placed on the end of the needle to prevent loss of CO_2 and addition of O_2 to the blood sample. Jugular venous blood samples can predict arterial blood gas values of pH, PCO_2, bicarbonate concentration, total CO_2, and base excess in animals that do not have respiratory disease, but only accurately predict blood pH in animals with respiratory disease.[14,15] Changes in jugular venous PO_2 over time are reflective of the direction and magnitude of the change in arterial PO_2.[16]

Generally, the blood sample should be analyzed as soon as possible and preferably within 30 minutes of collection. The method used for **storage** of an anaerobically collected blood sample for blood gas and pH analysis differs depending on whether the sample was collected from an artery or large vein. Venous blood samples should be stored in ice water (0°C) until analysis.[17] This will minimize any time-related changes in the measured values for pH and PCO_2 and therefore the calculated values for base excess and total CO_2, which occur when blood is held at room temperature (20°C) or higher ambient temperatures, particularly in blood samples with high white blood cell concentrations. If the primary interest is evaluation of the respiratory system, an arterial blood sample should

be obtained in the same manner as a venous sample; however, the sample should be kept at body temperature (preferable) or room temperature before blood gas and pH analysis is performed, which should be completed as soon as possible. This is because storing 3-mL polypropylene syringes in ice water (0°C) facilitates oxygen diffusion through the barrel of the syringe, causing a preanalytical increase in P_{O_2}. Partially evacuated blood collection tubes should never be used for blood gas and pH analysis because they are not completely evacuated; consequently, an anaerobic blood sample cannot be obtained for analysis. Use of partially evacuated tubes always results in higher values for blood P_{O_2} and lower values for blood P_{CO_2} because oxygen and carbon dioxide in the blood equilibrate with the oxygen-rich and carbon dioxide–poor air within the tube.[18]

Use of point-of-care clinical analyzing systems has greatly facilitated routine evaluation of acid-base status in domestic animals and, generally, point-of-care systems are sufficiently accurate for clinical use.[19] A thorough assessment of acid-base status requires blood gas analysis and serum biochemical analysis, with blood samples obtained from a major vein or any artery. If serum total protein, albumin, and phosphate concentrations are approximately normal, then acid-base status should be evaluated using blood pH, P_{CO_2}, and extracellular base excess concentration. This is the traditional Henderson–Hasselbalch approach. The presence of unidentified anions should be investigated by calculating the AG. If serum total protein, albumin, and phosphate concentrations are markedly abnormal, then acid-base status should be evaluated using blood pH, P_{CO_2}, measured SID, and A_{TOT}. This is the simplified strong ion approach. The presence of unidentified strong ions should be investigated by calculating the SIG.

Normal blood pH for most domestic animals varies from 7.35 to 7.45 (venous blood). The degree of acidemia encountered includes moderate acidemia (pH 7.30–7.25), severe acidemia (pH 7.25–7.20), and grave acidemia (pH 7.10–7.00), which is associated with a high fatality rate, except in neonatal animals.

Blood or Plasma L-Lactate Concentration

The blood or plasma L-lactate concentration provides valuable information about the adequacy of oxygen delivery to the tissues, providing a means for assessing the severity of cardiovascular or pulmonary dysfunction, monitoring the response to treatment, and formulating a prognosis for survival. The normal plasma L-lactate concentration in large animals is generally considered to be less than 1.5 mmol/L. Increases in plasma L-lactate concentration have been categorized as mild (2.5–4.9 mmol/L), moderate (5.0–9.9 mmol/L), and severe (≥10 mmol/L), with L-lactate concentrations greater than 10 mmol/L associated with a high mortality in humans, pigs, and horses.

A number of inexpensive handheld point-of-care devices are now available to measure blood L-lactate concentration. Most devices measure L-lactate concentration in whole blood through a two-step process on a specialized reagent strip. The L-lactate concentration is measured by placing a drop of blood onto the reagent strip; the blood seeps through a protective mesh on which the erythrocytes are retained and only plasma reaches the detection area. A chemical reaction takes place, and a change in color or current is rapidly detected and converted to an L-lactate concentration using a proprietary algorithm. Values can be displayed as whole blood or plasma based on a mathematical function of the analyzer. A number of method comparison studies have shown these units to be clinically useful, particularly when blood L-lactate concentrations are <15 mmol/L.

Studies in critically ill human patients have shown excellent correlations between blood L-lactate concentration in arterial blood, pulmonary arterial blood, central venous blood, and blood obtained from a peripheral vein, indicating that jugular venous blood L-lactate concentration provides an accurate reflection of pulmonary arterial or systemic arterial blood L-lactate concentrations, which are regarded as the gold standard sites for measuring blood L-lactate concentration. Consequently, jugular venous blood L-lactate concentrations are now routinely measured in critically ill large animals, with the clinical emphasis on evaluating the change in L-lactate concentration over time.[20-22] This is because the change in L-lactate concentration over time (particularly to an intervention) has greater prognostic ability than the actual L-lactate concentration at one point in time.

Serum Electrolytes

Serum electrolyte concentrations indicate the severity of the electrolyte losses and the necessity for replacement with either balanced electrolyte solution or specific electrolyte solution. Serum concentrations of **sodium, chloride, and potassium** are usually determined. The total deficit for each electrolyte can be estimated using the standard formula presented under calculation of electrolyte requirements.

Serum electrolyte concentrations depend on the initial cause and the severity of the disease. For example, in most cases of acute diarrhea there is hyponatremia and metabolic acidosis, which are usually marked in the horse with acute diarrhea. The serum concentration of chloride may be normal or subnormal in acute diarrhea. The serum concentration of potassium will be below normal initially, but as acidemia develops and becomes severe **hyperkalemia** may occur. In cattle with **abomasal hypomotility** there will be a **hypochloremic hypokalemic metabolic alkalosis.**

Water and electrolyte abnormalities are classified into three types based on the measurement of electrolytes and osmolality (assuming plasma osmolality in healthy large animals approximates 285 mosm/kg):

- **Hypertonic dehydration** (true dehydration/desiccation): Osmolality greater than 300 mosm/kg, associated with water deprivation, some acute gastrointestinal problems, and some types of diarrhea
- **Hypotonic dehydration** (acute desalting water loss): Osmolality less than 270 mOsm/kg, associated with acute diarrhea, particularly secretory diarrheas such as salmonellosis
- **Isotonic dehydration:** Normal electrolyte and osmolality levels, as in horses losing electrolytes and water in almost equal proportions

Urea and Creatinine

Urea and **creatinine** are metabolic breakdown constituents that can be used to assess the degree of dehydration and to distinguish among prerenal, renal, and postrenal uremia. The plasma/serum concentrations of urea and creatinine concentration will be elevated, depending on the severity of the dehydration and decrease in circulating blood volume. Following treatment with fluids and electrolytes in prerenal uremia, the concentrations of urea and creatinine will decline. Plasma creatinine concentration varies directly with the muscle mass in healthy animals, and, consequently, is much higher in beef bulls than dairy cows. Plasma urea concentration varies directly with the protein intake in healthy animals, and, consequently, is increased in ruminants on a high-protein diet.

Blood or Plasma Glucose

Plasma glucose concentration can be determined using conventional laboratory techniques (hexokinase assay), which require submission of heparinized blood samples to a laboratory as soon as possible to avoid erroneous results caused by erythrocyte glycolysis. Quantitative, rapid, low-cost point-of-care methods for determining blood glucose concentrations are now widely available, but many units are designed for analysis of human blood and are not suitable for use in large animals because they incorrectly assume intraerythrocyte glucose concentration is the same as plasma glucose concentration (which is the case in most primates). In all of the domestic animals examined, intraerythrocyte glucose concentration is lower than plasma glucose concentration, and, consequently, the measured blood glucose value depends on the hematocrit, which is usually assumed to be fixed and approximately 44%. Consequently, preferred point-of-care glucose meters should use a species-specific algorithm for correcting the

measured whole blood value, or should also measure hematocrit and use an additional algorithm to correct the measured whole blood value for deviations of hematocrit from the assumed value of 44%.

Anion Gap

Acid-base balance has traditionally been evaluated by using the Henderson–Hasselbalch equation to characterize four primary acid-base disturbances (i.e., respiratory acidosis and alkalosis, metabolic acidosis, alkalosis) and by calculating the AG to estimate the UA concentration. Evaluation of the AG has become routine in many medical institutions. The calculation takes little time, is essentially without cost, and is valuable in assessing a variety of clinical conditions in which electrolyte imbalances occur.

The reference range for AG depends partly on the formula used for calculation. Some investigators prefer not to include the potassium concentration when calculating the AG on the basis that $[K^+]$ varies to a much smaller degree than does $[Na^+]$, $[Cl^-]$, and $[HCO_3^-]$; therefore it exerts minimal influence on the AG. However, the consensus is that $[K^+]$ should be included in the calculation of AG in large animals. Other investigators substitute the measured total CO_2 value for $[HCO_3^-]$, permitting calculation of the AG from serum or plasma biochemical analysis without the need for blood gas determination.

The AG represents the difference between the concentration of [UA] and [UC] in serum (with square brackets representing concentration), which can be expressed in the equation:

$$[Na^+]+[K^+]+[UC]=[Cl^-]+[HCO_3^-]+[UA],$$

which can be rearranged to

$$[UA]-[UC]=AG=([Na^+]+[K^+])-([Cl^-]+[HCO_3^-])$$

A change in [UA] or [UC] will cause a change in the AG. Under normal circumstances, approximately two thirds of the AG originates from the net negative charge of serum proteins, and the remainder represents the serum concentration of phosphate and strong anions, such as L-lactate, sulfate, β-OH butyrate, aceto-acetate, and anions associated with uremia.

The reference range for an AG depends on the age and species. The normal range for 2- to 3-week-old foals is 9 to 22 mEq/L, which is higher than that for 2-year-old horses (range 8–13 mEq/L). The 95% confidence interval for the range of AG for adult animals varies for different species: 8 to 13 mEq/L (horse), 14 to 20 mEq/L (cow), and 17 to 29 mEq/L (sheep). The AG values greater than 30 mEq/L have been observed in critically ill cattle; the increase is attributed to an increase in blood lactate and keto-acid concentration as well as to anions associated with uremia (Fig. 5-15).

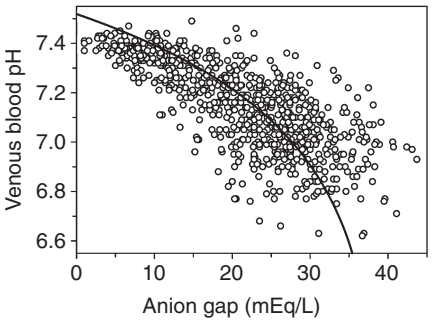

Fig. 5-15 Relationship between venous blood pH and anion gap (AG) in 806 neonatal calves with diarrhea. The thick line represents the result of nonlinear regression analysis: $pH = \log_{10}(39.7 - AG) + 5.92$. (Reproduced with permission from Trefz FM, Constable PD, Lorenz I. *J Vet Intern Med* 2015;29:678-687.)

A potentially valuable clinical use for the AG is in estimating a value for plasma L-lactate concentration, and this is why calculation of the AG has been considered a "poor man's plasma L-lactate concentration." The correlation between AG and plasma L-lactate concentrations is excellent in horses with intestinal disease. The AG in adult cattle is only moderately correlated with L-lactate concentrations and is similarly correlated with serum phosphate and creatinine concentrations in neonatal calves and adult cattle, as well as with serum albumin and total protein concentrations in adult cattle.[24] The AG determination is of limited usefulness in predicting blood L-lactate concentration in sick cattle, whereas the correlation between AG and serum concentration in sick cattle suggests that an increased AG should suggest the potential presence of uremic anions.

In summary, the determinants and utility of the AG in predicting hyperlactatemia are as follows:

- The AG in critically ill cattle is influenced by at least three factors: blood L-lactate concentration and the serum concentrations of phosphate and creatinine.
- There is a substantial quantity of UAs in sick cattle (approximately 7 mEq/L), which implies that either unidentified cations or anions other than chloride, bicarbonate, L-lactate, pyruvate, β-OH butyrate, or phosphate are present in critically ill cattle or that the formula used to assign protein charge was inaccurate.
- The correlation coefficient between AG and blood L-lactate concentration is similar to that observed in human patients and less than that seen in sick horses.
- The AG appears to predict blood L-lactate concentration more accurately in neonatal calves with experimental diarrhea than that in adult cattle with spontaneously occurring abomasal volvulus. The effects of acidemia on the AG and electrolyte concentration can vary depending on the cause of the acidosis and the species involved. Experimentally in horses, the infusion of L-lactic acid and D- and L-lactic acid results in acidosis with a high AG. An infusion of hydrochloric acid causes metabolic acidosis with a decreased AG. Infusions of isotonic saline (0.9% NaCl) cause mild acidosis with no significant change in AG.

Strong Ion Gap

The **SIG** represents the concentration of unmeasured strong ions in plasma and is more specific in detecting the presence of unmeasured strong ions in plasma than the AG. Moreover, the results of every study that has compared SIG with AG have demonstrated that SIG has greater explanatory power.

The SIG concept is a logical extension of the AG concept and was developed using the SID approach to express SIG in terms of other factors:

$$SIG=\{A_{TOT}/(1+10^{(pKa-pH)})\}-AG$$

where SIG represents the difference between unmeasured strong cation concentration and unmeasured strong anion concentration in plasma or serum. Calculation of the SIG requires species-specific values for the total plasma concentration of nonvolatile weak acids (A_{TOT}; i.e., the total concentration of plasma nonvolatile buffers such as albumin, globulin, and phosphate) and the negative logarithm to the base 10 (pK_a) of the effective dissociation constant (K_a) for plasma nonvolatile buffers. Values for A_{TOT} and pK_a have been determined for the plasma of horses (A_{TOT}, 15.0 mmol/L = 0.22 mmol/g of total protein or 0.47 mmol/g of albumin; pK_a, 6.66) and calves (A_{TOT}, 23.1 mmol/L = 0.41 mmol/g of total protein or 0.75 mmol/g of albumin; pK_a, 7.08).

The reference range for SIG is generally −5 to +5 mEq/L. An increase in SIG above 5 mEq/L (which occurs rarely) reflects an increase in unmeasured strong cations or a decrease in unmeasured strong anions. A decrease in SIG below −5 mEq/L (a common occurrence) reflects a decrease in unmeasured strong cations or, more likely, an increase in unmeasured strong anions (Fig. 5-16).

The SIG offers a more accurate approach to identifying unmeasured strong ions in plasma than does the AG. The critical difference between the AG and SIG is that the SIG provides an estimate of the difference between unmeasured strong cations and strong anions, whereas AG provides an estimate of the difference between UCs and anions (including strong ions and nonvolatile buffer ions such as albumin, globulin,

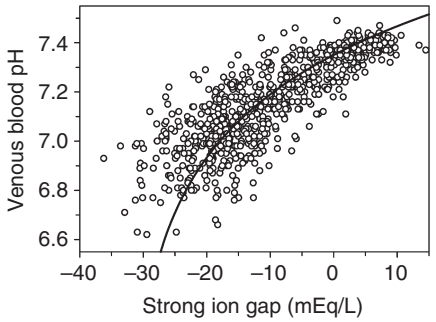

Fig. 5-16 Relationship between venous blood pH and strong ion gap (SIG) in 806 neonatal calves with diarrhea. The thick line represents the result of nonlinear regression analysis: pH = $\log_{10}$ (SIG + 32.4) + 5.84. (Reproduced with permission from Trefz FM, Constable PD, Lorenz I. *J Vet Intern Med* 2015;29:678-687.)

and phosphate). A change in SIG therefore provides a more specific method for detecting a change in unmeasured strong ions (such as lactate) than a change in AG.[23,24]

Osmolal Gap

Evaluation of the osmolal gap is a means of detecting an increased amount of abnormal osmotically active solute in the blood. The osmolal gap is the difference between the measured plasma osmolality and the osmolality calculated from the plasma concentration of normally measured solutes. Sodium and potassium and their associated anions, along with glucose and urea, constitute the majority of normal osmotically active solutes. The following formula is recommended with plasma/serum glucose and urea measured in units of mg/dL,[25] although many clinicians disregard the contribution of urea on the basis that it is an ineffective osmole that easily crosses cell membranes:

$$1.90\times([Na^+]+[K^+])+(glucose/18)+(urea/2.8)+5.0.$$

Examination of the triad of **calculated osmolality**, **measured osmolality,** and the **osmolal gap** is beneficial in the diagnosis and prognosis of a number of diseases.

Arterial, Jugular, or Central Venous Blood Pressure

Arterial blood pressure is occasionally measured in referral centers in which the technical assistance and instrumentation are readily available. Mean arterial blood pressure provides a rough guide for the presence and severity of terminal shock but not for the severity or extent of the initiating lesion. Methods for measuring mean arterial blood pressure are summarized in Chapter 10.

Jugular venous pressure (or preferably central venous pressure) is occasionally measured in referral centers to monitor the response to fluid administration. Normal pressure is 2 to 10 cmH_2O (0.3–1.0 kPa), referenced to the point of the shoulder (scapulohumeral joint). Below 2 cmH_2O (0.3 kPa) requires fluid therapy; above 15 cmH_2O (1.5 kPa) indicates cardiac failure and volume overload. Mean central venous pressure provided a sensitive method for detecting hypovolemia in horses having blood removed at 16 mL/kg; the significant reduction in mean central venous pressure occurred in the absence of a change in heart rate.[17] Methods for measuring jugular venous pressure or central venous pressure are summarized in Chapter 10.

Total Body Water

The most practical way to measure change in body water is to measure the **change in BW** by weighing the animal on admission and at a standard time each day, usually before the morning feeding. This is most valuable in animals admitted to a hospital with clinical signs consistent with severe dehydration. Simultaneous measurement of hematocrit and plasma protein concentration using refractometry provides a low-cost but clinically valuable method for monitoring changes in extracellular fluid volume from admission. The clinical utility of frequent weighing can be improved by periodically weighing the food offered and eaten as well as determining the weight of feces produced. More exact estimates are provided if urine is collected and weighed, although this is usually only feasible in neonatal calves and small ruminants. Losses in milk volume also need to be accounted for if the method is used in lactating dairy cattle.

Bioelectrical impedance analysis has been used in horses to detect acute changes in fluid volume in horses, although impedance analysis appears to have more applications in research studies than in the critical care of dehydrated or shocked animals. The method uses a head–tail configuration (although other configurations have been used) and requires shaving two areas of skin over the right cranial border of the first cervical vertebra and over the caudal aspect of the right tuber ischia and cleaning the skin with alcohol. Subdermal platinum electrodes are then fixed in place.[27,28] These electrodes provide the best signal-to-noise ratio but are not practical for use in the field; noninvasive carbon fiber electrodes appear to provide a good option for field work. Adhesive electrodes are used for humans but do not work well in horses. A multifrequency bioimpedance analyzer measures the resistance and reactance between the electrodes at multiple frequencies at the two sites and uses proprietary algorithms to calculate extracellular fluid volume, intracellular fluid volume, and total body water. As currently used, the method does not appear to have sufficient sensitivity for routine clinical use because it was unable to detect a 20% change in blood volume caused by hemorrhage and underestimated the actual contraction and expansion of the extracellular fluid volume in adult horses administered furosemide and intravenous large-volume crystalloid solutions.[27] In addition, when applied to 48 kg BW neonatal foals with an estimated extracellular fluid volume of 17.4 L, the 95% confidence interval for the volume estimated by bioelectrical impedance was 20% of the actual value with the estimate ranging from 15.6 to 19.2 L.[28]

The sodium dilution principle has also been used to estimate changes in extracellular and intracellular volume in horses. The method requires measurement of serum sodium concentration, urine sodium concentration, and BW, and makes the assumption that sodium ions and water remain constant over time in physiologic fluids, except for measured "ins" and "outs" that reflect intravenous fluid administration and urine production. The method requires validation in clinically ill horses before recommending its use.[29]

The reference method for measuring total body water in horses before and after exercise uses orally administered deuterium oxide followed by a series of blood samples taken for analysis. Mean total body water content is about 62%. This method is not used clinically.

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Principles of Fluid and Electrolyte Therapy

The most important principle is to prevent or minimize dehydration and electrolyte loss whenever possible. This means the provision of an adequate water supply, adequate drinking space, and a continuous supply of salt and the necessary minerals. The next most important principle is to treat potential losses of fluid and electrolytes as quickly as possible to minimize the degree of dehydration and acid-base imbalance that may occur in animals with diseases in which losses are occurring.

The **major therapeutic objectives** are to **correct the abnormalities** that already exist and to monitor and **provide maintenance therapy** until the animal has recovered. Correction of the abnormalities may require 4 to 6 hours, and maintenance therapy may be necessary for 2 to 4 days, depending on the cause of the disease. Recent studies have identified concerns with bolus fluid resuscitation in septic patients, such as 20 to 40 mL/kg in the first hour.[1-3] These findings suggest that rapid resuscitation should focus on the use of low-volume hypertonic saline, and that traditional high-volume crystalloid solution resuscitation should not use bolus administration. Instead, traditional high-volume crystalloid fluid resuscitation should focus on slower rates of administration (<20 ml/kg/h).

There are at least five possible free water, electrolyte, acid-base, and oncotic pressure abnormalities that could exist at the same time and must be corrected:

- **Fluid volume deficit (free water)**
- **Plasma osmolar deficits**
- **Specific electrolyte imbalances**
- **Acid-base imbalance**
- **Oncotic pressure imbalances**

The two major problems are to determine the nature and degree of the abnormalities present and to decide which fluid and electrolyte replacement solution should be used.

The ideal situation would be to make both a clinical and laboratory evaluation of the animal as described earlier. The history and the diagnosis will suggest the possibility of acidemia or alkalemia and the electrolyte imbalances that are likely to be present. The degree of dehydration can usually be recognized clinically. Severe dehydration and acidemia should be treated as quickly as possible. A summary of the disturbances of fluid and electrolyte balance that occur in some common diseases of cattle and horses, and the suggested fluid therapy, is presented in Table 5-2.

Calculation of Electrolyte Requirements

The electrolyte deficits can be estimated using the serum electrolyte values of the affected animal. The total deficit of the electrolyte in mEq is the product of the deficit of the electrolyte in mEq per liter (ΔmEq/L) and the distribution space for the electrolyte. For sodium, chloride, and bicarbonate, the distribution space is the extracellular fluid volume, which approximates 30% of BW in normally hydrated adults and 50% in normally hydrated neonates. In other words, for sodium, chloride, and bicarbonate, the total milliequivalent deficit = (ΔmEq/L) × (estimated euhydrated BW in kg) × (0.3 or 0.5).

There is much less certainty about the size of the potassium space because potassium is predominantly an intracellular ion.

Types of Intravenous Fluid

Fluids are categorized on the basis of their physical nature (**crystalloid** or **colloid**)

Table 5-2 Summary of disturbances of body water, electrolytes, and acid-base balance in some common diseases of cattle and horses, and suggested fluid therapy

Disease	Major abnormalities and deficits	Flue and electrolyte requirements
Neonatal calf diarrhea (including piglets and lambs)	Metabolic acidosis, low plasma bicarbonate, severe dehydration, loss of sodium, hyperkalemia when acidosis severe	Equal mixtures of isotonic saline and isotonic sodium bicarbonate with 5% dextrose, balanced electrolytes, intravenous and orally
D-lactic acidosis (carbohydrate engorgement of ruminants)	Metabolic acidosis, low plasma bicarbonate, severe dehydration	Sodium bicarbonate initially followed by balanced electrolytes, intravenously
Acute diffuse peritonitis	Dehydration, slight metabolic alkalosis caused by paralytic ileus	Balanced electrolyte solutions in large quantities intravenously for hydration and maintenance
Right-side dilatation/abomasal volvulus of cattle, abomasal impaction (dietary or vagal nerve injury).	Metabolic alkalosis, marked hypochloremia, hypokalemia, severe dehydration	Balanced electrolyte solutions or high-potassium and chloride-acidifying solution, intravenously; may give acidifying solutions orally; can also use mixture of 2 L of isotonic saline (0.9%), 1 L isotonic potassium chloride (1.1%), and 1 L isotonic dextrose (5%)
Peracute coliform mastitis	Severe dehydration, mild electrolyte deficits including mild hypocalcemia, metabolic acidosis if diarrhea present	Balanced electrolyte solutions intravenously in large quantities for hydration and maintenance for 24–48 hours (100–150 mL/kg BW per 24 hours)
Acute diarrhea in the horse (enteric salmonellosis)	Severe dehydration, marked hyponatremia, metabolic acidosis, hypokalemia occurs following bicarbonate therapy.	Hypertonic sodium bicarbonate (5%) 3–5 L/500 kg BW followed by high-sodium, high-potassium alkalinizing solution to correct hypokalemia following bicarbonate therapy, all by the intravenous route
Acute grain engorgement in the horse	Metabolic acidosis, dehydration, and shock	Hypertonic sodium bicarbonate (5%) 3–5 L/500 kg BW followed by balanced electrolytes intravenously
Water and electrolyte deprivation, esophageal obstruction in horses	Moderate dehydration	Balanced electrolytes intravenously, when obstruction relieved, provide electrolyte solution orally
Acute intestinal obstruction	Metabolic acidosis or alkalosis dependent on level of obstruction, severe dehydration in horse, moderate in cow	Isotonic sodium bicarbonate initially, 3–5 L/500 kg BW followed by balanced electrolytes intravenously, horses may develop hypokalemia following bicarbonate therapy and must be given potassium chloride

and osmolarity (**hypotonic**, **isotonic**, or **hypertonic**). Isotonic or slightly hypotonic crystalloid solutions are most commonly administered parenterally, although under specific circumstances hypertonic crystalloid solutions or isotonic 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% NaCl, 7.2% NaCl (hypertonic saline), 1.3% $NaHCO_3$, 8% $NaHCO_3$, calcium gluconate, and 50% dextrose. Sodium chloride is the classic example of a crystalloid solution, as table salt (NaCl) 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; therefore they are not confined to the intravascular space. Sodium-containing crystalloid solutions are always indicated in hypovolemia (circuit problem) but are contraindicated in congestive heart failure (pump problem) because they provide an additional sodium load, and animals with heart failure have already retained too much sodium. Sodium-containing crystalloid solutions are also contraindicated in the presence of severe hypoalbuminemia because sodium-containing crystalloids will further decrease plasma albumin concentration and oncotic pressure, resulting in the 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 1 mol of compound is equivalent to the molecular weight of the compound in grams (formula weights for NaCl, $NaHCO_3$, and KCl are 58.5, 85, and 74 g, respectively). Because body fluids are dilute, moles are expressed as millimoles (mmol = mol/1000) to facilitate readability.

Crystalloid solutions are commonly expressed 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 1 Eq is the number of each charged component that combines with or replaces 1 mol of hydrogen ion (this means that Eq is always a positive number). Because body fluids are dilute, equivalents are expressed as milliequivalents (mEq = Eq/1000) to facilitate readability. To calculate the number of mEq from mmol, simply multiply the number of millimoles by the valence (charge) or mEq/L = (mmol/L) × 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 (i.e., it completely dissociates into Na^+ and Cl^- in water). In comparison, 1 mmol of $CaCl_2$ 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.

The principal reason constituents of plasma are defined 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, nonesterified fatty acids, etc.) in plasma is called the SID, and this factor independently and directly alters blood pH and therefore acid-base status. The normal SID of plasma is approximately 40 mEq/L, although there are species differences in the actual value. Electrolyte solutions with an effective SID greater than 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; Table 5-3).

Table 5-3 Summary of effective strong ion difference and osmolarity of parenterally administered crystalloid solutions

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

The effective strong ion difference (SID) is the difference between the strong cation and strong anion concentration after metabolizable anions (such as lactate or acetate) have been completely metabolized to produce bicarbonate. Electrolyte solutions with an effective SID of more than 27 mEq/L are alkalinizing because they create a strong ion alkalosis. Electrolyte solutions with an effective SID = 0 are acidifying because they create a strong ion acidosis.

Isotonic, Hypertonic, and Hypotonic 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 large animals is approximately 285 mOsm/kg, and plasma osmolality is aggressively defended 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 L of lactated Ringer's solution closely approximates 1 kg of lactated Ringer's solution and because osmolarity can be easily calculated 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 kilogram (1 L) of plasma from an adult large animal 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% $NaHCO_3$ are therefore considered isotonic solutions because they distribute in plasma water and have calculated osmolarities of 309, 308, and 310 mOsm/L, respectively.

The normal plasma osmolarity for solutions to be administered to large animals is approximately 306 mOsm/L; solutions can therefore be defined as isotonic (300–312 mOsm/L), hypertonic (>312 mOsm/L), or hypotonic (<300 mOsm/L). Using this categorization, it is readily apparent that some routinely used crystalloid solutions are hypotonic; in particular, lactated Ringer's solution (275 mOsm/L) is mildly hypotonic and 5% dextrose (250 mOsm/L) is moderately hypotonic, although, as glucose is metabolized, 5% dextrose becomes an increasingly hypotonic solution. Erythrocytes are resistant to increases in plasma osmolarity, whereas they are susceptible to mild decreases in osmolarity; this is the basis of the red blood cell fragility test in which red blood cell suspensions are placed in solutions of decreasing osmolarity. Because of hypotonic-induced hemolysis, parenterally administered fluids should ideally be isotonic or hypertonic.

Hypotonic Crystalloid Solutions

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

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

The lactate in lactated Ringer's is a racemic, approximately equimolar mixture of L- and D-lactate. In healthy animals L-lactate is rapidly metabolized; however, animals have negligible D-lactate dehydrogenase activity, leading to slow clearance of D-lactate, which is primarily through the urinary system. DL-lactate solutions, such as lactated Ringer's, therefore have approximately half the alkalinizing ability of L-lactate solutions. The effective SID of lactated Ringer's solution is therefore less than the calculated value of 28 mEq/L. Lactated Ringer's solution is the standard intravenous fluid for neonates and adult horses, because these animals tend to become acidemic when inappetent. However, lactated Ringer's solution is theoretically inferior to acetated Ringer's solution, because critically ill animals may have increased blood L-lactate concentrations and it is incongruous to add L-lactate in this situation.

There has been recent interest in increasing the L-lactate concentration of lactated Ringer's and decreasing the chloride concentration to increase the alkalinizing effect. The inclusion of L-lactate at 56 or 84 mEq/L to an isotonic sodium solution provided a similar alkalinizing effect in healthy calves to the inclusion of bicarbonate at 56 or 84 mEq/L.[4]

Acetated Ringer's solution is a balanced, polyionic, alkalinizing, and hypotonic (294 mOsm/L) crystalloid solution. Commercially available formulations of acetated Ringer's solution contain physiologic concentrations of Na^+, K^+, Mg^{2+}, Cl^-, acetate (CH_3COO^-), and gluconate ($CH_2(OH)\{CH(OH)\}_4COO^-$); the gluconate is problematic because calves (and presumably all large animals) slowly metabolize gluconate.[5] Acetated Ringer's solution alkalinizes because acetate is metabolized to the bicarbonate ion:

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

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. Two acetated Ringer's solution formulations are commercially available in North America, Plasma-Lyte A and Normosol-R. Both have the same formulation, except Plasma-Lyte has a pH of 7.4 when administered compared with Normosol-R, which has a pH of 6.6 when administered. The difference in solution pH is unlikely to be of clinical significance. The main advantage of acetated Ringer's solution is that the sodium concentration (140 mEq/L) is approximately the same as that of livestock animals, whereas the sodium concentration in lactated Ringer's (130 mEq/L) is appreciably lower.

Five percent dextrose is 250 mOsm/L as administered, but plasma osmolarity decreases below 250 mOsm/L 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 is to provide free water or as a vehicle for pharmacologic agents.

Isotonic Crystalloid Solutions

Ringer's solution is a balanced polyionic nonalkalinizing isotonic crystalloid solution that contains physiologic concentrations of Na^+, K^+, Ca^{2+}, and Cl^-. This solution is mildly acidifying because its effective SID = 0 mEq/L. Addition of a fluid with a SID of 0 mEq/L to plasma (normal SID ≈ 40 mEq/L) will decrease plasma SID and therefore directly and independently decrease plasma pH because a 1 mEq/L decrease in SID decreases plasma pH by approximately 0.016. Ringer's solution is the standard intravenous fluid for adult ruminants because these ruminants tend to get alkalemic when inappetent.

Isotonic saline (0.9% NaCl solution) is an isotonic crystalloid solution that has little merit in the routine treatment of sick ruminants, principally because ruminants usually develop hypocalcemia and hypokalemia when inappetent. Accordingly, the use of 0.9% NaCl should be confined to horses, the 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 = 0 mEq/L.

Isotonic sodium bicarbonate (1.3% $NaHCO_3$ solution) is an alkalinizing isotonic crystalloid solution that is used to treat severe acidemia (indicated whenever blood pH <7.20 as a result of metabolic acidosis). This solution is alkalinizing because it buffers hydrogen ion, $HCO_3^- + H^+ \leftrightarrow CO_2 + H_2O$, and increases SID (effective SID = 155 mEq/L). Sodium bicarbonate is superior to sodium L-lactate and sodium acetate for the treatment of metabolic acidosis because it provides an immediate source of bicarbonate. On theoretical grounds, sodium bicarbonate ($NaHCO_3$) should not be used to treat severe respiratory acidosis, because additional CO_2 generated may worsen the respiratory acidosis. However, studies in critically ill large animals have failed to identify a clinically important effect of sodium bicarbonate infusion on increasing arterial P_{CO_2}, inducing respiratory acidosis and further decreasing blood pH. Moreover, concern has been raised that rapid large-volume sodium bicarbonate administration can result in systemic alkalinization but not **paradoxical CSF acidosis**, which may produce adverse neurologic sequelae. An in-depth review of the studies on this topic indicates that paradoxical CSF acidosis has only been observed in anesthetized animals with controlled ventilation. In other words, when sodium bicarbonate is administered to animals that control their own ventilation, even under anesthesia, paradoxical CSF acidosis does not occur because the animal detects the increase in arterial P_{CO_2} and reflexively increases minute volume to combat the bicarbonate-induced respiratory acidosis.[6]

Tromethamine (THAM, Tris-hydroxymethyl aminomethane, 300 mmol/L) is an isotonic solution of an organic amine that is a safe and effective buffer. After administration, 70% of the neutral compound $(CH_2OH)_3C–NH_2$ in tromethamine is immediately protonated to the strong cation $(CH_2OH)_3C–NH_3^+$ in plasma, with the net equation:

$$(CH_2OH)_3C–NH_2 + H^+ \rightleftharpoons (CH_2OH)_3C–NH_3^+$$

The remaining 30% of the administered tromethamine remains unprotonated, and can therefore cross cell membranes and potentially buffer the intracellular compartment. Tromethamine provides an alternative alkalinizing agent to sodium bicarbonate; however, tromethamine does not currently appear to offer any important clinical advantages over sodium bicarbonate in spontaneously breathing animals.

Isotonic formulations are available for intravenous administration with or without electrolytes; administration of tromethamine without electrolytes leads to hyponatremia, and it would appear preferable to administer tromethamine in conjunction with electrolytes.

Carbicarb is an isotonic buffer (300 mOsm/L) made from equimolar disodium carbonate (Na_2CO_3) and sodium bicarbonate; carbonate avoids generation of CO_2 when buffering acidemic blood:

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

Carbicarb was suspected to decrease the incidence and magnitude of hypercapnia when rapid alkalinization was needed in animals with mixed metabolic and respiratory acidosis. Despite numerous studies comparing Carbicarb with sodium bicarbonate, the potential clinical advantages of Carbicarb have only been demonstrated 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 over conventional isotonic sodium bicarbonate administration. Accordingly, there does not appear to be a compelling reason to prefer Carbicarb to isotonic sodium bicarbonate when rapid alkalinization of conscious animals is required.

Darrow's solution is an isotonic polyionic solution formulated by Darrow in 1946 for use in human infants; the solution has been administered to calves. Compared with other isoosmotic polyionic solutions, 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 large animals.

McSherry's balanced electrolyte solution is an isotonic polyionic solution formulated by McSherry and Grinyer in 1954 for intravenous and intraperitoneal administration to dehydrated diarrheic calves. On theoretical grounds, this is an excellent parenteral fluid for resuscitating dehydrated diarrheic calves that deserves more frequent use. Unfortunately, commercial formulations are currently unavailable.

Hypertonic Crystalloid Solutions

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

Table 5-4 Estimated daily energy requirements of fasting cattle

Body weight (kg)	Metabolic body size (kg $W^{0.73}$)	Metabolizable energy requirements (kcal)	Glucose 50% (L/day)
45 (1-month-old calf)	16	1760	7
90	27	2970	1.2
180	45	4950	2.0
360	74	8140	3.3
454	87	9519	3.8
544	100	12100	4.8

The necessity for glucose in fluid therapy has been controversial. Hypoglycemia occurs commonly in septicemic neonates and calves with diarrhea, but is uncommon in most other common diseases in which there is an acute fluid and electrolyte disturbance. Dextrose will promote the movement of extracellular potassium into the cell, will provide metabolic water, and is a source of carbohydrate. If glucose is indicated, large quantities of parenteral glucose are necessary to meet the maintenance energy requirements, and every effort must be made to restore the animal's appetite and to provide the necessary requirements through dietary intake. The energy requirements for maintenance are calculated on the basis of metabolic body size, $kg^{0.73}$, which is a measure of the fasting metabolism in an animal not eating and not doing any muscular work. If 1 g of dextrose given intravenously will provide 5 kcal (2.1 kJ) of energy, the approximate amounts of dextrose solution needed to meet the energy needs for maintenance in cattle are shown in Table 5-4. Table 5-4 provides a rough estimate of the requirements and should be used as a general guideline only. Every effort should be made to supply the energy needs through oral intake of energy-containing foods.

NaCl 7.2% (hypertonic saline) is 2460 mOsm/L (approximately eight times normal osmolarity), and is used for the rapid resuscitation of animals with hypovolemia. Hypertonic saline should be administered at 4 to 5m L/kg BW intravenously over 4 to 5 min (1(mL/kg BW)/min). Faster rates of administration lead to hemodynamic collapse caused by vasodilation and decreased cardiac contractility, whereas slower rates of administration provide no advantages over isotonic crystalloid solutions. Like high-volume 0.9% NaCl, small-volume hypertonic saline consistently induces a mild strong ion acidosis as its effective SID = 0 mEq/L. Generally, the decrease in pH following hypertonic saline administration is less than 0.08 pH units and rapidly dissipates with time. The effect of hypertonic saline on acid-base balance is therefore clinically inconsequential.

The use of small volumes (4–5 mL/kg BW) of hypertonic saline solution, ranging in concentration from 7.0% to 7.5%, has been extensively evaluated for the treatment of various forms of hemorrhagic, septic, and endotoxic shock. Plasma volume is increased by the movement of free water from the intracellular space, increasing cardiac output, mean arterial blood pressure, systemic oxygen delivery, and glomerular filtration rate. Total peripheral vascular resistance and pulmonary vascular resistance decrease, and mean circulatory filling pressure increases. Urine output is restored and acid-base equilibrium returns toward normal in conjunction with improved tissue perfusion.

Hypertonic saline (7.2–7.5%), with or without Dextran 70, has been used successfully in the initial resuscitation of diarrheic calves that have moderate to severe dehydration.[7-9] When used in this manner, resuscitation is optimized if calves receive 3 L of an isotonic oral electrolyte solution by esophageal intubation immediately before hypertonic saline is administered intravenously into the jugular vein through an 18-gauge needle at 4 to 5 mL/kg over 4 to 5 minutes. Combined intravenous hypertonic saline and oral electrolyte solution provides the fastest rate of resuscitation of dehydrated calves, as characterized by cardiac output and mean central venous pressure. It is important to note that the rate of resuscitation with hypertonic saline is even faster than that provided by administration of an equivalent sodium load of lactated Ringer's solution at 80 mL/kg over the first hour. The rapid infusion of small volumes of hypertonic saline should therefore be considered the preferred treatment for the initial resuscitation of severely dehydrated diarrheic calves. Moreover, more of the administered sodium in hypertonic saline is retained by the calf, resulting in more sustained resuscitation, whereas urinary sodium and free water loss is increased in calves administered lactated Ringer's solution or 0.9% NaCl solution.[7,8,10] Although the first studies to

demonstrate efficacy of hypertonic saline in resuscitating dehydrated calves also administered dextran to assist in sustained plasma volume expansion,[7,8] subsequent studies have demonstrated that the addition of dextran is not required for a beneficial response.[9,10]

Hypertonic saline solution is widely used for the treatment of dairy cattle with endotoxic shock and endotoxemia associated with coliform mastitis. Affected cows are given 2 L of hypertonic saline (4–5 mL/kg BW) intravenously, followed by immediate access to drinking water and other supportive therapy. The small volume of hypertonic saline followed by the oral water load increases circulatory volume rapidly, induces slight metabolic acidosis, increases renal perfusion and glomerular filtration rate, and induces homeostatic changes in serum calcium and phosphorus. In experimental endotoxin-induced mastitis of cattle, small volumes of hypertonic saline given intravenously (7.5%, 5 mL/kg BW) resulted in expanded plasma volume and increased the cows' voluntary water intake by about 12 times compared with cows treated with isotonic saline. The rapid intravenous administration of hypertonic saline successfully, but transiently, resuscitates calves in experimental endotoxic shock.[11] Hypertonic saline (7.2% NaCl, 2400 mOsm/L), 4 mL/kg BW intravenously over 4 minutes can be safely administered to endotoxic calves. On a comparative basis, the rapid infusion of large-volume isotonic saline is superior to small-volume hypertonic saline for initial resuscitation of experimentally induced acutely endotoxemic calves.

Hypertonic saline (7.2% NaCl, 2 L intravenously over 10 minutes) has been administered to cattle with RDA, followed by 10 L of 0.9% NaCl intravenously, and the resuscitative effects compared with cattle receiving an equivalent sodium load of 0.9% NaCl (26 L). Hypertonic saline produced a faster rate of initial resuscitation, based on mean central venous pressure and changes in plasma volume.[12] Hypertonic saline (7.5% NaCl, 5 mL/kg intravenously over 15 minutes) has been administered to cattle with experimentally induced acute ruminal acidosis, and the resuscitative effects compared with isotonic saline solution (0.9% NaCl). The response to both fluids appeared equivalent, except for a slighter larger reduction in blood pH in cattle treated with hypertonic saline.[13] It should be noted that hypertonic saline should not be administered to ruminants with acute ruminal acidosis on theoretical grounds. This is because rumen osmolality is markedly increased in acute ruminal acidosis, which minimizes the osmotic gradient that is generated following rapid intravenous small-volume hypertonic saline administration and the volume of free water translocated from the forestomach.

Hypertonic saline solutions have been extensively studied in horses and are widely used for the initial resuscitation of critically ill horses that are undergoing abdominal surgery for colic. Hypertonic saline has been associated with greater and more prolonged improvement in cardiopulmonary function and survival in horses with experimentally induced hemorrhagic and endotoxemic shock and in halothane-induced hypotension in horses. When given intravenously to normal conscious horses at 5 mL/kg BW, there are increases in plasma osmolality and serum sodium and chloride, but clinically normal horses rapidly regulate variable sodium loads. In horses with experimentally induced acute endotoxemia, horses resuscitated with intravenous hypertonic saline (5 mL/kg) and hydroxyethyl starch (10 mL/kg) had a higher cardiac output, lower mean pulmonary artery pressure and mean central venous pressure, higher ionized plasma calcium concentration, and improved respiratory gas exchange and arterial oxygenation than horses resuscitated with high-volume isotonic acetated Ringer's solution.[14,15] These results were consistent with increased interstitial water in the lung and volume overload as a result of conventional rapid high-volume isotonic solution administration.[14] Similar findings were reported earlier in the resuscitation of endotoxemic calves.[11] Hypertonic saline (7.2%) at 4 mL/kg provided a superior resuscitative solution than equivolume isotonic saline (0.9%) in horses eliminated from an endurance event because of dehydration. Dehydrated horses administered hypertonic saline had a greater plasma volume expansion and shorter time to first urination than horses receiving isotonic saline.[16]

Hypertonic solutions of sodium bicarbonate are highly effective for the initial treatment of acidosis associated with D-lactic acidosis in calves, acute diarrhea in calves, and strong ion (metabolic) acidosis in newborn calves. **Sodium bicarbonate 8.4%** is 2000 mOsm/L (approximately seven times normal osmolarity). This solution 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^-/mL of solution, which facilitates calculation of the volume to be administered. The speed of intravenous administration of 8.4% sodium bicarbonate should not exceed 1 (mL/kg BW)/min. There is one report of the intravenous administration of 8.4% sodium bicarbonate to normovolemic calves with experimentally induced mixed respiratory and metabolic acidosis; the study found that rapid administration of sodium bicarbonate (5 mL/kg intravenously over 5 min) rapidly corrected the metabolic acidosis, increased blood pH, and improved cardiovascular status without inducing paradoxical CSF acidosis, suggesting that this treatment may be of value in treating dehydrated diarrheic calves.[17] A study in dehydrated calves with naturally acquired diarrhea has been conducted comparing intravenous hypertonic sodium bicarbonate (8.4%, 10 mL/kg over 8 minutes) and hypertonic saline (5.9%, 5 mL/kg over 4 minutes); calves receiving either treatment also received 3 L of an oral electrolyte solution 5 minutes after injection. As expected, the hypertonic sodium bicarbonate solution was more effective in correcting profound acidemia and metabolic acidosis than hypertonic saline.[18] The results of a study that compared the intravenous administration of equivalent sodium loads of 8.4% to 1.3% $NaHCO_3$ to neonatal calves with naturally acquired diarrhea and severe dehydration indicated that isotonic sodium bicarbonate was more effective in rehydrating the calf, whereas the rapid administration of hypertonic sodium bicarbonate was more effective in rapidly correcting the acidemia and strong ion (metabolic) acidosis.[19]

There are recent studies evaluating the effect of hypertonic solutions of **sodium lactate** (11.2% at 5 mL/kg/h administered over 270 minutes); lactate provides an energy substrate that can be used by most cells in the body, while being alkalinizing after metabolism to bicarbonate. In a pig endotoxemia model, infusion of hypertonic sodium lactate increased mean arterial blood pressure and cardiac output and improved oxygenation, relative to hypertonic sodium bicarbonate or 0.9% NaCl solution.[20]

Sodium bicarbonate 5% is 1190 mOsm/L (approximately four times normal osmolarity). This solution is also used for rapid alkalinization in the presence of severe acidemia (pH <7.20). The speed of intravenous administration of 5.0% sodium bicarbonate should not exceed 2 (mL/kg)/min. Three to five liters of 5% sodium bicarbonate may be necessary as initial therapy to correct the severe hyponatremia and strong ion (metabolic) acidosis that occurs in the horse with acute diarrhea. Following this initial treatment, hypokalemia characterized by muscular weakness commonly occurs, which can be treated using a high-sodium, high-potassium, alkalinizing solution.

Calcium gluconate 23% or calcium borogluconate are 1069 mOsm/L (approximately three and a half 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 sodium bicarbonate solutions because a white precipitate ($CaCO_3$) forms immediately that 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 Hb, 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 are also contraindicated in the presence of oliguric or anuric renal failure because the sustained volume overload may lead to pulmonary edema. Although initial studies using colloid solutions appeared promising, influential studies promoting the use of commercially available solutions have been recently retracted from major journals,[21] and the majority of smaller reviews evaluating the safety and efficacy of colloid solutions were written by investigators that had or have since established ties to the manufacturers of colloid solutions.[22] Moreover, questions are being raised about the relative importance of the difference between plasma oncotic and interstitial oncotic pressures and transcapillary fluid dynamics in patients with normal or decreased capillary pressures. The net result of these recent developments is decreased enthusiasm for the administration of commercially formulated colloid solutions.

Whole blood is the perfect balanced colloid/crystalloid solution, with great O_2-carrying capacity. It has a short shelf-life (<24 hours at 4°C) and is expensive to obtain. Whole blood administration runs the risk of disease transmission and allergic reactions; the latter are extremely rare in ruminants with the first blood transfusion but common enough in horses for blood typing or crossmatching to be required. Descriptions for collecting, storing, and administering blood are available in Chapter 4.

Stroma-free Hb is a blood substitute containing a purified Hb glutamer-200 solution (13 g Hb/dL) derived from cattle blood. A commercially available solution 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 isotonic but hyperoncotic. Stroma-free Hb solutions are excellent at increasing oxygen delivery and carrying capacity while providing similar plasma volume expansion to dextrans and hydroxyethyl starches. The major theoretical concerns regarding administration of stroma-free Hb solutions are potent vasoconstriction and hemoglobinuric nephrosis. Some of the original experimental studies examining the effects of stroma-free Hb administration were completed in sheep, and there are occasional reports of its successful administration to critically ill horses in a clinical situation. It is likely that the high cost of this product will minimize its administration to large animals.

Plasma (fresh or frozen) 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 collection, harvesting, storing, and administering plasma are available elsewhere, and bovine, equine, and New World camelid plasmas are commercially available. Like blood, administration of plasma runs the risk of disease transmission and allergic reactions, although these risks are less than with blood transfusion.

Plasma is routinely administered to foals with inadequate transfer of passive immunity. Hyperimmune plasma is occasionally administered to neonatal foals and adult horses with gram-negative septicemia and endotoxemia. There appears 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 per dL) and electrolytes intravenously was 93% (37/40), which was significantly greater than the survival rate of calves receiving intravenous electrolytes alone (54%, 7/13). Another study failed to identify a beneficial effect of blood transfusion in treating diarrheic calves. Because blood is cheaper to obtain than plasma, whole blood transfusions are usually administered when a neonatal ruminant needs plasma. Human albumin solutions (5% or 25% human albumin in 0.9% NaCl) are available, but are very expensive relative to the use of other colloids such as plasma, blood, or Dextran 70. Consequently, there does not appear to be a persuasive reason for the administration of human albumin solutions to large animals.

Dextran preparations (such as Dextran 70 and Dextran 40) are high molecular weight glucose polymers obtained by bacterial fermentation of sucrose; the fermentation metabolites then undergo acid hydrolysis and fractionation. The molecular weight of dextran can therefore 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. Therefore Dextran 70 acts clinically as a plasma volume expander; this is in contrast to isotonic crystalloid solutions, which act as extracellular fluid volume expanders. Dextran 70 has been the most widely used dextran formulation in large animals, and is therefore the recommended product for administration. It is supplied as a 6% concentration in 0.9% NaCl, which provides a hyperoncotic but isotonic 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 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 maximum 24-hour dose in humans), and the molecular weight of dextran. The deleterious effects of dextrans are usually associated with large doses or prolonged administration.

The use of **hypertonic saline–dextran solution** (4 mL/kg, 2400 mOsm/L sodium chloride in 6% Dextran 70 administered intravenously once over 4 minutes) combined with an isotonic oral alkalinizing solution containing sodium chloride (3.22 g/L), potassium chloride (1.12 g/L), sodium acetate trihydrate (4.76 g/L), and glucose anhydrous (16.22 g/L), providing 300 mOsm/kg of water and administered at 55 mL/kg BW, was superior to either solution alone for the treatment of experimentally induced hypovolemic diarrhea in calves. The combined treatment resulted in immediate and sustained increases in plasma volume, cardiac output, and stroke volume, improving tissue perfusion. Rapid and sustained rehydration after the combined treatment was indicated by improvement in hydration and clinical depression scores and decreases in hematocrit; blood lactate concentration; and serum creatinine, albumin, and phosphate concentrations. Resuscitation with oral electrolyte solution alone was slower but was complete within 24 hours. Resuscitation with the hypertonic saline–dextran solution alone resulted in only transient benefit.

The administration of hypertonic saline–dextran solution (7.2% NaCl solution with 6% dextran at the rate of 4 mL/kg BW, intravenously during a 4-minute period, combined with oral administration of isotonic electrolyte solution at the rate of 50–60 mL/kg BW) provided a rapid and effective method for resuscitating severely dehydrated calves with experimentally induced diarrhea or with naturally acquired diarrhea.

Hydroxyethyl starch is a high molecular weight glucose polymer (mean molecular weight 450,000 g) that is chemically synthesized from amylopectin, producing a highly branched glucose polymer with a structure similar to that of glycogen. Hydroxyethyl starch is hydrolyzed in blood by α-amylase, and the addition of hydroxyethyl groups slows hydrolysis and prolongs the duration of plasma volume expansion. Hydroxyethyl starch solutions are categorized by the mean molecular weight and a molar substitution ratio (usually stated after a back slash) that

reflects the number of hydroxyethyl substitutions per glucose unit, with a higher number indicating more substitutions and a slower rate of degradation.[23] A variety of hydroxyethyl starch formulations have been developed world wide; Hetastarch (hydroxyethyl starch at 600,000 g/0.75 in 0.9% NaCl solution or 670,000 g/0.75 in lactated Ringer's solution), Pentastarch (200,000 g/0.4 in 0.9% NaCl solution), and Tetrastarch (130,000 g/0.4 or 130,000 g/0.42 in 0.9% NaCl solution). Pentastarch (200,000 g/0.4 in 0.9% NaCl solution), and Tetrastarch (130,000 g/0.4 in 0.9% NaCl solution). Because the molecular weight of hydroxyethyl starch is much greater than that of albumin (65,000 g), hydroxyethyl starch in Hetastarch preparations decreases endothelial permeability by sealing separations of endothelial cells. Hydroxyethyl starch is supplied as a 6% concentration in 0.9% NaCl; this provides a hyperoncotic but approximately isotonic solution. Reported administration rates are 5 to 40(mL/kg BW)/h but, like Dextran 70, it is safer to administer hydroxyethyl starch at less than 20(mL/kg BW)/h. Like Dextran 70, hydroxyethyl starch administration runs the risk of exacerbating preexisting coagulopathies. The risk of coagulopathy is dependent on the administration rate, total dose administered (20 mL/kg BW is the maximum 24-hour dose in humans), and size of the hydroxyethyl starch particles. Administration of 6% hydroxyethyl starch to anesthetized horses at 5 to 15 mL/kg over 90 minutes increased mean central venous pressure and cardiac output but did not correct inhalation anesthetic-induced systemic hypotension.[24] The rapid administration of 6% hydroxyethyl starch to horses with naturally occurring gastrointestinal disease at 10 mL/kg increased colloid osmotic pressure by approximately 20%, but did not return values to within the reference range.[25] High molecular weight hydroxyethyl starch formulations have been recently linked to nephrotoxicity, acute renal failure, and mortality in humans, particularly in septic patients or patients with preexisting renal disease, and the U.S. Food and Drug Administration recommended in 2013 that they not be used in critically ill adults and patients with preexisting renal dysfunction or severe liver disease. Low molecular weight hydroxyethyl starch formulations do not seem to demonstrate similar adverse effects, but are cleared at a faster rate because of their small size, resulting in a shorter duration of action. The relevance of these findings to the use of hydroxyethyl starch formulations in large animals is uncertain, because clinically relevant coagulation abnormalities caused by hydroxyethyl starch were not identified when administered to horses with experimentally induced acute endotoxemia at 10 mL/kg.[15] Hydroxyethyl starch solutions do exert dose-dependent in vitro effects on coagulation in horse blood, as assessed by platelet aggregation and function.[23] The clinical relevance of these in vitro findings has not been determined.

Pentastarch has two important differences to Hetastarch (hydroxyethyl starch) formulations: it appears to have a less exacerbating effect on preexisting coagulopathies and the rate of elimination is faster (elimination half-life of 5.6 hours in healthy horses and possibly 2 hours in critically ill horses); however, similar to hydroxyethyl starch, pentastarch has been associated with an increased incidence of acute kidney injury in humans.[26] Pentastarch has been administered preoperatively to horses with colic at 4 mL/kg, and this infusion produced a higher cardiac output in anesthetized horses for 150 minutes compared with the same volume of hypertonic saline (7.2% NaCl).[27] It should be noted that Pentastarch is considerably more expensive than 7.2% hypertonic saline when compared on a volume basis.

Tetrastarch has been the most recently introduced colloid and, consequently, there are fewer studies examining its efficacy and safety. In vitro studies suggest Tetrastarch produces less impairment of coagulation caused by its lower molecular weight and lower molar substitution formulation. Studies in healthy adult horses indicated Tetrastarch caused plasma volume expansion but a shorter duration of adverse effects on platelet function than a similar dose of Hetastarch.[28] The clinical significance of this difference remains to be determined.

Gelatins (modified bovine collagens) are available for veterinary use. The 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 appear to have less effect on coagulation. Generally, gelatins have not been evaluated as completely as dextrans and hydroxyethyl starches and, on this basis, are not currently preferred.

Practical Administration of Electrolyte Solutions

Under ideal conditions, with laboratory evaluation of the animal, the deficits can be accurately assessed and fluids containing the deficient electrolytes can be formulated. However, under most practice conditions this is not possible and **polyionic crystalloid solutions** are in general use. These usually contain sodium, potassium, chloride, and calcium or magnesium at a concentration similar to the electrolyte composition of extracellular fluid; the solutions may also contain lactate or acetate as bicarbonate precursors. Dextrose may be added to the solution to make an initial mildly hypertonic solution.

Polyionic crystalloid solutions are safe and can be used in large quantities without inducing electrolyte disturbances provided that circulating blood volume and renal function have been restored and are maintained. They can be used for most situations of dehydration and moderate acidemia or alkalemia and moderate electrolyte imbalances. They are not usually adequate for the treatment of severe acidemia or alkalemia, or severe hyponatremia, hypokalemia, or hypochloremia.

For the treatment of severe acidemia or alkalemia, and severe hyponatremia, hypokalemia, and hypochloremia, specific electrolyte solutions are necessary. Generally, they consist of a mixture of the common simple solutions with supplemented electrolytes to correct some major abnormality. These are considered necessary to correct abnormalities quickly that could not be corrected using balanced electrolyte solutions. These solutions are summarized in Tables 5-3 and 5-5. Many intravenous solutions for fluid therapy in calf diarrhea are available, and it is recommended that they should contain 150 mmol/L of sodium, 5 mmol/L of potassium, and about 50 mmol/L of a mixture of bicarbonate and precursors.

When acidemia is not present it is not necessary to use a fluid containing bicarbonate.

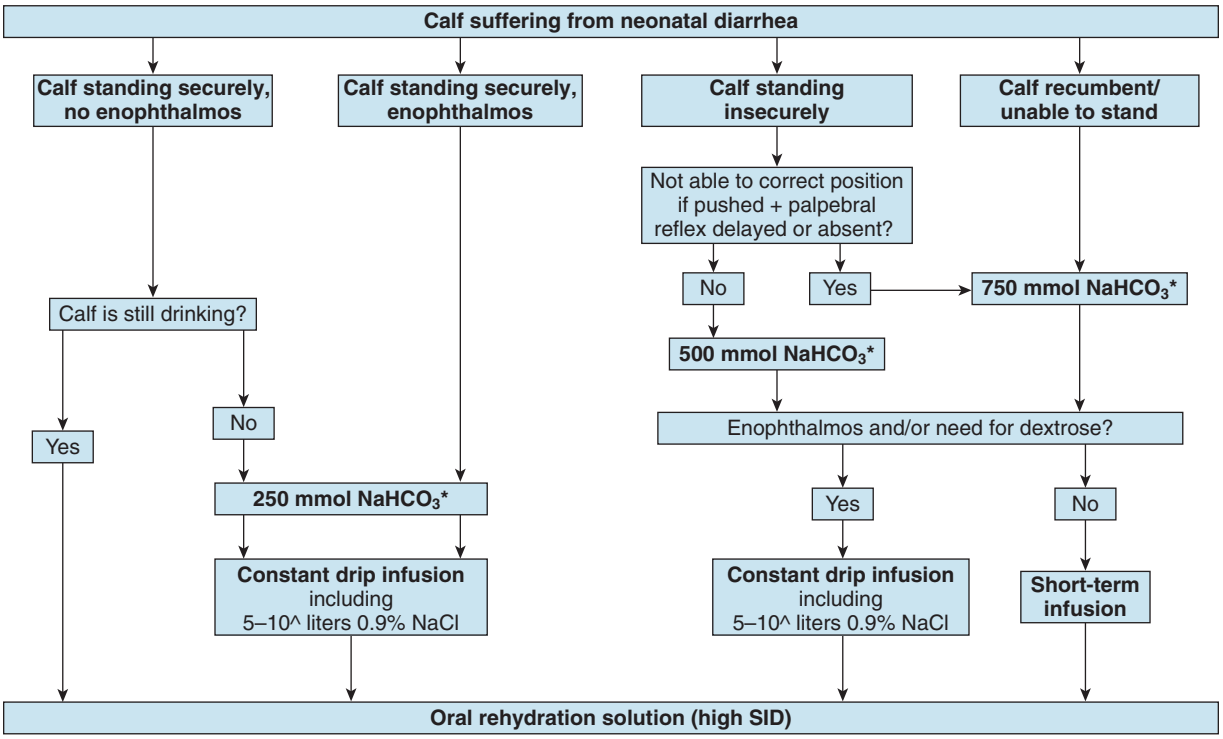
Mature cattle affected with metabolic alkalosis associated with diseases of the abomasum are usually hypokalemic, hypochloremic, and dehydrated. For such cases, a balanced electrolyte solution containing sodium, chloride, and potassium is satisfactory. A solution containing sodium (135–155 mEq/L), chloride (150–170 mEq/L), and potassium (10–20 mEq/L) is effective. In recently calved dairy cattle, calcium borogluconate is commonly added to the mixture.

Solutions containing potassium have been recommended for the treatment of the potassium depletion that occurs in calves with acute diarrhea and in inappetent ruminants and horses. However, in calves with severe acidemia and hyperkalemia, it is important to expand circulating blood volume, restore renal function, and correct the strong ion (metabolic) acidosis before providing additional potassium, which may be toxic. Solutions containing potassium may be indicated following correction of the acidosis and dehydration. However, if the animal's appetite is returned to normal, the oral potassium intake will usually correct any existing deficiencies.

In neonatal calves with dehydration caused by diarrhea, optimized decision trees for treatment have been developed based on clinical signs of hydration status and the presence of varying degrees of acidemia caused by metabolic acidosis (suckling strength, degree of enophthalmos, ability to stand, and presence or absence of palpebral reflex).[3,29] The decision tree is followed to determine the need for oral fluids or intravenous administration of isotonic solutions of sodium bicarbonate containing 250 mmol, 500 mmol, or 750 mmol of sodium bicarbonate, with supplemental glucose added when indicated[30] (Fig. 5-17).

Table 5-5 Composition (mmol/L) and indications for use of electrolyte solutions used in fluid therapy

Solution	Na^+	K^+	Cl^-	Mg^{2+}	Ca^{2+}	HCO_3^-	Lactate or acetate	Dextrose	Gluconate	Major indications
0.9% sodium chloride (isotonic saline)	155		155							Expansion of circulation blood volume
1.3% sodium bicarbonate (isotonic)	155					156				Metabolic acidosis
1.3% sodium bicarbonate in 5% dextrose	155					156		5%		Metabolic acidosis
5% sodium bicarbonate (hypertonic)	600					600				Severe metabolic acidosis
Equal mixture of isotonic saline and isotonic sodium bicarbonate	155		78			78				Metabolic acidosis and dehydration
Balanced electrolyte solution (i.e., McSherry's solution)	138	12	100	5	3		50 (acetate)			Metabolic acidosis electrolyte losses and dehydration
Lactated Ringer's solution	130	4	111		3		28 (lactate)			Metabolic acidosis
Normosol-R	140	5	98				27	23		Metabolic acidosis
Plasma-Lyte A	140	5	98				27	23		Metabolic acidosis
High sodium, alkalinizing solution, lactated Ringer's solution plus sodium bicarbonate (5 g/L)	190	4	111			60	27 (lactate)			Metabolic acidosis and hyponatremia
High-sodium, high-potassium, alkalinizing sodium, lactated Ringer's solution plus 1 g/L potassium chloride and 5 g/L sodium bicarbonate	190	18	125			60	27 (lactate)			Metabolic, acidosis, hyponatremia, hypokalemia
High-potassium acidifying solution, isotonic saline plus 2.5 g potassium, chloride per liter, mixture of 1 L isotonic potassium chloride (1.1%), 2 L isotonic saline (0.9%), and 1 L dextrose 9%	154	35	189							Metabolic alkalosis, hypochloremia, hypokalemia Metabolic alkalosis in cattle with abomasal disease



* Represents the intended amount of sodium bicarbonate
^ An infusion volume of 10 liters is recommended for calves with estimated enophthalmos ≥ 7 mm.

Fig. 5-17 Optimized decision tree for treating neonatal calves with diarrhea in a field setting. Examination of the ability to stand is evaluated by lifting recumbent animals. Enophthalmos reflects a visible gap of 3 to 4 mm between the corneal surface of the eye and the caruncula lacrimalis or normal position of the lower eyelid. (From Trefz FM et al. *BMC Vet Res* 2012;8:238.23).

For the treatment of hypochloremic hypokalemic metabolic alkalosis, acidifying solutions can be used but preferably only if constant laboratory evaluation of the animal is possible. Without laboratory evaluation, the use of Ringer's solution, 0.9% NaCl, or hypertonic saline for correction of strong ion (metabolic) alkalosis in adult cattle is recommended, along with the oral administration of potassium in animals that are inappetent. In experimentally induced hypochloremic hypokalemic metabolic alkalosis in 40 to 50 kg BW sheep, replacement of the chloride deficit using 2 L of hypertonic saline (1.8% sodium chloride) was effective in returning plasma sodium and chloride concentrations to normal within 12 hours, and the plasma potassium concentrations and acid-base balance returned to normal within 36 hours of treatment without providing potassium. Small volumes of hypertonic saline are also effective for the treatment of experimentally induced hypochloremic hypokalemic metabolic alkalosis in sheep.

In summary, five different kinds of solutions are used in large-animal practice:

- **Polyionic crystalloid solutions**, such as lactated Ringer's solution and acetated Ringer's solution, are indicated for dehydration and moderate degrees of acid-base and electrolyte imbalance.
- **Hypertonic saline solution and an oral water load** represent a practical and inexpensive alternative to parenteral administration of large fluid volumes.
- **Hypertonic or isotonic sodium bicarbonates**, such as 8.4, 5.0 (hypertonic), or 1.3% (isotonic) solutions of sodium bicarbonate, are used for severe strong ion (metabolic) acidosis and hyponatremia, particularly in dehydrated depressed calves with diarrhea.
- **Chloride-containing acidifying solutions,** such as Ringer's solution, are used for treatment of strong ion (metabolic) alkalosis.
- **Colloid solutions,** such as plasma or blood, are administered more frequently than Dextran 70 or hydroxyethyl starch solutions.

Because cost is a major consideration in large-animal fluid therapy, it may not be possible to use sterile solutions. Most of the previously mentioned solutions can be formulated using the necessary salts mixed with distilled water, boiled water, or ordinary tap water and are therefore prepared inexpensively.

Quantity of Fluids Required and Routes of Administration

The amount of fluid required depends on the degree of dehydration (an estimate of the volume losses that have already occurred); the continuous losses that occur during treatment; and the maintenance requirements of the animal during treatment presuming its dietary intake of water, electrolytes, and nutrients is minimal. The fluids are usually given in two stages:

- **Hydration therapy** in the first 4 to 6 hours at a rate of 100 to 150 mL/kg BW intravenously.
- **Maintenance therapy** (a combination of **continuous losses** and **maintenance requirements**) in the next 20 to 24 hours, depending on the severity and the course of the disease, at 60 to 80 mL/kg BW per 24 hours intravenously (approximately 3–4 mL/kg BW per hour). In some cases of profuse diarrhea, the continuous losses and maintenance requirements will be about 150 mL/kg BW over a 24-hour period. The daily maintenance water requirements of adult horses range from 54 to 83 mL/kg BW, with a mean of 64 mL/kg BW.

Some examples of the large quantities of fluid required for hydration and maintenance therapy in cases of acute diarrhea are outlined in Table 5-6.

Parenteral Fluid Therapy

The total amount of the estimated necessary hydration therapy should be given intravenously using indwelling intravenous catheters in the first 4 to 6 hours to expand and maintain circulating blood volume. If acidemia or alkalemia is present, it also should be treated immediately. Thus the most important abnormalities—decreased circulating blood volume and acid-base imbalance—are treated first. Restoring circulating blood volume will restore renal function, which will assist in correcting acid-base and electrolyte balance. The immediate correction of acidemia will return the tissues to their normal physiologic activity. The intravenous route is preferred for hydration therapy and for the correction of severe acid-base and electrolyte imbalances. All other routes (intraperitoneal, subcutaneous, and oral) are unsatisfactory in the presence of decreased circulating blood volume.

During the intravenous administration, the animal must be monitored for clinical and laboratory evidence of improvement or deleterious effects. A **favorable response** is indicated by urination within 30 to 60 minutes, an improvement in mental attitude, and some evidence of hydration. **Unfavorable responses** include **dyspnea** because of preexisting pneumonia or pulmonary edema because of too rapid administration, **failure to urinate** because of renal failure or paralysis of the bladder, and **tetany** because of the excessive administration of alkali. Unusual responses such as sweating, trembling, and depression within several hours following the intravenous administration of electrolytes or other substances such as commercial amino acids may occur if the infusion is contaminated during administration. If a laboratory is available, the determination of PCV, bicarbonate, and blood pH will provide an excellent monitoring system during the administration of the fluids.

Rate of Administration

The rate of administration will depend on the size of the animal, the severity of the illness, the type of fluids administered, and the response of the animal to the fluids. In calves, isotonic saline (0.9% NaCl) and sodium bicarbonate solutions can be given at the rate of 1 to 3 L/h; in a mature horse, fluids may be given at the rate of 10 to 12 L/h. Hypertonic solutions such as 5% sodium bicarbonate can be given to a mature horse at the rate of 3 to 5 L/h, followed by balanced electrolytes at 10 to 12 L/h. Solutions containing added potassium should be given cautiously, at the rate of 3 to 5 L/h. In a cow with severe dehydration and acidosis caused by carbohydrate engorgement, fluids may be given at the rate of 10 to 12 L/h.

Adverse reactions to intravenous fluid administration include **sudden muscle weakness** (suggests hypokalemia) and sudden **tachycardia** and **hyperventilation**, which suggest **overhydration**. When these occur the fluids should be stopped and the clinical findings assessed. If laboratory assistance is available, the determination of blood pH and bicarbonate may provide an explanation for the reaction.

Special care is needed when administering intravenous fluids to **hypothermic** animals because intravenous fluid therapy has the potential to further decrease core

Table 5-6 Examples of approximate amounts of fluid required for rehydration and maintenance therapy

Animal	Degree of dehydration (% BW)	FLUID REQUIRED FOR	
		Rehydration (L)	Maintenance (L/24 hours)
Mature horse (500 kg)	8	40	25–50
	12	60	25–50
Newborn calf (50 kg)	8	4	2.5–5
	12	6	2.5–5
Mature cow (700 kg)	8	56	35–70
	12	84	35–70

body temperature. Cooling is inevitable during intravenous fluid therapy whenever animals are housed at temperatures below their core body temperature. It is important to note that fluids initially warmed to 37°C are cooled after going through the fluid administration set. Placing commercially available heaters around the fluid administration line as close as possible to the catheter insertion site is effective in warming intravenous fluids to >36°C at flow rates between 60 and 300 mL/h.[31] When treating hypothermic neonates, many veterinarians place the distal part of the fluid administration set in a bucket of hot water to ensure that the fluid is as warm as possible when administered. The efficacy of this heating approach has not been evaluated, and because of the distance between the bucket and catheter insertion site, it is likely that this approach will not be as effective as use of commercially available heaters around the fluid line.

Intravenous Catheters and Complications

The administration of large quantities of fluids intravenously to farm animals is best done with an indwelling **jugular vein** flexible catheter (10–14 gauge) that is appropriately secured to the animal's neck to prevent withdrawal from the vein (Fig. 5-18). Standard aseptic technique must be used. A plastic, springlike coiled tube and suitable rubber tubing are used to deliver the fluids from large 20- to 25-L plastic containers (Fig. 5-19). The coiled plastic tubing allows the animal to lie down or stand up without disrupting the catheter and tubing. The use of a drip chamber in the rubber tubing system assists in determining the flow rate, which can be adjusted with a clamp. With a 14-gauge catheter, 20 L of fluids can be delivered as hydration therapy to a mature horse or cow over 4 hours.

Auricular Vein of Cattle and Calves

Intravenous fluids are commonly administered to adult cattle and calves in northern Europe using the auricular vein. The short neck, thick skin, and, in some breeds, pendulous dewlap of cattle make it difficult to introduce and secure indwelling jugular catheters for long-term use. The auricular vein of adult cattle can be successfully catheterized with an over-the-needle, 5-cm long, 14-gauge catheter, permitting 20 L of rehydration solution to be delivered over 4 hours. The auricular vein of neonatal calves can be successfully catheterized with an over-the-needle, 2.5-cm long, 22-gauge butterfly catheter, after clipping the external pinna and applying a tourniquet at the base of the ear to facilitate visualization of blood vessels and catheter advancement (Fig. 5-20).

Cecal Catheters in Horses

Percutaneous cecal catheters have been used to deliver fluid solutions in ponies. The advantages include less cost, but complications include peritonitis, diarrhea, laminitis, and hypocalcemia.

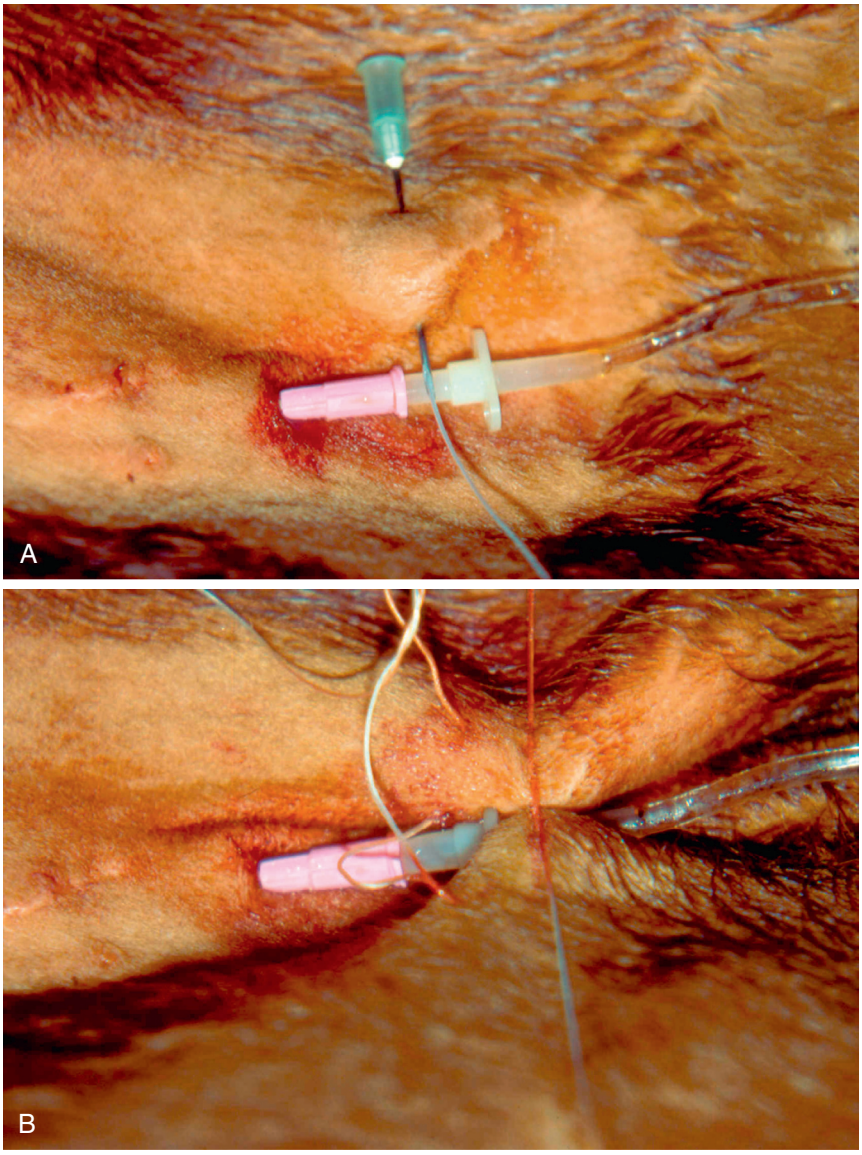


Fig. 5-18 Securing a 14-gauge 14-cm catheter into the jugular vein of a cow. The site of venipuncture is clipped and scrubbed for aseptic placement of a catheter. A 1-mL bleb of 2% lidocaine is placed intradermally at the proposed site of catheter insertion and a 5-mm long stab incision made through the skin, including the dermis. **A,** The catheter is then placed into the lumen of the vein and carefully advanced until the hub of the catheter is level with the skin. The catheter is secured by placing sutures through the skin using an 18-gauge needle and a synthetic multifilament suture material. The suture does a loop around the extension tubing near where it attaches to the hub of the catheter so that the catheter cannot back out. **B,** The 18-gauge needle is then passed through the ventral skin fold adjacent to the catheter, and the suture tightened to create a tunnel.

Thrombophlebitis

Long-term jugular vein catheterization (over a period of a few days) in adult cattle and particularly horses can result in thrombophlebitis, suppurative phlebitis, and catheter sepsis. Inspection of the affected jugular vein reveals swelling, firmness, and moderate pain. Careful digital and visual inspection is necessary to determine the patency of the vein; in about 50% of cases the vein is completely thrombosed and occluded and cannot be used for intravenous administration for 2 to 3 weeks. The extent and severity of the thrombophlebitis can be determined by ultrasonography of the neck, and patency of the vein can be assessed by compressing the vein with the transducer head.

The development of thrombophlebitis is dependent on the method used for skin preparation and the catheterization

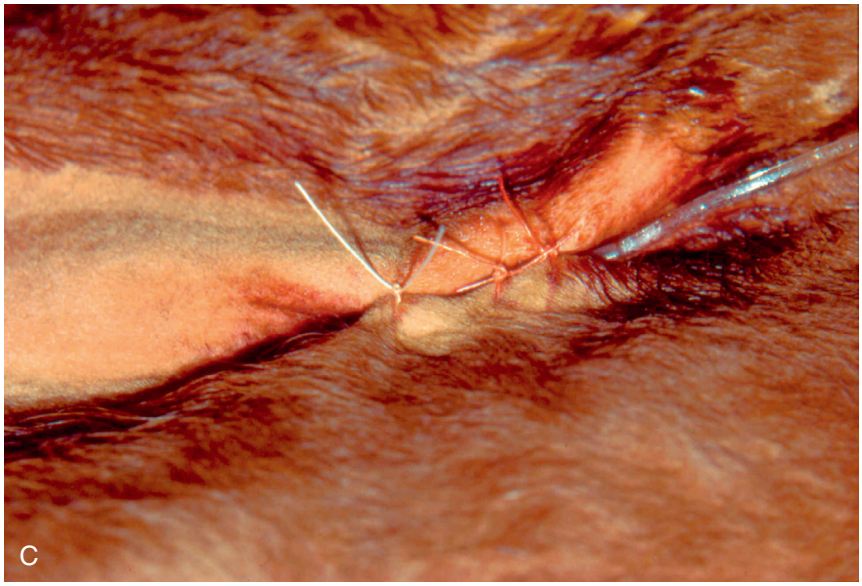


Fig. 5-18, cont'd **C,** Additional sutures are placed through the upper and lower skin folds to lengthen the tunnel and prevent excessive movement at the junction of the catheter with the hub.

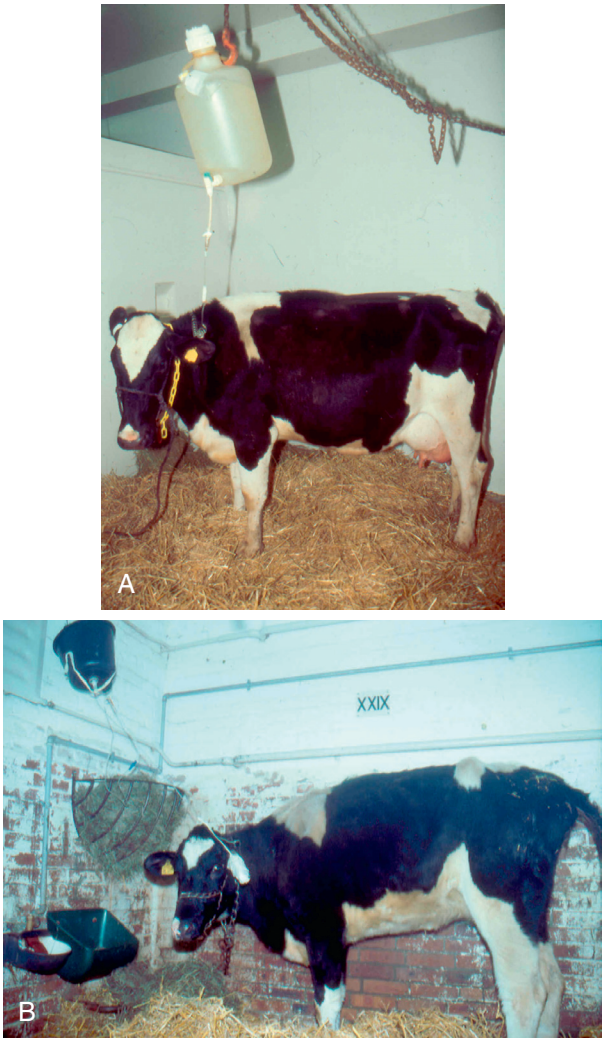


Fig. 5-19 Administering large-volume isotonic crystalloid solutions to Holstein–Friesian cows by the jugular vein **(A)** and auricular vein **(B)**.

technique. Careful preparation of the skin and aseptic technique during insertion and placement of the catheter are crucial in preventing this complication. Heparin subcutaneously, 150 IU/kg BW immediately after insertion of the catheter and repeated every 12 hours, has been used prophylactically, but this is not deemed necessary with good technique. Alternating catheters between jugular veins every 48 to 72 hours is standard practice in equine fluid therapy, but despite this precaution complications occur in 20% to 50% of horses whose jugular veins are catheterized for 48 hours. By using catheters made of materials that are less thrombogenic, inserting them in an aseptic manner, and observing simple management practices, the duration of catheter survival increases to about 14 days. The least reactive catheter is Silastic followed by polyurethane; polytetrafluoroethylene causes the most reaction. Catheters that are soft are superior to stiff and rigid ones.

Intravenous fluids for large animals are often stored in a carboy (a Persian and Arabic term meaning *big jug*), which is used to describe a rigid container that can hold 20 to 40 L of fluids. A retrospective study of the risk factors associated with vein thrombosis in horses treated with intravenous fluids in a veterinary teaching hospital found that the use of carboy fluids and diarrhea and fever were related; the incidence was lower in horses that had general anesthesia, surgery, and received antimicrobial agents. A variety of aerobic bacteria were cultured from about 50% of the intravenous catheters removed from horses. Bacteria were isolated from 7% of skin swabs taken from the area around the catheter after surgical preparation with iodine soap and before and after removal of the catheter. However, there was no correlation between bacterial culture and venous thrombophlebitis.

Oral Fluid Therapy

Whenever possible, the oral route can be used to deliver the maintenance requirements. Provided there are no abnormalities of the digestive tract that interfere with oral administration or the absorption of the fluids, the oral route is preferred for maintenance therapy. In ruminants such as adult cattle rumen function must be present for significant absorption of fluids and electrolytes. The oral administration of large quantities of fluid to cattle with rumen atony results in sequestration of the fluid in the rumen and the development of metabolic hypochloremic hypokalemic alkalosis.

Oral Fluid Therapy in Calves and Adult Cattle

A variety of oral electrolyte replacement solutions are available commercially. Most preparations are in the form of powders to be mixed with water or directly with milk. The formulations vary in their composition

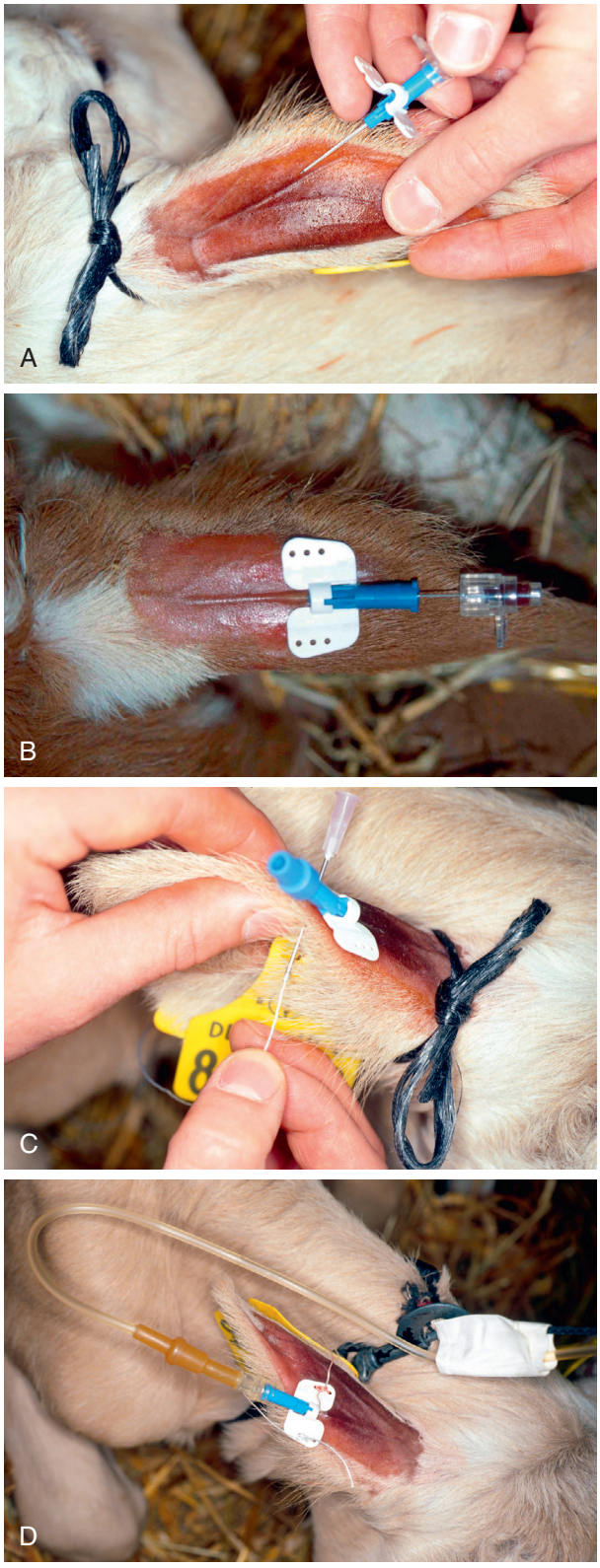


Fig. 5-20 Placement of a 22-gauge 2.5-cm over the stylet butterfly catheter into the auricular vein of a calf. The ear is clipped and scrubbed for aseptic placement of a catheter, and a tourniquet is placed at the base of the ear to facilitate visualization of the auricular veins **(A).** The catheter is then placed into the lumen of the vein and carefully advanced **(B).** The tourniquet is removed and the catheter is secured to pinna by placing a 20-gauge needle though the pinna and butterfly section and tying, taking care not to distort the ear **(C).** Intravenous fluids are then attached and the ear bandaged, taking care not to bandage below the end of the catheter **(D)**. (Pictures generously provided by Dr. Joachim Berchtold, Germany.)

but typically contain sodium, chloride, potassium, glucose, glycine, and bicarbonate or its precursors (acetate, propionate, or citrate). Some formulations contain other agents such as lecithin-coated pectin fiber that is reported to decrease the proliferation of *E. coli* and *Salmonella* spp., or other agents that facilitate normalization of the enteric bacterial population. Knowledge of the requirements for the ideal oral electrolyte solution for diarrheic calves continues to evolve. However, much progress has been made over the last 30 years, and the critical issues in formulating the ideal oral electrolyte solution are osmolality, sodium concentration, source of the alkalinizing agent, and the energy content (which is intimately tied to osmolality). It remains to be determined whether oral electrolyte solutions should contain agents such as glutamine that may facilitate repair of damaged intestinal epithelium. This issue is being actively researched at the moment and a clear consensus has not yet been reached.

Oral electrolyte solutions should be routinely administered to all neonatal calves <21 days of age at the first signs of diarrhea because it cannot be accurately predicted how quickly the calf will become dehydrated. Calves with a 4-mm or greater recession of the eye or calves that are unable to stand should receive intravenous fluids (small-volume hypertonic saline, small-volume sodium bicarbonate, or conventional large-volume isotonic crystalloid solution) in addition to an oral electrolyte solution. The initial treatment of a dehydrated calf should use an oral electrolyte solution that is not added to milk replacer because this provides superior plasma volume expansion.[32] The **osmolality** of the oral electrolyte solution should range from isotonic (300 mosm/kg) to hypertonic (700 mOsm/kg). The effective osmolality at the tip of the intestinal villus is approximately 600 mOsm/kg because of the presence of a countercurrent exchange mechanism. Although markedly hypertonic fluids should be avoided in animals with severe villous damage, it is currently not possible to predict which calves have severe villous damage on the basis of the physical examination findings and measurement of fecal pH or other body parameter. Low osmolality fluids (300 mosm/kg) have inadequate energy content because they have insufficient glucose. For this reason, if milk is withheld, then hypertonic oral electrolyte solutions (~600 mosm/kg) should be administered.[33,34] If milk is fed, then isotonic oral electrolyte solutions (300 mosm/kg) should be administered because inadequate energy content is no longer an issue.[34,35] Ideally fresh milk should be fed to diarrheic calves after 24 hours of treatment; fresh cow's milk is preferred to milk replacer or pasteurized waste milk because fresh milk contains trophic factors that facilitate repair of damaged intestinal

epithelium, and the energy content of milk is required to maintain BW. Generally, milk should not be withheld from diarrheic calves for more than 24 hours.[37]

The **sodium concentration** or the oral electrolyte solution should be between 90 and 130 mmol/L. Adequate sodium absorption is the fundamental determinant of successful expansion of the extracellular space, and is the main reason that oral electrolyte solutions are administered (the sodium concentration of milk is very low with an average value of 28 mmol/L). Sodium concentrations <90 mmol/L provide an inadequate sodium load, whereas sodium concentrations >130 mmol/L can lead to hypernatremia and additional free water loss.

The oral electrolyte solution should also contain **glucose** and either **acetate**, **propionate**, or **glycine** to facilitate sodium absorption and provide energy. There are cotransport mechanisms for sodium and glucose, sodium and volatile fatty acids such as acetate and propionate, sodium and citrate, and sodium and amino acids (such as glycine) in the luminal membrane of villous epithelial cells. Administration of glucose, acetate, propionate, glycine, or citrate therefore facilitates sodium absorption. These transport mechanisms are unimpaired in enterotoxigenic *E. coli* and are at least partially functional in malabsorptive/maldigestive diarrheas. A recent study in healthy normally hydrated neonatal calves raised questions about the relative importance of glucose-coupled sodium transport in rehydrating diarrheic calves with diarrhea, and suggested that the ratio of glucose to sodium (which is thought to range between 1.0 and 3.0 with an optimum ratio of 1.4 based on human infant oral rehydration solutions) may not be an important component of treatment efficacy in neonatal calves.[38] The choice of glycine in oral electrolyte solutions as an amino acid coupled sodium transport was based primarily on its low cost and wide availability, and because glycine was included in early human infant oral rehydration solutions.

The oral electrolyte solution must contain an **alkalinizing agent**, such as acetate, propionate, or bicarbonate, at a concentration range of 40 to 80 mM/L.[39-41] Acetate-containing fluids are as effective as bicarbonate-containing solutions at correcting mild to moderate acidosis: [acetate- = CH_3COO^-] + H^+ + $2O_2$ ↔ $2CO_2$ + $2H_2O$. Acetate must be metabolized to be effective, and metabolism may be impaired in severely dehydrated or acidemic animals, although this has not been proven in severely dehydrated calves. Acetate- or propionate-containing fluids can be fed with milk as acetate and propionate do not raise abomasal pH or inhibit milk clotting. In comparison, bicarbonate containing oral electrolyte solutions, when fed without milk, excessively alkalinize the abomasum and proximal small intestine, decreasing the effectiveness of the "abomasal sterilizer" in killing ingested enteric pathogens, and potentially promoting enterotoxigenic *E. coli* attachment to epithelial cells and STa enterotoxin production. Moreover, bicarbonate does not inhibit growth of *Salmonella i*n the intestinal lumen, whereas acetate and propionate both inhibit *Salmonella* growth. However, it is important to note that bicarbonate-containing oral electrolyte fluids are theoretically more effective at rapidly correcting severe acidemia than acetate and propionate, because bicarbonate reacts directly with H^+ ions (HCO_3^- + H^+ ↔ H_2CO_3 ↔ H_2O + CO_2). The main disadvantage of bicarbonate-containing oral fluids is that the pH of the abomasum (a natural defense mechanism) is increased, raising concerns that bicarbonate may decrease the ability to form a clot in the abomasum. This theoretical disadvantage regarding bicarbonate does not appear to be true, at least when low concentration bicarbonate solutions (25 mmol/L) are fed.[37]

The alkalinizing potential of an oral electrolyte solution can be estimated by calculating the **effective SID** of the formulation as fed. Because electroneutrality must be preserved at all times, the difference between the charge assigned to all strong cations in an oral electrolyte solution (usually only sodium and potassium) and strong anions in an oral electrolyte solution (usually only chloride) is called the effective SID and reflects the concentration of metabolizable strong anions, such as acetate, propionate, and citrate, as well as the concentration of bicarbonate.[39] Oral electrolyte solutions should have an effective SID of approximately 40 to 80 mmol/L. Electrolyte solutions with an effective SID = 0 are acidifying because they create a systemic strong ion acidosis; such solutions are not recommended for the treatment of dehydrated calves with diarrhea.

The **rate of abomasal emptying** influences the rate at which an oral electrolyte solution is delivered to the small intestine, which is the major site of fluid absorption. The rate of abomasal emptying is therefore an important determinant of the rate of rehydration in a dehydrated calf with diarrhea. The volume and caloric content of an ingested fluid meal are the most important determinants of abomasal emptying rate.[40] Other important determinants of emptying rate are the type of protein or fat, osmolality, and duodenal pH, with a solution osmolality of 600 mosm/kg or a luminal pH of <2.0 or >10.0 decreasing the abomasal emptying rate in suckling calves.[40] Studies in healthy calves suggest that oral electrolyte solutions that provide >2.4 g of glucose per kilogram BW may lead to a slower rate of rehydration as a result of a slower delivery of free water, sodium, and glucose to the small intestine, although it has been difficult to detect clinically important differences in the rate of resuscitation when oral electrolyte solutions are fed to calves with naturally acquired diarrhea.

For diarrheic calves, the total 24-hour maintenance requirement is calculated and given orally in divided doses, ideally three times a day. Compared with parenteral therapy, there is less danger from overhydration and electrolyte toxicity, and in acute diarrhea the maintenance of oral fluid and electrolyte intakes will replace continuous losses that occur during the diarrhea. Livestock owners should be informed of the value of providing newborn animals affected with diarrhea associated with dehydration, depression, inactivity, or failure to suck with oral fluids and electrolytes as soon as possible and of the value of continuing this treatment until the animal has returned to normal. Oral electrolyte solutions and water should be made available at all times to animals affected with diarrhea and other diseases in which there is continuous loss of fluid and electrolytes.

The **continued feeding of milk to diarrheic calves** while they are receiving oral fluids and electrolytes has been controversial. In the past, it was conventional to withhold milk from diarrheic calves for 1 to 2 days and then gradually reintroduce milk over the next few days when there is evidence of recovery. An extreme practice was to totally deprive the calf of milk until the diarrhea ceased. The rationale for this practice was that the ability of the calf's intestine to digest milk was impaired, particularly lactose digestion in the rotavirus and coronavirus diarrheas of young calves. It was also thought that the presence of milk in the intestine would provide a substrate for continued growth of enteric pathogens. Recent studies in calves with naturally acquired and experimentally induced diarrhea have demonstrated the benefit of feeding milk to diarrheic calves receiving oral electrolyte solutions[35]; such practice results in more rapid recovery from diarrhea (fewer days of diarrhea), less debilitation, continued weight gain, greater fat stores, faster rate of regeneration of the intestinal mucosa, and less thymic atrophy than calves deprived of milk. Adding the oral electrolyte solution to the milk of calves with diarrhea is effective and practical; this treatment approach requires that water be readily available to treated calves at all times.[36]

In adult ruminants, both water and sodium must be absorbed to produce sustained expansion of the extracellular fluid space. Acetic, propionic, and butyric acids are absorbed rapidly from the forestomach in their nonionized form but are absorbed more slowly in conjunction with a sodium ion in their ionized form. Cattle produce up to 180 L of saliva per day with a sodium concentration of 126 mEq/L, and approximately half of the sodium secreted with saliva is reabsorbed by the forestomach primarily through active transport mechanisms. Based on this physiology, orally administered

sodium is well absorbed in adult ruminants, and sodium absorption is accompanied by the passive movement of water from the rumen into the extracellular space.

Oral sodium bicarbonate administration can be an important part of treating adult ruminants with grain overload. The oral administration of sodium bicarbonate to adult ruminants (2.5 g/kg BW) causes a profound metabolic alkalosis (strong ion alkalosis). Drenching of dairy cows with 700 mL of 40% sodium bicarbonate solution or 46% sodium propionate solution (both markedly hyperosmotic) increases blood pH to an equivalent degree. Oral administration of sodium salts with a high effective SID therefore causes a metabolic alkalosis (strong ion alkalosis) in adult ruminants, as they do in neonatal ruminants.

The vast ruminal capacity for sodium and water absorption can be used by administering hypotonic oral electrolyte solutions to dehydrated adult ruminants. The optimal formulation of an oral electrolyte solution for adult ruminants is unknown, but such a solution should contain sodium, potassium, calcium, 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 hypotonic 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. An isotonic fluid containing 6.17 g of NaCl, 0.34 g of KCl, and 2.89 g of $NaHCO_3$ (providing 140 mmol/L of sodium, 4.5 mmol/L of potassium, and 110 mmol/L of chloride) was effective in treating dehydrated goats when administered by nasoruminal intubation.[42] Another recommended formulation for adult ruminants, particularly those with **hypochloremic hypokalemia metabolic alkalosis**, contains 7 g of NaCl, 1.5 g of KCl, and 1 g of $CaCl_2$ (providing 120 mmol/L of sodium, 20 mmol/L of potassium, 9 mmol/L of calcium, and 158 mmol/L of chloride).[44] Formulation of a practical, effective, inexpensive, and commercially available oral electrolyte solution for adult ruminants remains an important need in fluid and electrolyte therapy.

Oral Fluid Therapy in Horses

Intravenous fluid and electrolyte therapy has been used extensively for the treatment of dehydration and electrolyte disturbances in the horse with diarrhea. However, oral fluid therapy, as used in calves and adult cattle, has not been used to the same extent. Oral fluid therapy offers may be an effective, practical, and economical method of rehydration of horses with diarrhea that has not yet been fully explored.

In the horse with acute diarrhea, several factors contribute to the nature of the fluid and electrolyte losses. There are increases in fecal sodium and water loss, but the fecal potassium excretion may remain unchanged. The lack of feed intake, which affects primarily the potassium intake, can result in losses of 2500 to 3000 mmol of potassium per day. Although urinary water and potassium losses are reduced, potassium depletion continues; thus potassium losses are very high and need to be replaced, especially in the anorexic horse. The large potassium deficit in diarrheic horses should also be considered when formulating the composition of oral fluids. Administration of 30 to 40 g of potassium chloride or, if chloride administration is inappropriate, 30 to 40 g of potassium bicarbonate in 2 to 4 L of water given by nasogastric tube several times daily to an inappetent horse with diarrhea, can complement intravenous fluid therapy and replace the potassium deficit.

The optimum electrolyte composition of oral fluids and the amount to be used have not yet been determined for the horse. The amount given depends on the degree of dehydration. Dehydration in horses becomes clinically apparent when about 5% of BW has been lost. In a 500-kg horse, assuming 90% water loss, the fluid deficit is about 23 L. Abdominal discomfort may occur following the nasogastric tube administration of a series of 8- to 10-L doses of oral rehydration fluid. The administration of large amounts may result in rapid transit through the stomach and intestines and decreased absorption. A slower rate of administration, such as 8 to 10 L every few hours, may be tolerated more effectively and the transit time in the intestine may be decreased, enhancing absorption. Volumes of 6 to 8 L can be given by nasogastric tube as often as every 15 to 20 minutes by funnel; as much as 20 to 30 L is possible during the first hour and 40 L is possible during a 2-hour period. Oral fluids may also be administered through a small-diameter indwelling nasogastric tube, as is used for prolonged enteral nutrition of horses with dysphagia.

Commercially available **oral electrolyte solutions** are inadequate for horses because the concentrations of sodium and potassium are too low to adequately replace losses. When treating horses with acute diarrhea, the ratio of sodium to chloride ions in the oral solution should be approximately 1.4:1, and the need for glucose in an oral rehydration solution for adult horses has not been clearly demonstrated. One formulation contained 5.27 g of NaCl, 0.37 g of KCl, and 3.78 g $NaHCO_3$ per liter of tap water; this produced a suitable electrolyte composition for oral administration (Na 135 mmol/L, K 5 mmol/L, Cl 95 mmol/L, and HCO_3 45 mmol/L).

Oral administration of bicarbonate will result in a pronounced alkalemia within 3 to 6 hours, with the maximum change in pH occurring at a sodium bicarbonate dose of 1 g/kg BW (which represents 40% of normal extracellular sodium). Doses above this level do not induce additional alkalinization, presumably because of limited absorption of bicarbonate from the intestinal tract. The oral administration of sodium bicarbonate to normal mature resting horses without ad libitum access to water induces metabolic alkalosis, hypernatremia, hypokalemia, and hyperosmolality for at least 8 hours. The oral doses were 0.25, 1, and 1.5 g/kg BW in 3 L of water; the intravenous dose was 0.25 g/kg BW in 3 L of water. The effects were dose dependent: in the horses given the 1 and 1.5 g/kg BW oral doses the hypercapnia persisted for 12 hours, whereas hypercapnia lasted 2 hours in horses given the 0.25 g/kg BW dose orally or intravenously. The effects of these large doses of sodium bicarbonate on the renal function of horses indicated increases in urine flow, fractional clearance of electrolytes and bicarbonate, electrolyte-free water reabsorption, urine concentrations of sodium and bicarbonate, urine excretion, clearance of sodium and bicarbonate, urine pH, and AG.

The temperature or glucose concentration of the fluid does not appear to be important because the rate of fluid absorption was similar in dehydrated horses administered an oral rehydration solution at 5°C, 21°C, or 37°C or containing glucose at 0%, 2.5%, or 3.5%. The tonicity of the oral rehydration solution is of minor clinical importance; however, oral administration of hypertonic solutions (628 mOsm/kg BW) to dehydrated horses caused a transient increase in plasma protein concentration that was attributed to movement of water into the bowel lumen. **Continuous flow administration** of a hypotonic solution at 15 (mL/kg)/h through a **small-diameter nasoesophageal tube** is effective in increasing plasma glucose concentration in healthy adult horses, with maltodextrin (15 g/L) providing a greater glycemic response to that provided by glucose (15 g/L). This treatment protocol appears to provide a useful low-cost method for treating horses that are slightly dehydrated and hypoglycemic, but safety studies using a larger number of horses are required.[43] A practical limitation of oral rehydration solutions in horses is that they should be ingested voluntarily rather than by nasogastric intubation. This limitation has led to recent interest in the oral administration of pastes.

The oral administration of an **electrolyte paste** has been shown to be effective in correcting mild to moderate dehydration in horses, provided animals are monitored to ensure that they drink water. Oral electrolyte pastes may be formulated as follows: 30 g of 1:1 mixture of sodium chloride and potassium chloride, potassium chloride and sodium bicarbonate, or potassium chloride and potassium carbonate, and administered every 6 hours; 120 g of the latter mixture provides 1400 mmol or more of potassium

in a 24-hour period. Administration of higher doses of oral pastes (0.5 g of NaCl/kg BW, 0.5 g of KCl/kg BW, or a mixture of 0.25 g of NaCl/kg BW and 0.25 g of KCl/kg BW) to dehydrated horses induced a transient period of hyperhydration and apparent plasma volume expansion that lasted 12 hours. Although the absorbed electrolytes from an oral paste are subsequently eliminated via the urine, this treatment is potentially of benefit in horses with disease processes associated with ongoing fluid loss, such as diarrhea.

There is no published information on the use of oral fluid therapy in horses that are diarrheic as a result of disease of the small intestine such as enteritis or proximal enteritis (duodenitis). It would seem unlikely that oral fluid therapy would be indicated or effective for anterior duodenitis. In horses with colitis, the small intestinal absorptive capacity is probably intact and oral fluid therapy before transport of the horse to a clinical center for intensive fluid therapy may delay the onset of more serious complications. Horses with mild dehydration can be rehydrated effectively with oral fluid therapy. Horses treated with oral fluid therapy must be monitored clinically, and the hematocrit, total plasma protein concentration, and serum electrolytes should be measured.

Oral fluid therapy provides an effective and inexpensive treatment in horses with impaction of the large colon and dorsal displacement of the colon. An absolute requirement for oral fluid therapy in the horse is that there is no gastric reflux. Generally, although 6 to 8 L of water can be administered by nasogastric tube and funnel (gravity flow) every 15 to 20 minutes, and the administered fluid is rapidly transported to the large intestine, some horses do not tolerate oral fluid administration at 10 L/h and exhibit mild signs of abdominal discomfort. Accordingly, oral fluid rates are more commonly administered at 8 to 10 L every 2 hours using a nasogastric tube and a funnel.[45] Volumes exceeding 10 L should be administered over at least 15 minutes,[46] even though 90% of 10 L of an electrolyte solution is emptied from the stomach within 15 minutes.

It is generally recommended that the osmolality of the fluids should be isotonic, ranging from 280 to 360 mOsm/L; the upper range of tonicity that is safe to administer is unknown. Plain water has been administered at 50 to 150 mL/kg BW over 24 hours in four treatments to horses with experimentally induced dehydration. The administration of water was safe and effective in hydrating the large intestinal luminal contents.[46] One isotonic formulation that was successful in a case series involving 108 horses contained 6 g of sodium chloride and 3 g of potassium chloride per liter of tap water, equivalent to the following electrolyte concentration: 103 mEq/L of Na, 40 mEq/L of K, and 143 mEq/L of Cl.[45] Potassium is an important component of the isotonic formulation in horses with impaction of the large colon or dorsal displacement of the colon. Oral administration of 60 L of lactated Ringer's solution or an isotonic solution over 12 hours was superior in hydrating the contents of the right dorsal colon compared with intravenous administration of an equivalent volume of lactated Ringer's solution or enteral administration of 1g/kg BW of $MgSO_4.7H_2O$ (Epsom salts) or anhydrous Na_2SO_4 as a 1-L solution. Moreover, enteral administration of Epsom salts has been associated with hypermagnesemia, and anhydrous Na_2SO_4 has been associated with hypocalcemia.

Fluid and Electrolyte Therapy in Newborn Piglets and Lambs

The most common cause of fluid and electrolyte imbalance in newborn piglets and lambs is acute neonatal diarrhea. There is severe dehydration, acidemia, hyponatremia and, in some cases, hyperkalemia caused by the acidosis. Balanced electrolyte solutions or isotonic saline and sodium bicarbonate initially followed by balanced electrolytes are indicated and successful. These are given subcutaneously or intraperitoneally at the rate of 15 mL per piglet every 2 hours plus the same amount orally. The safe amount of sterilized porcine serum or saline and 5% dextrose that can be given to piglets is equivalent to about 8% BW intraperitoneally, in two divided doses given 8 hours apart. Lambs are also treated subcutaneously (30–40 mL) and orally (50–100 mL) every 2 hours.

Parenteral Nutrition

Parenteral nutrition is used to provide adequate nutrition intravenously, as long as necessary, when feeding by the gastrointestinal tract is impractical, inadequate, or impossible. The term parenteral nutrition is preferred to total parenteral nutrition because the complete nutritional requirements of large animals are either not completely known or not addressed by intravenous fluid administration. It should be recognized that enteral nutrition represents state-of-the-art medicine because enteral nutrition supports the repair, maintenance, and growth of the gastrointestinal tract to a much greater extent than parenteral nutrition. It should also be recognized that parenteral nutrition should only be contemplated after at least 5 days of inappetence.

The technique is used to supply the nutrient requirements, most importantly protein, of the animal until it returns to normal. In calves affected with persistent diarrhea caused by chronic disease of the alimentary tract, or that cannot or will not eat, total intravenous feeding may be indicated. High concentrations of glucose, protein hydrolysates, lipid emulsions, and electrolytes are given by continuous slow intravenous infusion over a period of several days. Some encouraging results in calves have been published, but the cost-effectiveness of the technique has not been examined.

Parenteral nutrition is an acceptable method of maintaining nutrition in the healthy horse over a period of 10 days. Body weight was maintained at 94% of initial values without clinical evidence of dehydration. No problems were encountered with the long-term intravenous catheterization. The total daily amounts given are calculated on the basis of daily caloric requirement. The intravenous catheter must be inserted down into the cranial vena cava, in which a large volume of blood will dilute the hypertonic concentration of the solution. The potential problems associated with parenteral nutrition include difficulty in the maintenance of a steady intravenous drip, hypertonicity of the solutions used, venous thrombosis, excessive diuresis, catheter sepsis, and bacterial contamination of the solutions.

Parenteral nutrition in foals usually starts with a parenteral daily initial digestible energy of 50 to 55 kcal/kg BW that is designed to address resting energy requirements; the daily energy intake is increased gradually up to a daily target of 120 kcal/kg using a combination of parenteral and enteral nutrition.[47] Because of the cost of components, energy density, and availability of products, there are two philosophical approaches to parenteral nutrition in foals: (1) intravenous dextrose and lipid emulsion with 30% to 40% of the caloric intake provided by lipids or (2) intravenous dextrose, amino acids in a nonelectrolyte solution, and lipid emulsion. The latter formulation has been used for parenteral nutrition in alpacas.[48] B-complex vitamins are usually added to the final parenteral nutrition solution, and there is no clear consensus on the need for concurrent insulin administration. Typical commercially available products administered in North America are designed for use in humans in a critical care setting and include 50% dextrose solution, an 8.5% amino acid solution without electrolytes, and a 20% lipid emulsion solution, with the lipid solution as the most expensive component. In a retrospective study of 53 foals that received parenteral nutrition including lipids, 32% developed hypertriglyceridemia (>200 mg/dL), and this development was significantly associated with nonsurvival.[47] This finding suggests that parenteral nutrition in foals should use limited amounts of lipid for energy, and current recommendations in septic human patients are to provide no more than 5% of the caloric intake from lipid emulsions. Fifteen percent of the 53 foals developed catheter-related complications such as thrombophlebitis or sepsis.[47] This emphasizes the need for strict aseptic technique whenever attaching or flushing fluid administration lines and catheters in animals receiving parenteral nutrition.

A practical and effective parenteral nutrition solution for sheep, goats, and New

World camelids contains the following components and is administered at a rate of 5% of BW per day:[43,44]

- 5 L of a commercial balance electrolyte solution (such as lactated Ringer's solution)
- 1 L of 8.5% amino acids (commercially available)
- 500 mL of 50% dextrose
- 20 mL of B-complex vitamins
- Potassium chloride (20–40 mEq/L) and calcium gluconate 23% (20–50 mL/L) as indicated

The components should be mixed aseptically in this order. Administration is best performed using a centrally located catheter and strict attention should be given to aseptic technique. **Hyperglycemia** is a common finding in neonatal animals undergoing parenteral nutrition, and the occurrence of hyperglycemia (glucose >180 mg/dL, equivalent to >10 mmol/L) has been associated with an increased likelihood of nonsurvival.[49] The widespread availability of low-cost blood glucose point-of-care units has made it much easier to monitor blood glucose concentration every 1 to 2 hours and adjust the fluid administration rate accordingly.

Parenteral nutrition in adult cattle focuses on the administration of 50% dextrose as a continuous rate infusion as part of the treatment of ketosis and hepatic lipidosis and in the supportive treatment in cows that are inappetent or recumbent or have gastrointestinal or infectious diseases.[50] Concentrated (50%) dextrose solutions are administered to keep the infused volume low and minimize plasma volume expansion and diuresis. Cows with hepatic lipidosis or prolonged anorexia sometimes require continuous intravenous infusion of dextrose for several days until they can maintain energy balance. The continuous intravenous infusion of 50% dextrose (0.3 g/kg/h) to healthy lactating dairy cows resulted in hyperglycemia and hyperinsulinemia and a marked reduction in plasma phosphorus concentration. Other effects of intravenous dextrose infusion included decreased plasma potassium concentration, decreased dry matter intake and fecal production, and a transient increase in milk production followed by a sustained decrease. All of these effects were reversed after dextrose infusion was stopped.[50] The results suggest a slower rate of glucose administration (0.1–0.2 g/kg/h) is more appropriate in lactating dairy cattle.

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