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TREATMENTS AFFECTING FLUID AND ELECTROLYTE STATUS DURING EXERCISE

Harold C. Schott II, DVM, PhD,
and Kenneth W. Hinchcliff, BVSc, MS, PhD

Body fluid and electrolyte homeostasis may be affected by management practices, diet, administration of fluid and electrolyte supplements, and medication administration. Medications may be given to specifically manipulate body fluid and electrolyte content in an attempt to improve performance (i.e., sodium bicarbonate) or to ameliorate potentially detrimental effects of other disorders, including exercise-induced pulmonary hemorrhage and hyperkalemic periodic paralysis (administration of furosemide and acetazolamide, respectively). Manipulation of body fluid and electrolyte homeostasis can be demonstrated in both resting and exercising horses, but the primary interest is in how these manipulations affect subsequent performance and recovery. The reader is referred to previous publications by the authors[104] and others[9, 11, 97] for review of the fluid and electrolyte shifts that accompany exercise. In this article, we will:

- review the alterations in fluid and electrolyte status accompanying feed ingestion
- discuss the importance of the contents of the equine gastrointestinal tract as a "reservoir" of water and electrolytes during exercise
- review the numerous strategies for hyperhydration of the equine athlete and for replacement of fluid and electrolytes lost via sweating that were developed and tested in preparation for the equestrian events at the 1996 Atlanta Summer Olympic Games

From the Department of Large Animal Clinical Sciences, Michigan State University, East Lansing, Michigan (HCS); and the Department of Veterinary Clinical Sciences, The Ohio State University, Columbus, Ohio (KWH)

- discuss several specific medications that are commonly used in equine athletes, including sodium bicarbonate, furosemide, and acetazolamide.

FEEDING AND MANAGEMENT PRACTICES AFFECTING FLUID AND ELECTROLYTE HOMEOSTASIS

Nutrition of the athletic horse has been the subject of numerous research studies (reviewed by Hintz,[52] Meyer,[77] and Lawrence[65]). The majority of this research has focused on nutritive value of feed stuffs or the increased energy requirements of exercising horses, and much less attention has been paid to the manners by which equine athletes are actually fed. Consequently, many feeding practices remain more firmly based in tradition than on supportive scientific data. Recently, several studies have addressed the effects of both feed type and postprandial interval on exercise performance. Although the emphasis of these studies has been on substrate utilization and metabolic responses,[67, 68, 115] investigators have also specifically addressed the effects of diet on fluid and electrolyte homeostasis in resting and exercising horses.

Effects of Meal Ingestion

Ingestion of a meal leads to significant perturbations of fluid and electrolyte homeostasis.[15] For example, in the hour after ponies or horses were fed a completely pelleted meal, plasma protein and sodium concentrations increased approximately 1.0 g/dL and 3.0 mmol/L, respectively, and plasma volume decreased by approximately 15%.[14, 16] These changes were attributed to the production of large volumes of saliva and pancreatic secretions (20–25 L and 2–3 L, respectively, for a 450-kg horse) in the upper alimentary tract. In addition, these fluid shifts and electrolyte alterations were accompanied by activation of the renin-angiotensin system, an increase in plasma aldosterone concentration, and a decrease in urine flow and sodium excretion. Although substantial, these perturbations were transient, and plasma constituents and volume returned to prefeeding values within 2 to 3 hours after feeding. Feeding of a pelleted meal was also accompanied by a second, smaller decrease in plasma volume 6 to 8 hours after meal ingestion. The latter fluid shift was attributed to colonic secretions associated with increased fermentation as the soluble carbohydrates escaping small intestinal digestion entered the colon. Although these studies were performed using a completely pelleted feed, complementary studies showed that these meal-associated perturbations of fluid and electrolyte homeostasis could be reproduced with a more typical meal of hay and grain,[15] and an earlier study by Kerr and Snow[61] revealed similar findings when a meal of only hay was fed. In contrast, when the total daily ration was provided in smaller portions at 2- or 4-hour intervals throughout the day (similar to natural grazing), the alterations in fluid and electrolyte homeostasis were essentially abolished.[14, 16]

Bowel Fluid and Electrolyte Reservoir

The contents of the gastrointestinal tract of the equine athlete (unlike those of its human counterpart) also represent a substantial fluid and electrolyte reservoir which may be utilized during prolonged exercise.[77] For example, Meyer and Coenen[78] measured the total water content of ingesta by collecting the contents of the gastrointestinal tract of ponies immediately after euthanasia. In ponies on an all-hay diet, water content of ingesta was 183 mL/kg of body weight. In another group of similarly fed ponies subjected to 1 hour of low-intensity treadmill exercise (3.3 m/s), water content was 138 mL/kg of body weight. After correction for greater intakes of feed and water by the nonexercised ponies, this difference suggested absorption of approximately 5 L of water from the intestinal tract (or absorption of ≈15 L of water in a 450-kg horse). In contrast, water content of the ingesta of nonexercised ponies fed a completely pelleted diet was 101 mL/kg of body weight, a value only 55% that of the hay-fed ponies. Similarly, the sodium, chloride, and (to a lesser extent) potassium contents of the ingesta were significantly lower in the exercised ponies, in comparison with the nonexercised ponies, indicating that the gastrointestinal contents also provide a reservoir of electrolytes (especially sodium) which can be absorbed during prolonged endurance exercise.

Danielsen et al[21] recently studied the effects of roughage intake on fluid and electrolyte status in Thoroughbred horses performing repeated bouts of low-intensity exercise. In a crossover design, horses received either free-choice grass hay or a limited hay diet (overnight fast of ≈16 hours) prior to an exercise test consisting of six 15-minute bouts of treadmill exercise (5 minutes at 4 m/s followed by 10 minutes at 7 m/s, producing heart rates of 110–120 beats per minute), with each bout separated by 15 minutes of hand walking (total duration of 2.75 hours). Body weight loss during exercise was 2.8% for both feeding programs, and there were no differences in heart rates, rectal temperatures, or changes in plasma protein or electrolyte concentrations between the two treatments. In a second experiment in the same report, the investigators subjected the horses to a more demanding exercise test consisting of four 30-minute bouts of treadmill exercise (two cycles of 5 minutes at 2 m/s followed by 10 minutes at 8.5 m/s, producing heart rates of 140–145 beats per minute), with each each bout separated by 10 minutes of hand walking (total duration of 2.5 hours). Further, the limited hay diet (5.0 kg of a pelleted feed and 4.4 kg of grass hay daily) was fed for 7 days (with a similar overnight fast of ≈16 hours) prior to the exercise test. Body weight loss (≈4%), heart rate, and rectal temperature were not different between the limited and free-choice hay diets, but plasma

protein concentration was significantly greater after limited hay feeding. Thus, feeding of a limited roughage diet for 1 week appeared to limit the amount of water that could be recovered from gastrointestinal tract contents during exercise, which is similar to the findings in ponies fed a completely pelleted feed.[78] In an attempt to increase the water reservoir of the ingesta, Cinotti et al[13] recently fed four horses 0.3 mg/kg of psyllium daily for 8 days prior to a 120-km endurance ride. No difference in performance or changes in plasma protein or electrolyte concentrations were observed between the two groups. The results of these studies suggest that it may be more practical to provide free-choice access to roughage rather than attempt to increase the fiber content of the gastrointestinal tract with supplements. Despite increasing the total water content of the ingesta, it has been suggested that high-fiber diets may actually limit water availability due to binding by hydrophilic polysaccharides in the fiber.[19] The results of the work of Meyer and Coenen[78] and Danielsen et al[21] would seem to discount this suggestion, but comparing the ability of exercising horses to absorb water from different types of roughage warrants further study. As an example, although water intake and fecal moisture content (≈75% of fecal weight) are essentially the same for horses on grass and alfalfa hay diets, urine water output is lower and fecal water output is greater (due to greater amounts of fecal material) when horses are fed grass (Table 1).[20, 36, 116] The difference in water turnover between grass and alfalfa diets has been attributed to the higher protein and lower fiber content of alfalfa and suggests that an alfalfa-based diet may result in a lesser water reserve in the gastrointestinal tract.

Although the total "available reserve" in the ingesta has not been determined, these studies illustrate the importance of the equine gastrointestinal tract as a source of fluid and electrolytes which may be utilized during or after prolonged endurance exercise. Utilization of this intestinal reserve is further supported by development of the typical "tucked-up" appearance of the abdomen in endurance horses towards the end of a ride. Finally, depletion of this gut reservoir is likely the major factor responsible for the persistent body weight losses that may be observed during recovery from prolonged endurance exercise.[57, 105, 106]

Table 1. WATER AND ELECTROLYTE BALANCE IN HORSES RECEIVING A LOW-SODIUM DIET (ALFALFA-TIMOTHY HAY) AND A HIGH-SODIUM DIET (ALFALFA-CHAFF HAY)

Source	Intake	Urinary Loss	Fecal Loss	Unmeasured*
Tasker (1967)†				
Water (L)	27.4	4.9	14	8.5 (31%)
Sodium (mmol)	329	7	116	206 (63%)
Potassium (mmol)	3930	2196	993	741 (19%)
Groenendyk et al (1988)‡				
Water (L)	27.6	9.9	7.2	10.5 (38%)
Sodium (mmol)	986	527	253	206 (21%)
Potassium (mmol)	3320	2661	504	155 (5%)
Chloride (mmol)	3008	2347	174	487 (16%)

*Unmeasured losses include insensible water losses as well as electrolyte losses thought to occur in sweat; the value in parentheses is the percentage represented by these unmeasured losses.

†*Data from* Tasker JB: Fluid and electrolyte studies in the horse. III. Intake and output of water, sodium, and potassium in normal horses. Cornell Vet 57:649, 1967.

‡*Data from* Groenendyk S, English PB, Abetz I: External balance of water and electrolytes in the horse. Equine Vet J 20:189, 1988.

In comparison with prolonged endurance exercise, the effects of feeding practices on fluid and electrolyte homeostasis during shorter bouts of high-intensity exercise have received less attention. Surveys of racehorse trainers and endurance riders have revealed that essentially all of the former either limit or eliminate hay feeding on the day of the race[58, 103] and that a much lower percentage of endurance riders restrict access to feed prior to competition.[89] Similarly, many racehorse trainers will either remove or limit access to water in the hours preceding a race, although endurance riders almost never limit access to water. These feeding practices are speculated to benefit the racehorse, because a transient reduction in body weight is thought to improve performance. In a recent study of the timing of hay feeding on plasma volume and metabolic responses to strenuous treadmill exercise (J.D. Pagan, PhD, personal communication, 1996), Thoroughbred horses had greater pre-exercise body weight when they had free-choice access to hay and were fed 2.3 kg of sweet feed 3 hours prior to exercise in comparison with when they were either fasted for 12 hours or only fed 2.3 kg of sweet feed 3 hours prior to exercise (with no hay for 12 hours). Further, pre-exercise plasma volume was 9% lower in the free-choice hay-fed horses in comparison with the other feeding states (fasted or grain-fed horses). During treadmill exercise, heart rates during the canter (8 minutes at 9.0 m/s) and the gallop (2 minutes at 10.7 m/s) were lower in the fasted horses in comparison with the free-choice hay-fed horses (176 versus 191 beats per minute and 191 versus 206 beats per minute at the canter and the gallop, respectively). Although not measured, the lower heart rates suggested that plasma and stroke volume may have been greater in the fasted horses during exercise.

Dietary Recommendations for Athletic Horses

Feeding a large (especially concentrate) meal 1 to 2 hours before exercise would be expected to alter both metabolic responses (due to increased insulin) and fluid and electrolyte status and could negatively affect performance during both short-term, high-intensity racing exercise and prolonged endurance exercise. Other manipulations, including water withholding and furosemide administration, could be expected to exacerbate and prolong the transient shifts associated with upper alimentary tract secretions. The effects of feeding 3 to 6 hours prior to competition (as is common practice with racehorses and show horses) on meta-

bolic responses and fluid and electrolyte balance during exercise are less clear. Although data are limited, results of studies to date suggest that it may be preferable to avoid morning grain rations and limit hay intake on days when horses are entered in high-intensity competitions of relatively short duration (<5–10 minutes). Similarly, feeding a large concentrate meal to endurance horses on the morning of the ride is probably better avoided. In the latter athlete, the delayed fluid shift associated with colonic secretions 6 to 8 hours after ingestion of a large concentrate meal on the morning of the ride could potentiate the competition for blood flow between muscle and the so-called *nonessential* organs of the gastrointestinal tract during exercise. In contrast, feeding small amounts of concentrate (0.5–1.0 kg) 1 to 2 hours before the ride and offering similar amounts at each rest stop, along with free access to hay may be beneficial in maintaining plasma glucose concentrations later in the ride as glycogen stores become depleted. The metabolic benefits of these frequent, small meals would likely outweigh any adverse effects on fluid and electrolyte status.

Feeding Considerations for Multiday Events

Horses that compete over a period of several days (multiday endurance ride, 3-day event, or multiday horse show) are occasionally faced with the challenge of both having enough time to eat as well as to recover/rest before another day of demanding performance. There are only limited data on the effects of feed deprivation on subsequent exercise performance by horses. For example, to assess whether draught horses could perform satisfactorily for several days with limited feed intake (because transport of roughage into certain field environments could prove challenging), Swedish Warmbloods were fed only oats and natural roughage sources (limited grass, heather, birch and pine twigs, and dried leaves) for 1 week, during which time, they walked 180 km.[6] Cumulative body weight loss reached 12% by the end of the study, and performance deteriorated considerably on the final days of exercise. Subsequently, Sticker et al[114] fasted a group of mares for 72 hours prior to an exercise bout consisting of 5 minutes of a fast trot on a lunge line. Although metabolic responses (energy substrates and associated hormones) were different between the fasted and fed horses, no difference in exercise performance was reported. Nevertheless, the exercise bout was a rather minimal effort in comparison with multiday events.

In horses competing in a 5-day, 424-km endurance ride, body weight loss did not progressively increase during the course of the ride. After a loss of 6.2% on the first day of the ride, horses replaced about one half of this deficit during the overnight recovery period.[105] On subsequent days, body weight losses of 3% to 4% were experienced, but these were largely replaced during the overnight recovery periods. These horses, which were all provided supplemental electrolytes, were able to establish a balance between feed intake and weight loss during this challenging multiday competition. A problem faced by these endurance athletes, however, was a decrease in the time available for actual feed intake, as many horses were exercising for 8 to 12 hours each day. For these and other types of equine athletes participating in multiday events, it would seem advisable to provide free-choice access to hay during all rest periods and throughout the night. As mentioned above, concentrates should also be provided in small amounts (0.5–1.0 kg) frequently, during rest periods and several times during the night. Beet pulp, which is high in both energy and fiber content, is another beneficial feed source for these athletes. In addition, fat supplementation may be a further method of increasing energy intake by horses competing in these multiday events.

Fat Supplementation

Addition of animal or vegetable fat to the diet has been receiving considerable attention as a means of increasing dietary energy content and has been touted to increase anaerobic capacity and enhance performance during short bouts of high-intensity exercise.[24, 41] With regard to the latter, fat supplementation has been reported to increase muscle glycogen content and thereby delay fatigue associated with glycogen depletion.[41] In theory, providing energy as fat (rather than carbohydrates) should ameliorate some of the alterations in fluid and electrolyte homeostasis associated with feeding a large, predominantly carbohydrate, concentrate meal. Further, increasing dietary fat has been anectdotically reported to be of benefit in horses suffering from exertional rhabdomyolysis as well as gastric and colonic ulcers. To specifically investigate the effects of fat supplementation on fluid and electrolyte status, Hoyt et al[55] performed electrolyte balance studies (using metabolism stalls to document urinary and fecal output) in Thoroughbred horses before and after dietary supplementation with 10% animal fat. No differences in fluid and electrolyte balance were detected. Further, sweat production and composition during an exercise test were not different in fat-supplemented horses. Fat supplementation has also been advocated as a means of reducing thermal stress (due to less heat generation by colonic fermentation) in horses exercising in hot and humid environments.[109] To determine if fat supplementation was beneficial for horses exercising in hot environments (August in Texas with a mean daily temperature of 29.2°C and relative humidity of 46%), Hower et al[54] studied electrolyte balance (also using metabolism stalls) and measured aldosterone responses to a 1200-m gallop (designed to achieve a heart rate of 185 beats per minute) in Thoroughbred horses. As in the previous study, no differences in electrolyte balance due to diet were observed when horses were fed fat-supplemented or control diets, and plasma aldosterone responses were also similar in the two diets. Thus, although fat supplementation could have glycogen-sparing effects and thereby delay fatigue, it remains unclear if and to what extent fat

supplementation may affect fluid and electrolyte status in exercising horses. If fat feeding is associated with decreased roughage intake, horses competing in short-duration, high-intensity events may benefit from a decrease in "bowel ballast," although endurance athletes may suffer from the loss of potential fluid and electrolyte reserves in the ingesta.

Daily Electrolyte Supplementation

Investigations of electrolyte balance have revealed that most horses on a predominantly hay or pasture diet ingest excess potassium and chloride. In contrast, sodium intake is variable and may be marginal in some diets.[36, 97, 108, 116] Maintenance requirements for a sodium intake of 10 to 15 g/d for a 450-kg horse have been recommended,[36, 108] and although voluntary salt intake by horses licking a salt block is quite variable, in most instances, it is adequate to meet maintenance needs for nonexercised horses (when coupled with sodium intake in feed).[60, 108] Nevertheless, exercising horses that lose considerable amounts of sodium in sweat (500–1000 mmol/h) or are treated with furosemide will have greater dietary requirements to replace such losses.[97] Consequently, it has become rather common to recommend addition of 50 to 75 g of loose salt (which will provide 850–1275 mmol of sodium, because 1 g of sodium chloride provides ≈17 mmol of sodium) to the diet when horses are stabled in a hot and humid environment, exercised heavily, or repeatedly treated with furosemide.

In horses, the stimuli for electrolyte intake ("salt appetite") have received much less attention than the study of water balance. Houpt et al[53] found that horses that were treated with furosemide ate more salt in the hours after treatment in comparison with placebo-treated horses on the same diet (which provided 15 g of sodium per day). Nevertheless, the salt intake (which was comparable for licking a salt block and drinking a 0.9% sodium chloride solution) was excessive in both treatment groups (in excess of 100 g). Thus, salt appetite unlike water intake is not closely regulated to balance intake to match losses. In fact, when free-choice salt is available, it appears that most horses consume more than their maintenance needs (14–143 g/d in one study).[108] Although this salt appetite may not seem appropriate, it could be considered advantageous for the exercising horse. Further, increased intake is considered harmless, as the excess is readily eliminated by increasing urinary sodium excretion.

The data from the water and electrolyte balance studies performed by Tasker[116] and Groenendyk et al[36] (see Table 1) provide a good illustration of the equine kidney's capacity to conserve sodium when dietary intake is low (Tasker's data) or to excrete excess sodium when dietary intake is not limited (Groenendyk's data). Further, these studies demonstrate that urinary excretion is the major route for the loss of both potassium and chloride. Although the dietary intake of potassium is usually excessive, equine kidneys do not appear to have a great capacity to conserve potassium during periods of food and water deprivation or with anorexia associated with disease.[97, 100, 116] Thus, urinary potassium concentration and total excretion can remain substantial in the face of decreased intake. Consequently, horses with decreased feed intake may develop significant total body potassium depletion and often benefit from supplemental dietary potassium (25–50 g/d of potassium chloride will provide 375–750 mmol of potassium, because 1 g of potassium chloride provides ≈15 mmol of potassium).

Despite most nonsupplemented equine diets being marginal in sodium content, it is difficult to experimentally produce total body sodium depletion by restricting dietary sodium intake alone. For example, Lindner et al[69] had to limit sodium intake of ponies to less than 5 mg/kg of body weight per day (<2.5 g/d for a 450-kg horse) and subject them to 2 hours of treadmill exercise every third day before a sodium deficit could be induced. Although the sodium content of the ingesta decreased by 75% in comparison with sodium-replete control ponies, sweat sodium concentration was minimally reduced, because equine sweat (unlike human sweat) does not become progressively more hypotonic as exercise continues.[76] Of interest, sweat production by the sodium-restricted ponies progressively decreased over the 30-day exercise period, suggesting that horses may adapt to sodium depletion by modifying their thermoregulatory responses to exercise. For example, minute ventilation (and therefore respiratory heat loss) has been documented to progressively increase during prolonged treadmill exercise.[3]

At present, there are no data to support the concept of "electrolyte loading" of equine athletes by feeding supplemental electrolytes for several days prior to competition. As discussed, the additional electrolytes are readily excreted within a few hours by the kidneys. Nevertheless, electrolytes administered in the few hours immediately before a prolonged exercise competition may be of benefit as long as adequate water is also ingested (see below). Further, there are also no data to suggest that daily electrolyte supplementation will lead to decreased renal and gastrointestinal compensatory abilities to conserve electrolytes during exercise. Thus, daily electrolyte supplementation should be considered a means of ensuring that daily losses induced by exercise, exposure to heat and hot weather, or during long-distance transport to an event are adequately replaced. Another touted benefit of daily electrolyte supplementation is that equine athletes may learn to accept the supplement as part of their daily feed rather than having the supplement potentially discourage feed intake when it is only provided at competitions. For example, horses appear to be able to "learn" to drink salt water if it is offered to them as part of their daily diet (always with fresh water as well). Although Randall et al[91] reported that horses did not readily drink (in comparison with water) salt water with a concentration in excess of 0.6% of sodium chloride, others have reported that horses performing endurance exercise or treated with furosemide can be trained to drink 0.9% saline solutions.[53, 60, 62] Finally, if electrolytes

are to be administered as a paste, it would also be advisable to condition a horse to receive this form of supplementation during training rides.

FLUID AND ELECTROLYTE SUPPLEMENTATION DURING EXERCISE

Ingestion of fluid and electrolyte products by human athletes during prolonged exercise has been the focus of considerable research over the past few decades.[30, 75, 82, 83] Because both fluid and electrolyte depletion (leading to thermoregulatory failure) as well as marked reductions in plasma glucose concentration contribute to decreased performance and fatigue in human endurance exercise,[2, 8, 101, 102] these products are used for two complementary effects: maintenance of plasma volume and composition in the face of substantial losses of water and electrolytes in sweat and provision of a carbohydrate energy source to maintain plasma glucose concentrations in the later stages of prolonged exercise. Although ingestion of plain water appears to be adequate during exercise lasting 1 hour or less, performance during longer bouts of endurance exercise appears to be enhanced by the presence of both a carbohydrate source and sodium in the rehydration product.[30] A number of factors, including volume, temperature, tonicity, and composition of the ingested solutions, however, appear to play important roles in how well these products are emptied from the stomach and subsequently absorbed from the gastrointestinal tract of exercising humans. Further, there is considerable interindividual variation in gastric emptying and absorption of these products in human athletes.[18]

Over the past few decades, the philosophy about fluid replacement for human athletes has changed dramatically. Historically, water was often withheld from military recruits and athletes to "toughen the psyche"; unfortunately, this practice resulted in numerous fatalities from heat injury.[101, 102] Similar disasters have also occurred in poorly supervised equine endurance events. Today, the combination of increased recognition of heat-related illness and popular marketing strategies has led to the opposite extreme; human athletes force themselves to consume beverages early in the course of endurance competition well before thirst is perceived. Although such fluid replacement practices are generally beneficial, excessive consumption of water or electrolyte-poor "sports drinks" has been implicated as a contributing factor to development of clinical hyponatremia or "water intoxication" in some human endurance athletes.[84, 85]

At present, most human sports drinks consist of 4% to 10% carbohydrate solutions (containing glucose, sucrose, fructose, or glucose polymers) and have sodium concentrations of 0 to 25 mmol/L. Higher carbohydrate concentrations (>10%) appear to decrease gastric-emptying rates, and beverages with tonicities exceeding that of plasma delay fluid absorption and may transiently exacerbate dehydration by initially pulling water into the lumen of the small intestine.[81] A general problem with many available sports drinks is that the ratio of glucose to sodium is in excess of 12:1.[31, 81] In contrast, maximal water absorption appears to occur with lumenal ratios in the range of 1:2 to 2:1, because the mucosal channel (transport protein) functions by cotransporting two sodium ions with each glucose molecule.[22, 31] To achieve these ratios, 30 to 110 mmol/L of sodium would be required for absorption of each 1% (10 g/L) of glucose in the replacement solution; however, higher concentrations of sodium would also make the beverages hypertonic. As can be appreciated, the formulation of the ideal sports drink remains a confusing issue and involves a trade-off between several physiologic ideals as well as beverage palatability.[18]

Although substantial depletion of fluid and electrolytes has been recognized for several decades to contribute to fatigue and the development of medical problems in endurance horses,[10, 104, 111] only recently have controlled studies been performed to investigate the effects of administration of fluid and electrolyte replacement solutions in exercising horses.

Intravenous Fluid and Electrolyte Supplementation in Exercising Horses

Although administration of intravenous fluid "jugs" remains a common racetrack practice, an improved understanding of the magnitude of fluid and electrolyte shifts that accompany high-intensity exercise[104] makes administration of 500 to 1000 mL of a polyionic solution difficult to justify in terms of maintenance or restoration of fluid and electrolyte balance. Although a number of other medications may be added to these jugs we are unaware of any reports documenting beneficial effects of such treatments. Further, adverse effects are anecdotically reported, and in a recent report of 21 cases of pulmonary infarction, all horses in the series were racehorses, many of whom had recently raced.[12] Although the authors of this report did not attempt to associate recent medication administration with the development of pulmonary infarction, repeated intravenous medication administration would be a suspected risk factor.

Oral Fluid and Electrolyte Supplementation in Exercising Horses

In addition to daily electrolyte supplementation (discussed above), many horse owners provide even greater amounts of oral electrolytes (in feed or as a paste) to horses competing in hot and humid climates or over long distances. In the first such study of which we are aware, Ralston and Larson[90] administered a commercial electrolyte product to horses competing in a 96-km endurance ride. Although supplemented horses (which received the product the evening before the ride and at the 19- and 50-km veterinary checkpoints) were reported to recover

slightly faster at the 50-km checkpoint, no differences were observed at the end of the ride. The study was complicated by the fact that the unsupplemented group consisted of only three horses (in comparison with the 14 supplemented horses) which finished first, 14th, and last. Further, the commercial supplement contained predominantly amino acids and carbohydrates (50% molasses), and the three doses provided a total of less than 5 g (85 mmol) of sodium chloride. As a consequence, it is impossible to draw any valid conclusions from this study.

In a series of recent studies, Sosa-León et al[110, 110a, 110b] evaluated the effects of administration of oral fluid and electrolyte solutions to resting and exercising horses. In resting horses, the effects of tonicity, glucose concentration, and temperature on absorption and elimination of an oral rehydration solution (ORS) were evaluated 3 hours after induction of an approximately 4% loss of body weight by furosemide administration (1 mg/kg intramuscularly).[110] The volume of ORS administered was equal to the urinary fluid loss (17.5–18.5 L), and the fluids were given via nasogastric intubation as two doses separated by 30 minutes. Neither temperature (isotonic ORS at 5°, 21°, or 37°C) nor inclusion of glucose (isotonic ORS with glucose to sodium ratios of 0:1, 2:1, or 4:1 [using glucose concentrations of 0%, 2.5%, or 3.5%]) had any significant effects on fluid absorption. In the tonicity study, administration of a hypertonic ORS (628 mOsm/kg, sodium concentration of 246 mmol/L) resulted in a further increase (in addition to the furosemide-induced increase) in plasma protein concentration for the initial 2 hours following ORS administration. In contrast, the plasma protein concentration in horses treated with water or an isotonic ORS (314 mOsm/kg) started to decrease by 1 hour following ORS administration. By 3 hours after ORS administration, there were no differences in the plasma protein concentration between the three treatment groups. These findings suggested that plasma volume transiently decreased after administration of the hypertonic ORS likely due to movement of water into the bowel lumen. Although such a fluid shift would be detrimental to the exercising horse, it should be mentioned that these horses were not provided access to water during the study period. Varying ORS tonicity produced expected changes in plasma osmolality and sodium concentrations, which increased with the hypertonic ORS, remained stable with the isotonic ORS, and decreased with water treatment. Importantly, however, the latter decreases measured after water treatment provide strong support for electrolyte inclusion in ORS products in order to minimize the risk of developing hyponatremia, which has also been reported in exhausted endurance horses.[110a]

In their initial exercise study, Sosa-León et al[110a] administered approximately 17.5 L of a hypotonic (230 mOsm/kg) commercial electrolyte solution to six horses via repeated nasogastric intubation (90 minutes prior to exercise). Fluid administration resulted in lower plasma protein, sodium, and bicarbonate concentrations and a higher plasma chloride concentration before and during exercise (90 minutes of treadmill exercise at 30% of maximal oxygen consumption) in comparison with values measured in the same horses during a control run (without fluid administration). Nevertheless, the expansion of plasma volume indicated by the lower plasma protein concentration in fluid-treated horses was not accompanied by differences in weight loss, core body temperature (right atrial blood temperature), or hemodynamic and metabolic responses to exercise. Although the differences were not significant, fluid-treated horses tended to have higher values for heart rate, stroke volume, and cardiac output during the exercise bout. In a subsequent exercise study by the same investigators,[110b] seven horses received approximately 26 L of isotonic fluid (3:1 ratio of sodium chloride to potassium chloride without glucose) prior to performing treadmill exercise (98 minutes at 20%–60% of maximal oxygen consumption) simulating the second day of a 3-day event. Similar to their previous findings, fluid-treated horses had apparent plasma volume expansion (based on lower plasma protein concentrations), higher plasma chloride concentration, and a lower mixed venous pH and bicarbonate concentration compared with when they were exercised without fluid treatment. Differences in thermoregulatory responses (right atrial blood temperature) were not observed, but exercise heart rate was again higher in the fluid-treated horses. The authors also reported that the fluid-treated horses, which received volumes approximating 6% of their body weight, developed diarrhea and suggested that they had probably reached the volume limit of pre-exercise hyperhydration of horses. The finding of higher exercise heart rates in both studies is difficult to interpret, because plasma volume expansion would be expected to produce no change or a decrease in heart rate (assuming that cardiac output is primarily coupled to the metabolic demands of exercising muscle) as has been reported in studies of human subjects.[75, 83, 101] Nevertheless, higher exercise heart rates following hyperhydration may reflect an important species difference between human and equine athletes. If hyperhydration increases the demand for blood flow by the gastrointestinal tract (to absorb the fluid), a greater exercise heart rate (and associated cardiac output) would be expected. In fact, Duren et al[23] reported that exercising ponies had higher values for heart rate, cardiac output, and intestinal blood flow in the fed state compared with when they had been subjected to a 24-hour fast. Decreased blood flow to the intestinal tract would also explain the lower exercise heart rates observed after an overnight fast in the study of Thoroughbreds described above (J.D. Pagan, PhD, personal communication, 1996).

In another recent study comparing the responses of resting and exercising horses to a smaller dose of ORS (4 L of an isotonic solution containing 140 mmol/L of sodium and 70 mmol/L of dextrose [1.25% solution]) or 4 L of water, there was no difference in uptake of the solutions as assessed by the appearance of deuterium in plasma (D.J. Marlin, PhD, personal communication, 1997). Uptake of both ORS and water was apparent within 10 minutes and peaked 30 to 60 minutes after nasogastric intubation, and in the resting study, the decrease in plasma protein concentration and measured increase in plasma volume

were greater for the ORS (attributed to absorption of both water and osmoles into the vascular compartment). When 4 L of the ORS or 4 L of water was administered 30 minutes prior to exercise (20 minutes of walking at 1.7 m/s and 40 minutes of trotting at 3.7 m/s), however, differences in body weight loss (≈4%), plasma volume, plasma osmolality, or plasma concentrations of protein, glucose, and electrolytes were not observed.

A practical limitation of using ORSs in exercising horses is that they should be ingested voluntarily rather than require administration via nasogastric intubation; however, both human and equine athletes experience what has been termed both *voluntary*[56] and *involuntary*[35] dehydration during endurance exercise. Regardless of which term is more appropriate, it refers to the development of a state of 2% to 5% dehydration (in terms of percentage of body weight loss) before individuals develop a sensation of thirst and elect to voluntarily consume water or another ORS.[35, 56] Although the physiologic mechanisms responsible for this dehydration are incompletely understood, a common explanation is that the loss of electrolytes with water (in sweat) leads to isotonic dehydration. Because an increase in plasma osmolality is a more potent stimulus for thirst than hypovolemia, thirst is not triggered until a significant loss of fluid (body weight) occurs. Although voluntary dehydration during exercise has not been well documented in horses, the common observation that endurance horses usually drink little during the first half of a ride supports its occurrence in this species as well. Further, because electrolyte losses in equine sweat may be greater than those in human sweat,[76] it could be hypothesized that horses are more susceptible to the development of isotonic (and voluntary) dehydration.

As horses typically do not drink during the early stages of endurance exercise, electrolyte supplements are often administered as a paste before and during competition. Nyman et al[86] recently studied voluntary drinking in a group of endurance-trained horses. The horses, which had been conditioned to drink salt water at their home stables, were divided into three groups which were offered either water, water after administration of 30 g of sodium chloride as a paste (total of three doses or 90 g during the ride), or salt water (0.9% sodium chloride solution) at multiple stops during a 62-km exercise bout. Differences between the three groups in body weight loss (15–18 kg) and fluid intake (10–13 L) during the ride were not observed; however, plasma sodium concentration increased in the horses administered the salt paste (despite a higher total intake of sodium chloride by the horses that drank saline). Of interest, drinking replaced only 38% to 45% body weight losses in these horses, providing support that voluntary dehydration does occur in equine endurance athletes. During a 3-hour recovery period, fluid intake and body weight recovery were greater in the salt paste and saline groups as compared with the water group, and plasma aldosterone concentration increased only in the water group (suggesting a persistent sodium deficit). These authors concluded that provision of a source of salt (either as a paste or as salt water) during endurance exercise resulted in more rapid restoration of body fluid and electrolyte content after endurance exercise and recommended its use, especially during competition in a multiday event. Based on the mild increase in plasma sodium concentration observed during exercise, these authors cautioned against administration of salt as a paste. This caution was not supported by other data such as decreased performance or drinking during the ride, however, and further study would be required before the common practice of electrolyte administration as a paste should be discouraged.

ORSs have also been used to restore fluid and electrolyte balance and thereby improve recovery from exercise during acclimatization to hot and humid ambient conditions. In a study by Hyyppä et al[57] approximately 8 L of an ORS (an isotonic 0.5% glucose solution containing ≈40 mmol/L of sodium) was administered via nasogastric intubation 30 minutes after completion of a treadmill exercise bout simulating the endurance phase of a 3-day event (competition exercise test [CET]). To study acclimatization, the bout was repeated five times at biweekly intervals under conditions of high heat (28°C) and relative humidity (58%). Further, after the final CET, horses were administered approximately 8 L of water instead of the ORS. Body weight loss during all five CETs was similar (2.8%–3.4%) and, although incomplete, overnight recovery of body weight improved by the third CET. Another response to acclimatization was a progressive increase in plasma volume during the course of the experiment. Rehydration with water rather than with the ORS after the final CET resulted in the lowest value for voluntary water intake during overnight recovery as well as the greatest value for persistent body weight loss on the morning after completion of the CET (2.5%). Plasma aldosterone concentration reached the highest values after overnight recovery after all five CETs, indicating that despite acclimatization responses, pre-exercise fluid and electrolyte status had not been completely restored. Similar findings have also been reported for endurance horses competing in 80- and 160-km rides.[106] In that report, endurance horses that failed to complete the ride were also documented to experience the greatest body weight losses and increases in plasma aldosterone concentration, which is consistent with more severe perturbations of fluid and electrolyte homeostasis.

In another investigation of restoration of fluid and electrolyte balance after exercise, Jansson et al[59] reported that despite a dietary intake of 38 g of sodium chloride per day, urinary sodium excretion was markedly reduced for 2 days following completion of a strenuous exercise test (90% of maximum oxygen consumption) which resulted in an approximate 2% loss of body weight. In contrast, nasogastric administration of 10 L of a 0.9% sodium chloride solution (90 g of sodium chloride) 1 hour before a similar exercise test abolished the subsequent decrease in urinary sodium excretion, indicating that electrolyte administration prior to exercise improved restoration of fluid and electrolyte balance. Coenen et al[17] further investigated the timing of pre-exercise electrolyte supplementation by feeding small horses (mean body weight, 220 kg) a supplement (48% grass meal, 33% sugar beet syrup, 19% sodium chloride) providing 300 mmol or approximately 18 g of sodium (in addition

to a dietary intake of ≈18 g per day) at 1 or 4 hours prior to 2 hours of low-intensity treadmill exercise (3.3 m/s). Body weight loss during exercise (2.0%–2.5%) was not different between the two treatments or in nonsupplemented controls, but heart rate was higher in the horses supplemented 1 hour prior to exercise. More importantly, voluntary water intake during the 4 hours preceding exercise and the 6 hours following exercise was significantly greater for both supplemented groups in comparison with controls. The authors concluded that supplementation 4 hours prior to exercise was preferable because it produced a greater pre-exercise water intake. Nevertheless, further scrutiny of their data suggests that overall retention of the supplemental sodium chloride may have been greatest when it was administered 1 hour prior to exercise due to lesser urinary losses of water and electrolytes.

It warrants mention that the majority of the recent studies investigating the effects of ORSs on fluid and electrolyte status during exercise and recovery were completed as a part of the heroic research effort which culminated in the ability to have horses successfully acclimatize to and compete in the hot and humid conditions accompanying the 1996 Atlanta Summer Olympic Games. Further, the results of these studies are of great benefit to equine athletes competing in many disciplines. They have also laid the groundwork for investigators to address remaining questions. Specifically, although it is of obvious benefit to administer supplemental electrolytes to horses performing exercise resulting in a body weight loss of 2% or greater, the need for a carbohydrate source in an equine ORS has not been clearly demonstrated. Studies to date have not shown improved absorption of carbohydrate-electrolyte solutions over plain electrolyte solutions. In contrast, an additional carbohydrate source during prolonged exercise may have glycogen-sparing effects and may delay fatigue. For example, Farris et al[25] recently reported that an intravenous glucose infusion prolonged run times in Standardbred horses performing low-intensity treadmill exercise. Similarly, pre-exercise administration of 3 L of a popular carbohydrate-electrolyte supplement (Perform'N Win; Buckeye Feed Mills, Dalton, OH) is advertised to prolong treadmill run time by 23%. In contrast, another supplement prepared specifically for the 1996 Summer Olympic Games (Summer Games Electrolyte; Kentucky Equine Research, Versailles, KY) contains no carbohydrate source. Whether addition of a carbohydrate source is of benefit to an endurance horse but not to a 3-day event horse remains an unanswered question. Next, it is not clear whether the common practice of administering electrolytes as a hypertonic paste is detrimental or not. The practice seems reasonable as long as horses have access to water and voluntarily drink. Use of these pastes may occasionally exacerbate fluid and electrolyte disturbances in endurance horses when they fail to drink or have reduced intestinal blood flow, however.

In addition to providing a source of replacement electrolytes, with or without carbohydrates, an ideal formulation would also stimulate voluntary water intake. Human athletes can force themselves to drink in moderation early in the course of endurance exercise. Some horses have been anecdotally reported to learn to drink, and recent studies have shown that they can be trained to drink saline at concentrations of up to 0.9%.[53, 60, 62] Nevertheless, there also appears to be considerable variation between horses' drinking habits during and following exercise, with some horses always described as poor drinkers.[62] In an attempt to stimulate voluntary water intake, one of the authors (HCS) has recently been investigating the effects of administering a glycerol-containing ORS to horses. Glycerol is a natural metabolite which, in addition to having caloric value, appears to rapidly enter all body fluid compartments and improve hydration status in resting humans.[28, 92] Thus, when administered as an oral hypertonic solution, it results in minimal fluid movement into the bowel in comparison with an electrolyte solution of similar tonicity and is accompanied by a rapid increase in plasma osmolality (the major stimulus for drinking). For example, in the hour after nasogastric administration of glycerol (1 g/kg) in 8 L of 0.9% of sodium chloride (tonicity, ≈1200 mOsm/kg) to four euhydrated horses, plasma osmolality increased by approximately 10 mOsm/kg and horses voluntarily drank an additional 5 L. In contrast, voluntary drinking was not observed after nasogastric administration of either glycerol (1 g/kg) in 8 L of water or 8 L of 0.9% of sodium chloride.[107] Further, in contrast to electrolyte solutions (which are largely limited to absorption and distribution into the extracellular fluid compartment), glycerol solutions can increase extracellular and intracellular water content. As a consequence, glycerol solutions are less rapidly eliminated via renal excretion than electrolyte solutions.[28, 92] In horses, renal water retention was enhanced during the 5-hour study period following administration of the glycerol-saline ORS.[107] Administration of glycerol prior to exercise has been reported to improve thermoregulatory responses during exercise in a hot environment[72] and to prolong exercise time in cyclists.[79] Although promising, potential problems with glycerol are plasma hypertonicity and excessive intracellular accumulation leading to cell swelling. Some human athletes have complained of headache following glycerol ingestion, but adverse effects have not been observed in preliminary treadmill studies during which horses received a total of 3 g/kg of glycerol (H.C. Schott II, DVM, PhD, unpublished observations, 1997).

Although this discussion of oral fluid and electrolyte supplementation has focused almost exclusively on fluid and electrolyte supplementation of horses performing endurance exercise, it warrants mention that manipulation of fluid and electrolyte status prior to high-intensity racing exercise may also affect performance. As horses are not likely to absorb significant amounts of water and electrolytes from the ingesta during bouts of intense exercise lasting only a few minutes, manipulations that induce a 2% to 3% loss of body weight (e.g., decreasing intestinal bulk by withholding hay or decreasing body fluid by furosemide administration or withholding water) have been suggested to enhance performance. Mild hypohydration has recently been suggested to have less obvious detrimental effects on performance, however. For example, low levels of

dehydration (<3%) have been shown to impair high-intensity rowing and cycling performance, possibly due to alterations in cellular metabolism and glycogen utilization.[7, 118]

MEDICATIONS AFFECTING FLUID AND ELECTROLYTE STATUS

Sodium Bicarbonate

Sodium bicarbonate administration to horses alters body fluid, electrolyte, and acid-base status. Along with changes in other variables, sodium bicarbonate induces dose-dependent changes in serum sodium, potassium, and bicarbonate concentrations and alters renal function.[70, 95, 96] These effects are first detectable within 30 minutes of administration and may persist for hours. In this section, we will review the effects of sodium bicarbonate administration on the fluid and electrolyte status of resting and exercising horses. The effect of, or potential for, sodium bicarbonate to affect athletic performance has been addressed elsewhere[40, 71, 104] and will not be repeated here.[74]

Effects of Sodium Bicarbonate on Acid-Base Status

Ingestion of sufficient sodium bicarbonate will induce a metabolic alkalosis, the extent of which is related to some extent to the amount of sodium bicarbonate administered and the route by which it is administered.[32, 34, 38, 45, 66, 70, 95] Oral administration of sodium bicarbonate to horses results in increases in blood pH and bicarbonate concentration which are dependent on the amount of sodium bicarbonate given. Lower doses (0.25–1.0 g/kg of body weight) cause dose-dependent increases in blood pH and bicarbonate concentration.[32, 70, 95] Oral doses of 1.0 and 1.5 g/kg of body weight induce a similar degree of alkalemia (Fig. 1).[95] The reason for this plateau in the dose-response relationship is unknown, but one could speculate that it is related to limited absorption of bicarbonate from the gastrointestinal tract. It therefore appears that a dose of sodium bicarbonate of 1 mg/kg induces the maximum change in blood pH and bicarbonate concentration for a given sodium and bicarbonate load and that larger doses do not induce a more severe alkalemia.

The time to peak change in blood pH and bicarbonate concentration after oral administration of sodium bicarbonate is about 4 hours, with a range of 3 to 6 hours, regardless of dose.[32, 70, 95] A significant alkalemia is apparent within 1 hour of oral administration of sodium bicarbonate and persists for a variable period of time, depending, in part, on the dose. In horses denied access to water for 12 hours, sodium bicarbonate at doses of 0.25 to 1.5 g/kg increased blood pH for at least 12 hours, although after 12 hours, the effect was much less marked with the lower doses.[95] When water was freely available to horses after sodium bicarbonate administration (0.3, 0.5, and 0.6 g/kg), blood pH declined rapidly after 12 hours to values at 24 hours after dosing that were not different from values before dosing.[32, 70] Horses allowed access to water

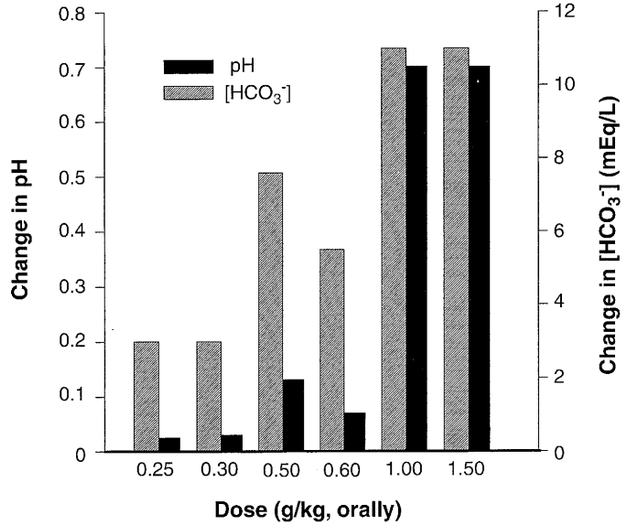

Figure 1. Effect of varying dose of sodium bicarbonate on blood pH and bicarbonate. ($[HCO_3^-]$) concentration in horses. (*Data from* Greenhaff PL, Snow DH, Harris RC, et al: Bicarbonate loading in the Thoroughbred: Dose, method of administration and acid-base changes. Equine Vet J 9(suppl):83, 1990. Lloyd DR, Rose RJ: Effects of sodium bicarbonate on fluid, electrolyte, and acid-base balance in racehorses. Br Vet J 151:523, 1995. Rivas LJ, Hinchcliff KW, Kohn CW, et al: Effect of sodium bicarbonate administration on blood constituents of horses. Am J Vet Res 58:658, 1997)

can excrete the sodium and bicarbonate load and restore normal blood pH and bicarbonate concentration 24 hours after oral administration of sodium bicarbonate at doses up to 0.6 g/kg. Whether or not a similar situation occurs in horses administered larger doses of sodium bicarbonate or in those denied access to water is unknown.

Effect of Sodium Bicarbonate on Serum Electrolyte Concentrations

Administration of sodium bicarbonate at a dose rate of 0.3 g/kg (3.9 mmol of sodium per kilogram) represents a quantity of sodium equal to approximately 12% of extracellular sodium. Not surprisingly then, ingestion of sodium bicarbonate (0.25–1.5 g/kg) increases serum osmolality, and the increase is largely due to an increase in serum sodium concentration.[34, 45, 95] Serum potassium concentrations decrease[34, 95] and serum concentrations of chloride have been reported to be unaffected by or to decrease after sodium bicarbonate administration.[34, 37, 70, 95]

Changes in serum electrolyte concentrations are dependent upon the dose of sodium bicarbonate and on access to water. Increasing doses of sodium bicarbonate result in higher serum sodium concentrations up

to doses of 1 g/kg. Doses of sodium bicarbonate of 1.0 and 1.5 g/kg to horses denied access to water resulted in similar increases in serum sodium concentration. The increases in serum sodium concentration at doses of 0.25 to 0.6 g/kg peak at approximately 4 to 6 hours, whereas higher doses in horses denied access to water resulted in serum sodium concentrations that peaked at 6 hours and remained at approximately these values until 12 hours (the end of the observation period).[95]

Serum (or plasma) osmolality increases after sodium bicarbonate administration as a result of the sodium bicarbonate-induced increase in serum sodium concentration.[70, 95] The effect of sodium bicarbonate on serum osmolality and sodium concentration is attenuated if horses are allowed access to water.[37, 70]

Effect of Sodium Bicarbonate on Plasma Volume

Serum protein concentrations of horses administered sodium bicarbonate (0.5 or 0.6 g/kg) and allowed access to water are lower than those of control horses,[34, 70] suggesting that sodium bicarbonate increased plasma volume. Nevertheless, there was no detectable effect of sodium bicarbonate (1 g/kg) either with or without water on plasma volume as measured by Evan's blue dye dilution.[37] Similarly, in splenectomized horses, in which changes in plasma volume can be readily and unequivocally detected through changes in hematocrit and hemoglobin concentration, there was no effect of oral sodium bicarbonate (1 g/kg) or sodium chloride (0.7 g/kg) administration on plasma volume (K.W. Hinchcliff, BVSc, MS, PhD, unpublished observation, 1993).

Effects of Sodium Bicarbonate on Renal Function

The administration of large quantities of sodium as sodium bicarbonate results in an increase in urine production (Fig. 2), a decrease in urine concentration, and an increase in urine pH.[70, 96] These changes occur both in horses denied access to water and in horses provided water after dosing and likely reflect a homeostatic response to the hypernatremia and alkalosis in which the horse attempts to excrete a sodium and bicarbonate load and to conserve plasma volume.

The decrease in urine osmolality in the presence of an increase in urine sodium concentration noted with 1.0- and 1.5-g/kg doses of sodium bicarbonate is associated with an increase in electrolyte free-water resorption.[96] Because the changes in sodium excretion are not associated with an increase in glomerular filtration rate, the fractional clearance of sodium increases as the dose of sodium bicarbonate increases.[96] The amount of sodium excreted in the urine of treated horses after sodium bicarbonate administration is significantly greater than that in untreated horses.[70, 96]

Apparently in an attempt to restore a normal acid-base status, horses administered sodium bicarbonate excrete a more alkaline urine than horses treated with water.[96] The increase in urine pH is attributable

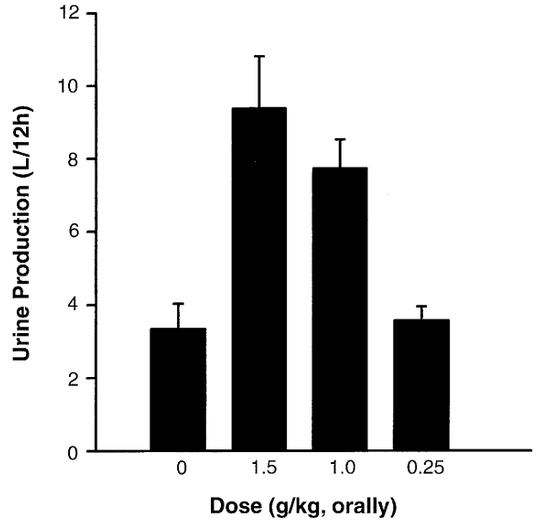

Figure 2. Effect of sodium bicarbonate dose on urine production of horses (mean ± SE). (*Data from* Rivas LJ, Hinchcliff KW, Kohn CW, et al: Effect of sodium bicarbonate administration on renal function of horses. Am J Vet Res 58:664, 1997)

to an increase in urine bicarbonate concentration and anion gap.[96] The concentration of bicarbonate in urine continues to increase over a 12-hour period in horses administered 1.0 or 1.5 g/kg of sodium bicarbonate and denied access to water.[96] The absolute increases in urine pH may be quite small (0.6 pH units), however, because of the normally alkaline urine of horses.

Mechanism of Alkalosis

Classic acid-base theory, based on the Henderson-Hasselbalch equation in which the pH of a solution is calculated as follows:

$$pH = pKa + \log([base/acid])$$

where *pKa* is the ionization or dissociation constant and *[base]* and *[acid]* are the concentrations of a weak acid and its associated base, explains the increase in blood pH after sodium bicarbonate administration by an increase in blood bicarbonate concentration. Mathematically, this relationship can be represented as follows:

$$pH = 6.10 + \log([HCO_3^-]/0.03\ P_{CO_2})$$

where *6.10* is the pKa in plasma at 37°C, $[HCO_3^-]$ is the concentration of bicarbonate, and P_{CO_2} is the partial pressure of carbon dioxide in plasma. For example, a plasma bicarbonate concentration of 24 mmol/L

and a P_{CO_2} of 40 mm Hg will yield a pH of 7.40. An increase in the bicarbonate concentration to 30 mmol/L without a change in the P_{CO_2} will increase the pH by 0.09 U to 7.49.

Quantitative acid-base theory states that changes in pH are determined by changes in the relative concentrations of strong ions, the concentration of weak acids, and the P_{CO_2} of a solution.[113] For plasma, the principal strong ions are sodium, chloride, potassium, and lactate [La^-], and protein is the significant weak acid. The quantitative relationship among the strong ions is termed the *strong ion difference* (SID) and is calculated as follows:

$$SID = [Na^+] + [K^+] - [Cl^-] - [La^-]$$

Increases in the SID are associated with a higher pH; conversely, a reduction in the SID is associated with a lower pH given that the P_{CO_2} and protein concentration are constant.[113] The acid-base response to sodium bicarbonate ingestion can be explained using the quantitative approach. Ingestion of sodium bicarbonate increases plasma sodium concentration, and concentrations of chloride, lactate, and potassium remain unchanged, thus:

$$SID_{(normal)} = 140 + 4 - 98 - 1 \ (= 45 \text{ mEq/L})$$

and

$$SID_{(bicarbonate)} = 152 + 4 - 98 - 1 \ (= 57 \text{ mEq/L})$$

Effects of Sodium Bicarbonate During Running

Sodium bicarbonate alters the acid-base, plasma lactate, and muscle metabolite responses to exercise. The magnitude of these changes varies with the dose of sodium bicarbonate used, the type of exercise (including duration and intensity), and the site of blood sampling (arterial, arterialized venous, peripheral venous, or mixed venous). Nevertheless, there are some consistent changes associated with sodium bicarbonate administration.

At similar work intensities, blood pH and bicarbonate concentrations are higher in animals or human beings administered sodium bicarbonate than in those not treated.[33, 64, 66, 71] This occurs because bicarbonate-induced alkalosis does not increase the rate of appearance of hydrogen ions in the plasma during exercise.[64] At exhaustion, however, the mixed venous blood pH of horses is unaffected by sodium bicarbonate,[45] suggesting that the higher initial pH in horses receiving bicarbonate increases the quantity of hydrogen ions buffered. Arterial pH at fatigue after exercise at 110% of maximum oxygen consumption is higher after sodium bicarbonate administration than after saline administration[71]; however, this may be a result of the acidifying effect of sodium chloride as values after water (or control) treatment are not reported.[71] Sodium bicarbonate administration increases plasma or blood lactate concentrations over those of untreated horses or horses treated with sodium chloride during submaximal or exhaustive exercise.[41, 45, 66, 71]

Adverse Effects

Gastrointestinal discomfort is frequently reported in human beings who ingest large quantities of sodium bicarbonate (>0.4 g/kg) or insufficient water and has been reported to occur in horses.[96] Theoretically, cardiac arrhythmias may develop secondary to the serum electrolyte abnormalities encountered after sodium bicarbonate ingestion, but sodium bicarbonate–induced arrhythmias are not reported in the horse. The concurrent administration of furosemide and sodium bicarbonate to horses induces a profound metabolic alkalosis and severe serum electrolyte abnormalities[26] and should be avoided. Fatal aspiration pneumonia has been observed in horses after the inadvertent intratracheal administration of sodium bicarbonate solution.

Furosemide

Furosemide is a diuretic commonly used in the prophylaxis of exercise-induced pulmonary hemorrhage in racehorses in North America and other parts of the world. In the United States, it is common for well over one half of all Thoroughbred racehorses entered to race on a given day to be administered furosemide before racing according to the Daily Racing Form. This widespread use of furosemide has prompted numerous investigations of its pharmacology in horses, and much of this work has been reviewed elsewhere.[29, 43, 44, 50]

Serum Electrolyte Concentration

Furosemide induces a profound and rapid diuresis, natriuresis, and chloruresis in horses[1, 27, 63] which results in a significant reduction in plasma and blood volume, serum chloride, potassium and hydrogen ion concentrations, and total body sodium concentration. These effects are achieved through inhibition of the reabsorption of sodium and chloride in the thick ascending limb of the loop of Henle.[119] This effect of furosemide is dependent upon normal prostaglandin metabolism within the kidney and is inhibited by the prior administration of nonsteroidal anti-inflammatory drugs, including phenylbutazone.[51, 119]

The losses of electrolytes in urine alter body composition and are evident as reduced plasma concentrations of potassium, chloride, calcium, and hydrogen, with unchanged sodium concentrations, following furosemide administration to horses.[27, 80, 117, 120] The slight increase in blood pH after furosemide administration can be attributed to furosemide-induced hypochloremia and to a subsequent increase in the blood bicarbonate concentration.[39, 44] The furosemide-induced increase in pH, bicarbonate and, presumably, total carbon dioxide concentration may be

problematic for testing, requiring assessment of the acid-base status of horses similar to testing for administration of sodium bicarbonate.

Urine Production and Composition

The effect of furosemide on urine production is both dose and route dependent, with larger and intramuscular doses inducing the production of greater quantities of urine.[117] Urine production during the 4 hours after furosemide administration (1 mg/kg) to horses averages 25 mL/kg of body weight and is produced at rates of up to 270 mL/min.[47, 63] Urine produced immediately after furosemide administration is isosothenuric, it has sodium and chloride concentrations higher and potassium concentrations lower than those in the urine before furosemide administration.

Effect of Furosemide on Blood Volume

The furosemide-induced diuresis results in a reduction in the plasma volume of resting horses denied access to water.[47, 80] The furosemide-induced reduction in plasma and blood volume is likely important in mediating the hemodynamic effects of furosemide, including a reduction in pulmonary artery, pulmonary wedge, and right atrial pressure during exercise.[73, 87] There is a significant relationship between right atrial pressure and blood volume of splenectomized horses (Fig. 3).[94] A reduction in blood volume is associated with a reduction in right atrial pressure, and subsequent restoration of blood volume increases right atrial pressure.[94] These changes were interpreted as indicating that the predominant mechanism by which furosemide reduces right atrial pressure is through a reduction in intravascular volume. Further evidence to support this hypothesis was provided by the observation that restoration of the plasma volume of intact horses administered furosemide restored the normal hemodynamic responses to exercise.[42] In that study, furosemide reduced right atrial and pulmonary artery pressures of horses during an exercise test, and administration of polyionic fluids to the horses 3 hours after furosemide administration restored these pressures as well as the atrial natriuretic peptide concentration to values similar to those of untreated horses.[42] In anesthetized horses with ligated ureters (to prevent the loss of urine and hence plasma volume depletion by furosemide), furosemide did not reduce pulmonary artery or right atrial pressures as it did in anesthetized horses with intact ureters.[49] Together, these results provide persuasive evidence that furosemide exerts its hemodynamic effect through blood volume depletion.

The hemodynamic effects of furosemide may be important in mediating any effect of furosemide on the incidence or severity of exercise-induced pulmonary hemorrhage given the recent demonstration that high pulmonary vascular pressures and alveolar rupture may be involved in the pathogenesis of this disorder.[88] Nevertheless, the reduction in blood and plasma volumes of horses caused by furosemide is also

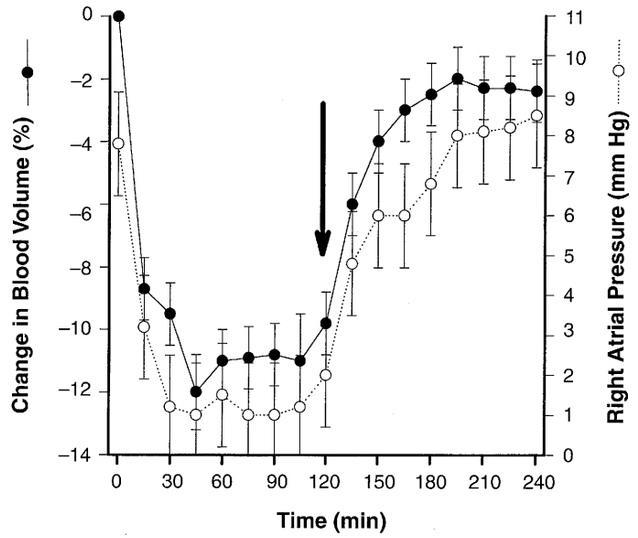

Figure 3. Time course of effect of furosemide, administered at time 0 min, on right atrial pressure (open circles) and blood volume. (expressed as a percent change, closed circles) in five splenectomized horses. (*Data from* Rivas LJ, Hinchcliff KW: Effect of furosemide and subsequent intravenous fluid administration on right atrial pressure of splenectomized horses. Am J Vet Res 58:632, 1997)

inextricably linked to a reduction in body weight, and there is recent evidence that this reduction in body weight may be related to an ergogenic effect of furosemide.[4, 46, 48]

Acetazolamide

Acetazolamide is a carbonic anhydrase inhibitor used in humans and horses for the treatment of hyperkalemic periodic paralysis.[5, 93, 112] The dosage used for treatment of hyperkalemic periodic paralysis in horses (2.2 mg/kg orally twice daily) is much less than the dosage required to induce severe acidosis (30 mg/kg orally twice daily), although, to our knowledge, the effect of the lower dose on the acid-base status of horses has not been reported. Acetazolamide induces a hyperchloremic acidosis in dogs and horses, and these effects are likely related to inhibition of carbonic anhydrase. The effects of acetazolamide are characterized by decreases in blood pH and base excess bicarbonate and potassium concentrations.[98, 99] Serum chloride concentrations are higher after acetazolamide administration.

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Address reprint requests to
Harold C. Schott II, DVM, PhD
Department of Large Animal Clinical Sciences
D–201 Veterinary Medical Center
Michigan State University
East Lansing, MI 48824–1314

 0749–0739/98 $8.00 + .00

THE EXHAUSTED HORSE SYNDROME

Jonathan H. Foreman, DVM, MS

All muscular work if continued long enough results eventually in fatigue. In some events such as power events like weight lifting, recovery from fatigue is quite rapid, and work can soon be resumed. In other events such as endurance running or riding, this fatigue is different in that it cannot be rapidly overcome. It can sometimes actually result in severe physiologic changes which may become life threatening. The onset or development of endurance fatigue is particularly sensitive to the effects of increased ambient heat and humidity.

HISTORY AND RISK FACTORS

Endurance exercise as defined by exercise physiologists includes all types of exercise in which horses work at submaximal speeds for a number of hours. Endurance exercise is typified by competitions such as endurance races and competitive trail rides. Endurance races in North America range from 25 miles to more than 100 miles, with the most common competitive distance being 50 miles. The exhausted horse syndrome is not, however, associated only with true endurance riding. Other competitive events such as 3-day eventing or combined training involve sufficient endurance work so that they may also lead to exhaustion. Pleasure riding for lengthy periods of time such as trail riding, backpacking, mountainous hunting, fox hunting, and bird hunting by horseback may also lead to endurance-related exhaustion.

The onset of exhaustion associated with endurance exercise is exac-

From the Department of Veterinary Clinical Medicine, University of Illinois, College of Veterinary Medicine, Urbana, Illinois