Exercise-associated hypotension in Alaskan sled dogs: urinary and hormonal responses

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Hinchcliff, K. W., G. A. Reinhart, J. R. Burr, and R. A. Swenson. Exercise-associated hypotension in Alaskan sled dogs: urinary and hormonal responses. J. Appl. Physiol. 83(3): 824–829, 1997.—Exercise-associated hypotension occurs in horses and humans, both species that sweat, and in sled dogs, which do not sweat. To investigate the mechanism of exercise-associated hypotension in sled dogs, we measured water turnover, serum electrolyte concentrations and osmolality, plasma renin hormone concentrations, and urine composition of 12 fit Alaskan sled dogs before, during, and after a 490-km sled dog race (Ex group). Water turnover and serum electrolyte concentrations were measured in six similarly fit dogs that did not run (Sed group). Water turnover was significantly larger (P < 0.001) in Ex [190 ± 19 (SD) ml·kg⁻¹·day⁻¹] than in Sed dogs [51 ± 13 ml·kg⁻¹·day⁻¹]. There were significant (P < 0.001) decreases in serum sodium concentration (from 148.6 ± 2.8 to 139.7 ± 1.9 mmol/l) and osmolality (from 306 ± 9 to 296 ± 5 mosmol/kgH₂O) of Ex, but not Sed, dogs during the race. Plasma concentrations of arginine vasopressin decreased, whereas aldosterone and plasma renin activity increased significantly (P < 0.01) during the race. Urine osmolality was unchanged, whereas urine sodium, potassium, and chloride concentrations decreased significantly (P < 0.05) and urine urea concentration increased (P = 0.06). These results demonstrate increased water turnover associated with hypotension and renal sodium conservation with maintained high urine osmolality in exercising Alaskan sled dogs.

Hypotension, a reduction in serum sodium concentration to abnormally low levels (25), occurs during or after prolonged exercise in humans, horses, and sled dogs (2, 4, 9, 10, 12, 22, 23, 27). Symptomatic hypotension of human athletes is related to the high metabolizable energy intake of these dogs is attributable to solute diuresis and urine sodium loss mandated by the large solute (urea) intake related to the high metabolizable energy intake of racing Alaskan sled dogs (13), although an increase in TBW cannot be excluded as a factor contributing to the hypotension.

HYPERSONTREMIA, a reduction in serum sodium concentration to abnormally low levels (25), occurs during or after prolonged exercise in humans, horses, and sled dogs (2, 4, 9, 10, 12, 22, 23, 27). Symptomatic hypotension is associated with very low serum sodium concentrations (<130 mmol/l), whereas lesser reductions in serum sodium concentration in humans, horses, and dogs are not associated with clinical signs (10–12, 14, 23). Symptomatic and asymptomatic hypotension in human athletes is typically associated with participation in races of >4-h duration (11, 27), whereas in horses symptomatic and asymptomatic hypotension occurs during or immediately after endurance racing (50–100 miles) or after participation in a 3-day event (4, 22, 23). Hypotension without associated clinical signs is reported in dogs competing in the 1,100-mile Iditarod Trail sled dog race and in dogs competing in shorter races (2, 14).

The pathogenesis of symptomatic exercise-associated hypotension in human athletes is debated (11, 16, 21). Symptomatic exercise-associated hypotension in humans is attributed to either water intoxication secondary to ingestion of large quantities of hypotonic fluids (10, 16) or to a disproportionately large loss of sodium, compared with net losses of body water, during running (11). Symptomatic hypotension of human runners is associated with increased total body water (TBW) (16). In contrast, hypotension after exercise in clinically normal horses is believed to be attributable to large losses of sodium with a lesser reduction in TBW (4, 22). Regardless of the role of each of these mechanisms, exercise by humans and horses is associated with a reduction in body sodium content, both of individuals that develop hypotension and those that do not, because of losses of large quantities of sodium in sweat (e.g., 155 mmol sodium and 4.1 liters sweat during a 4-h treadmill run by humans and 5.9 mmol sodium and 37 liters sweat during a 7-h run by horses) (5, 16, 19, 25). Exercise-associated hypotension is unexpected in dogs because they do not sweat appreciably and, therefore, loss of significant quantities of sodium by this route is unlikely.

To our knowledge, apart from our previous reports (2, 14), the development of exercise-associated hypotension has not been reported in species that thermoregulate during exercise by mechanisms other than evaporation of sweat or in species that exercise in frigid conditions. Here we document the development of hypotension in a race (serum sodium concentration <140 mmol/l; see Ref. 6) with renal sodium and potassium conservation and maintenance of high urine osmolality in Alaskan sled dogs during prolonged exercise. We speculate that exercise-associated hypotension in these dogs is attributable to solute diuresis and urine sodium loss mandated by the large solute (urea) intake related to the high metabolizable energy intake of racing Alaskan sled dogs (13), although an increase in TBW cannot be excluded as a factor contributing to the hypotension.

MATERIALS AND METHODS

Experimental design. Blood and urine samples were collected from dogs before, at the midpoint, and at the finish of a 490-km sled dog race. Water turnover during the race was measured by using deuterium oxide. Another group of dogs did not participate in the race but had blood collected and water turnover measured coincident with that of dogs participating in the race.

Dogs. Seventeen fit Alaskan sled dogs were studied (12 males, 5 females, weighing 26.7 ± 2.9 kg, 2–7 yr old) that were competing in the 1994 Copper Basin 300. The dogs were all from the same kennel and had completed 1,200 miles of training during the previous 4 mo. Twelve dogs (Ex group) were administered deuterium oxide (0.25 mg/kg, 99.9%,
deuterium enrichment was measured by a commercial labora-

tory, Hoffman LaRoche, Nutely, NJ), and osmolality. Serum

potassium, chloride, calcium, phosphate, creatinine, and total

serum or plasma. Samples were prevented from freezing before separation of

containing EDTA (Vacutainer, Becton Dickinson). Blood

(1,500 g) after centrifugation of the blood (1,500 g for 30 min), and we assume that most of their water was

supplied with feed. The dogs were fed the above diet as a

running, and we assume that most of their water was

eliminated from the study because of lameness after

completing ~300 km of the race.

average temperature during the 3 days of the race

was –36, –34, and –27°C (minimum temperatures of

–40, –40, and –32°C), with wind speed of 10 km/h on
each day. The dogs completed the 490-km race in 65 h at
an average speed of 7.5 km/h. Two labeled dogs were
eliminated from the study because of lameness after completing ~300 km of the race.

Water turnover. TBW of the Ex dogs was 18.7 ± 2.2

liters (0.69 ± 0.04 ml/kg), which was not significantly different (P > 0.05) from that of the Sed dogs (15.6 ± 4.7
liters, 0.68 ± 0.1 ml/kg). Water turnover was signifi-
cantly different (P < 0.001) between Ex (5.0 ± 1.8 l/day, 190 ± 19 ml·kg⁻¹·day⁻¹) and Sed (1.13 ± 0.3 l/day, 51 ± 13 ml·kg⁻¹·day⁻¹) groups.

Serum constituents. There were significant (P < 0.001) decreases during the race in serum sodium (6%),
potassium (20%), calcium (8%), and total protein (14%) concentrations and osmolality (3.4%) of Ex dogs (Fig. 1,
Table 1). There were no significant (P > 0.05) changes in these variables in Sed dogs. Serum creatinine and
chloride concentrations did not change significantly (P > 0.05) in either Ex or Sed dogs. Serum urea
nitrogen concentrations increased (30%, P < 0.05) during the race in Ex but not in Sed dogs (Table 1).

Plasma concentrations of AVP decreased significantly (48%, P < 0.001), Aldo and plasma renin activity
increased significantly (190 and 220%, respectively,
P < 0.01), and ANP was unchanged (P = 0.08) during the race (Figs. 1–2, Table 2).

Urine. Urine osmolality was unchanged during the race (P = 0.5), whereas decreases in urine sodium (73%), potassium (57%), and chloride (79%) concentrations of Ex dogs were significant (P < 0.05) (Table 3). There was a trend for urine urea nitrogen concentration to increase during the race (22%, P = 0.06). Fractional clearance of sodium and chloride decreased significantly (P < 0.05) during the race (Fig. 2, Table 3).

Diet. Ensuring collection of complete samples of a representative diet proved to be problematic because of the severe weather conditions. However, the samples collected indicated a minimum intake by dogs of 8,200 mg of sodium, 17 g of potassium, and 960 g of protein during the race.

DISCUSSION

This study confirms the development of hyponatremia during prolonged exercise by sled dogs and demonstrates that this phenomenon is associated with large water turnover, renal sodium conservation, and high urine osmolality. Urine osmolality was maintained during the race at its initial high concentration, despite a marked reduction in urine sodium and potassium concentrations, by an increase in urine urea concentration. The increase in urine urea concentration likely reflected the increased protein intake and, hence, renal solute load mandated by the dogs’ large energy requirements while racing (13).

Exercise-induced hyponatremia can be attributed to one or more of several mechanisms including (21, 27) 1) a reduction in total body exchangeable cation content, 2) an increase in TBW, or 3) a permutation of these changes (for instance, a reduction in total exchangeable cation content with a lesser reduction in TBW). It is assumed that the empirical relationship between serum sodium concentration ([Na]s), total body contents of exchangeable sodium and potassium (Na e and K e, respectively), and TBW (7), i.e.

\[ [Na]_s = \frac{(Na_e + K_e)}{TBW} \]

demonstrated for humans applies to dogs as well (18).

Human athletes with symptomatic hyponatremia have an increased TBW (estimated from excess fluid excretion) at the time that hyponatremia is diagnosed (16). Thus hyponatremia in these symptomatic individuals with serum sodium concentrations <130 mmol/l is likely in large part dilutional and attributable to the intake of large volumes of sodium-poor fluid while running (21). We cannot exclude a relative water excess as a cause of the hyponatremia observed in these dogs, as a small (~800-ml) increase in TBW could account for the observed decrease in serum sodium concentration if

Table 1. Serum constituents of 12 Alaskan sled dogs before, during, and after a 490-km sled dog race and of 6 dogs that did not run

<table>
<thead>
<tr>
<th>Variable</th>
<th>Prerace</th>
<th>Midrace</th>
<th>Postrace</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Ex</td>
<td>Sed</td>
<td>Ex</td>
</tr>
<tr>
<td>Sodium concn, mmol/l</td>
<td>148.6 ± 2.8</td>
<td>146.8 ± 2.7</td>
<td>144.9 ± 2.7*</td>
</tr>
<tr>
<td>Potassium concn, mmol/l</td>
<td>4.8 ± 0.2</td>
<td>4.4 ± 0.3</td>
<td>4.7 ± 0.2</td>
</tr>
<tr>
<td>Chloride concn, mmol/l</td>
<td>115.7 ± 2.2</td>
<td>115.3 ± 2.8</td>
<td>114.7 ± 3.2</td>
</tr>
<tr>
<td>Calcium concn, mmol/l</td>
<td>2.4 ± 0.0</td>
<td>2.4 ± 0.1</td>
<td>2.2 ± 0.1*</td>
</tr>
<tr>
<td>Total protein concn, g/l</td>
<td>63 ± 3</td>
<td>63 ± 4</td>
<td>58 ± 4*</td>
</tr>
<tr>
<td>Urea nitrogen, mmol/l</td>
<td>8.7 ± 3.0</td>
<td>5.4 ± 7.1</td>
<td>11.6 ± 13.1*</td>
</tr>
<tr>
<td>Creatinine concn, µmol/l</td>
<td>61.9 ± 17.7</td>
<td>55.7 ± 13.7</td>
<td>61.9 ± 17.7</td>
</tr>
<tr>
<td>Osmolality, mosmol/kgH2O</td>
<td>306.2 ± 9.3</td>
<td>305.8 ± 7.6</td>
<td>303.4 ± 9.5</td>
</tr>
</tbody>
</table>

Values are means ± SD. Ex, dogs that participated in the race (n = 12 except n = 10); Sed, sedentary fit dogs (n = 6). Prerace, Midrace, Postrace values measured before, during, and after the race, respectively. *P < 0.05 vs. Prerace value for that group.
of electrolytes and urea nitrogen and urine osmolality have been suggested as causes of exercise-associated hyponatremia. Ingestion of inappropriately large quantities of water or impaired renal function have been implicated as causes of this disorder. An increased free water excretion. Ingestion of inappropriately large quantities of water in the body and may be viewed as a failure in free sodium concentration indicates a relative excess of solute in the plasma that may have increased extracellular volume. The presence of an unmeasured solute in the plasma that may have increased extracellular volume was excluded by the correlation between plasma Aldo concentrations (7), and serum protein concentration could be a decrease in total body exchangeable cation content. Before the race, dogs had low plasma Aldo concentrations and produced concentrated urine that contained substantial quantities of sodium (96 mmol/l) and potassium (157 mmol/l). Renal conservation of sodium during the race was indicated by the significant reductions in fractional clearance of sodium and urine sodium concentration and by an increase in plasma Aldo concentration (Fig. 1). The decrease in the sum of urine sodium and urine potassium concentrations from values greater than serum sodium concentration before the race to values below serum sodium concentration at the end of the race indicates marked renal cation conservation and could be interpreted as a change from negative free water clearance before the race to positive free water clearance at the end of the race, and would be appropriate for the observed decline in serum osmolality and AVP concentration (Fig. 2). In contrast to these dogs, renal sodium conservation and an increase in free water clearance are associated with a marked decrease in urine osmolality in humans during prolonged exercise (10, 17). Similarly, urine osmolality of horses decreases during prolonged running (25).

The large urine volume apparently mandated by the dogs' diet imposes an obligatory urinary sodium loss. The excretion of 4 l/day of urine with a sodium concentration of 50 mmol/l (a conservative estimate of the average urine sodium concentration of the dogs in the present study) results in the excretion of 200 mmol sodium/day of the race. If sodium intake does not equal this rate of sodium excretion, then sodium depletion must occur. Unfortunately, our estimates of sodium intake by the dogs of this study were not reliable. Our measured intake of sodium by Ex dogs was 360 mmol (8,200 mg) for the duration of the race. Were this estimate of intake accurate, then the dogs would have developed an estimated sodium deficit of 240 mmol at the end of the race. This quantity of sodium is equivalent to 20% of a 25-kg dog's exchangeable sodium content, assuming an extracellular fluid volume of 250 ml/kg (3) and it would have yielded a serum sodium concentration at the end of the race of 118 mmol/l. In fact, the reduction in serum sodium concentration was much less (6%) and was likely attributable to a greater sodium intake than was measured or a lower sodium excretion than was estimated. Regardless of the precise estimates, our results suggest that the obligatory excretion of urea by racing Alaskan sled dogs mandates excretion of a physiologically significant quantity of sodium even in the face of homeostatic mechanisms.

### Table 2. Plasma concentrations of Aldo, ANP, AVP, and of PRA in 12 Alaskan sled dogs before, during, and after a 490-km sled dog race

<table>
<thead>
<tr>
<th>Hormone</th>
<th>Prerace</th>
<th>Midrace</th>
<th>Postrace</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aldo, ng/l</td>
<td>28 ± 26</td>
<td>104 ± 63*</td>
<td>82 ± 46*</td>
</tr>
<tr>
<td>ANP, ng/l</td>
<td>67 ± 19</td>
<td>71 ± 45</td>
<td>93 ± 39</td>
</tr>
<tr>
<td>PRA, µg·l⁻¹·h⁻¹</td>
<td>2.1 ± 1.5</td>
<td>4.1 ± 1.8</td>
<td>6.8 ± 5.2*</td>
</tr>
<tr>
<td>AVP, ng/l</td>
<td>2.3 ± 0.5</td>
<td>2.0 ± 0.5</td>
<td>1.2 ± 0.3*</td>
</tr>
</tbody>
</table>

Values are means ± SD. *P < 0.05 vs. prerace value.

### Table 3. Urine concentration and fractional clearance of electrolytes and urea nitrogen and urine osmolality of 12 Alaskan sled dogs before, during, and after a 490-km sled dog race

<table>
<thead>
<tr>
<th>Variable</th>
<th>Prerace</th>
<th>Midrace</th>
<th>Postrace</th>
</tr>
</thead>
<tbody>
<tr>
<td>Osmolality, mosmol/kg H₂O</td>
<td>1,500 ± 390</td>
<td>1,370 ± 480</td>
<td>1,410 ± 450</td>
</tr>
<tr>
<td>Sodium concn, mmol/l</td>
<td>96 ± 38</td>
<td>70.6 ± 94.9</td>
<td>26.4 ± 19.5*</td>
</tr>
<tr>
<td>Potassium concn, mmol/l</td>
<td>157 ± 56</td>
<td>88 ± 38*</td>
<td>66 ± 35*</td>
</tr>
<tr>
<td>UNa + UK, mmol/l</td>
<td>253 ± 89</td>
<td>159 ± 91*</td>
<td>90 ± 44*</td>
</tr>
<tr>
<td>Chloride concn, mmol/l</td>
<td>165 ± 58</td>
<td>60 ± 20*</td>
<td>35 ± 20*</td>
</tr>
<tr>
<td>Phosphate concn, mmol/l</td>
<td>70.1 ± 21.0</td>
<td>67.2 ± 32.6</td>
<td>44.3 ± 18.1*</td>
</tr>
<tr>
<td>Calcium concn, mmol/l</td>
<td>0.70 ± 0.35</td>
<td>0.72 ± 0.40</td>
<td>0.71 ± 0.63</td>
</tr>
<tr>
<td>Urea nitrogen, mmol/l</td>
<td>940 ± 247</td>
<td>997 ± 350</td>
<td>1,150 ± 403</td>
</tr>
<tr>
<td>FC Na, %</td>
<td>0.66 ± 0.26</td>
<td>0.59 ± 0.31</td>
<td>0.42 ± 0.19*</td>
</tr>
<tr>
<td>FC K, %</td>
<td>20.6 ± 8.3</td>
<td>18.3 ± 9.5</td>
<td>14.8 ± 6.9</td>
</tr>
<tr>
<td>FC Cl, %</td>
<td>0.82 ± 0.66</td>
<td>0.48 ± 0.37*</td>
<td>0.36 ± 0.08*</td>
</tr>
<tr>
<td>FC OS, %</td>
<td>2.9 ± 0.7</td>
<td>4.2 ± 1.2*</td>
<td>4.2 ± 0.8*</td>
</tr>
</tbody>
</table>

Values are means ± SD; *P < 0.05 vs. Prerace value.
that act to reduce urinary sodium concentration. The large losses of sodium in the urine, if not offset by an increase in sodium intake or a decrease in TBW, may result in hyponatremia.

Urine osmolality of humans and horses decreases during prolonged exercise (10, 25), and in humans this is associated with an increase in free water clearance (10). There was no reduction in urine osmolality of dogs during the race despite the renal cation conservation. The reduction in osmolality attributable to the decreases in sodium and potassium urea levels was offset by an increase in urine urea concentration during the race; the sum of sodium and potassium urea declined by ∼170 mmol/l, and urine urea nitrogen concentration increased by 200 mmol/l (Table 3). Thus urine osmolality was unchanged, in the face of a significant decline in plasma AVP concentration, because of an increase in urine urea nitrogen concentration. Had there been an increase in free water excretion due to ingestion of excess volumes of water, urine osmolality would have declined. The decline in plasma AVP concentration may have contributed to the increased urea concentration in urine-AVP increases tubular permeability to urea (1).

Water turnover in running Alaskan sled dogs substantially exceeds that of similarly trained and housed sedentary dogs (14). The greater water turnover of running dogs may be attributable to higher respiratory and renal water losses than occur in sedentary dogs. Respiratory losses likely account for only a fraction of the measured water turnover (8), and fecal losses are also likely to be minimal (20, 24). Estimated respiratory water loss was 800 ml/day (8), assuming a total respiratory water loss of 60 breaths/min. Together, fecal and respiratory losses were likely <1 l/day, indicating that water loss in the urine must have been substantial (4.5 l/day).

Urine volume is related to urine osmolality and the renal solute load of the diet; for a given urine osmolality, urine volume increases as intake of solutes that are excreted in the urine increases (18). Urine production can, therefore, be estimated from the renal solute load [principally urea, sodium, and potassium (18)] in the diet and urine osmolality. Racing Alaskan sled dogs consume over 45,000 kJ/day, of which ∼900 g are contributed by protein (13). An intake of 900 g/day of protein, equivalent to ∼5.1 mol/day of urea, necessitates the excretion of 4.6 liters of urine with a urea concentration of 1,100 mosmol/kgH2O. This estimate of urine volume, although approximate, is similar to the water turnover, less estimated respiratory water losses, measured in the dogs in the present study. Obviously, a smaller renal solute load or greater urine osmolality would result in a smaller obligatory volume of urine. The high water turnover of Alaskan sled dogs during a race appears to be related to their large metabolizable energy intake and, hence, large renal solute load.

Conclusions. This study documents the development of exercise-associated hyponatremia and hypoosmolality in Alaskan sled dogs, a species that does not have large sodium losses in sweat. Furthermore, we demonstrate the occurrence of renal sodium conservation and maintained high urine osmolality associated with an increase in plasma Aldo and decrease in plasma AVP concentrations. We speculate that exercise-associated hyponatremia in sled dogs is a result of loss of sodium in urine combined with inadequate intake of sodium. However, an abnormality in regulation of extracellular fluid volume cannot be excluded as contributing to the hyponatremia.

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REFERENCES


