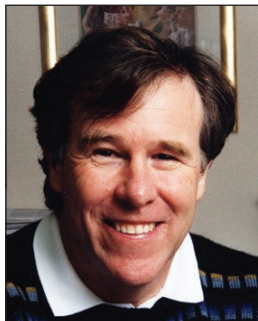


Carol Rees Parrish, R.D., M.S., Series Editor

Water Intoxication—Considerations for Patients, Athletes and Physicians



Timothy D. Noakes

Prior to 1969 athletes were advised to avoid drinking any fluids during exercise. But beginning in the 1970's, the idea gained credence that not to drink during exercise was “criminal folly” that could lead to dehydration-induced heat stroke. As a result athletes were advised to drink “beyond thirst” by ingesting “as much as tolerable” during exercise. The clinical sequelae of this advice became apparent in 1981 when the first reported case of exercise-associated hyponatremic encephalopathy in a female runner during a 90 km ultramarathon foot race in South Africa was reported. This article reviews exercise-associated hyponatremia (EAH) and exercise-associated hyponatremic encephalopathy (EAHE) and provides safe guidelines for hydration during exercise.

INTRODUCTION

Prior to 1969 athletes were encouraged to avoid drinking any fluids during exercise since it was believed that fluid ingestion would impair exercise performance, in particular by causing gastrointestinal distress, the so-called “stitch.” Athletes in those years actively followed that advice, priding themselves on their ability to run even 26 mile (42 km) marathon races without drinking (1). Furthermore, the rules then governing competitive distance running restricted the amount of fluid to which athletes had access.

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In 1981 the first case of exercise-associated hyponatremic encephalopathy (EAHE) occurred in a 46-year-old female marathon runner in a 90 km Comrades ultramarathon in South Africa. She presented with the symptoms and signs typical of EAHE as listed in Table 1 (2).

In 1991 we provided definitive evidence that exercise-associated hyponatremic encephalopathy (EAHE) is due to abnormal fluid retention in those who overdrink during prolonged exercise and to which a sodium deficit plays little or no part (3). Shortly after the publication of this compelling evidence, influential sporting organizations began to promote the value of drinking “as much as tolerable” but failed to warn of the proven dangers of overdrinking during exercise. As a result, more than 10 documented deaths from EAHE, an entirely preventable condition, have been reported in the scientific literature since 1991 (4).

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Table 1.
Diagnostic features of exercise-associated hyponatremia (EAH) and hyponatremic encephalopathy (EAHE)

EAH	EAHE
Symptoms	
Nausea	Headache
Vomiting	Altered level of consciousness
Unexplained fatigue	Coma
Impaired exercise performance	Convulsion/Seizure
Signs and clinical findings	
Evidence for weight gain	Evidence of weight gain
Serum [Na ⁺] <135 mmol/L	Serum [Na ⁺] <130 mmol/L
	Cerebral edema
	Pulmonary edema

There is no historical evidence that the absence of regular drinking during exercise produced any adverse consequences. The first purported case of heat injury in a marathon runner who did not drink during competition—Jim Peters in the 1954 Commonwealth (Empire) Games marathon in Vancouver—may not have been due to heat stroke (5). Instead, a series of publications in the 1960's showed that marathon runners who drank little or nothing seemed to do rather well, often winning races despite finishing with advanced grades of "dehydration" and high core body temperatures (6–8). This outcome might be expected if humans evolved their modern form specifically because of a superior capacity to run prolonged distances in (dry) heat with little or no fluid replacement (9–11).

HUMANS EVOLVED AS RUNNERS ABLE TO EXERCISE FOR PROLONGED PERIODS IN DRY HEAT WITH MINIMAL FLUID REPLACEMENT

This novel theory first proposed in the early 1900's (12,13) holds that humans evolved our particular biological features including long legs and short arms; relative hairlessness associated with an unmatched ability to lose heat by sweating; strong core abdominal muscles; and the capacity to rotate the upper and lower bodies in opposite directions, because all these adaptations gave early humans an evolutionary advantage over other non-sweating mammals with whom we shared the hot African

savannah more than 2 million years ago. Thus, it is proposed that our early hominid ancestors discovered that they could capture non-sweating mammals, especially swifter antelope, by chasing them in the mid-day heat. Profuse sweating allowed early hominids to safely regulate their body temperatures as they chased these antelope for many hours in midday heat. Provided they could chase the antelope for long enough in sufficiently hot conditions, the antelope's brain temperature would finally become too high causing it to seek shade and to stop running. There the temporarily paralyzed animal could be more easily dispatched even by hunters, who as recently as 100,000 years ago, lacked more modern implements like spears and knives. The theory is that the high energy diet provided by these antelope

allowed the rapid growth of the human brain and hence the development of *Homo sapien*.

Naturally the best hunters would be those who were neither overcome by thirst nor incapacitated by the loss of a large volume of body water caused by the heavy sweating during the three-to-six hours required for a successful hunt (11). Like all the great runners of the past (1), the most successful hunters would have drunk little since carrying water would have impeded their progress and reduced their probability of success whilst hunting.

PROMOTION OF THE CONTRARY BELIEF THAT HUMANS ARE POORLY ADAPTED TO EXERCISE IN THE HEAT

Two separate events that happened between 1965 and 1969 led to a contrary perception that humans are poorly adapted for exercise in the heat and are at risk of death from heat stroke if they sweat profusely and do not drink copious amounts of fluid during exercise thereby developing "dangerous dehydration."

First was the development of the world's first sports drink at the University of Florida, beginning in 1965. The drink was developed by a renal physician, Dr Robert Cade, who was certain that fluid ingestion during exercise would prevent the development of "heat" illness including heat stroke and heat cramps during exercise. But the drink became an overnight commercial success especially in the United States, because of

its alleged capacity to enhance the performance of American football teams, first collegiate and later professional, in the fourth quarter of football matches (14).

Second, a group of South African researchers showed an apparently causal relationship between fluid ingestion during exercise, the prevention of “dehydration” and lower body temperatures in athletes competing in a series of 20 mile (32 km) running races (15). These researchers concluded that athletes who do not drink sufficient fluids during marathon running are at risk of developing heat stroke and that the international ruling then in place which restricted fluid availability during marathon running was “criminal folly.”

Together these concepts led to the idea that athletes needed to drink “as much as tolerable” during exercise in order to maximize their performance and to insure that they do not die from heat stroke (16,17). Skillful marketing (18,19) soon led to the universal acceptance that not to drink “as much as tolerable” during exercise was extremely unwise. Soon it became the accepted truism that any weight loss during exercise is detrimental to both health and performance (16,17).

The defining event which invited a re-assessment of this new “truth” occurred on June 1, 1981 when an athlete competing in the 56 mile (90 km) Comrades Marathon in South Africa was admitted to hospital in an unconscious state having developed a grand mal epileptic seizure. Her serum sodium concentration on hospital admission was 115 mmol/L confirming a diagnosis of EAHE. She regained consciousness after two-days and was released from hospital four-days later. Subsequent investigation over the next two years uncovered three additional cases of EAH and EAHE in South African ultra-endurance athletes. Their case reports were subsequently published in 1985 in a paper entitled “Water intoxication: A possible complication during endurance exercise” (2). In time the term EAH would supercede that of water intoxication (20). The paper drew the following conclusion: *“The etiology of this condition appears to be voluntary hyperhydration with hypotonic solutions combined with moderate sweat sodium chloride losses . . . advice (on fluid replacement) should be tempered with the proviso that the intake of hypotonic fluids in excess of that required to balance sweat and urine losses . . . may be hazardous in some individuals.”*

In 1988, to evaluate this novel theory, PhD student Anthony Irving hospitalized eight Comrades Marathon runners with exercise-associated hyponatremic encephalopathy (EAHE) in order to study their fluid and sodium balance during recovery (3). He showed that all athletes had drunk to excess during the race gaining between two-to-six kilograms (four-to-12 pounds). However, there was no evidence that subjects with EAHE had incurred a greater sodium deficit than had control runners who completed these races with normal serum sodium concentrations. Thus we concluded that EAH *“results for fluid retention in subjects who ingest abnormally large fluid volumes during prolonged exercise”* since this study found *“that each of eight subjects who collapsed with the hyponatremia of exercise (mean plasma sodium concentration 122.4 ± 2.2 mM) were fluid overloaded by an amount ranging from 1.22 to 5.92 liters. These fluid volumes are conservative because no allowance was made for insensible water losses during recovery”* and that *“sodium chloride losses alone cannot explain the hyponatremia of exercise”* (3). The key findings are presented in Figure 1.

Our finding that subjects with EAHE did not have a larger sodium deficit than controls is historically important because this evidence has essentially been ignored. Instead, theoretical arguments without experimental support (21–23) were advanced to explain why some might develop EAH or EAHE as the result of unreplaced sodium deficits incurred during prolonged exercise. However, no study has yet been able to document a sodium deficit in patients with EAH or EAHE whereas many studies have either confirmed our original finding (24–28) or shown that sodium chloride ingestion during exercise does not influence the serum sodium concentration in those who do not overconsume fluids during exercise (29,30). Since EAH and EAHE are due to abnormal fluid retention, only drinks containing sodium at a concentration well in excess of that found in blood (>140 mmol/L) would theoretically play some role in the prevention of these conditions (31). In reality, such drinks are unpalatable and likely to induce nausea and vomiting.

Unfortunately, our original findings had little practical impact. For 10 years after the publication of our original paper, a number of influential organizations produced drinking guidelines which promoted the con-

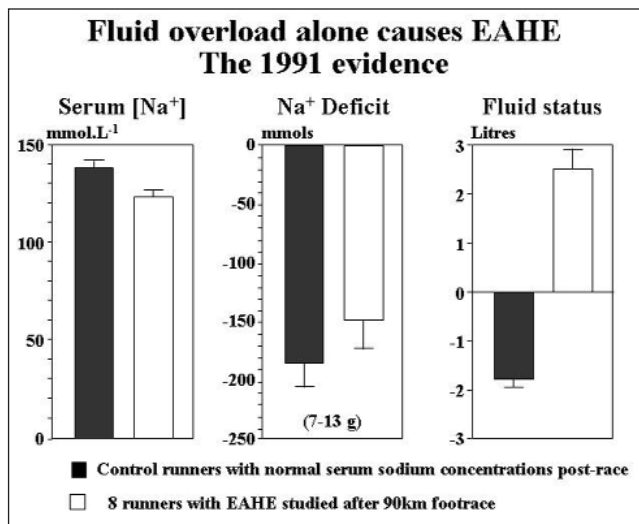


Figure 1. The study of Irving, et al (3) compared sodium chloride (middle panel) and fluid (right panel) balance in athletes who finished the 90 km Comrades Marathon with either normal or reduced (EAH and EAHE) serum sodium chloride concentrations (left panel).

Whereas sodium chloride losses (middle panel) were the same in both groups of athletes, athletes who maintained their serum sodium concentrations during the race lost about two litres of fluid. In contrast, athletes who developed EAH or EAHE during the Comrades Marathon finished with a fluid excess that ranged from two-to-six litres.

Thus this study conclusively established already in 1991 that EAH and EAHE is due to fluid retention to which a sodium chloride deficit plays little if any role. In 2005 the International Consensus Conference on EAH (20) confirmed that this conclusion is correct.

cept that only if athletes drank “as much as tolerable” could they exercise safely (16,17,32,33). These guidelines failed to emphasize the established finding that the overconsumption of sodium-poor fluids during exercise could have fatal consequences (18).

This danger was first acknowledged only after the 2002 Boston Marathon at which the next two critical events occurred. First Cynthia Lucero died as a result of drinking too much of an electrolyte-containing sports drink during the race (34). Second, residents from the Children’s Hospital at Harvard Medical School chose that particular race to study the factors associated with EAH and EAHE in runners in that specific race (28). That study found that 13% of the stud-

ied runners developed EAH. This compares with the absence of a single case ever of EAH in 42 km marathons in South Africa and New Zealand (19).

The authors proved that the same four risk factors previously surmised (4,35) predicted the risk of EAH during the marathon race:

- Substantial weight gain (odds ratio, 4.2)
- Consumption of more than 3 liters of fluids during the race, consumption of fluids every mile, a racing time of >4:00 hours (odds ratio, 7.4)
- Female sex
- Low body-mass index

In 2005 the First International Consensus Conference on EAH concluded that EAH is caused by excessive fluid consumption to which a sodium deficit plays little if any role (20). A subsequent collaborative research paper combining this information (36) concluded that 3 factors cause EAH:

1. Voluntary overdrinking caused almost certainly by behavioral conditioning in those who have been instructed to drink “as much as tolerable” in order “to stay ahead of thirst” during exercise.
2. A failure to suppress the secretion of ADH in the face of increased total body water content—the syndrome of Inappropriate ADH secretion (SIADH).
3. Relocation of internal sodium stores. There is growing evidence that the sodium present in the body is not located only in the extra-cellular compartment. Rather it seems that there may be a substantial amount of sodium stored in an osmotically-inactivate form (Na) within certain cells. Extracellular sodium may then be added to that store in the process of inactivation of osmotically-active sodium (Na⁺). Alternatively, osmotically inactive sodium may be activated and added to that already present in osmotically-active form in the extracellular fluid.

We also found that approximately 70% of athletes who gain weight during exercise (because they both over-drink and fail appropriately to suppress ADH secretion) do not develop EAH (36). Since these athletes could not have ingested enough sodium during exercise to maintain the serum sodium concentration in the face of a large increase in total body water, they

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Table 2.

Key factors in the prevention of EAH and of fatal outcomes in EAHE

1. Teach athletes to drink according to the dictates of thirst before, during and after exercise.
2. Physicians treating collapsed athletes with an altered level of consciousness should not infuse any fluids intravenously until a diagnosis of EAHE has been excluded.
3. Once a diagnosis of EAHE has been established only hypertonic (3% or greater) saline solutions should be used for intravenous therapy.

must have relocated Na⁺ from an internal body store. Alternatively abnormal osmotic inactivation of extracellular Na⁺ could worsen EAH in those who overdrink during exercise and who fail appropriately to suppress ADH secretion.

The point is that the development of the condition will occur only in those who are pre-disposed because (i) they fail appropriately to suppress ADH secretion in response to overdrinking resulting in an expansion of the total body water and (ii) they are either unable to mobilize Na⁺ from internal stores of osmotically-inactive Na or (iii) they inactivate osmotically-active circulating Na⁺ present in the extracellular space, storing it as Na in an intracellular site.

It therefore follows that the real etiology of EAH can only be studied in persons who exhibit all these abnormalities. For example, attempting to show that sodium ingestion can prevent EAH by studying subjects who are not predisposed to its development because they lack these biological variants, will not likely uncover the truth.

PRACTICAL CONSIDERATIONS

1. EAH is an iatrogenic disease caused by the promotion of a false physiology. Humans are highly adapted for exercise in the heat and do not need to drink to excess to optimize their performance during exercise. Nor is there any evidence that high rates of fluid ingestion are required to prevent ill health during exercise. When athletes drank little during exercise, they did not develop EAH and EAHE. Only after the introduction of the drinking guidelines which encouraged

athletes to drink “as much as tolerable” in order to prevent a novel medical disease—“dehydration”—and to optimize athletic performance, did the prevalence of EAH and EAHE suddenly increase.

2. EAHE is not a benign condition. At least 10 deaths from the condition have been described in the scientific literature (4). All these deaths were foreseeable and preventable.
3. Not everyone who overdrinks during exercise will develop EAH or EAHE. Rather it appears that only those with genetic variants which cause (i) the oversecretion of ADH even when they are overhydrated, (ii) the relocation of extracellular Na⁺ to an intracellular osmotically-inactive Na store or (iii) the inability to activate the reverse process in the face of a large increase in total body water, are at risk of developing EAH and EAHE.
4. Prevention of EAH and EAHE is simple. It requires only that athletes drink according to thirst before, during and after exercise.
5. Some patients with EAH or EAHE have died because of inappropriate treatment—specifically the provision of hypotonic or isotonic intravenous fluids in large volumes—for the treatment of “dehydration.” Yet these athletes were overhydrated because they had drunk to excess during exercise and had retained that fluid because of SIADH. Fluid restriction, not the provision of isotonic or hypotonic NaCl solutions in large volumes, is the basis for the safe treatment of EAHE.
6. A fatal outcome can be prevented by a high level of clinical suspicion. It requires clinicians to understand that an altered level of consciousness is NOT caused by the mild levels of “dehydration” experienced by athletes competing in modern athletic events (36) in which fluid is readily available during exercise. Typically, an altered level of consciousness in athletes in whom there is no other obvious cause (such as cardiac arrest or a cerebrovascular accident) will be due to either heatstroke or EAHE. Heatstroke can be excluded by the measurement of a rectal temperature less than about 41°C in which case EAHE becomes the most likely diagnosis in athletes who do not exhibit other overt clinical signs indicating intracerebral or cardiovascular pathology. EAHE often presents initially as

confusion and withdrawal, similar to that seen in persons with mild head injury (concussion).

7. Treatment is simple and life-saving. The key is that no fluids with a NaCl concentration less than 3% (i.e. hypertonic saline) should be used. For severe cases of EAH, 3%–5% NaCl solutions given intravenously at slow rates are life saving (20).

The adoption of these guidelines has minimized the incidence of EAH and its potential fatal complication, EAHE, in New Zealand and South Africa.

SUMMARY

There is and never was a need for EAH or EAHE to occur. There is no need ever for a fatal outcome. Deaths are always due to lack of awareness on the part of athletes, their coaches, their doctors, race organizers and powerful commercial interests, all of which have conspired to encourage overdrinking during exercise. The knowledge deficit extends to those emergency ambulance personnel and emergency care physicians who believe that “dehydration” can cause an altered level of consciousness including the development of coma and who, as a result, have treated overhydrated athletes suffering from EAH and EAHE, with the rapid infusion of large volumes of iso- or hypotonic NaCl solutions. The only effect of such treatment is acutely to increase intracerebral pressure, with the production of cerebellar coning, respiratory arrest and brain death. ■

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