Statement of the Third International Exercise-Associated Hyponatremia Consensus Development Conference, Carlsbad, California, 2015

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Abstract
The third International Exercise-Associated Hyponatremia (EAH) Consensus Development Conference convened in Carlsbad, California in February 2015 with a panel of 17 international experts. The delegates represented 4 countries and 9 medical and scientific sub-specialties pertaining to athletic training, exercise physiology, sports medicine, water/sodium metabolism, and body fluid homeostasis. The primary goal of the panel was to review the existing data on EAH and update the 2008 Consensus Statement. This document serves to replace the second International EAH Consensus Development Conference Statement and launch an educational campaign designed to address the morbidity and mortality associated with a preventable and treatable fluid imbalance.

The following statement is a summary of the data synthesized by the 2015 EAH Consensus Panel and represents an evolution of the most current knowledge on EAH. This document will summarize the most current information on the prevalence, etiology, diagnosis, treatment and prevention of EAH for medical personnel, athletes, athletic trainers, and the greater public. The EAH Consensus Panel strove to clearly articulate what we agreed upon, did not agree upon, and did not know, including minority viewpoints that were supported by clinical experience and experimental data. Further updates will be necessary to both: (1) remain current with our understanding and (2) critically assess the effectiveness of our present recommendations. Suggestions for future research and educational strategies to reduce the incidence and prevalence of EAH are provided at the end of the document as well as areas of controversy that remain in this topic. [excerpt]

Keywords
EAH, exercise-associated collapse, hydration

Disciplines
Other Medicine and Health Sciences | Sports Sciences

Authors

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CONSENSUS STATEMENT

Statement of the Third International Exercise-Associated Hyponatremia Consensus Development Conference, Carlsbad, California, 2015

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Key Words: EAH, exercise-associated collapse, hydration


INTRODUCTION

The third International Exercise-Associated Hyponatremia (EAH) Consensus Development Conference convened in Carlsbad, California in February 2015 with a panel of 17 international experts. The delegates represented 4 countries and 9 medical and scientific sub-specialties pertaining to athletic training, exercise physiology, sports medicine, water/sodium metabolism, and body fluid homeostasis. The primary goal of the panel was to review the existing data on EAH and update the 2008 Consensus Statement.1 This document serves to replace the second International EAH Consensus Development Conference Statement and launch an educational campaign designed to address the morbidity and mortality associated with a preventable and treatable fluid imbalance.

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CONSENSUS METHODOLOGY

The third International Exercise-Associated Hyponatremia Consensus Development Conference utilized National Institutes of Health guidelines, amended for a more holistic approach to fit the needs of both the group and the topic. Twenty-two individuals (17 accepted) were invited to participate in the consensus conference who: (1) have made scientific and/or clinical contributions to the topic of water and sodium homeostasis and/or hyponatremia and (2) represented a specific group (eg, nephrology, endurance medicine, etc.) or had unique topical expertise (eg, cystic fibrosis, muscle cramps, fluid balance, etc.). The present document is intended to serve as the scientific record of the conference with intent to widely disseminate this information to achieve
maximum impact on both current health care practice and future medical research.

The methodology governing the conduct of this consensus development conference is summarized below:


2. These experts presented data on EAH in a day long public session, followed by open question/answer and discussion periods with the audience. The panel members met the following day in a closed session to prepare the consensus statement.

3. Workgroups were created 3 months prior to the February 2015 meeting to update the following EAH target areas: epidemiology, etiology and pathophysiology, diagnosis, treatment, and prevention. Each workgroup was asked to present updated drafts for discussion during the closed session.

4. A systematic, comprehensive and updated literature review was shared by the panel members prior to the February 2015 meeting, using a cloud storage service that was organized into workgroup categories (epidemiology, etiology and pathophysiology, diagnosis, treatment and prevention). All panel members had unlimited access to the cloud storage service and could add digital versions of published manuscripts to the EAH manuscript section at any time.

The panel chairperson (MHR) was responsible for monitoring the progress of each work group, directing the closed session and guiding the panel’s deliberations. Using the previous 2 EAH consensus statements as a starting point, each work-group was asked to: (1) incorporate new data into each assigned section and (2) update any outdated information. All recommendations were graded based on clinical strength, using the grading scale described by the American College of Chest Physicians (Table 1).2 Particular emphasis was placed on creating more generalized recommendations so as to prevent and treat EAH across a wider variety of athletic events, rather than the endurance sports focus of the 2 prior EAH Consensus Statements.

**Sponsorship**

The travel (except R.J.M. and I.R.R., who supported their own travel), hotel and meal expenses for the participants were funded by CrossFit, Inc (Solana Beach, CA). The open conference was also sponsored by CrossFit, Inc. However, no members from CrossFit, Inc participated in any of the closed discussions or contributed to the development of the consensus guidelines. Furthermore, no members from CrossFit, Inc had access to the consensus document prior to publication.

**RESULTS AND DISCUSSION**

**Definition**

EAH is used to describe hyponatremia occurring during or up to 24 hours after physical activity. It is defined by a serum, plasma or blood sodium concentration ([Na⁺]) below the normal reference range of the laboratory performing the test. For most laboratories, this is a [Na⁺] less than 135 mmol/L.1 The main determinants of the serum [Na⁺] are the total content of exchangeable body sodium and potassium relative to total body water and thus hyponatremia can result

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**TABLE 1.** American College of Chest Physicians Classification Scheme for Grading Evidence and Recommendations Utilized in This Statement

<table>
<thead>
<tr>
<th>Grade</th>
<th>Description</th>
<th>Benefits vs Risks and Burdens</th>
<th>Methodological Quality of Supporting Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>1A</td>
<td>Strong recommendation, high-quality evidence</td>
<td>Benefits clearly outweigh risks and burdens or vice versa</td>
<td>RCTs without important limitations or overwhelming evidence from observational studies</td>
</tr>
<tr>
<td>1B</td>
<td>Strong recommendation, moderate-quality evidence</td>
<td>Benefits clearly outweigh risks and burdens or vice versa</td>
<td>RCTs with important limitations or exceptionally strong evidence from observational studies</td>
</tr>
<tr>
<td>1C</td>
<td>Strong recommendation, low-quality or very low quality evidence</td>
<td>Benefits clearly outweigh risks and burdens or vice versa</td>
<td>Observational studies or case series</td>
</tr>
<tr>
<td>2A</td>
<td>Weak recommendation, high-quality evidence</td>
<td>Benefits closely balanced with risks and burdens</td>
<td>RCTs without important limitations or overwhelming evidence from observational studies</td>
</tr>
<tr>
<td>2B</td>
<td>Weak recommendation, moderate-quality evidence</td>
<td>Benefits closely balanced with risks and burdens</td>
<td>RCTs with important limitations or exceptionally strong evidence from observational studies</td>
</tr>
<tr>
<td>2C</td>
<td>Weak recommendation, low-quality or very low quality evidence</td>
<td>Uncertainty in the estimates of benefits, risks and burden; benefits, risk and burden may be closely balanced</td>
<td>Observational studies or case series</td>
</tr>
</tbody>
</table>

RCT, randomized controlled trial.

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from loss of solutes (sodium, potassium), a relative excess of total body water or a combination of both. However, in most clinical scenarios, the driving force for the development of hyponatremia is a relative excess of total body water. The symptoms associated with EAH depend on both the magnitude of the serum sodium decrease from baseline level along with the rate at which this decrease occurs. Symptomatic EAH can occur if the rate of fall approaches 7% to 10% within 24 hours. Thus, more severe degrees of hyponatremia (typically <125 mmol/L) as well as more modest serum sodium values (in the range of 125-130 mmol/L), that develop over a short period of time, can both be associated with signs and symptoms.

**Epidemiology**

The vast majority of recreationally active individuals begin endurance races with a blood [Na⁺] above 135 mmol/L. Based on data pooled from 27 separate studies, encompassing 2262 participants with a verifiable pre-race blood [Na⁺] measurement, only 0.8% (19/2262) presented with hyponatremia prior to race start. These pooled data represent blood [Na⁺] measurements collected in 7 countries and between 5 minutes to 72 hours pre-competition. This 0.8% also includes 16 questionable below-normal [Na⁺] values possibly confounded by fingerstick hemolysis and/or outdated techniques. Thus, baseline (pre-event) hyponatremia in recreational exercisers appears to fall within the expected range for a normal population distribution (1%-2%), and at a frequency well below what has been observed in individuals presenting for non-hyponatremia related clinical treatment situations or in hospitalized patients. We thereby believe that EAH largely develops during or immediately following exercise.

Exercise-associated hyponatremia can present in 2 forms: asymptomatic or symptomatic. Asymptomatic athletes with [Na⁺] <135 mmol/L have largely been detected by blood samples taken post-exercise from athletes participating in research protocols or obtained for reasons other than suspicion of EAH. Athletes with the symptomatic form of EAH can present with mild, non-specific symptoms (eg, lightheadedness, nausea) but typically present with headache, vomiting, and/or altered mental status (eg, confusion, seizure) resulting from cerebral edema (termed exercise-associated hyponatremic encephalopathy or EAHE) that may or may not be associated with non-cardiogenic pulmonary edema. EAHE is a life-threatening condition that has been observed across a wide variety of activities (Table 2). The incidence of asymptomatic and symptomatic cases of EAH varies widely with regard to type and duration of activity, location of the event, characteristics of the participants (see risk factors) and heat or cold stress during the event.

**Epidemiology of Asymptomatic EAH**

The reported incidence of asymptomatic EAH has ranged from 0% to 51% immediately post-race. In a study of an ultramarathon, 67% of the participants were hyponatremic (asymptomatic) at some point during the race, but only 27% finished the with serum [Na⁺] <135 mmol/L (40% self-corrected prior to finishing the event). The highest reported incidence of asymptomatic hyponatremia post-race has been consistently noted in 161-km ultramarathons, in which the reported incidence of EAH has ranged between 5% and 51%. The incidence of asymptomatic EAH in Ironman triathlons in different environments has been reported to range from negligible to as high as 18% and 25%. In studies on endurance cyclists the incidence of asymptomatic EAH has ranged from 0% in a 720-km race to 12% in a 109-km race. In a 26.4-km swim, 17% of swimmers developed asymptomatic hyponatremia. In a study of an ultramarathon, 67% of the participants were asymptomatic hyponatremic (asymptomatic) at some point during the race, compared to 6% of finishers. Additionally, asymptomatic hyponatremia was observed in 33% of premier league UK rugby players following an 80 minutes rugby competition and 70% of elite rowers during a 28-day training camp.

**Epidemiology of Symptomatic EAH**

Symptomatic EAH is rare and occurs with considerably less frequency than asymptomatic EAH, but complications associated with EAH have led to at least 14 athlete related deaths since 1981. Symptomatic EAH generally occurs as an isolated case or in small clusters during or following endurance events with participants reporting to the race medical facilities or to hospital emergency departments within 24 hours after participation. In general, participants seek treatment for a constellation of symptoms ranging from feeling unwell to convulsions. Clusters of cases have occurred in military training exercises, marathons, Ironman triathlons and ultramarathons. The incidence of asymptomatic EAH has been reported to be as high as 23% and 38% of athletes seeking medical care in an Ironman Triathlon and an ultramarathon, respectively, but most endurance events report no cases of asymptomatic EAH, especially at the marathon distance and below.

Two studies have examined large compilations of data to help define the incidence of symptomatic and asymptomatic EAH. In the first study of 2135 athletes from 8 endurance events ranging in length from 42.2 to 161 km, the incidence of symptomatic EAH was 1% (compared to 6% with asymptomatic EAH) among study participants. In the
second study of 669 161-km ultramarathon runners, only one case (0.1% among study participants) of symptomatic EAH presented during the 5-year sampling period (compared to 13% with asymptomatic EAH), but considering the total number of race participants over this time period, the actual incidence of symptomatic EAH was approximately 0.06%.

Symptomatic EAH has also been reported in hikers and military personnel. Symptomatic EAH accounted for 16% of Grand Canyon hikers seeking medical care for exercise-associated collapse or exhaustion from May 31, 1993 through September 31, 1993 providing an estimated incidence rate between 2 and 4 per 100,000 persons. Furthermore, suspected hyponatremia was found to account for 19% of non-fatal suspected heat-related incidents in the Grand Canyon National Park from April through September during 2004 through 2009 hiking seasons. In the US active duty military, the annual incidence rate of hyponatremia from 1999 through 2012 has ranged from 1.9 to 13% with asymptomatic EAH, but considering the total person-years (averaged 6.7 cases per 100 000 person-years). However, this incidence is probably inflated as the data were derived from a medical coded database that does not have a specific designation for EAH and likely includes hyponatremia from both exercise and non-exercise related conditions.

Alarmingly, symptomatic EAH is now being reported in a more diverse set of sporting activities. For instance, symptomatic EAH has been reported in shorter distance endurance competitions, such as a half marathon with slower finishers completing the distance in 2 to 3 hours and a sprint triathlon with slower finishers taking approximately 2 hours to complete. In addition, EAH has been reported in US professional and college American rules football players and has led to the deaths of 3 US high school football players after the development of hyponatremia during prolonged heat or cold exposure. Suspected hyponatremia was found to account for 16% of non-fatal suspected heat-related incidents in the Grand Canyon National Park from April through September during 2004 through 2009 hiking seasons. In the US active duty military, the annual incidence rate of hyponatremia from 1999 through 2012 has ranged from ~4 to 13 cases per 100,000 person-years (averaged 6.7 cases per 100 000 person-years). However, this incidence is probably inflated as the data were derived from a medical coded database that does not have a specific designation for EAH and likely includes hyponatremia from both exercise and non-exercise related conditions.

TABLE 3. Risk Factors for the Development of Asymptomatic and Symptomatic EAH1

<table>
<thead>
<tr>
<th>Risk Factors for EAH</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overdrinking water, sports drinks, and other hypotonic beverages</td>
</tr>
<tr>
<td>Weight gain during exercise</td>
</tr>
<tr>
<td>Exercise duration &gt;4 h</td>
</tr>
<tr>
<td>Event inexperience or inadequate training</td>
</tr>
<tr>
<td>Slow running or performance pace</td>
</tr>
<tr>
<td>High or low body mass index (BMI)</td>
</tr>
<tr>
<td>Readily available fluids</td>
</tr>
</tbody>
</table>

 involving a male pledge performing calisthenics. It is likely that other cases of symptomatic hyponatremia have either not been recognized or reported.

Risk Factors

The major risk factors for developing EAH are listed in Table 3. The single most important risk factor is sustained, excessive fluid (water, sports drinks or other hypotonic fluids) intake in volumes greater than loss through sweat, respiratory and renal water excretion so that a positive fluid balance accrues over time. Almost all cases of symptomatic EAH have occurred in individuals who have gained or maintained weight during activities in which some weight loss would represent fluid balance and euhydration. Body weight losses of <0.75 kg after a standard marathon and <1% after an 80 minutes rugby match have been associated with asymptomatic EAH. All sports beverages are hypotonic to plasma (typical sodium content in sports drinks are approximately 10-38 mmol/L); thus the magnitude of excessive fluid volume ingestion will overwhelm any protective effect of the beverages’ sodium content on maintaining serum [Na+].

From a practical standpoint, it is the smaller individuals and those who participate at a slower pace and drink more than sweat losses that are more likely to develop EAH. Although the incidence of women experiencing EAH is greater than that of men, adjusted for BMI and racing time, the apparent sex difference is not statistically significant.

Nonsteroidal anti-inflammatory drugs (NSAIDs) have been implicated as a risk factor in the development of EAH presumably by potentiating the water retention effects of arginine vasopressin (AVP) at the level of the kidney collecting duct. However, data are conflicting, and further investigation is necessary to determine whether NSAID usage—with respect to both classification and dosage—is a risk factor for the development of EAH. The possible pathophysiological contributions of intrinsic renal disease and low solute diets on water retention, high sweat sodium concentrations in extreme environments, and the potentiation of thirst by non-osmotic stimuli during exercise warrant further investigation as secondary risk factors for EAH. Whether common medications that are associated with hyponatremia and the syndrome of inappropriate anti-diuretic hormone secretion (SIADH) in the general population, such as selective serotonin reuptake inhibitors, can potentiate the development of EAH is not known and warrants further investigation.

There is a paucity of evidence suggesting that those developing symptomatic EAH have either been a “salty sweater” or a heterozygous carrier of the cystic fibrosis genotype. Athletes with homozygous CF, however, are at risk for developing hyponatremia as demonstrated by numerous instances when an individual is diagnosed with CF after the development of hyponatremia during prolonged physical exertion or prolonged exposure to high ambient temperatures. As individuals with CF experience a longer lifespan (median predicted survival age in 2012 was 41.1 years) and are encouraged to consider exercise as...
one of their therapies,\textsuperscript{112} this population may be at increased risk for EAH due to the combination of high sweat fluid and sweat $[\text{Na}^{+}]$ loss.

**Etiology and Pathophysiology of EAH**

The predominant pathophysiology of EAH, and of most serious medical concern, is dilutional hyponatremia caused by sustained overdrinking and AVP induced impaired water clearance, which overwhims the ability of the kidney to excrete the excess water load. Dilutional hyponatremia is the primary pathophysiological variant of clinically symptomatic EAH and largely (if not exclusively) associated with all reported cases of morbidity and mortality that are listed in Table 2. Dilutional EAH is an acute onset form of hyponatremia, which is now occurring in non-endurance sports, with 3 deaths, recently reported amongst the approximately 7.5 million American high school football-player-years from 2008 through the 2014 seasons.$^{63,64,69}$ These football players were encouraged to ingest copious volumes of hypotonic fluids and sports drinks to prevent or relieve exercise-associated muscle cramps (EAMC).$^{63,64,69}$ in the belief that EAMC was caused by dehydration and electrolyte imbalance.$^{113}$ However, experimental$^{114,115}$ and observational$^{116,117}$ studies speculate that EAMC may reflect neurological changes due to fatigue rather than uncompensated water and sodium losses incurred during exercise in some cases. Muscle cramping and tremor have also been associated with overdrinking and hyponatremia in athletes.$^{82,100,118,119}$

Symptoms associated with EAH are due to osmotically-induced shifts of water into the intracellular compartment. In the confined space of the cranium these shifts of water into the central nervous system (CNS) tissues lead to cellular edema and pathological increases in intracranial pressure. Acutely, this may manifest in symptoms previously described and in the extreme may lead to brain herniation and death.

**Etiology of Euvolemic/Hypervolemic EAH**

Total body water expansion relative to the amount of total body exchangeable sodium is the main pathogenic cause of asymptomatic and symptomatic EAH.$^{34,41,45,52,57,58,61,71,73,75,76,84,119,122–126}$ Dilutional EAH can be euvolemic (total body water expansion without changes in total exchangeable sodium) or hypervolemic (total body water expansion above concomitant increases in total exchangeable sodium). The primary etiologic factor in dilutional hyponatremia is consumption of fluids (water, sports drinks or other hypotonic fluids) in excess of total body fluid losses, which includes the sum of insensible (cutaneous, respiratory, and gastrointestinal),$^{127,128}$ sweat and renal (urine) fluid losses.$^{34,45,52,57,58,61,71,73,75,76,84,119,122–125}$

Hyponatremia caused solely by the overconsumption of fluids, above known maximal urine excretory rates of 800 to 1000 mL,$^{129}$ has been demonstrated at rest in athletes with and without a history of EAH.$^{34,36,87}$ Although some cases of EAH may be due to pure water intoxication from overconsumption of fluids, non-osmotic AVP secretion is a key contributing factor in most athlete-related symptomatic cases.$^{5,19}$ Known stimuli to AVP secretion that are commonly associated with exercise include: nausea/vomiting$^{130}$, interleukin-6 release$^{2}$, plasma volume contraction$^{11}$, hypoglycemia$^{131}$; elevated body temperature$^{132}$; and/or other hormonal mediators.$^{16}$ Even small increases in circulating AVP levels can markedly reduce renal water excretion well below maximal levels,$^{133}$ resulting in retained body water not only when drinking rates do not exceed those necessary to prevent excessive dehydration, but also when drinking rates are well in excess of fluid replacement need.$^{49,134}$

**SUMMARY STATEMENT**

The primary etiology and pathophysiological mechanism underlying EAH—and all known fatalities—is the overconsumption of hypotonic fluids relative to exchangeable sodium in likely combination with non-osmotic AVP secretion (Grade 1A).

**Etiology of Hypovolemic EAH**

There is persisting debate as to the relative contribution of under-replaced sodium losses to the lowered sodium concentrations observed in EAH. While in clinical medicine, electrolyte depletion without expansion of total body water or hypovolemic hyponatremia is well described,$^{5,6,135–138}$ in EAH this variant has been more difficult to define and is much less likely to be encountered except in extreme events usually over prolonged periods (such as ultra-marathons)$^{139}$ or hot Ironman distance triathlons.$^{19,20}$ The data regarding sodium losses during exercise (as measured during recovery) and their potential contribution to the development of symptomatic hyponatremia in longer and hotter races$^{139}$ have been consolidated in Table 4 against data collected from relatively shorter and cooler races$^{123,140,141}$ where fluid overload hyponatremia has been verified. From the standpoint of the clinical literature, hypovolemic hyponatremia reflects a loss of total body exchangeable sodium that manifests as volume depletion.$^{5,6,135,142}$ Hypovolemic EAH would be predicted$^{89}$ to occur in athletes exercising for longer periods of time (such as 161 km ultramarathons; $>20$ hours),$^{11,54–56}$ and/or in hotter$^{11,19,20,55,108,109}$ environments and/or with higher sweat sodium losses.$^{99,101}$ Clinical confirmation of the hypovolemic form of hyponatremia is supported by a spot urine sodium concentration ($U[\text{Na}^{+}]$) below 30 mmol/L,$^{136,137,144}$ in conjunction with a serum or plasma $[\text{Na}^{+}]$ below 135 mmol/L. A spot $U[\text{Na}^{+}]$ $<30$ mmol/L is 100% specific and 80% sensitive for predicting a sustained increase ($>5$ mmol/L) in serum $[\text{Na}^{+}]$ following isotonic saline administration$^{136}$ in clinical patients. Elevated blood urea nitrogen levels ($>20$ mg/dL)$^{136,139}$ and weight loss$^{19,20,55}$ may also suggest volume depletion as a pathogenic contributor to EAH. However, these biochemical tests are not always available at the point of care and thus clinical assessment (vital signs, weight change, and physical examination) may be the only indication of volume depletion.

**SUMMARY STATEMENT**

Under-replaced sodium losses contribute to serum $[\text{Na}^{+}]$ independent of distance (Grade 1A). However, there
is paucity of data supporting sodium loss as the primary mechanism of symptomatic EAH even in those who exercise for prolonged periods of time and in warm weather (Grade 2C). In these cases, relative over-drinking of hypotonic fluids with sustained non-osmotic AVP secretion is likely involved in the development of symptomatic EAH.

The Role of Thirst

Since drinking fluid volume above sweat and urinary losses during and after activity is the main pathophysiological mechanism underlying asymptomatic, symptomatic and fatal cases of EAH, prevention is dependent on drinking less. Thirst should provide adequate stimulus for preventing excess dehydration and markedly reduce the risk of developing EAH in all sports. Physiologically-driven thirst has been defined as a “generalized, deep seated feeling of desire for water” and is an evolutionarily conserved, finely tuned, regulatory mechanism serving to protect both plasma osmolality and circulating plasma volume. Osmoreceptors located within the circumventricular organs of the brain (highly vascularized structures located around the third and fourth ventricles and characterized by the lack of a blood–brain barrier that are points of communication between the blood, the brain parenchyma, and the cerebral spinal fluid) and baroreceptors located within the aortic arch, carotid sinus and great veins provide “real-time” neural input to higher centers of the brain which continuously and simultaneously coordinate the regulation of both thirst and AVP secretion. Thus, there are physiological sensing mechanisms in place to prompt when to drink and therefore guard against excessive dehydration. Earlier published recommendations to begin drinking before thirst was largely meant for situations where sweating rates were high, above maximal rates of gastric emptying, and dehydration would rapidly accrue over time. Unfortunately, this advice has fostered the misconception that thirst is a poor guide to fluid replacement and has facilitated inadvertent overdrinking and pathological dilutional EAH.

Clinical Classification and Diagnosis of EAH

The diagnosis of EAH is made when the blood, serum or plasma [Na⁺] is below the normal reference range of the laboratory performing the test (typically <135 mmol/L) and is associated with typical clinical constellation of symptoms and signs. In our collective experience, EAH is best classified by clinical severity (symptoms) and not the absolute numerical [Na⁺] value to best guide treatment strategies.

Characteristics of Asymptomatic EAH

Asymptomatic EAH represents a biochemical finding, diagnosed by blood electrolyte testing for research or unrelated metabolic screening purposes. This group of subjects presents without any discernable symptoms or may have mild, generalized and transient complaints commonly experienced by other participants who do not typically seek medical care following exercise. In normally distributed populations, up to 5% of all athletes tested would fall outside of the normal range for [Na⁺], with half of those (2.5%) falling in the range of asymptomatic EAH values.

Characteristics of Mild EAH

Mildly symptomatic EAH typically presents with non-specific signs and symptoms without clear signs of encephalopathy (Table 5). Athletes with mild EAH may have normal vital signs, may not have any orthostatic hypotension, and the symptoms do not resolve after placing athletes in the Trendelenburg position as would be expected with exercise.
associated postural hypotension. The clinical symptoms of mild symptomatic EAH are not specific or sensitive, but should raise the index of suspicion for EAH and necessitate a low threshold for [Na+] measurement, as athletes can rapidly progress from mild symptoms to severe and life-threatening EAHE (Table 5).

EAH must be differentiated from other causes of collapse that may present with similar signs and symptoms including exertional heat illness, acute mountain sickness, and exercise associated postural hypotension. It is important for medical staff to perform a rapid history and physical examination to help determine the etiology of these nonspecific symptoms. However, any clinical suspicion of EAH should lead to prompt measurement of [Na+], if possible. It is common for athletes with EAH to maintain or gain weight during exercise. However, any symptoms listed in Table 5 is an indication to measure [Na+] if available. EAHE can present with a wide range of symptoms ranging from nonspecific mild complaints to severe encephalopathy. The severity of symptoms and not the absolute value of the [Na+] should guide the choice of therapy (Grade 1A). Rapid determination of [Na+] is critical in confirming clinical suspicion but may not always be available.

**Treatment of EAH**

Any athlete exhibiting signs or symptoms consistent with acute hyponatremia (Table 5) should be screened for EAH. The capacity for onsite [Na+] analysis is optimal for management of EAH and is recommended for any large-scale endurance event. However, this capability is not always practical or possible (eg, small or remote events). Treatment should be based on the degree of neurological impairment, not simply the [Na+] level; as brain edema is dependent upon both the magnitude and rate of fall of [Na+] not just the lowest level reached, as stated previously. The following treatment protocols are recommended for EAH and EAHE based on either [Na+] measurement and clinic assessment or clinical assessment alone if [Na+] measurement is not available.

**Onsite Treatment of Asymptomatic EAH Found Via [Na+] Measurement**

Asymptomatic hyponatremia is not normally detected unless an athlete has blood electrolyte concentrations tested for some other reason. In athletes with this incidental biochemical diagnosis, oral or intravenous hypotonic fluid intake should be restricted until the onset of urination to reduce the risk of further decreasing [Na+] with continued AVP-mediated water retention. Furthermore, isotonic intravenous fluids should be administered with great caution or withheld until urination as, in the setting of elevated AVP levels and a concentrated urine, these fluids may lower the [Na+] or delay recovery.

Although there is no compelling reason to actively treat asymptomatic EAH, it is clinically appropriate to administer oral hypertonic saline solutions (HTS), to reduce the risk of progression to symptomatic hyponatremia, this is particularly relevant for those with a [Na+] <130 mmol/L. Upon departure from the event site, athletes with asymptomatic EAH should be advised to seek urgent medical attention if any neurologic signs or symptoms of EAH develop within 24 hours of event discharge from the medical area to observe the affected athlete for signs and symptoms of evolving EAH, since the neurological impairments associated with EAH may limit the athlete’s ability to accurately self-assess his or her status.

**SUMMARY STATEMENT**

EAH can present with a wide range of symptoms ranging from nonspecific mild complaints to severe encephalopathy. The severity of symptoms and not the absolute value of the [Na+] should guide the choice of therapy (Grade 1A). Rapid determination of [Na+] is critical in confirming clinical suspicion but may not always be available.

**TABLE 5. Signs and Symptoms of Mild and Severe (Life-threatening) EAH. Signs and Symptoms Related to Other Conditions Associated With Exercise-Associated Collapse Noted With an Asterisk (*)**

<table>
<thead>
<tr>
<th>Symptoms and Signs Associated With Mild EAH</th>
<th>Symptoms and Signs Associated With Severe EAH and EAHE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lightheadedness*</td>
<td>Vomiting*</td>
</tr>
<tr>
<td>Dizziness*</td>
<td>Headache*</td>
</tr>
<tr>
<td>Nausea*</td>
<td>Altered mental status* (confusion, disorientation, agitation, delirium, feelings of “impending doom,” obtundation)</td>
</tr>
<tr>
<td>Puffiness</td>
<td>Phantom running</td>
</tr>
<tr>
<td>Body weight gain from baseline</td>
<td>Seizure*</td>
</tr>
<tr>
<td>Frothy sputum (non-cardiogenic pulmonary edema)</td>
<td>Coma*</td>
</tr>
<tr>
<td>Dyspnea (non-cardiogenic pulmonary edema)</td>
<td>Signs of impending brain herniation (decorticate posturing, mydriasis)</td>
</tr>
<tr>
<td>Frothy sputum (non-cardiogenic pulmonary edema)</td>
<td></td>
</tr>
</tbody>
</table>
SUMMARY STATEMENT

The major clinical relevance of asymptomatic EAH lies in its potential for asymptomatic athletes to quickly transition and progress into symptomatic stages if hypotonic fluids are given intravenously or ingested (Grade 1C). Thus, in patients identified with EAH, hypotonic or isotonic fluids should be withheld until urination is documented (Grade 1C).

Onsite Treatment of Symptomatic EAH Found Via [Na+] Measurement

Severe EAH (EAHE)

Acute severely symptomatic hyponatremia is a rapidly progressing, life threatening emergency that requires immediate administration of IV hypertonic saline (HTS) (such as 3% sodium chloride).38,42,49,51,62,72,82,91 Because EAHE is an acute rather than chronic process, athletes presenting with symptomatic hyponatremia can and should be treated with HTS as there is no risk of osmotic demyelination after exposure to HTS, but there is grave risk of brain herniation and non-cardiogenic pulmonary edema if HTS is not administered.5,6,38,47,50,62

Any athlete with EAHE associated with signs or symptoms of encephalopathy should be immediately treated with an IV bolus or infusion of HTS to acutely reduce brain edema, with additional IV boluses administered until there is clinical improvement42,51,72 (Table 6). The dose and route of HTS administration should be based upon the severity of clinical symptoms and the available HTS formulations, as discussed in Table 6. Numerous case reports and case series have validated the efficacy and safety use of IV HTS administration in symptomatic EAH8,38,48,49,52,62,72,82,91,100,122,154 with one runner receiving 950 mL of 3% over a 7-hour period without complications42 and another swimmer receiving 40 mL of 20% HTS51 without complication.

In the event that an athlete presents with symptoms of severe, life-threatening encephalopathy (eg, seizures, coma, or signs of impending brain herniation) it is acceptable and highly recommended to administer the first bolus of HTS before [Na+] is measured. Confirmed symptomatic dilutional (euvolemic or hypervolemic) EAHE is a contraindication to the administration of IV hypotonic fluids, lactated Ringer’s, or isotonic (normal) saline, all of which can worsen the degree of hyponatremia41,47,50,134 or delay recovery.91,118,122,151,154,157

The efficacy of IV HTS as the definitive treatment of acute hyponatremic encephalopathy has been validated extensively in both hospital and field settings since it was first utilized successfully in 1938.158 This treatment is based on the capacity of an IV HTS bolus to increase the serum [Na+] 2 to 5 mmol/L, resulting in a concomitant decrease of intracranial pressure and improvement in symptoms.5,6 This approach does not pose any substantial danger to the patient, because osmotic demyelination syndrome has not been associated with either the rapid correction of acute hyponatremia (ie, <48 hours duration) in clinical159 or exercise settings8,38,48,49,52,62,72,82,91,100,122,154 or with the limited increase in [Na+] produced by a single bolus of HT.139,160 Also, of note, if the athlete was wrongly assumed to have EAHE, the administration of HTS in small boluses is not associated with any negative consequences and serves as an excellent volume expander.139

The goal of this therapy is to stabilize the athlete for transfer to an advanced medical care facility for further evaluation, monitoring and treatment. Ideally, the athlete should be transported with knowledgeable event medical personnel able to maintain the same level of care en route and to ensure that the treatment is not interrupted for evaluation such as computerized tomography (CT) imaging of the brain or treatments that may worsen hyponatremia, such as administration of hypotonic fluids, lactated Ringer’s, or isotonic (normal) saline. The diagnosis of EAHE or EAHE must be communicated to the receiving physician upon transfer of care.

TABLE 6. Recommended Treatment for Both Mild and Severe (Life-threatening) Symptomatic EAH in Field or in the Hospital

<table>
<thead>
<tr>
<th>Treatment of Mild EAH</th>
<th>Treatments of Severe EAH</th>
</tr>
</thead>
<tbody>
<tr>
<td>Observation (restrict hypotonic and isotonic fluids until urinating freely)</td>
<td>Administration of intravenous HTS (see below for severe symptomatology) Administration of oral HTS:</td>
</tr>
<tr>
<td>Administration of intravenous HTS (see below for severe symtomatology) Administration of oral HTS:</td>
<td>Equivalent volumes of other solutions of high sodium concentration (eg, 3%-9%)</td>
</tr>
<tr>
<td>Concentrated bouillon (4 bouillon cubes in 125 mL, ½ cup, of water) 3% NaCl (100 mL), preferably with the addition of a flavoring (eg, Crystal Light, Kool Aid) Equivalent volumes of other solutions of high sodium concentration (eg, 3%-9%)</td>
<td></td>
</tr>
<tr>
<td>Mild EAH</td>
<td>Administration of intravenous HTS:</td>
</tr>
<tr>
<td>100 mL bolus of 3% NaCl, repeated twice if there is no clinical improvement (10 min intervals have been recommended, but this should be determined by the clinical judgment of the treating physician)</td>
<td>100 mL bolus of 3% NaCl, repeated twice if there is no clinical improvement (10 min intervals have been recommended, but this should be determined by the clinical judgment of the treating physician)</td>
</tr>
<tr>
<td>Comparable amounts of more concentrated Na+–containing solutions (eg, 10 mL of 20% NaCl; 50 mL of 8.4% NaHCO3) may be used as an alternative to 3% NaCl</td>
<td>Comparable amounts of more concentrated Na+–containing solutions (eg, 10 mL of 20% NaCl; 50 mL of 8.4% NaHCO3) may be used as an alternative to 3% NaCl</td>
</tr>
<tr>
<td>In some situations (ie, more severe encephalopathic symptomatology such as seizures, coma or signs of impending brain herniation) it may be appropriate to administer larger HTS boluses initially rather than waiting to assess clinical improvement after repeated smaller boluses.</td>
<td>In some situations (ie, more severe encephalopathic symptomatology such as seizures, coma or signs of impending brain herniation) it may be appropriate to administer larger HTS boluses initially rather than waiting to assess clinical improvement after repeated smaller boluses.</td>
</tr>
</tbody>
</table>

HTS, hypertonic saline.

SUMMARY STATEMENT

For those athletes presenting with signs and symptoms consistent with EAHE, emergent intravenous treatment therapy with hypertonic saline is indicated and should not be delayed pending laboratory measurement or other diagnostic testing (Grade 1B).

Mild EAH

Any athlete with mild EAH symptoms (Table 6) may be treated with an IV bolus of HTS as described above. Alternatively, a mildly symptomatic athlete may be treated with oral hypertonic solutions when tolerated3,139,155,160 (Table 6) or observation until urination, as seen in clinical settings.6,120 Oral sodium tablets may not be as efficacious as hypertonic solutions, as suggested in a single case report124 and requires further investigation. The efficacy and tolerance of oral HTS has been supported by limited field
the intravascular volume by increasing the serum \( \text{Na}^+ \), neurological status and (2) a bolus of HTS will expand

In Hospital Treatment of Symptomatic EAH

but Unable to Confirm Via \( \text{Na}^+ \)

Onsite Treatment of EAH Suspected Clinically but Unable to Confirm Via \( \text{Na}^+ \)

Measurement

The situation may arise where EAH is strongly suspected based on the clinical evaluation of the athlete (ie, history and physical examination showing neurological symptoms or signs of EAH; Table 3) but \( \text{Na}^+ \) cannot be determined,\(^7^2\) such as in a remote setting.\(^3^9,118,151\) In this situation empiric treatment is justified using the same treatment recommendations described above for EAH documented with a \( \text{Na}^+ \) (Table 6). This empiric approach can be lifesaving and is unlikely to do harm, since: (1) the additional small increase in serum osmolality from a single bolus of HTS will not significantly worsen the neurological status and (2) a bolus of HTS will expand the intravascular volume by increasing the serum \( \text{Na}^+ \), partially reducing any hypovolemic component of the hyponatremia.\(^13^9\)

In Hospital Treatment of Symptomatic EAH

Athletes presenting to a hospital or medical facility, whether primarily or as a transfer from the event site, with signs or symptoms of hyponatremia will require immediate measurement of electrolytes and should be treated as described above without delay once EAH is confirmed (Table 6). If symptomatic EAH persists or worsens following the initial intervention with IV HTS, current treatment guidelines for acute symptomatic hyponatremia should be instituted and the patient managed in an intensive or critical care setting with care provided or guided by a specialist familiar with this life threatening condition.\(^5^6\)

SUMMARY STATEMENT

Athletes presenting to a medical facility with EAH should be treated as per other settings (Grade 1C). However, diagnostic testing in these scenarios should not delay potentially life-saving therapy with HTS (Grade 1C).

Prevention

Athletes and support crews need to carefully consider fluid and electrolyte supplementation during and after exercise and the rationale behind those decisions. Excessive fluid replacement beyond thirst (whether water, sports drinks or other hypotonic fluids) is not a panacea for all instances of fatigue, collapse, muscle cramping, or exertional heat stroke (Table 7). The drinking of fluid volumes sufficiently above sweat and urinary losses before, during and after activity and the accrual a positive water balance, is the primary underlying pathophysiological mechanism of symptomatic and fatal EAH cases.\(^3^4,41,45,52,57,58,61,71,73,75,76,84,119,122–126,162,163\) Therefore, prevention strategies must target drinking behavior. Fluid intake recommendations suggesting that athletes begin to drink fluids before the onset of the sensation of thirst were targeting those exercising in situations where high sweat rates were present and dehydration could evolve rapidly with known medical and performance outcomes. Unfortunately, this advice fostered the misconception that thirst is a poor guide to fluid replacement in lower sweat rate situations. We believe that this has facilitated individuals choosing to inadvertently adopt overdrinking and develop pathologic dilutional EAH, as demonstrated in 41 cases evaluated in Table 7.

Modest to moderate levels of dehydration are tolerable and pose little risk to life in otherwise healthy individuals. Laboratory and field studies indicate that fluid deficits less than and up to a volume approximately equal to 3% of normal body mass (or \(-5\%\) total body water) can be tolerated without a reduction in endurance performance or muscular power when in cool to temperate (\(-10^\circ\text{C}-20^\circ\text{C}\)) temperatures.\(^16^4\) Therefore, aggressive drinking to prevent dehydration is unnecessary and carries with it greater risk of developing symptomatic EAH.

Body weight is a reasonable surrogate measure of hydration state when measured day to day after sleep\(^16^5\) and can be used to relatively accurately assess changes in hydration state accompanying upwards to 1 to 2 hours of activity. However, it is a very imprecise measure during the athletic events where EAH is most likely to develop, that is, multiple hours of sustained activity. This is in large part due to body mass changes accompanying energy combustion\(^12^8\) and unknown amounts of food consumed, bathroom stops, etc. Moreover, consolidation of 4 studies (786 athletes) comparing body weight changes taken at registration (1-3 days prior) and again within 60 minutes of race start demonstrate an average 1% increase in body weight\(^5^,1^0,1^2,1^6^6\) from registration to race start. However, this average value conceals that fact that large gains in weight (up to at least 4% of body mass)\(^1^6^6,1^6^7\) occur in some individuals while substantial weight losses occur in others over that last day or 2 before competition. This weight increase further confounds the accuracy of bodyweight as a proxy measure of body water in field events. With that said, a body mass measured after several hours of activity that is equal to or above the individuals normal body mass is a positive indicator for the presence of fluid overload.

SUMMARY STATEMENT

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The safest individualized hydration strategy before, during and immediately following exercise is to drink palatable fluids when thirsty (Figure). Marathon runners with hypernatremia report “thirstiness” as a physiologically expected symptom while a weak but statistically significant relationship has been demonstrated between thirst ratings and plasma [Na⁺] immediately following a 161 km race. Studies verify that participants allowed free access...
to fluids during treadmill walking in the heat\textsuperscript{169} or running 30 km under different ambient conditions\textsuperscript{170} maintain plasma osmolality by drinking to thirst. Moreover, the cues to drink provided by osmolality and blood volume persist in both hot\textsuperscript{101} and cold\textsuperscript{171} environments. Thus, drinking to thirst will, in most cases, prevent both dilutional EAH and performance decrements due to excessive dehydration.\textsuperscript{10}

Potential exceptions to this fluid replacement strategy are thirst stimulated by confounding oral variables such as dry mouth (xerostomia),\textsuperscript{102,172} genetic influences,\textsuperscript{103}

### FIGURE

Primary recommended fluid intake strategy to prevent symptomatic EAH.

### TABLE 8. Four Case Reports Reporting Symptomatic EAH While Drinking Either ad libitum (First 2 Cases) or in Response to Thirst (Second 2 Cases)

<table>
<thead>
<tr>
<th>Study</th>
<th>Subjects Age (yo), Sex (♂♀), Activity</th>
<th>Plasma [Na\textsuperscript+} mmol/L (Initial)</th>
<th>Symptomatic EAH With ad libitum Drinking (Comments From Report)</th>
</tr>
</thead>
</table>
| Baker et al\textsuperscript{85} | 65, ♀, Lab trial                       | 126                                           | 46kg♀ drank 2.8L water and gained 2.4 kg in 2.5 hr intermittent cycling trial 30°C  
Subjects were not encouraged to drink but told that more fluid was readily available if needed |
| Hew-Butler\textsuperscript{134} | 28, ♀, cyclist                          | 114                                           | Subject followed her normal practice of ingesting a GU packet with 200mL of water every 45 minutes with Coke and water ad libitum for an estimated fluid consumption rate of ~550ml/hr |
| Khodaee et al\textsuperscript{100} | 44, ♂, Mountain biker                   | 116                                           | 84kg♂ drank 29L water and 5.3 g sodium during plus after race (~14 hrs total)  
History of muscle cramping after 5-6hr cycling. Felt “very thirsty” after the race  
Initial labwork in hospital: urine[Na\textsuperscript+] = 31 mmol/L and BUN = 19 mg/dl  
Labwork 2 months after hospitalization: plasma [Na\textsuperscript+] = 133 mmol/L, BUN = 10 mg/dl  
Subject began using “regular sodium supplementation” and “very thirsty” at 100km  
2.2% weight gain noted at 126km and dropped out of race at 145km (28 hrs)  
Initial labwork in hospital: BUN = 22 mg/dl  
17 hrs later in hospital (>10.4L 0.9% saline), plasma [Na\textsuperscript+] = 136 mmol/L and BUN = 10 mg/dl  
Subject received 20L of IV fluids in hospital and discharged with positive fluid balance of 6.6L |
| Hoffman et al\textsuperscript{72} | 53, ♂, Ultra-runner                     | 122                                           | 84kg♂ drank 29L water and 5.3 g sodium during plus after race (~14 hrs total)  
History of muscle cramping after 5-6hr cycling. Felt “very thirsty” after the race  
Initial labwork in hospital: urine[Na\textsuperscript+] = 31 mmol/L and BUN = 19 mg/dl  
Labwork 2 months after hospitalization: plasma [Na\textsuperscript+] = 133 mmol/L, BUN = 10 mg/dl  
Subject began using “regular sodium supplementation” and “very thirsty” at 100km  
2.2% weight gain noted at 126km and dropped out of race at 145km (28 hrs)  
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Subject received 20L of IV fluids in hospital and discharged with positive fluid balance of 6.6L |
known discrepancies between drinking “ad libitum” versus drinking according to the dictates of thirst, excessive sodium intake and/or other non-osmotic or hypovolemic factors that are yet to be determined and require further investigation (Table 8).

**SUMMARY STATEMENT**

Given that excessive fluid consumption is a primary etiologic factor in EAH, using the innate thirst mechanism to guide fluid consumption is a strategy that should limit drinking in excess and developing hyponatremia while providing sufficient fluid to prevent excessive dehydration (Grade 1C).

**Additional Strategies to Prevent EAH**

**Sodium Supplementation**

When fluid intake matches or even slightly exceeds sweat losses, the ingestion of sodium-containing sports drinks can attenuate the rate of fall of [Na⁺] over the course of 2 hours of continuous or intermittent cycling and ~4 hours of running. However, it is critical to emphasize that sodium containing sports drinks, which are hypotonic, will not prevent EAH in athletes who overdrink during exercise, as all sports drinks have a significantly lower [Na⁺] (10-38 mmol/L) than serum (~140 mmol/L). The dilutional effect of volume excess overwhelms any positive effect of sodium and electrolytes in sports drinks. Therefore, while modest salt replacement is likely not harmful and has been associated with significant increases or no change in serum [Na⁺] during competitive field events it will be of modest to no benefit in situations where excess fluids are being consumed. The potential detrimental effects of excessive sodium supplementation are not clear.

**SUMMARY STATEMENT**

Sodium supplementation is a strategy for attenuating sodium concentration reductions that can develop when fluid intakes approximate sweat losses during prolonged exercise but cannot prevent EAH in the setting of a persistent excessive fluid intake that produces fluid overload (Grade 1C).

**Education and Event Management Efforts**

Athlete and support team educational strategies should be instituted to improve knowledge of safe hydration practices and reduce the overemphasis on high fluid intakes. For example, an education program for an Ironman triathlon advising athletes of the risks incurred by overdrinking coupled with decreasing the number of fluid stations to limit the fluid availability reduced the incidence of EAH. Dissemination of appropriate drinking advice alone has also been shown to reduce the incidence of EAH in a 90 km footrace. Past studies have demonstrated that cycling fluid stations placed 20 km apart in an Ironman triathlon and running fluid stations placed 5 km apart in a standard marathon have reduced or prevented EAH. However, this proposed strategy and its effect on the incidence of EAH needs further study to determine the optimal number and spacing of fluid stations in different terrains and ambient temperatures. Furthermore, alternative strategies will be needed in settings where EAH has been noted but either aid stations are not provided or in situations where drinks are freely available and/or athletes transport their own fluids.

Athletes who seek more quantitative guidance are encouraged to weigh themselves before and after training to assess their sweating rates and fluid replacement needs. Some weight loss associated with activity will be unrelated to fluid status as non-water mass is lost as energy is expended and is increased with increasing duration and intensity of exercise. The presence of weight gain is positive indicator that fluid intake has been in excess of fluid losses and water overload is present.

**SUMMARY STATEMENT**

Educational efforts regarding the risks of overhydration should be encouraged and disseminated widely to athletes, coaches, and event management personnel (Grade 1C). These efforts should include all sporting events where EAH has been encountered. Event management strategies such as limiting access to fluids may be of benefit, but require broader study.

**Dissemination of Advice for Prevention and Treatment of EAH**

**Athletes, Coaches, Parents**

Educational strategies and programs are needed that effectively communicate to coaches, athletes, and parents rational fluid replacement, avoidance of overconsuming fluids (water, sports drinks or other hypotonic fluids), to recognize the signs and symptoms of EAH, and to understand the critical need for immediate medical attention for suspected casualties. Athletes, coaches and parents must be alert to the risks of excessive fluid consumption and understand that high fluid intakes will not necessarily prevent exercise-associated maladies such as muscle cramps or exertional heat stroke.

**On-site Medical Professionals (Medics, Paramedics, Emergency Medical Technicians, Athletic Trainers, Physiotherapists, and Others)**

The educational strategies for on-site medical personnel must address the circumstances (during or following events or practices during acclimatization), identification, evaluation and management of EAH and EAHE, and emphasize that the life-threatening nature of these rare conditions require immediate intervention. The pathophysiology of EAH and the drinking behaviours involved in the evolution of EAH must be clearly recognized. It should be stressed that: (1) EAH is caused primarily by the consumption of hypotonic fluid in excess of sweat and urinary losses and (2) excessive fluid intake (water, sports drinks or other hypotonic beverages) may not prevent muscle cramps or exertional heatstroke and in rare cases may even be associative. On-site personnel must understand that oral fluid intake and IV fluid infusion of hypertonic and isotonic fluids is contraindicated in all suspected cases.
of EAH and rapid transfer to a hospital is necessary. The potential life-saving role of HTS requires wide-spread education and should be considered the equivalent of automatic external defibrillators and ice/cold water immersion in the “first aid” of sudden cardiac arrest and exertional heat stroke, respectively.

Team Physicians and Medical Directors of Athletic Events

Team physicians and medical directors of athletic events should be involved in all decisions regarding medical management including overseeing medical protocols, medical supplies/equipment, strategies for fluid replacement that optimize safe hydration practices, placement of fluid stations, and the use of intravenous rehydration. Important athletic event decisions include spacing and placement of fluid stations, distribution of fluid replacement advice to athletes, and training of the aid station personnel and spectators. Drinking advice distributed to participants by sponsors should be reviewed by and approved by the event medical team to avoid conflict with the official race educational information.

Team physicians and event medical directors should ideally have onsite point of care [Na⁺] analysis available and hypertonic saline on hand for management of EAH and EAHE. The event organizer/medical director should be in contact with the local emergency medical services to ensure that transportation to an advanced care medical facility is available during events with high risk for EAH (Table 2).

A record of EAH cases should be kept, including follow up and outcome, to aid in planning for future events and to establish both incidence and prevalence for different events.

Emergency Medical Services and Hospitals

Prior to the race or athletic event, the medical team should establish a relationship with the local emergency response and transport teams, medical facilities and emergency department physicians. This may include specific collaborative education programs aimed at all of these groups and pre-event checklists to ensure that the appropriate course of action is taken and the needed supplies are available in the emergency room when an athlete arrives in extremis.

SUMMARY STATEMENT

Prevention of EAH requires broad educational programs with consistent messages that stress the importance of appropriate hydration practices, recognition of EAH and proper therapy (Grade 1C).

Controversies in EAH

Hypovolemic Hyponatremia

It is unclear whether the hypovolemic variant of EAH has medical consequences. At present, we have apparent evidence of hypovolemic hyponatremia developing over the course of ultra-endurance event, but we lack data regarding: (1) the relative contribution of solute deficits versus fluid status and (2) whether or not the hypovolemic component is somehow compromising the afflicted individual. Most of the contributions of sweat and urinary sodium losses are negligible to the overall pathogenesis of EAH with the possible exception of volume depleted athletes with low serum sodium levels. Thermoregulatory sweat is hypotonic, with sweat sodium concentrations ranging between 10 and 70 mmol/L, which are well below the normal (isotonic) range of values for serum [Na⁺] (135-145 mmol/L). While there will always be some contribution of sodium loss to the pathogenesis of EAH—which will vary significantly in magnitude depending on: exercise intensity, exercise duration, body size, and relative ambient temperature—it is not clear whether or not sweat sodium losses alone can account for the changes in hypovolemic hyponatremia in athletes. The potential role of urinary sodium losses from exercise-induced brain natriuretic peptide secretion contributing to EAH is also unclear.16,188

There are 3 distinct groups of athletes that demonstrate extreme sodium conservation which may increase the susceptibility towards the development of hypovolemic hyponatremia: (1) runners participating in 161 km races under hot conditions, (2) Ironman triathletes participating in hot and humid Ironman triathlons and (3) football players during the first week of training camp. These 3 groups would hypothetically be at greater risk for developing the hypovolemic variant of EAH from more vigorous and sustained sweating (and associated sweat sodium and potassium losses) coupled with an inability to eat sufficient foods to offset the sodium and potassium losses. Football players may also lack adequate adaptations to heat stress, at the onset of pre-season training, which would prevent excessive sweat sodium losses with repeated exposure.

Treatment of Hypovolemic Hyponatremia

Participants with suspected hypovolemic EAH and developing signs of encephalopathy would be best treated initially with an IV HTS bolus to reverse intracerebral edema and expand the intravascular volume. The initial bolus of HTS can be followed by IV 0.9% saline, if neurological symptoms improve. At least one panel member has successfully treated athletes who were clinically volume depleted, with measures of [Na⁺] as low as 124 mmol/L, with IV normal saline infusion. As in all cases of EAH, it would be harmful to treat with hypertonic IV solutions.

Clinical Importance of Asymptomatic EAH

The clinical relevance of the asymptomatic form of EAH continues to be disputed. We agree that the main clinical relevance of asymptomatic EAH lays in the potential for asymptomatic athletes to transition to symptomatic EAH with the continued ingestion of hypertonic fluids. Moreover, symptomatic EAH can rapidly progress to life-threatening symptomatic hyponatremia if large volumes of hypertonic fluids are ingested after identification of asymptomatic EAH is present or are administered intravenously during recovery from exercise.

SUGGESTIONS FOR FUTURE RESEARCH

Prospective and controlled clinical trials should be performed both in the laboratory and in the field to best
determine optimal preventative and therapeutic strategies. Some of the remaining issues for study include:

- Examining nutritional requirements and/or role of diet on the risk for EAH.
- Examining tolerance versus risk for various forms (tablets vs solution) and amounts of sodium supplementation on health, performance and natremia status.
- Gathering evidence with regards to the success of the “drink to thirst” strategy on prevention and/or reduction of the incidence of EAH in athletic events.
- Determining if the development of EAH increases the risk for recurrence and/or long-term health problems.
- Identifying genetic markers which may predispose individuals to developing EAH.
- Additional research is necessary to understand whether individuals consuming NSAIDS are at heightened risk of developing EAH.
- Investigating the efficacy of alternative treatments for non-life threatening EAH, including oral hypertonic sodium solutions, sodium tablets and vasopressin receptor antagonists.
- Clarifying the etiology behind the apparent hypovolemic variant of EAH and the potential for pathophysiological consequences.
- Evaluating the variability in [Na+] in the days leading up to the event, at event start and during the event.
- Evaluating the variability in body weight in the days leading up to the event and at event start.

**SUMMARY OF RECOMMENDATIONS**

**Etiology of EAH**

1. The primary etiology and pathophysiological mechanism underlying EAH—and all known fatalities—is the over-consumption of hypotonic fluids relative to exchangeable sodium in likely combination with non-osmotic AVP secretion (Grade 1A).

2. Under-replaced sodium losses contribute to serum [Na+] independent of distance (Grade 1A). However, there is paucity of data supporting sodium loss as the primary mechanism of symptomatic EAH even in those who exercise for prolonged periods of time and in warm weather (Grade 2C). In these cases, relative over-drinking of hypotonic fluids with sustained non-osmotic AVP secretion is likely involved in the development of symptomatic EAH.

**Clinical Classification and Diagnosis of EAH**

1. EAH can present with a wide range of symptoms ranging from nonspecific mild complaints to severe encephalopathy. The severity of symptoms and not the absolute value of the [Na+] should guide the choice of therapy (Grade 1A). Rapid determination of [Na+] is critical in confirming clinical suspicion but may not always be available.

**Treatment of EAH**

1. The major clinical relevance of asymptomatic EAH lies in its potential for asymptomatic athletes to quickly transition progression into symptomatic stages if hypotonic fluids are given intravenously or ingested (Grade 1C). Thus, in patients identified with EAH, hypotonic or isotonic fluids should be withheld until urination is documented (Grade 1C).

2. For those athletes presenting with signs and symptoms consistent with EAHE, emergent intravenous treatment therapy with hypertonic saline is indicated and should not be delayed pending laboratory measurement or other diagnostic testing (Grade 1B).

3. Athletes presenting with mild symptoms associated with EAH can be treated with an IV bolus of HTS (Grade 1B), oral hypertonic saline fluids or observation until the onset of urination as dictated by clinical symptoms (Grade 2B).

4. Athletes presenting to a medical facility with EAH should be treated as per other settings (Grade 1C). However, diagnostic testing in these scenarios should not delay potentially life-saving therapy with HTS (Grade 1C).

**Prevention of EAH**

1. Given that excessive fluid consumption is a primary etiologic factor in EAH, using the innate thirst mechanism to guide fluid consumption is a strategy that should limit drinking in excess and developing hyponatremia while providing sufficient fluid to prevent excessive dehydration (Grade 1C).

2. Prevention of EAH requires broad educational programs with consistent messages that stress the importance of appropriate hydration practices, recognition of EAH and proper therapy (Grade 1C).

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**REFERENCES**


