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WILDERNESS MEDICAL SOCIETY CLINICAL PRACTICE GUIDELINES

Wilderness Medical Society Clinical Practice Guidelines for the Management of Exercise-Associated Hyponatremia: 2019 Update

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Exercise-associated hyponatremia (EAH) is defined by a serum or plasma sodium concentration below the normal reference range of 135 mmol·L^{-1} that occurs during or up to 24 h after prolonged physical activity. It is reported to occur in individual physical activities or during organized endurance events conducted in environments in which medical care is limited and often not available, and patient evacuation to definitive care is often greatly delayed. Rapid recognition and appropriate treatment are essential in the severe form to increase the likelihood of a positive outcome. To mitigate the risk of EAH mismanagement, care providers in the prehospital and in hospital settings must differentiate from other causes that present with similar signs and symptoms. EAH most commonly has overlapping signs and symptoms with heat exhaustion and exertional heat stroke. Failure in this regard is a recognized cause of worsened morbidity and mortality. In an effort to produce best practice guidelines for EAH management, the Wilderness Medical Society convened an expert panel in May 2018. The panel was charged with updating the WMS Practice Guidelines for Treatment of Exercise-Associated Hyponatremia published in 2014 using evidence-based guidelines for the prevention, recognition, and treatment of EAH. Recommendations are made based on presenting with symptomatic EAH, particularly when point-of-care blood sodium testing is unavailable in the field. These recommendations are graded on the basis of the quality of supporting evidence and balanced between the benefits and risks/burdens for each parameter according to the methodology stipulated by the American College of Chest Physicians.

Keywords: hydration, water, arginine vasopressin, exercise physiology, hypertonic saline

Introduction

In the 3 decades since the first report of exercise-associated hyponatremia (EAH),[1] there have been great efforts to prevent what is now recognized as an important cause of preventable morbidity and mortality in endurance and other physical activities throughout the world. To date, review articles and international consensus statements have documented risk factors, pathophysiology, signs and symptoms, prevention, and patient management strategies.[2-6]

These reports have primarily focused on incidences of EAH in organized endurance events that are conducted in the front country, where medical tents and local emergency medical services (EMS) are available onsite and can transport participants as needed to a local hospital for appropriate management.

Beyond front country endurance events, many prolonged individual exertional activities (eg, backpacking, cycling, ultramarathons, and multiple-day endurance events) take place in the backcountry. EAH has been documented in hikers, trekkers, climbers, and cold climate endurance athletes.[7-11] Thus, EAH is not solely associated

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with activities in warm climates but is reported in both environmental extremes. Furthermore, it is likely that many individuals with asymptomatic or symptomatic EAH go underreported.[10] Fortunately, the lessons learned from current evidence-based EAH guidelines can be extended to those providing care in wilderness environments. It was the intent of this panel to develop evidence-based practice guidelines for the acute care of EAH for use in resource-limited environments, including wilderness, military training and operations, multihour and multiday endurance competition, and during transport by EMS. This set of guidelines is an updated version from 2014.[12] It is beyond the scope of this practice guideline to provide an in-depth discussion of fluid hydration; this is a controversial topic for specific endurance activities to prevent the onset of EAH and to minimize the occurrence of >2% total body water loss.[13,14] There is no single recommendation (ie, drinking to thirst or preplanned scheduled drinking) that fits all individuals during varied outdoor activities in a range of ambient temperatures and with varied sweat rates, body masses, and exercise intensities and durations.[15-17] Our intent is to provide evidence to mitigate the morbidity and mortality from EAH and to recommend safe hydration guidance for preventing overhydration during exertional activities in heat and during varied exercise intensities and durations. However, when overhydration inadvertently results in signs and symptoms of mild to severe EAH, we present evidence for the most effective treatment protocols. The reader is highly encouraged to see other important resources for gaining a broad understanding about how to prevent significant dehydration (hypohydration) and overhydration (hyperhydration) exertional heat illness and how they interrelate in the prevention and treatment of EAH.[15-19]

Methods

The expert panel was convened in May 2018. Members were selected on the basis of prehospital EAH treatment experience, clinical expertise, or research experience. Relevant articles were identified by a search of MEDLINE as the primary database, US National Library of Medicine, and National Institutes of Health. Key search terms used were hyponatremia, EAH, arginine vasopressin, syndrome of inappropriate antidiuretic hormone, hyponatremic encephalopathy, and hypertonic saline (HTS). See Table 1 for key definitions. Articles published between 2014 and 2018 were the focus of the 2019 update. Peer-reviewed studies related to EAH, including randomized controlled trials, observational studies, and case series, were reviewed, and the level of evidence supporting the conclusions was assessed. Abstract-only studies were not included. Conclusions from review articles were not considered in the formulation of recommendations but are cited in an effort to provide context. When no relevant studies were identified, the panel recommendation was based on risk versus benefit perceptions derived from patient-care experience. The panel used a consensus approach to develop recommendations regarding management of EAH in the wilderness. These recommendations have been graded on the basis of clinical strength as outlined by the American College of Chest Physicians (see online Supplemental Table).[20]

SCOPE OF THE PROBLEM

EAH is defined by a serum, plasma, or blood sodium concentration below the normal reference range of 135 $mmol \cdot L^{-1}$ that occurs during or up to 24 h after prolonged physical activity.[4] The reported incidence of EAH varies widely, in part because the diagnosis is based solely on an abnormal biochemical result in an appropriate clinical setting. EAH cases were initially considered rare findings. However, through greater awareness, research, and documentation, incidence rates are now reported in a greater breadth, from low- to moderate- to high-intensity individual activities and sport/endurance events. An extensive list of EAH cases for a wide variety of activities has been given elsewhere.[6]

EAH may be either asymptomatic or symptomatic. Asymptomatic EAH is largely detected in screening protocols as part of research or blood analyzed for other reasons, with the highest reported rates of asymptomatic EAH being as high as 30 to 51% in 161 km (100 mi) single-stage ultramarathon foot races in North America.[21] Symptomatic EAH, a biochemical diagnosis of EAH combined with clinical symptoms and signs, has a much lower incidence. Severe EAH manifests as significant mental status changes such as confusion, delirium, seizures, or a coma resulting from cerebral edema (termed exercise-associated hyponatremic encephalopathy, which may be associated with noncardiogenic pulmonary edema).[5,21] Confirmed deaths of public record have been directly attributed to complications associated with severe EAH[22-25] and have been reported in detail elsewhere.[6] The overall incidence of symptomatic EAH in all marathon participants is typically less than 1%,[25,26] but the percentage of EAH seen in all symptomatic athletes seeking medical care has been reported to be as high as 23% in an Ironman Triathlon[27] and 38% in runners participating in a marathon and ultramarathon in Asia.[28] Symptomatic EAH is now being reported in much shorter distance events, such as a half marathon[29] or a sprint triathlon,[30] which takes approximately 90 min to complete. Symptomatic cases of EAH have been reported in recreational hikers and were found to account for 19% of nonfatal heat-related incidents in Grand Canyon National Park from April through September during 2004 through 2009.[31] From 2002 through 2017, there were 1552 incident

Table 1. Definition of terms

Terms	*Definition*
Ad libitum drinking	Consuming fluid whenever and in whatever volume desired.
Arginine vasopressin	A hormone secreted by cells of the hypothalamic nuclei and stored in the posterior pituitary for release as necessary; also known as antidiuretic hormone.
Dehydration	A loss of body water; an acute condition brought about by the net loss of hypotonic body fluids when free water loss exceeds free water oral intake due to physical activity or in high environmental temperature.
Dilutional hyponatremia	A potentially life-threatening condition that occurs when a person consumes too much water without an adequate intake of electrolytes, resulting in below normal blood sodium concentration.
Drinking to thirst	The use of thirst sensation as the stimulus to drink fluids for hydration.
Euhydration	A normal daily fluctuation in body water content; also referred to as normovolemia.
Exercise-associated collapse	A conscious individual who is unable to stand or walk unaided as a result of light-headedness, faintness and dizziness, or syncope, causing a collapse that occurs after completion of exertional physical activity.
Exercise-associated hypernatremia	A serum, plasma, or blood sodium concentration >145 $mmol \cdot L^{-1}$ that occurs during or up to 24 h after prolonged physical activity; this condition can present symptoms similar to exercise-associated hyponatremia.
Exercise-associated hyponatremia	A serum, plasma, or blood sodium concentration below the normal reference range of 135 $mmol \cdot L^{-1}$ that occurs during or up to 24 h after prolonged physical activity.
Exercise-associated hyponatremia with encephalopathy	A severe form of exercise-associated hyponatremia associated with neurologic changes resulting from cerebral edema and can be associated with noncardiogenic pulmonary edema.
Heat exhaustion	A condition when one is exposed to high ambient temperature or strenuous exertion; manifests nonspecific symptoms that range from uncomfortable to debilitating and may limit continuation of physical activity in the heat.
Heat stroke	A core temperature above 40°C (104°F) with altered mental status and generally divided into 2 categories: classic heat stroke, resulting from passive exposure to high environmental temperatures, and exertional heat stroke, resulting from pathologic hyperthermia during strenuous physical activities.
Hyperhydration	A state of elevated body water (excess) induced acutely before physical activity by means of excessive fluid (isotonic or hypotonic) ingestion.
Hypertonic saline	Any crystalloid solution containing more than 0.9% sodium chloride (ie, 3% sodium chloride).
Hypervolemia	A condition of fluid overload characterized by excessive body fluid volume with an expansion of the extracellular fluid volume, including the intravascular or interstitial space.
Hypohydration	Body water deficit and a form of chronic dehydration; hypohydration during exercise with >2% of body mass can occur from sweat loss during exercise and high environmental temperatures and is usually characterized as hyperosmotic hypovolemia (the term dehydration conveys both acute and chronic loss of body water and hypohydration in this practice guideline).
Hyponatremic encephalopathy	When serum sodium rapidly decreases (eg, exercise-associated hyponatremia), there is an osmotic shift of fluid into the intracellular spaces, resulting in cerebral edema and increased intracranial pressure.
Hypovolemia	A state of decreased blood volume, specifically blood plasma, due to things such as bleeding or water depletion.
Oliguria	Diminished urine excretion.
Overhydration	Excessive oral intake of hypotonic fluids (eg, water and sport electrolyte drinks) resulting in the amount of salt and other electrolytes in the body becoming diluted (ie, hyponatremia).
Syndrome of inappropriate antidiuretic hormone	A syndrome in which secretion of vasopressin (antidiuretic hormone) is not inhibited by hypotonicity of extracellular fluid, and hyponatremia occurs.

diagnoses of exertional hyponatremia among active component Department of Defense service members, with an overall incidence rate of 7.1 cases per 100,000 person-years.[31] The overall incidence rate during the 16-y period (2002−2017) was highest in the US Marine Corps, followed by the US Army and US Air Force, respectively.[32]

PATHOGENESIS OF EAH

It is known that the primary mechanism leading to the majority of EAH cases is overconsumption of hypotonic fluids, likely in combination with nonosmotic stimulation of arginine vasopressin (AVP, also known as antidiuretic hormone) secretion.[3,4] Additionally, a hypovolemic form of EAH, although far less common than the symptomatic hypervolemic form, may be more prevalent in certain circumstances.[33]

Overhydration with hypotonic fluids

In the majority of individuals who develop hyponatremia during prolonged exertional activities (eg, endurance athletic events, backpacking, hiking), there is an increase in total body water relative to total body exchangeable sodium.[3,34,35] Hyponatremia occurs by ingestion of large amounts of hypotonic fluids (water or sports drinks) in excess of sweat, urine, and insensible (mainly respiratory and gastrointestinal) losses.

The data supporting overhydration as the major mechanism involved in EAH are largely derived from observations of weight gain seen in the majority of athletes who become symptomatic with EAH after endurance athletic events in which pre- and post-race weights were taken.[35] However, extrapolation of these weight data in EAH development to other endurance wilderness events such as prolonged hiking is limited. As an example of the magnitude of these fluid intakes, individuals with normal renal function who ingest a regular diet can excrete between 500 and 1000 $mL \cdot h^{-1}$ of water. With the additional nonrenal losses of water as a result of sweat and insensible fluid losses, individuals undertaking prolonged physical activity should be able to consume as much as 1000 to 1500 $mL \cdot h^{-1}$ before developing water retention and dilutional hyponatremia (fluid intake > total body fluid losses).[3] Ingestion of more fluid than this maximal excretory limit will lead to water retention, weight gain, and hyponatremia. However, many individuals who develop EAH do not drink more than 1000 to 1500 $mL \cdot h^{-1}$; thus, additional factors must be involved in the development of EAH.[35] The single most important factor other than hypotonic fluid ingestion is the presence of AVP, which limits renal water excretion and promotes water retention.

Nonosmotic AVP secretion

AVP secretion may play a role in the majority of individuals with EAH.[36-40] Release of AVP leads to water retention in the distal tubule of the kidney and has a net result of lowering serum sodium as this water is returned to the extracellular fluid. Several potential stimuli to AVP release in these circumstances include nonspecific stresses (pain, emotional stress, physical exercise), nausea/vomiting, hypoglycemia, exposure to heat, and possibly medication use (eg, nonsteroidal anti-inflammatory drugs, selective serotonin reuptake inhibitors).[41-46]

Sweat sodium loss

Whether sweat sodium loss contributes to the development of EAH remains controversial. Sodium loss from sweat is highly variable between individuals. The direct effect of losing hypotonic sweat alone would be an increase in serum sodium (loss of water from the body in excess of loss of sodium). However, sweat loss could contribute to the development of hyponatremia via 2 mechanisms: (1) if the degree of fluid loss were sufficient to produce significant volume depletion and provide a stimulus to AVP release, thereby impairing excretion of water, or (2) through ingestion of replacement fluids that were more hypotonic than the sweat losses. This scenario may contribute to the finding of EAH in some individuals with hypovolemia from exertional activity.

RISK FACTORS

The major risk factor for development of hypervolemic EAH is excessive hypotonic fluid intake beyond the capacity for renal water excretion.[47,48] High ambient temperatures appear to increase the risk of EAH,[49,50] as do longer exercising times[51] and nausea (with or without vomiting).[45] Although the incidence of women experiencing symptomatic hyponatremia appears to be greater than that of men in some environments,[4,27,29] when adjusted for body mass index and racing time, the apparent sex difference was not statistically significant,[38] meaning men and women are at equal risk for developing EAH and adverse consequences. Along with other nonosmotic stimuli to AVP secretion, nonsteroidal anti-inflammatory drugs have been implicated as a potential risk factor by potentiating the water retention effects of AVP at the kidney,[23,52] although direct causal evidence remains conflicting.[53,54]

The far less common variant of hypovolemic EAH has been associated with chronic diuretic use,[55,56] higher ambient temperatures, and longer duration of physical activity,[4,56,57] especially in older men participating in long-duration exercise in remote settings. Individuals with higher sweat sodium concentrations, with and without cystic

fibrosis, have also been shown to be more at risk for developing the hypovolemic variant of EAH over time.[51] Nausea and vomiting may contribute to both solute losses and nonosmotic fluid retention through AVP stimulation in both the hypervolemic and hypovolemic variants of EAH.[45]

Recommendation. Sustained overhydration during exercise is the primary risk factor in the development of all variants of EAH and should be avoided. **Recommendation grade:** 1A.

PREVENTION

Education of event participants, support crews, and medical personnel

Appropriate education and coordination among participants, event directors, support crews, park rangers, and first responders and EMS transport personnel are essential in the prevention of EAH. EMS providers should also have a basic understanding of EAH to avoid the provision of improper hydration.[58] Pre-site visits to the receiving medical facilities and emergency department triage staff will increase EAH awareness and collaboration. It has been previously shown that runners have a poor understanding of the relationship between drinking habits and hyponatremia[59,60]; this likely extends to wilderness recreationalists. EAH educational materials should be provided via in-person briefings, written statements, or educational videotapes prior to the activity.

Recommendation. Participants and medical staff should be educated about proper hydration strategies for exertional activities. **Recommendation grade:** 1C.

Avoidance of overhydration

Several strategies are available to prevent overdrinking during exercise. Because the clinical consequences of hypoosmotic hyponatremia are largely driven by acute osmotic disturbances in water balance (ie, when water passes through the cell membrane down an osmotic gradient from outside the cells to inside the cells, causing cellular swelling), drinking according to the dictates of osmotically driven thirst remains the primary strategy to prevent EAH. Because fluid losses through sweat and urine are highly dynamic and variable across individuals participating in a variety of outdoor and indoor activities, fixed (nonindividualized) range guidelines are inappropriate.[61-64] Using the sensation of osmotic- or volemic-driven thirst as a real-time guide for fluid ingestion during such activities appears safe and effective and largely eliminates both of the detrimental extremes of dysnatremia (hypernatremia and hyponatremia), irrespective of body weight losses.[61,62,65] Therefore, participant education on this (osmotically driven) "drinking to thirst" approach is an important prevention strategy.

Another strategy used to prevent overdrinking is estimation of individual fluid replacement needs. This can be done in advance of a wilderness excursion by monitoring body weight changes across a variety of climates, activities, and intensities and then calculating fluid replacement needs per hour (ie, every 1 pound of body weight lost should be replaced with 470 mL [16 oz] of fluid). This strategy is commonly used during 161-km ultramarathons to help prevent overhydration. However, EAH has been reported with substantial weight loss and lack of weight loss,[35,49,66-68] and thus weight changes are not a reliable approach for excluding a diagnosis of EAH. In the presence of weight gain during exercise, fluid intake should be reduced because no person should gain weight during exercise. Although largely impractical in a wilderness setting, weight scales might be helpful in organized endurance athletic events, but care should be taken to ensure scale calibration and placement on solid, level surfaces, and participants should be educated in proper use of body weight information. Another helpful strategy that has been shown to reduce the incidence of EAH during endurance events is to reduce fluid availability.[65]

Recommendation. Participants in endurance athletic events or strenuous wilderness activities should focus on avoiding overdrinking during the activity. **Recommendation grade:** 1A.

Participants should drink according to thirst, or they should determine an estimation of their individual fluid needs during pre-event training activities (by assessing body weight losses per hour), which limits the potential for weight gain. **Recommendation grade:** 1C.

Supplemental sodium and oral intake

Sodium supplementation during exercise with overhydration has not been shown to prevent the development of EAH during physical activity lasting less than 18 h.[65-70] Supplemental sodium (in foods, fluids, or capsules) may attenuate the decline in blood sodium concentration when drinking beyond thirst to fully replace weight losses. However, sodium supplementation will not prevent the development of EAH if overdrinking continues.[70] Supplemental sodium has no effect on blood sodium concentration when exercising individuals drink according to thirst,[70,71] although those who drink the least amount of fluid during exercise will often finish the activity with elevated blood sodium concentrations.[72-75] Collectively, these observations demonstrate that it is the amount of fluid ingested during exercise rather than the amount of sodium that has the

more pronounced effect on blood sodium concentrations. Studies suggest that sweat sodium losses augment the palatability of salty beverages,[76,77] which may support the utility of having sodium-rich foods and beverages available during long and hot activities. For example, a salt packet from a fast food restaurant contains 300 mg of sodium, or 13 meq. Assuming that sweat losses are typically between 20 to 50 meq·L^{-1}, with wide variability of sweat rate and sodium losses, ingestion 1 to 2 salt packets per hour—or ingestion of salty foods—may be appropriate during prolonged activities as long as fluids are freely available.

Recommendation. Sodium and/or salty snacks should be freely available for consumption along with the appropriate fluid intake, particularly in long, hot events in non–heat acclimatized persons, but this strategy will not prevent EAH when combined with overdrinking. **Recommendation grade:** 2B.

PREHOSPITAL ASSESSMENT AND TREATMENT

Assessment

When symptomatic EAH is a consideration in the at-risk individual and when point-of-care serum sodium concentration analysis is available, the diagnosis is straightforward. However, the reality is that point-of-care diagnostic testing is problematic and expensive, and the devices and cartridges require a narrow ambient temperature range of 16 to 30°C (61 to 86°F) to ensure functionality. All of these factors make on-site analysis of serum sodium concentrations in most wilderness environments impractical.[58] Correct field diagnosis when point-of-care sodium testing is unavailable is mostly predicated on obtaining an accurate history of total fluid intake. When a history of hypotonic fluid ingestion supports excessive fluid intake relative to suspected losses, EAH should be considered as a possible diagnosis. The absence of major signs and symptoms common to symptomatic hypovolemia (or heat illness), such as thirst, postural dizziness, dry mucous membranes, and orthostatic changes in vital signs (tachycardia or hypotension while standing compared to supine), support EAH as a diagnosis.[8,19,78,79] Weight gain may be indicative of the diagnosis. Urine output is another clinical parameter used to assess volume status; however, because of the aforementioned water retention effects from AVP at the kidney, urine output is variable with EAH and may be an unreliable differentiator from dehydration or heat exhaustion or heat stroke.

Table 2. Signs and symptoms associated with mild exercise-associated hyponatremia

Weakness,[a] malaise,[b] and fatigue[a]
Irritability[a]
Headache[a]
Bloated feeling and body weight gain
Nausea and vomiting[a]
Dizziness[a]
Variable urine output[a,b]

[a] Overlapping signs and symptoms with heat exhaustion/dehydration.
[b] Urine output is often unreliable for diagnostic purposes because of variable arginine vasopressin effects. Thus, urine output in itself should not be relied upon to make a diagnosis of exercise-associated hyponatremia versus heat exhaustion/dehydration.

Table 3. Signs and symptoms associated with severe exercise-associated hyponatremia

Collapse[a]
Vomiting
Altered mental status (confusion/altered sensorium, ataxia, collapse)[a]
Normothermic
Dyspnea (noncardiogenic pulmonary edema)
Frothy sputum (noncardiogenic pulmonary edema)
Seizures[a]
Coma[a]

[a] Overlapping signs and symptoms with heat stroke.

Recommendation. When available, point-of-care testing should be done on at-risk, symptomatic patients. If unavailable, integrate all available clinical and historical information into an assessment of the patient's hydration status (history of fluid intake, food intake, presenting signs and symptoms, body weight if available, and urine output). **Recommendation grade:** 1C.

Treatment

Appropriate management of EAH depends first on correctly diagnosing the condition. EAH must be routinely considered as part of the differential diagnosis, with mild to severe heat illness,[8,18] as there are overlapping signs and symptoms (Tables 2 and 3).[8,78,79] As a result, EAH is commonly misdiagnosed as either heat exhaustion or exertional heat stroke in an individual presenting with collapse or exhaustion during or shortly after prolonged, low- to moderate-intensity exertion during hot conditions.[8] Accurately differentiating EAH from heat exhaustion or exertional heat stroke is critical because inappropriately treating one as the other can lead to adverse outcomes.[19,80]

Like EAH, heat exhaustion can develop over several hours with prolonged, low- to moderate-intensity exertion in warm or hot weather with inadequate fluid replacement and excessive fluid losses (ie, sweating). Although dehydration has a number of competing definitions in clinical

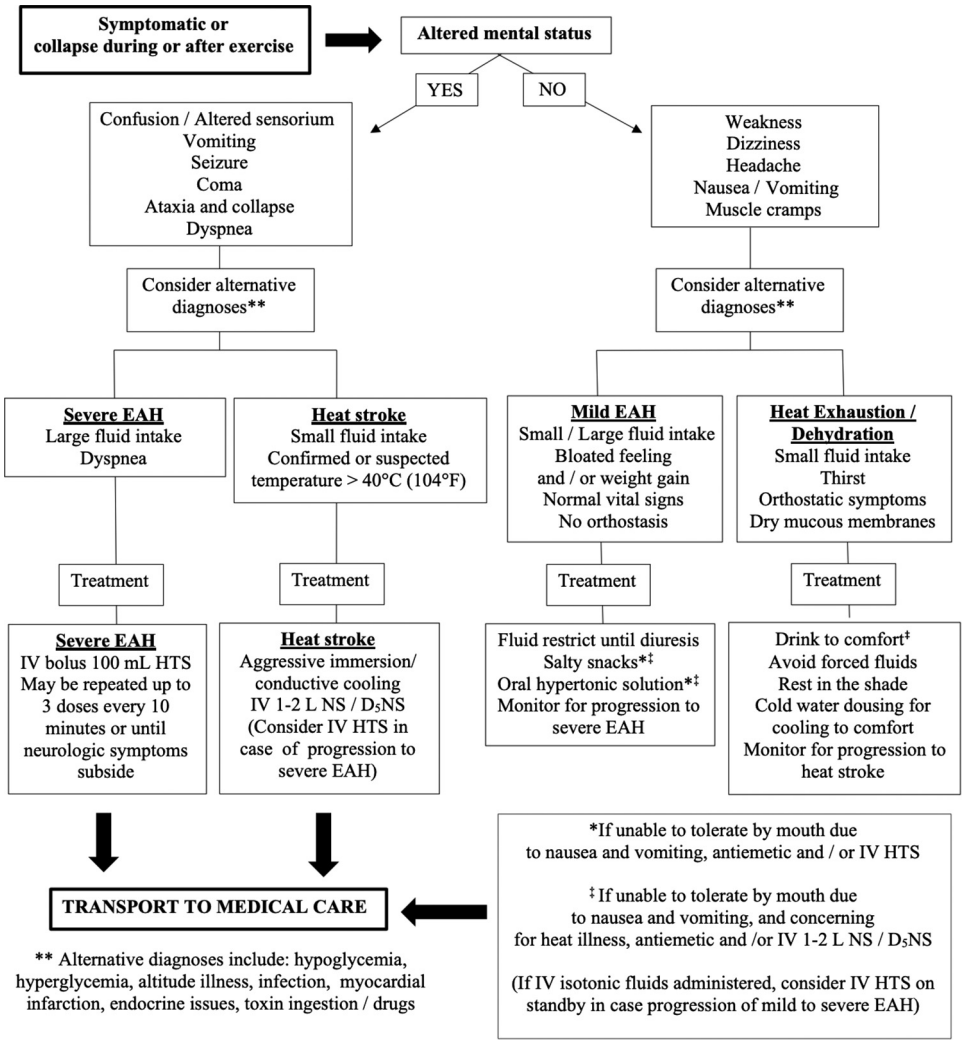

Figure. Clinical approach for field treatment of suspected EAH. D_5NS, 5% dextrose 0.9% normal saline; EAH, exercise-associated hyponatremia; HTS, hypertonic saline (3% sodium chloride); IV, intravenous; NS, normal saline (0.9% sodium chloride).

medicine,[58,79] for this practice guideline we will define it in association with heat illness as any total body water deficit (>2% of body weight) that can occur from sweat loss during physical activity in high environmental temperatures that may impede the ability to continue the physical activity or prolonged exercise.

When the diagnosis of EAH is confirmed or strongly suspected, empiric treatment of symptomatic EAH is an acceptable option.[4,58,81] Treatment options should be predicated on the presence (or absence) of neurologic impairment to differentiate mild EAH from severe EAH and guide resuscitative choices (Figure).[4,81] This algorithmic, empiric approach for clinically suspected EAH can be lifesaving and is unlikely (but unconfirmed) to induce harm.[4,81,82] Treatment has been recommended based on degree of neurologic manifestations[4] because cerebral edema and symptoms are dependent on the magnitude and rate of decline of serum sodium, not simply the serum sodium nadir.[83,84] Because individuals can rapidly progress from mild to severe EAH,[85] initial resuscitation and symptomatic care to minimize morbidity and progression of disease are of paramount importance.

MILD EAH

Oral fluid restriction

Suspected mild EAH from overhydration with fluid retention (ie, from nonosmotic AVP secretion) can be treated with oral fluid restriction until the onset of free water excretion (osmotic AVP suppression). Again, correctly differentiating EAH from dehydration is critical because treatments

are in opposition. Although administration of oral isotonic or hypotonic fluids is appropriate for the dehydrated or heat-stressed individual,[80] isotonic or hypotonic oral fluids may cause deleterious consequences in an individual with mild EAH and progression to severe EAH.[86,87]

Recommendation. Oral fluid restriction is indicated if EAH from fluid overload is associated with mild symptoms. Hypotonic fluids are contraindicated with suspected EAH. **Recommendation grade:** 1C.

Oral sodium

Oral hypertonic solutions may increase serum sodium levels similar to an intravenous (IV) bolus of the same solution (100 mL of 3% sodium chloride) in runners with asymptomatic or mild EAH.[57,88] Another study suggests that oral HTS reduces symptomatology from EAH faster than an IV bolus.[85,89] Unfortunately, oral hypertonic fluids may be unpalatable,[90] which limits their treatment utility. Symptomatic individuals with suspected EAH who are neurologically intact and have minimal nausea may thereby respond favorably (and more quickly) to an oral bolus of a hypertonic solution, such as concentrated broth (3−4 bouillon cubes [880 mg sodium per cube] in 125 mL [0.5 cup] of water) or 100 mL of HTS with flavoring. Another potentially effective alternative (from author experience) is 3 Top Ramen seasoning packets (contain 900 mg of sodium), ingested with 0.5 cup (125 mL) of water. Likewise, foods with high sodium content (ie, Rold Gold pretzels: 450 mg per 23 g for a 17-pretzel serving size) are another option.

Recommendation. Oral sodium in hypertonic solutions or foods with high sodium content (salty snacks) may increase serum sodium levels and enhance symptom relief (over fluid restriction) for mild EAH, if tolerated. **Recommendation grade:** 2B

Given the risk of hyponatremia worsening after the initial presentation, individuals should be closely monitored for this occurrence, particularly without biochemical confirmation of EAH. Although the exact time for observation is not known, clinicians should be cautious in letting individuals leave their care before at least 60 min of observation.[57,88,89] This is primarily due to water remaining in the gastrointestinal tract that can be absorbed at the cessation of exercise and may result in progression of EAH symptoms.[23,26,81,91] Longer observation periods may be appropriate depending on the presenting symptoms, amount of fluids ingested, or other circumstances, such as the absence of family or friends who can monitor the individual after the initial care period. Antiemetic medication, if available, may be a useful adjunct. More urgent medical attention, including planning for transfer to definitive care, is required if there is deterioration in the patient's condition with any neurological symptoms or signs that include altered mental status (eg, confusion/altered sensorium, ataxia, collapse), loss of consciousness, dyspnea, seizures, or decorticate posturing. If these signs and symptoms of central nervous system involvement develop, urgent treatment with an IV bolus of 100-mL of HTS is recommended.

Recommendation. Observe patients for at least 60 min after exercise to ensure no decompensation from delayed symptomatic EAH after cessation of exercise. **Recommendation grade:** 1C.

Intravenous solutions

An important element in the treatment of EAH is avoidance of exacerbating the condition with improper fluid management. The inability to tolerate oral fluids secondary to nausea and vomiting is common in both EAH and intracellular dehydration.[8,90,92] Intravenous isotonic fluids are discouraged in fluid overload EAH because nonosmotic AVP secretion exacerbates the dilutional effects of these fluids, with potentially devastating consequences.[23,24,26,55,84] Therefore, one should balance the risks and benefits of isotonic fluid administration with clear indications (eg, cardiovascular instability or intractable vomiting). If the history of fluid intake, vital signs, and physical examination do not support moderate to severe heat illness or dehydration as a likely cause, either hypotonic or isotonic IV fluids should be avoided and careful monitoring of neurological status advised.

Recommendation. IV hypotonic fluids are contraindicated with suspected fluid overload EAH. **Recommendation grade:** 1C.

Isotonic fluid intake should be restricted in known or suspected severe hypervolemic EAH until urination begins. **Recommendation grade:** 1C.

SEVERE EAH

Although the early symptoms of EAH may be nonspecific, the presence of altered mental status, coma, seizures, and/or respiratory distress (suggesting noncardiogenic pulmonary edema) in the absence of obvious hyperthermia supports the diagnosis of severe EAH and should be promptly recognized and treated immediately with an IV bolus of 100 mL of HTS.[23,24,26,81,91,93] If collapse occurs in hot conditions, severe EAH may present similarly to exertional heat stroke

(Table 3), and cases of their (paradoxical) coexistence have been reported, with 1 fatality.[94,95]

If the diagnosis is uncertain or there are signs of obvious hyperthermia, immediate cooling should be initiated while preparing to give possible HTS until the diagnosis is clarified (Figure).[19,78,79] Because severe, life-threatening severe EAH is an acute process, an IV bolus of 100 mL of HTS is considered a safe intervention, with no reported cases of osmotic demyelination to date. Although a 100-mL bolus of IV HTS, which can be repeated twice at 10-min intervals, is recommended (3 doses in total), larger volumes of HTS (950 mL 3% sodium chloride over 7 h and 600 mL over 1 h) have been successfully given without complications.[81,93] Without IV HTS administration there is significant risk for noncardiogenic pulmonary edema, progressive cerebral edema, brainstem herniation, and death.[23,37,86,96] The efficacy of IV HTS administration in hyponatremic encephalopathy has been validated, resulting in a decrease of edema and intracranial pressure and symptom resolution.[36,83]

Of note, when EAH encephalopathy is suspected and point-of-care testing unavailable, one or multiple boluses of HTS has been lifesaving. The theoretical risk from administration of an IV bolus of HTS, without biochemical confirmation of EAH, would be elevation of serum [Na+] 1 to 2 $mmol \cdot L^{-1}$ in person with hypernatremia. Collapsed marathon and ultramarathon runners have been found to be more frequently hypernatremic than hyponatremic and more likely to report vomiting than those who are normonatremic.[23,34,49] The common signs and symptoms of hypernatremia mirror EAH and include nausea, vomiting, diarrhea, headaches, and muscle cramping.[66] The vomiting observed in hypernatremia likely contributes to dehydration and the development of worsening hypernatremia.[49] In the case of hypernatremia where oral hydration cannot be tolerated, IV isotonic fluids augment plasma volume expansion, which has been shown to quickly reverse adverse symptomatology.[90,92]

Recommendation. An IV bolus of 100 mL of HTS should be administered immediately if signs and symptoms of encephalopathy (with or without noncardiogenic pulmonary edema) develop and severe EAH is strongly suspected. **Recommendation grade:** 1C.

APPROPRIATE TRANSFER OF CARE TO EMS TRANSPORT AND RECEIVING HOSPITAL

Prehospital transport

The intent of field management is to stabilize the patient until he or she can be transferred to a definitive care medical facility. Unfortunately, EAH symptom recognition is challenging and appropriate management conflicting. Therefore, when transferring care from on-site medical personnel to either EMS providers or directly to in-hospital providers, it is critical to relay the potential diagnosis of EAH and awareness of the dangers of aggressive oral or IV fluid hydration. Ideally, if intravenous access has been obtained, an IV saline lock should be placed for EMS transport, and the provision of IV fluids should be based on clear indications of clinical instability (eg, thready pulse, altered mental status, chest pain, shortness of breath). However, if the transport team does administer isotonic or hypotonic fluids, close observation is needed because a patient with mild EAH could experience progressive neurological symptoms associated with hyponatremic encephalopathy. If signs and symptoms of encephalopathy appear (see Table 3), isotonic or hypotonic IV fluid administration should be replaced with an immediate bolus of HTS (100 mL of 3% or closest equivalent).

Recommendation. When transferring care, receiving caregivers should be alerted to the potential diagnosis of EAH and appropriate fluid management (withhold hypotonic fluids). **Recommendation grade:** 2C.

Table 4. Acute in-hospital assessment and management of exercise-associated hyponatremia

Assessment	Urgent measurement of blood sodium by the most rapidly available means. Assess for clinical signs suggestive of developing cerebral edema. Obtain and store specimens, if possible, for later analysis of blood serum osmolality and urine sodium and osmolality.
Management	Supplemental oxygen to maintain oxygen saturation above 95%. Restrict fluids (both intravenous and oral) until onset of urination. Avoid intravenous normal saline until sodium correction is initiated. Normal saline may be required for hypovolemic shock or in renal protection therapy for rhabdomyolysis. In severe exercise-associated hyponatremia (signs of cerebral edema or serum sodium [125 $mmol \cdot L^{-1}$]) administer intravenous 3% sodium chloride as a 100-mL bolus repeated twice at 10-min intervals aiming to reverse cerebral edema. Aim to increase serum sodium by approximately 4 to 5 $mmol \cdot L^{-1}$ or until neurological symptoms are reversed by active treatment, then allow the remaining correction to occur spontaneously via urinary free water excretion.

Acute in-hospital treatment of symptomatic EAH

On arrival to definitive care, EAH symptom recognition is challenging. Appropriate management in an emergency department is not universally understood, and in-hospital medical providers must differentiate from other causes that present with similar signs and symptoms.[8,9,66,97] Patients arriving with signs or symptoms of EAH will require immediate measurement of electrolytes and should be treated as described in the Treatment section without delay once EAH is confirmed. In cases of severe hyponatremia, these patients require management in an intensive care or critical care unit and should be managed with accepted clinical guidelines (see Table 4 for an overview of in-hospital assessment and management steps).[4,83,98] The following recommendations are based on the level of evidence in the Treatment section.

Recommendations. Oral and IV hypotonic or isotonic hydration should be avoided early in the management of EAH, although it may be appropriate in certain clinical contexts once sodium correction has been initiated or hypovolemia is confirmed. **Recommendation grade:** 1C.

With suspected EAH, and particularly in those with altered mental status, sodium estimation should be obtained as rapidly as possible after hospital arrival. **Recommendation grade:** 1A.

A rapid assessment for signs and symptoms of cerebral edema or noncardiogenic pulmonary edema should be done in all patients with possible EAH. **Recommendation grade:** 1A.

Severe EAH biochemically confirmed or symptomatic EAH should be treated with a 100-mL bolus of IV HTS, which can be repeated twice at 10-min intervals (3 doses in total) or until improvement of neurologic symptoms, with the aim of acutely increasing serum sodium concentration by about 4 to 5 $mmol \cdot L^{-1}$ and reversing cerebral edema. **Recommendation grade:** 1A.

Conclusions

EAH has a complex pathogenesis and multifactorial etiology. The primary mechanism leading to the majority of EAH cases is overhydration of hypotonic fluids, likely in combination with nonosmotic stimulation of arginine vasopressin secretion. In the majority of cases, EAH is asymptomatic; however, it can be insidious, debilitating, and in rare cases present with severe symptoms and potentially devastating outcomes.

Preventing EAH is the key factor in protecting participants in endurance events and other wilderness recreation activities. Currently, there is no single hydration recommendation that fits all individuals for fluid and salt consumption during all exercise scenarios. We recommend for the majority of participants a hydration strategy that relies on their innate thirst mechanism. Thirst is triggered by changes in serum osmolality and should prevent severe dehydration while minimizing the risk for overhydration and hyponatremia (especially if ADH is present). We recognize that there are situations in which body fluid losses may be excessive and rapid. In these circumstances, thirst may not keep up with body fluid losses, and other hydration strategies may be needed. In these situations, participants should consider increasing their fluid intake to account for these excessive losses.

There is an ongoing need for education to ensure that participants understand the risk of overhydration. Furthermore, a knowledge gap persists internationally among practitioners and prehospital EMS personnel about the assessment and treatment of EAH, which is compounded by many of its nonspecific presenting signs and symptoms. The typical field response is to encourage oral hypotonic fluid intake or administer rapid isotonic IV fluids to endurance activity participants with the suspicion they are dehydrated. However, such universal treatment may result in increased morbidity and mortality in the EAH patient.

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Appendix A. Supplementary data

Supplementary material associated with this article can be found in the online version at: https://doi.org/10.1016/j.wem.2019.11.003.

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