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The Evaluation and Management of Heat Injuries in the Emergency Department

A 14 month old boy is brought into the ED by EMS after being left in a locked car while his babysitter was shopping. His rectal temperature is 105.6°F, his skin is dry, and he is hypotonic and unable to be aroused. The paramedics are already actively cooling the child with ice packs in his groin and axillae. Are there any pharmacologic options for therapy?

A 32 year old Hazardous Materials specialist, recently activated from the military reserves, is at the scene of a possible biologic terrorist attack in full protective clothing when he collapses and begins seizing. The temperature outside is only 50°F, his skin is soaked with sweat, and his skin feels hot to the paramedics. Could he have developed heat stroke during the winter while profusely sweating? Is there anything that could have been done to prevent this?

A 16 year old high school athlete is competing in the county track meet on an unusually hot and humid day. Several of the athletes are experiencing muscular cramping, and the only water available is from the city water fountain. After standing for a long time, one of the parents lost consciousness, but has now recovered. Are there any guidelines to better manage these events?

The heterogeneous and ubiquitous nature of heat induced illnesses has presented a timeless challenge to healthcare providers. Heat illnesses comprise a constellation of conditions that vary from the superficially annoying miliaria rubra, to the often fatal heat stroke with multi-organ dysfunction. Etiologies, risk factors and those affected are equally diverse, ranging from the

June 2006
Volume 8, Number 6

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CME Objectives

Upon completion of this article, you should be able to:

1. Understand and be able to define the various terms pertinent to the whole spectrum of heat illnesses;
2. Understand the differences between exertional and classic heat stroke;
3. Understand the key components to prehospital and emergency department management;
4. Understand available methods of cooling patients;
5. Understand physiologic systems affected by heatstroke

Date of original release: June 30, 2006.
Date of most recent review: June 25, 2006.
See "Physician CME Information" on back page.

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very young to the very old, from world class athletes to disabled individuals, and from world superpowers to third world countries. As a result, a review of this nature is inherently limited in its attempted scope. We will try to address those educational needs germane to emergency providers. This includes not only the obvious question of how to approach a hyperthermic patient both diagnostically and therapeutically, but out of necessity the various risk factors and pathophysiology involved. As in many aspects of medicine, prevention and planning often present the greatest opportunity to impact morbidity and mortality. Increasingly, emergency physicians are reaching out of the ED and are involved in the medical oversight of a wide range of special populations, including EMS, firefighters, military personnel, athletes, and refugees. This demands more than just a cursory knowledge of the subject matter, and will allow emergency physicians to positively affect medical oversight as well as management.

Critical Appraisal Of The Literature

A search of MEDLINE® was performed using the search strings "heat illness," "heat-related illness," "heat stroke," and "heat injury" with limits placed on articles no more than 10 years old unless deemed to be classic. The resulting articles were then individually reviewed. Additional bibliographic references not revealed during the MEDLINE® search were also retrieved if deemed relevant. The National Guideline Clearinghouse, Cochrane Database of Systematic reviews, BestBets, American Healthcare Research and Quality, Database of Abstracts of Reviews of Effectiveness, and Prime Answers were all reviewed with generally poor results. The American College of Emergency Physicians (ACEP) does not, as of this writing, have a clinical policy regarding the management of heat injuries.

Much of the literature surrounding the elucidation of the pathophysiology of severe heat related illnesses originates from animal studies and case-series that detail the myriad of multisystem effects that can occur. A number of epidemiologic studies have provided valuable insight into the various risk factors in developing a heat related illness. Several experimental studies have also been conducted to attempt to validate and quantify the effect of these risk factors. However these studies apply to, and utilize healthy adults simulating occupational duties or involve athletes. This obviously limits the applicability of the findings and leaves us to make assumptions on how the typical victims of classical heat stroke, the elderly and very young, would respond.

The literature addressing treatment modalities for heat stroke is generally poor. The studies that do address the various treatments for heat stroke are fraught with generally poor methodology, are usually case studies, and involve very small numbers (from 3-52 patients). While echoing the above concerns, JE Smith wrote an evidence-based meta-analysis in 2005 in the British Journal of Sports Medicine.[68] He was able to find 17 studies in the literature that provide original data on cooling times, and to-date this provides the best assessment of the literature regarding cooling methods in exertional heat stroke. In 2002, Bouchama and Knochel wrote a review in the New England Journal of Medicine which provides some helpful information regarding evaluation and treatment of heat stroke.[4] Specifically looking at the evidence for treating heatstroke with dantrolene sodium, Hadad et al. were only able to find two human studies and three animal studies appropriate for inclusion in his paper.[87] These above studies exemplify the difficulties researchers have had in providing evidence-based recommendations for the treatment of heat injuries.

Recognizing the paucity of organizational position statements addressing heat-related illnesses, the National Athletic Trainers Association (NATA) organized a conference in 2003. The panel consisted of representatives comprising 18 different medical, nutrition and sports related organizations, including ACEP, and produced "The Inter-Association Task Force of Exertional Heat Illness Consensus Statement". This document reflects a collection of expert opinion only and has been directly endorsed by only a few of the professional organizations from which the panel was comprised.[61]

Epidemiology, Etiology, And Pathophysiology

As could be deduced, heat illnesses have been documented throughout all of history, from biblical times and ancient Greece to modern day.[1] Historically, descriptions of heat illness involve fatal cases pro-

duced most often by exertion, or environmental extremes. Often missing are the nonfatal effects of heat illness and its varied presentation. Recent epidemiologic studies have provided some insight to better characterize the impact of heat related illness on society, its various risk factors, and has delineated especially vulnerable populations. A significant underestimation of the magnitude is still thought to exist however, as there is both under-diagnosis as well as varying definitions of heat-related illness.[2]

The incidence of heat illness understandably rises during periods of warm weather. Between 1979 and 1999, the CDC reported 8,015 heat related deaths in the U.S. From 1979 to 2002, a total of 4,780 heat-related deaths were attributable to hostile weather conditions. Epidemiologically, a heat wave is defined as ≥3 consecutive days of air temperatures ≥90°F (32.2°C). Heat-related deaths are usually defined as exposure to hot weather, a body temperature ≥40.6°C and an absence of alternate causes of hyperthermia.[3-6] Global average temperatures are projected to increase between 1.4°C and 5.8°C by the end of this century. There has been a recently demonstrated causal link between global warming and the occurrence of regional heat waves, and as a result, heat related illnesses can be expected to increase not withstanding additional interventions. Heat waves are not only predicted to be more frequent, but also to increase in duration.[7]

Studies of several recent heat waves emphasize the persisting relevance of heat-related illnesses. In July 1995, Chicago experienced a heat wave resulting in 485 heat related deaths.[6] In 2003, a heat wave across Europe resulted in the largest death toll in recent history. France alone experienced a loss of 14,800 lives in 9 days during which the temperature reached 37°C, with an average temperature of 35.7°C. For reference, the average temperature in 2002 during the same period was 25.1°C. This was estimated as probably the hottest summer in 500 years. The largest fatalities were seen among the elderly with a 70% and 120% increase in deaths in the ages 75-94 and ≥95 respectively.[5, 7, 8] One of the public hospitals in Paris reported an additional 2600 ED visits with an eventual 475 fatalities. Italy, Spain, Portugal, and England were estimated to have fatalities between 1,000 and 5,000 people during the same heat wave.[7, 8]

Not surprisingly, military organizations of many countries have been interested in the effects of heat on soldiers. A database study from 1980 to 2002 involving the U.S. military revealed that 5,246 soldiers were hospitalized and 37 died secondary to heat illness. There was an approximately 60% reduction in hospitalization rates (fewer heat exhaustion cases) over the 22-yr period, but a five-fold increase in heat stroke hospitalization rates (1.8 per 100,000 in 1980 to 14.5 per 100,000 in 2001) with an obvious association to the recent desert operational environment.[10] The recent death of a British neurosurgeon supporting allied troops in Iraq secondary to heatstroke exemplifies the far reaching and nondiscriminatory danger.[11]

Physiology of heat control

Discussion of the physiology of thermoregulation, even when limited to that of heat production and elimination, is a daunting task spanning not only a discussion of physics, but includes the microbiology and genetics of all the major organ systems as well. As emergency health care providers, not all of this information is immediately applicable to the presenting heatstroke victim. However, many of us are involved in activities that allow us to make a preventative impact on heat illness, i.e. event medical management, EMS/Fire, etc. Thus, the following is but an overview that will hopefully lay a foundation by which to better understand, plan for, and rationally treat heat illness.

Humans maintain body temperature within a strict range, usually 36.5°C - 37.5°C, in order to avoid enzymatic and cellular dysfunction. The central nervous system must compare information from thermal sensors to the desired "set-point" in the preoptic nucleus of the anterior hypothalamus and determine upon the activation of mechanisms to dissipate any excess heat. Thermal sensors exist both cutaneously as well as centrally in the hypothalamus. Heat production arises from both metabolic processes as well as the surrounding environment. The basal metabolic rate for a 70 kg person is approximately 100kcal and would result in a 1.1°C/hour rise in body temperature in lieu of any cooling mechanism.[1] Sympathetic nerves stimulate cutaneous vasodilatation and sweating in response to increased body heat. Blood flow to the skin increases from a baseline of approximately 250ml/min to approximately 6-8 L/minute with a concomitant increased demand on cardiac output.[12] These adaptive mechanisms will continue to intensify in order to match any additional heat production or absorption. Remarkably, it has been found that

elite athletes may reach a steady state of 104°F without any degradation in performance.[13]

There are four physical mechanisms by which heat exchange occurs: conduction, convection, evaporation and radiation. As these elements are crucial to the understanding of not only the physiology and etiology of heat related illnesses but its treatment as well, those are reviewed below.

Conduction

Conduction is heat exchange between two surfaces in direct contact and is usually considered the least important of the mechanisms of heat transfer. The thermal conductivity of air is poor, and as such when examined in the context of heat related illnesses, it is primarily the amount of direct contact with a solid or liquid surface that needs to be considered. The thermal conductivity of water is approximately 25-32 times greater than air. While contact with hot sand, concrete or water are all potential sources of additional heat stress, the application of ice packs to the axillae or groin is a potential tool for the elimination of heat in heat stroke.[1, 14, 15]

Convection

Convection is heat exchange from one region to another by a moving gas or fluid. The rate of heat transfer is affected by several variables including the density of the medium (fluid greater than gas), rate of flow, surface area, and temperature gradient. Heat is efficiently transferred from the body's core to the periphery through blood with changes in cardiac output affecting flow, and peripheral vasodilatation or vasoconstriction affecting surface area. Skin surface air velocity also modifies convective heat exchange with loose-fitting clothing maximizing both convective and evaporative heat loss. Once the ambient air temperature has exceeded skin temperature, heat is gained by the body from the environment.[1, 14]

Radiation

Radiation is heat transfer by electromagnetic waves. Estimates of heat gain from solar radiation range from 250-300 kcal/hr, approximately the same as walking. Clothing introduces a barrier, reducing this gain to approximately 100 kcal/hr. Interestingly, non-pigmented skin absorbs approximately 20% more heat than highly pigmented skin and may be a risk factor for developing a heat related illness. [1, 14]

Evaporation

Evaporation is the transfer of heat from the conversion of a liquid to a gas. As the ambient temperature rises and the other mechanisms of heat transfer become insufficient to maintain body temperature, evaporative heat exchange from sweating becomes the dominant mechanism of heat loss. During exercise evaporative heat loss is the primary thermoregulatory mechanism when the ambient temperature is above 20°C (68°F).[15, 16] Evaporative heat loss secondary to sweat is approximately 1 kcal/1.7 ml or 580kcal/L. Individuals exercising in hot environments commonly lose 1-2 L/hr of sweat, with up to 4L/hr for short periods. Though these rates may increase greatly, estimates of the upper limit of heat dissipation secondary to sweating is approximately 650kcal/hr, since much of the sweat at high rates is lost from the skin prior to evaporation. Sweat evaporated from clothing is also significantly less effective. In hot dry environments with sufficient air flow, the rate of evaporative cooling is primarily a function of the rate of sweating; however, as humidity rises and approaches 100% the role of evaporative cooling becomes minimal. Sufficiently hot and humid environments combined with even minor exertion may present the individual with a situation of uncompensable heat stress (UHS). This becomes especially important when using protective clothing which is detailed later, along with the special circumstances that UHS presents.[1, 14]

As evaporation becomes the primary method of heat loss at an appreciable level of exertion or environmental heat stress, rehydration becomes a crucial consideration. Rehydration rate depends on both gastric and intestinal transit time, which is dependent on several factors including volume ingested, exercise intensity and ambient temperature. Gastric emptying rates under optimal conditions can reach 1.8L/hr with the intestines absorbing 1.4-2.2 L/hr.[14] It has been assumed previously that with increased exercise intensity, decreased splanchnic blood flow secondary to increased muscle blood flow would decrease transit time. Interestingly however, it has been shown in one study that exercise <70% VO_{2max} results in increased gastric emptying, while >70% VO_{2max} decreased emptying.[17, 18]

Acclimation

Acclimation is defined as a series of physiologic changes as a result of repeated exposures to heat stress that allow a person to work safely at levels of

heat that were previously intolerable or life threatening.[1, 19] Studies of military populations have provided epidemiologic support for the efficacy of acclimation. A study of over 5000 U.S. Army heat illness hospitalizations showed greater rates of hospitalizations among recruits from northern (cooler), than from southern (warmer) states, where they were already presumably acclimated. Additionally, a decreasing prevalence of heat injury with increasing months of military experience supports the role of increased fitness and duration of exposure in long term adaptation.[10]

Table 1 below lists the physiologic adaptations that take place with acclimations. Decreased core and skin temperature with decreased perceived exertion during exercise are also seen.[13,14, 18] The rate of evaporation is related to the difference in the vapor pressure of water at the skin and that of the surrounding air. A lowered sweat salt content seen in acclimated individuals increases this difference and hence also increases the evaporative rate.[14] Daily exposure to work and heat for 100 min/day results in near maximal acclimation in 7-14 days.[1] Improvement in cardiac performance through physical conditioning may also be seen and is beneficial, but requires longer periods of training. Heat acclimation is a transient phenomenon, with a rate of decay occurring over several weeks once removed from the heat stress. Plasma volume however decreases considerably within 1-2 weeks. Re-induction of heat acclimation can however be achieved rapidly.[1, 14, 18]

Pathophysiology of heat illness

Irrespective of the initial etiology of severe heat exhaustion or heat stroke, there is a common final physiologic pathway involving tissue and cellular structure swelling and disruption with widespread hemorrhaging. Heat stress causes damage to the body by at least three prominent mechanisms. (1) Denaturation of proteins disrupts cellular functions, causing direct damage. Exposure to temperatures above 41.6°C to 42°C for even a few hours will cause cellular damage. Extreme temperatures above 49°C result in almost immediate cell death. Especially vulnerable organs to hyperthermia induced apoptosis include the thymus, spleen, lymph nodes and the mucosa of the small intestine. (2) Several inflammatory cytokines are released including tumor necrosis factor-α, interleukin-1 (β) and interferon γ, as well as the anti-inflammatory cytokines IL-6, IL-10 and TNF receptors p55 and p75. Concentrations of the various cytokines and receptors have been shown to correlate with outcome.[20] Additionally, infusion of IL1 and or TNF-α into animals has been shown to result in similar pathophysiologic changes as heat stroke.[21] (3) Significant temperatures also injure the vascular endothelium, increasing vascular permeability, and result in the activation of the coagulation cascade and subsequent development of disseminated intravascular coagulation (DIC). This is evidenced by increased concentrations of markers of endothelial activation or damage in heat stroke patients, including endothelin, intracellular adhesion molecule 1 (ICAM-1, CD54) and von Willebrand factor antigen.[4, 12, 14, 21, 22]

Table 1: Physiologic Changes with Acclimation

- Increased plasma volume
- Increased rate of sweating
- Decreased threshold for initiation of sweating
- Increased maximum capacity of cutaneous vasodilatation
- Decreased electrolyte content of sweat
- Decreased heart rate at a given work load and stress
- Increased aldosterone production with resulting decreased urinary sodium excretion and greater volume retention
- Lower core and skin temperature

Adapted from [13, 14]

Differential Diagnosis Of Heat Related Conditions

Heat Edema

Heat Edema is a benign condition that is often seen in non-acclimatized individuals when presented with a heat stress and is described as a mild edema that develops in dependent areas. More prominently seen in the elderly, the etiology is believed to be a combination of orthostatic pressure, peripheral vasodilatation and vascular leak that leads to increased interstitial fluid. Afflicted individuals often are sitting or standing for long periods of time resulting in an increased orthostatic pressure in dependent extremities. This condition will resolve once the individual acclimates, though symptomatic treatment includes rest, lower extremity elevation, and possibly compression stockings. Diuretic therapy has not been shown to be effective and may actually precipitate dehydration and a more severe heat illness.[1, 12, 13, 16]

Heat Tetany

Heat tetany has been described as carpopedal spasms that result from hyperventilation in response to heat stress. Symptoms of tetany appear to be related more to the rate of PCO_2 change than the absolute value.[23] Removal from the heat stress will allow the resolution of the compensatory hyperventilation, hypocarbia, and the resulting spasms. Rebreathing in a paper bag may also be used, but with caution for the development of hypoxemia. [13, 14]

Heat Syncope

Heat syncope is an orthostatic hypotensive event resulting in loss of consciousness that is the result of peripheral vasodilatation in response to heat, and is often seen in conjunction with prolonged standing or a rapid flat to upright postural change. As presented previously, the normal physiologic adaptation to heat stress includes increased peripheral circulating volume in an attempt to disperse heat from the body core. This, however, may be at the expense of a diminished central venous return, which when stressed with an upright posture can result in syncope. The condition is self limiting as the syncope returns the body to the horizontal position improving central venous return. Oral rehydration should be instituted, and the patient placed in a cool area to recover. Prevention measures include avoidance of prolonged standing in hot environments, adequate hydration, periodic flexing of the lower extremities to promote venous return, and lying down during symptoms of lightheadedness or weakness. Acclimation appears to also be helpful as the incidence of heat syncope decreases with increasing number of days worked in the heat.[1, 12-14, 16]

Heat Cramps

Heat cramps are fleeting painful spasms of the large voluntary muscle groups that occur after strenuous exertion. The condition is thought to be secondary to large amounts of sweat that is subsequently replaced by hypotonic solutions, resulting in a dilutional hyponatremia. Cramps commonly involve the thighs, calves, abdominal wall and shoulder. Elevated core temperature is not a required feature as the cramps may present several hours after the exertion. In a heat stress environment, non-acclimated individuals are at risk due to the increased electrolyte concentration of their sweat. Acute treatment consists of oral hydration with an electrolyte solution, or intravenous normal saline, and rest. Likewise, preventative measures include the use of an electrolyte rehydration solution rather than water, or the use of supplemental salt, either in the form of tablets or salty foods. Salt tablets are gastric irritants, however, and if used must be done with caution. They are not recommended for the acute treatment of heat cramps.[1, 12, 13, 15, 16]

Miliaria rubra

Miliaria rubra, also known as Prickly Heat or Heat Rash, is a pruritic papulovesicular rash that develops over clothing covered areas when exposed to hot humid environments. Additional risk factors include fever and a few drugs, i.e. isotretinoin, and bethanechol. It is the result of occluded sweat glands deep within the dermis, which subsequently dilate and rupture causing intensely pruritic vesicular lesions. Miliaria rubra may progress to miliaria profunda in which duct obstruction is evident in the dermoepidermal junction, with a common complication of chronic dermatitis. Understandably, the affected areas are often anhidrotic and may also become secondarily infected by staphylococcus. The resulting anhidrosis may place the affected individual at increased risk for hyperthermia. The complete pathogenesis is still unclear as the keratin plug observed microscopically obstructing the sweat gland ducts develops only later in the clinical course. Current theories involve primary duct disruption rather than occlusion which may develop later. Primary treatment includes drying and cooling of the skin to avoid further sweating. Chlorhexidine cream or lotion, and salicylic acid (1%) have also been used as adjuncts in treatment of the infection and assistance in desquamation respectively. Preventative measures include the avoidance of situations resulting in prolonged continuous sweating. [1, 13, 24, 25]

Heat Exhaustion

Heat exhaustion is the most common form of heat related illness. In contrast to the previously described conditions, heat exhaustion presents with systemic symptoms. Though nonspecific, they include profuse sweating, malaise, fatigue, headache, nausea and possible vomiting. Affected individuals are tachycardia, and often demonstrating orthostatic hypotension. Core temperature is less than 104°F. Importantly, mental status is relatively intact, without evidence of coma or seizures, though dizziness and emotional lability may occur.[1, 12, 13]

Classically, heat exhaustion is divided into two categories, water depletion and salt depletion. The water depletion form of heat exhaustion occurs sec-

ondary to inadequate rehydration during strenuous exertion in a hot environment. It is more rapid than the salt depletion form because of its relationship to overall volume status. It is often seen in day laborers, military personnel, and athletes. An involuntary dehydration of 2% or more of body weight may occur before a strong drinking response is observed. [26] Even with easily available fluid, and instructions to freely drink as needed, intake rarely matches the rate at which fluid is lost.[27] Salt depletion heat exhaustion is the result of rehydration of large volumes of sweat with hypotonic solutions. The resulting hyponatremia and hypochloremia produce systemic symptoms in contrast to heat cramps. Providing confusion to disease definitions, salt depletion heat exhaustion may produce an altered mental status or seizures secondary to severe hyponatremia, but not meet the hyperpyrexia definition for heat stroke.[12] Defined by some as exertional hyponatremia, this necessitates an aggressive electrolyte replacement strategy rather than primary cooling as required in heat stroke.[13] Rarely is either form of heat exhaustion seen purely, but rather in combination.[1]

Treatment of heat exhaustion includes, as with most of the minor heat related illnesses, removal from the heat, and oral rehydration with an electrolyte solution. Typically, recovery should be rapid with the patient feeling better in two to three hours.[16] In cases with more significant electrolyte disturbances or orthostatic hypotension intravenous normal saline should be used.[1, 16] Significant free water deficits should not be corrected faster than 2 mOsm/hr, as this has been associated with seizures secondary to cerebral edema.[1] As has already been stated, heat illness is a spectrum of disease, and as such treatment for heat exhaustion is based on its clear diagnosis, or more importantly the clear exclusion of heat stroke. It may be difficult to clearly differentiate heat stroke from exhaustion on initial presentation and thus aggressive treatment is recommended.

Heat Stroke

The most serious type of heat related illness is heat stroke. Variably defined, heat stroke usually includes; (1) A core body temperature of more than 105°F (40.5°C), though the temperature may be lower (2) Central nervous system dysfunction, (3) Exposure to heat stress, endogenous or exogenous, and (4) Exclusions to include CNS infection, sepsis, neuroleptic malignant syndrome or malignant hyperthermia secondary to anesthetic agents. (Table 2 below) Some sources include a marked elevation of hepatic transaminases, however this is not universal.[1, 2] An alternate definition based on pathophysiology is as follows: a form of hyperthermia associated with a systemic inflammatory response leading to a syndrome of multiorgan dysfunction in which encephalopathy predominates.[4] The mortality in heat stroke patients is commonly cited as high as 10 percent, but may vary widely.[16]

Heat stroke in its severe form can lead to multiorgan dysfunction with a clearly increased mortality rate. Common complications include acute respiratory distress syndrome (ARDS), disseminated intravascular coagulation (DIC), shock, rhabdomyolysis, renal failure, cerebral edema, seizures, and hepatic dysfunction.[2] In a retrospective chart study of patients with near fatal classic heatstroke that were admitted to an ICU in Chicago during the 1995 heat wave all had multi-organ dysfunction with neurologic impairment, 45% developed moderate to severe renal insufficiency; 10% developed ARDS; 57% had evidence of infection on admission. The inpatient mortality was 21%. In those discharged, a moderate to severe functional impairment existed in one third with no significant improvement at 1 year and an additional 28% of the patients had died.[28]

Several studies have attempted to characterize predictors of the development of multi-organ dysfunction in heat stroke. One of the most recent, a retrospective chart review of heatstroke patients admitted to teaching hospitals from 1998-2001 in India found the presence of metabolic acidosis, elevated creatinine kinase (CK) (>1000 IU/L), and elevated liver enzymes at initial presentation to be associated with the development of multi-organ dysfunction. Not surprisingly, those that progressed to multiorgan dysfunction presented for medical care later (4.1 vs. 2.3 mean days of hyperthermia prior to

Table 2: Diagnosis of Heat Stroke

- A core body temperature of generally more than 105°F (40.5°C), though may be slightly lower.
- Central nervous system dysfunction
- Exposure to heat stress, endogenous or exogenous
- Exclusions to include CNS infection, sepsis, neuroleptic malignant syndrome or malignant hyperthermia secondary to anesthetic agents.
- Some sources include a marked elevation of hepatic transaminases, however this is not universal.

Adapted from [1, 2]

admission). The study included a shockingly high overall case fatality rate of 71.4%, increasing to 85% with concomitant multi-organ dysfunction. Delayed presentation, tertiary care facility with a possibly increased disease severity, and a delay in the initiation of treatment were all proposed factors contributing to the high mortality rate.[2]

Though the final common pathway of heat stroke is similar, there exist two distinct forms, classic (epidemic) and exertional heatstroke. Each has unique etiologies, risk factors, populations and presentations. Also known as epidemic heatstroke from its relation to heat waves, classic heat stroke typically is seen in the elderly and debilitated. Classic heatstroke primarily develops secondary to an external thermal insult. Exertion is not required or common in the development of classic heat stroke, with its development over days rather than minutes or hours. Several risk factors include lower socioeconomic status, alcoholism, and psychiatric medications. A case-control study revealed that those at greatest risk had pre-existing medical conditions, were socially isolated, confined to bed, lived on the top floor, or did not have access to air conditioning.[29] Classical heat stroke victims often present anhidrotic secondary to the duration over which the condition develops, though this is not a diagnostic requirement. It is thought that failure of, or loss of sweating may play a more important role in the development of classical heat stroke than exertional.[22] Hyperventilation, resulting in respiratory alkalosis with concomitant metabolic acidosis, is common in classical heat stroke with a pure lactic acidosis more typically seen in exertional heat stroke.[1, 12, 14]

Exertional heat stroke typically occurs in previously healthy young adults exercising or working in a hot and humid environment without prior acclimation, and is primarily due to internal heat production.[30] It is typically reported in athletes, miners, foundry workers, firefighters and military recruits. Risk factors predisposing to the development of exertional heat stroke are similar to classical heat stroke, see Table 3.

Women have been cited to be relatively protected from exertional heat stroke as the body temperature at which thermoregulatory reflexes are activated are lower in women than men, and women appear to store less heat than men for a given workload. Proposed etiologies include lager muscle mass in men.[22] This does not seem to be a universal finding however as a study of US Army soldiers revealed greater rates of hospitalizations and heat strokes among women than men.[10] Patients usually present still sweating, tachycardic and hypotensive. Exertional heat stroke victims more commonly develop disseminated intravascular coagulation, acute renal failure, lactic acidosis, hypokalemia, and rhabdomyolysis when compared to classical heat stroke.[16]

Prehospital Care

The prehospital evaluation can be the most crucial part in the overall treatment of the heat-injured patients. The first step in treating this disorder is recognizing it. While in certain circumstances this would seem obvious (e.g. marathon runner, etc.), there are other times where the initial evaluation will be more subtle. During the summer months, history has shown us that elderly people are susceptible to rapid climate changes, resulting in increases in the number of heat injured patients. As such, it is crucial that prehospital caregivers be aware of heat stroke in the setting of altered mental status.

Once a patient is identified as potentially being a heat injury, basic measures should be undertaken to facilitate care and transport to the nearest appropriate medical facility. Prior to transport, measures

Table 3: Risk factors for Development of Heat Stroke by Type

Classic	Both	Exertional
• Elderly • Children • Social isolation • Confined to bed • Debilitated • Lack of air conditioning • Live on top floor of a building • Heat Wave • Chronic mental illness • Cardiopulmonary disease • Chronic illness	• Drugs (see Table 4 page 10) • Obesity • Current febrile illness • Prior dehydrating illness • Skin diseases (i.e. anhydrosis, psoriasis) • Metabolic conditions increasing heat production (i.e. thyrotoxicosis) • Lack of acclimatization • Prior heat stroke • Previous days heat exposure • Elevated Heat Index	• Protective clothing • Recent alcohol consumption • Lack of sleep, food or water • Lack of physical fitness • Lighter skin pigmentation • Motivation to push oneself/warrior mentality • Reluctance to report problems • Lack of coach or athlete education regarding heat illness.

Adapted from [3, 10, 12, 22, 29, 61, 114, 115]

should be taken to dissipate core body heat and mitigate factors that could increase heat transfer into the body. The patient should be placed in a shaded area. Tepid water may be applied to the patient in order to initiate the evaporation process. Manual fanning may also be performed if possible. The patient should be removed from any external heat sources if applicable.

EMS transport should be initiated with the appropriate level of transport capability. Patients with any changes in sensorium should have ALS trained personnel, if available, for advanced procedures such as intubation. Gradual rehydration may be initiated as patients with exertional heat stroke will most likely have some degree of dehydration. Care must not be too aggressive with this rehydration in that patients might already be hyponatremic and additional intravenous or oral water administration could make this worse. Alternatively, aggressive rehydration with normal saline can overcorrect as well. Clothing removal, external cooling through fanning or air-conditioning, and continuous monitoring are all appropriate prehospital measures that can be undertaken. Providers must be cautious with these patients and understand that in addition to altered mental status, they might have to treat seizure activity and content with vomiting and potentially diarrhea as well.

Currently, there is very little literature specific to prehospital care and outcomes from which to draw our conclusions. There is some observational data suggesting that having medical providers at the scene of mass gathering events will decrease the amount of hospital transports to include patients with heat injuries.[31] Additionally, medical rehydration units at mass gathering events can significantly impact the amount of patients requiring transport to the hospital. This has proved to be a successful method of treating mild to moderate heat-related illness.[32] Hopefully, with the expansion of emergency medicine and EMS training, new research will help to better define the appropriate level of treatment for heat-related illnesses in the prehospital setting.

Emergency Department Evaluation

Initial Stabilization

Heat injury patients will require a varying amount of monitoring based on their severity of illness. Heat stroke patients will require a significant amount of monitoring and emergency department resources. In addition to basic ED monitoring including pulse oximetry, the core body temperature must be determined as soon as possible. This can be established with a long rectal core body thermometer, esophageal probe, or probes imbedded within Foley catheters. These special thermometers can measure above 41.0°C (105.8°F) which will be necessary in some heat injury patients to establish the true magnitude of the hyperpyrexia. A Foley catheter will be an essential item in patient management, as urine output will be a key measurement in the resuscitation of the patient with heat injury. Fortunately, urinary bladder temperature variation with urine flow rates has been shown to clinically insignificant, and still reliable.[33]

In terms of intravascular access, consideration must be given as to when a central line should be placed; this is particularly relevant in light of new initiatives promoted by goal directed therapy seen in other disorders such as sepsis. Many heat stroke patients will require central venous pressure (CVP) monitoring in the ICU, and early knowledge of their intravascular status can potentially improve morbidity and mortality in these patients. Obviously, frequent neurological assessments are required to monitor the patient's progress, and an ECG is also warranted in this early period.

Historical Questions

If the patient's mental status is significantly altered, information must be sought from EMS personnel, witnesses, and family members whenever possible. Every attempt to find out what medications the patient is on should be made in that there are a number of drugs that predispose to heat injury, see Table 4 on next page. Obtain as much history as possible regarding the preceding events in order to understand the circumstances of the heat injury, e.g., medical illness or exertional activities.

Physical Exam

There are two things that must be done on the initial physical examination. Treatment of all patients on the spectrum of hyperthermic injury starts with reviewing the ABC's and reviewing the initial vital signs. Certain patients with significant mental derangement during heat stroke might need to be intubated for airway protection. Fluid resuscitation needs to be initiated, and good access must be achieved. The vital signs can provide clues as to what interventions might be necessary to resuscitate

the patient. Tachycardia is a good indicator that the patient is fairly sick and will need fluid resuscitation and cooling. Hypotension is a very concerning sign that demonstrates the patient will need serious goal directed therapy during the cooling process. Patient may also demonstrate varying degrees of tachypnea and tachycardia.[28] All patients in classic heat stroke will have tachycardia and hyperventilation[4], and up to 25% will have hypotension.[34]

After the initial stabilization, a more detailed physical examination can be performed. First, evaluate the patient's mental status. Not only will this provide a sense of the patient's ability to protect his airway, it will also give a good idea of how far down the spectrum of heat injury the patient is. Headache, incoherent speech, irritability, ataxia, global confusion, seizures, and coma are all reported central nervous system effects from heat stroke.[4] Less commonly reported are extrapyramidal syndromes, pancerebellar syndromes, and flaccid paraparesis.[35] An assessment of the patient's hydration status is also very helpful at this point: Evaluate skin turgor; see if the patient has moist mucous membranes, and if the eyes are sunken back. Sweating may be present, or the patient may demonstrate frank anhydrosis in severe cases. The skin may also be notable for bruising or petechaie which may be visible in cases that have progressed to disseminated intravascular coagulation (DIC). A good auscultory examination must be done; patients with tachypnea and/or hypoxia demonstrated by pulse oximetery could have pulmonary edema secondary to heat stroke.

Table 4: Medications that Contribute to Heat Injury

- Alcohol
- Alpha Adenergics
- Amphetamines
- Anticholinergics
- Antihistamines
- Benzodiazepines
- Beta-blockers
- Caffeine
- Calcium-channel Blockers
- Cocaine
- Diuretics
- Ephedra
- Heroin
- Inhaled Anesthetics
- Laxatives
- Lysergic Acid Diethylamide (LSD
- Ma Huang
- Monoamine Oxidase Inhibitors
- Neuroleptics
- Phencyclidine Hydrochloride (PCP)
- Phenothiazines
- Pseudoephedra
- Sympathomimetics (Other)
- Thyroid Agonists
- Tricyclic Antidepressants

Adapted from [16, 110, 112, 113]

Diagnostic Studies

Diagnostic Imaging

Chest radiograph A chest radiograph should be ordered in patients presenting with significant heat injury. Findings can demonstrate evidence of pulmonary edema, pulmonary congestion, acute respiratory distress syndrome (ARDS), and cardiomegaly. Additionally, one may find ancillary issues such as an infiltrative process that could have predisposed the patient to heat injury in the first place.

Computed tomography (CT) of the Head There are a large number of abnormalities that can occur in patients with heat stroke. Findings include edema, ischemic changes, or, in patients who become coagulopathic, hemorrhage.[36] Within four hours of developing heat stroke , significant findings such as neuronal swelling can occur.[37] CT is an appropriate early step in the management of these patients who have any degree of altered mental status. Long term damage to the CNS has been described in numerous reports[38], and a brain MRI might be needed to further delineate the scope of injury at a later point.

Electrocardiogram (ECG)

Cardiac disturbances are commonly found in patients suffering from heat injuries, especially those suffering from heat stroke. In one study, 21% of patients showed changes consistent with myocardial ischemia.[39] Although many of these changes are reversible with resolution of the heat syndrome [40], there are case reports of myocardial infarction with normal coronary arteries[22] and global hypokenesis identified by echocardiogram.[41]

Electrocardiographic alterations are also very commonly discovered in patients with heat stroke.[39] These findings are fairly non-specific and can include rhythm changes such as atrial fibrillation, conduction deficits such as QT segment prolongation, and ST segment changes and T wave abnormalities, see Table 5 on next page[42]. Of these potential abnormalities, the prolongation of the Q-T interval

appears to be the most common abnormality seen in patients with severe heat injury. This is thought to be due to electrolyte abnormalities such as hypocalcemia, hypokalemia, or hypomagnesaemia.[22]

Echocardiography

If available, echocardiography can be a helpful diagnostic tool in the workup of a heatstroke patient. As previously stated, many of the patients who demonstrate ECG findings consistent with myocardial infarction, do not, in fact, end up having such disease. The same is true for echocardiography[43]. Additionally, echocardiography can be helpful in the evaluation of myocardial function and injury. Patients demonstrating global hypokenesis without regional wall motion abnormalities suggest that there isn't a true hypoperfusion event occurring even in the presence of my elevated myocardial laboratory markers.[40] These events are theorized to either be due to transient coronary vasospasm, or Tako-Tsubo cardiomyopathy which is characterized by ECG findings consistent with acute myocardial infarction, transient left ventricular dysfunction, with normal coronary angiography.[40]

Although still controversial, it is theorized that patients with heat injury, particularly exertional heat injury, can be divided into two groups. The first is a hypodynamic group characterized by low cardiac index, an elevated CVP, and high systemic vascular resistance (SVR). Conversely, the hyperdynamic group has an elevated cardiac index, low SVR, and elevated CVP.[22, 39] Patients have been observed with both phenomena, and it is unclear as to whether these are separate entities, or just different physiologic responses existing on a continuum of disease. Some suggest that the initial response is hyperdynamic, and if untreated, this progresses to a hypodynamic physiologic state.[44]

Table 5: Electrocardiographic Findings in Heat Injured Patients

- Rhythm Disturbances
  - Sinus Tachycardia
  - Atrial Fibrillation
  - Supraventricular Tachycardia
- Conduction Defects
  - Right Bundle Branch Block
  - Intraventricular Conduction Delay
  - Q-T Interval Prolongation (most common)
  - ST Segment Changes (usually localized)

Adapted from references [22, 42]

Laboratory Studies

Laboratory studies will reflect the degree of organ dysfunction present, and help determine where on the spectrum of heat injury the patient lies. The most serious derangements will be seen in heatstroke, which involves a constellation of signs and symptoms from multi-organ dysfunction.[28, 45] Generally there is evidence of muscle breakdown, acute renal failure, and potentially disseminated intravascular coagulation (DIC). As such, a wide spectrum of laboratory abnormalities could potentially be encountered.

A complete blood count and serum chemistries with calcium, magnesium, and phosphate should be ordered. Evidence of hemoconcentration may be seen on the CBC secondary to dehydration. Additionally, heatstroke patients will most likely present with evidence of both leukocytosis and lymphocytosis.[46] DIC is also a feature of heatstroke[47] with rates as high as 45%.[28]

Serum Chemistries

Changes in serum sodium are more a reflection of water imbalances, and one could expect to see hyponatremia from dehydration and water ingestion. Changes in potassium are very common. Early on, hypokalemia can be seen, and this is thought to be associated with catecholamine effects, hyperventilation with respiratory alkalosis, sweat losses, and potentially renal wasting from hyperaldosteronism from training in the heat.[22] As heat injury progresses, hyperkalemia is more predominant and is thought to be due to the failure of the magnesium dependent sodium/potassium ATPase pump and exacerbated by acute renal failure.[22] Hypocalcemia is common, and can exacerbate hypokalemia in the heat injured patient.[48] Additionally, hypophosphatemia is commonly seen in heat stroke patients, and this appears to be related to an increase in the fractional excretion in the kidneys.[49] A metabolic acidosis is the predominant acid-base disorder seen in heat stroke.[50]

Renal failure is one of the most common abnormalities seen in heat injured patients.[47, 51-53] Renal insufficiency rates have been reported as high as 53% in classical heat stroke[28], and similar rates can be found regarding exertional heat stroke. This is thought to be due to a combination of direct thermal injury, pre-renal insult to the kidney from dehydration, renal hypoperfusion, rhabdomyolysis, and disseminated intravascular coagulation[22, 43]. Creatinine

phosphokinase (CK) is also elevated in not only exertional heat stroke as is traditionally taught, but also in classic heat stroke to a lesser, but still clinically significant degree.[28]

Additional Laboratory Tests

Although certainly not always the case, there have been case reports of elevated cardiac enzymes in patients with heat stroke.[40] However, it is important to point out that there aren't any substantiated reports of patient with electrocardiographic and laboratory evidence of acute myocardial infarction that have had the diagnosis supported with findings on cardiac catheterization.

There is sufficient documentation of hepatic failure to recommend that patients have persistent monitoring of liver function enzymes. Both splanchnic redistribution with subsequent hypoxia and direct injury from heat are theorized mechanisms of failure. [54, 55] Many of these patients will come in with normal lab values, but the majority of them peak around day three in terms of liver dysfunction or failure.[28] Although there is historical reference to liver transplantation following severe failure from heatstroke, both documented cases eventually resulted in patient death.[55] More recent literature suggests that many of these patients will do well with conservative management and not require transplantation after getting through the acute phase of the event.[54, 56, 57]

Both hyperthyroidism and less commonly hypothyroidism have been implicated or been found to be a diagnosis following treatment of heatstroke. [58, 59]

Treatment

Minor heat illness

The myriad of what could be described as minor heat illnesses have already been addressed in previous sections of this review. Beyond general supportive measures, these illnesses are self-limiting in nature and shouldn't require large amounts of emergency department resources. The focus really lies in the evidenced based treatment of heat stroke as described below.

Heat stroke

General supportive measures must be undertaken and will not be explained in great detail in this forum. Intubating patients to secure the airway in the presence of altered mental status might be warranted. Fluid rehydration is paramount to the resuscitation of heat inured patients. Various electrolytes can be altered in heat illness as previously stated, and fluids should be supplemented as is deemed appropriate. Additionally, renal failure in the presence of elevated CK and evidence of rhabdomyolysis should be treated with standard measures. Intravenous fluids will need to be pushed aggressively, and alkalinization of the urine can be initiated. Coagulapathies from DIC and hepatic failure must be monitored with appropriate interventions germane to emergency practice. Finally, cooling is the cornerstone to good outcomes in heat injured patients and must be done in an appropriate manner.

Cooling Methods

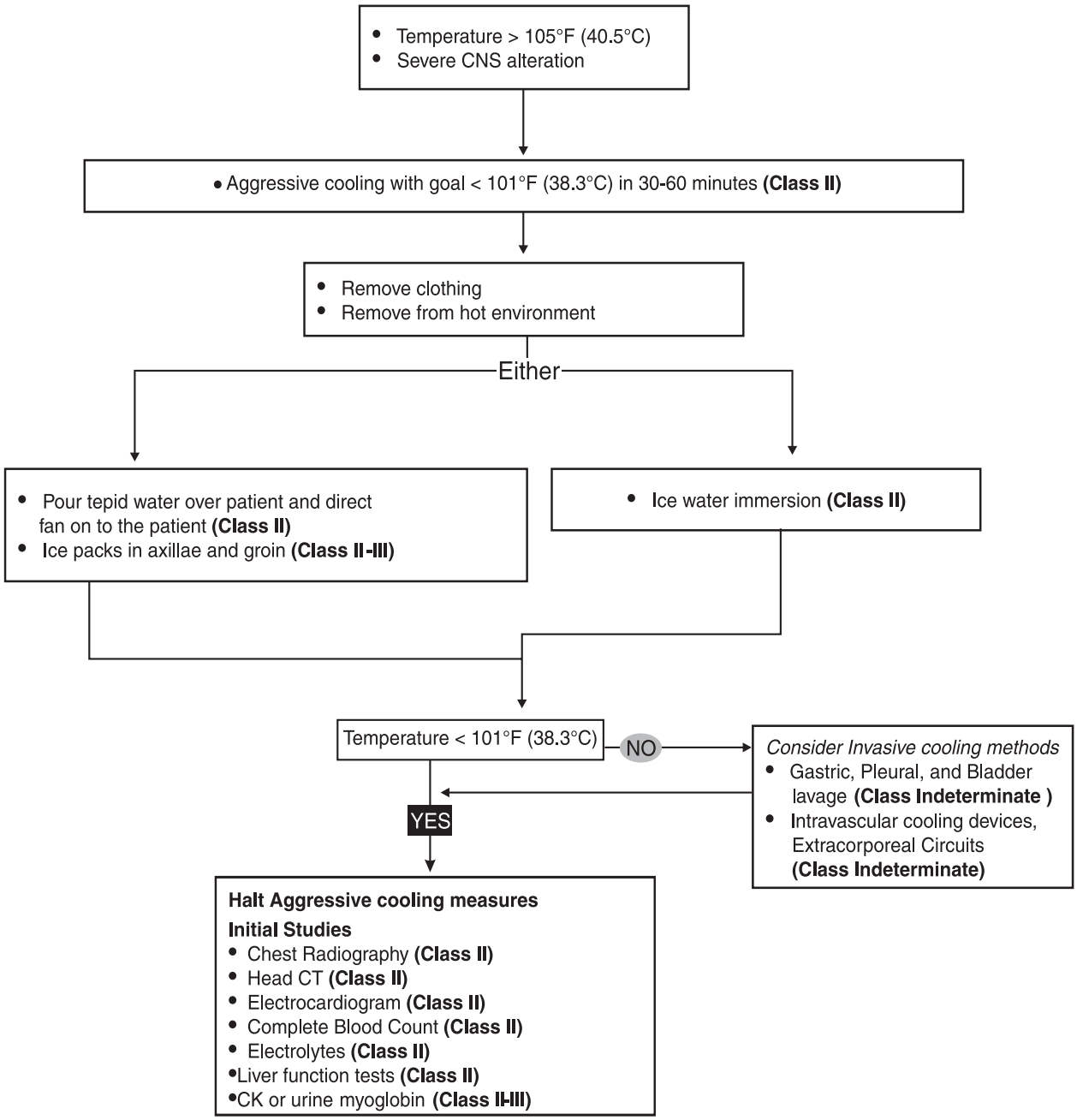
Cooling is the cornerstone of therapy in the treatment of heatstroke. The duration and degree of hyperthermia are the key factors in determining long-term outcome in patients with heatstroke. The most widely held belief is that rapidly lowering patients' core temperature below 38.9°C improves survival. In one retrospective review of 39 heat stroke patients, patients cooled to or below 38.9°C within 60 minutes demonstrated an improved outcome with a decreased mortality of 21%.[60] Another study showed a similar trend in patients cooled within 30 minutes of initial cooling measures.[28] The Inter-Association Task Force on Exertional Heat Illness consensus statement provides guidance that patients should be rapidly cooled to a temperature of 38.3°C (101°F) before ceasing such aggressive measures.[61]

There are a number of different methods of cooling patients which have been studied with varying degrees of success. The main two practical methods of cooling patients are through the utilization of evaporation and through the direct immersion of patients in cold water. In general, pharmacologic measures for the treatment of heatstroke, as well as experimental and invasive measures, have been met with varying success.

Techniques using Evaporative and Convective Cooling

Evaporation is one of the four methods of heat transfer, and is one that can be utilized in rapidly cooling patients. Convection can also be utilized to cool patients in the emergency department. The combination of both evaporation and convection has been utilized in previous studies to rapidly lower body tem-

Clinical Pathway: Heat Stroke Clinical Treatment Pathway



perature. This involves rapidly removing clothing, pouring tepid water over the body, and directing a fan on the patient. Fanning increases heat loss through both evaporation and convection and was first demonstrated in 1959 to be a preferred method of cooling heatstroke patients.[62] This approach has persisted as a recommended cooling technique however its efficacy is impacted by the ambient humidity.[63]

More recently, a body cooling unit was developed to maximize these principles of cooling. The basic suit was initially described as having patients lying in a net with 15°C water sprayed from both sides of the patient. At the same time warm air is circulated over the patient in an effort to maintain skin temperature between 32-33°C. It is proposed that keeping the body temperature at 30-35°C with warm air and good air circulation is the best and most comfortable way to lower a patients body temperature.[64] There is also the theoretical advantage of minimizing peripheral vasoconstriction with this method which could further assist in decreasing core body temperature.

The research on these cooling units can best be described as mixed. An early case series demonstrated cooling times of roughing 0.05°C/min, with cooling times ranging from 30 to 300 minutes. This is not significantly better than other evaporative methods nor immersion techniques, see below.[65] A randomized controlled trial done in 1986 demonstrated no difference in cooling times between classic evaporative cooling techniques and those patients who received the cooling unit.[66] Another 25 patient case series utilized a simplified cooling bed and was able to demonstrate slightly better cooling rates than could be expected with standard evaporative cooling techniques.[67] Further studies need to be done with these devices to determine if the units are cost-effective, and any better than alternative evaporative or immersion techniques of cooling heatstroke patients.

Techniques Using Immersion for Rapid Cooling

Ice water immersion is the other preferred method of cooling patients who are suffering from heatstroke. There is evidence to support this method as having a more rapid cooling effect on patients, and the most recent review on the topic reports immersion as having the best evidence-based support.[68] Critics site a number of problems with this method. For one, it is very difficult to monitor patients immersed in ice water, especially those with altered mental status. Following immersion, intravenous access is increasingly difficult as well. Furthermore, those that believe peripheral vasoconstriction inhibits dissipation of core body heat cite this method as being flawed due to the significant peripheral vasoconstriction that results from ice-water immersion.

The first case series using immersion was in 1982 which demonstrated that 26 of 28 patients achieved cooling below 38.9°C (102°F) within 30 minutes and all within 45 minutes. Patients were removed form the immersion if they could not tolerate it and had ice massage as an alternative. This certainly confounded the data to some degree, but the overall cooling times were impressive none-the-less.[69] Another case series of 27 patients using ice water immersion to a temperature less that 39°C achieved a mean cooling rate of 0.15C/min, with a mean cooling time of 19.2 minutes.[70] The final study was done in 1996 which took 21 heat stroke patients and compared treatment by ice water immersion to using wet towels placed over the torso. The study demonstrated a much more rapid cooling in the ice water immersion group (0.20C/min vs. 0.11C/min).[71] However, it is important to point out that this was a non-randomized observational study. In summary, these studies all have flaws in their design which should be taken into account. It is apparent that there is cooling benefit to immersion therapy, and it perhaps is the most rapid way to achieve goal-directed cooling.

Additional Cooling Options

Classic teachings sometimes call for icepacks in both axillae and the groin. The thought is that this will have a larger affect on core body cooling that peripheral skin cooling. There is limited evidence on the subject, though there is one study which demonstrated that in combination with evaporative cooling it assisted in lowering the core body temperature.[72] It is important to point out that in this study icepacks alone were worse than evaporative cooling. Considering this as an adjunct therapy appears appropriate based on the best available evidence.

The arteriovenous anastomosis and venous plexus in the palms of the hands and soles of the feet are ways in which core body heat can be transferred out of the body.[73] Early studies demonstrated that the submersion of hands in cold water resulted in significant temperature drops in normal patients.[68] More recently, the significance of the hands in the redistribution of elevated core temperature has been further elucidated. In one recent experimental study of 26

patients, utilizing a newly developed device that increases blood flow through negative pressure and creates a heat sink, the authors demonstrated that heat could successfully be removed from the body. The study also showed that patients who had the device attached could actually function in a heat stressful environment longer than the controls.[73]

Invasive cooling methods are another option for the patient who is perhaps resistant to classic cooling methods. Most of these would be considered investigational in nature, but there is some data on gastric lavage to suggest that it may be helpful in lowering core body temperature in hypothermic patients.[60, 74] More recently, there was a case report utilizing a new intravascular cooling device which appeared to play a role in return to euthermia in the patient. This device requires more testing but holds promise as an adjunct to treating heatstroke patients.[75]

Conclusions

One of the biggest issues when evaluating the literature on cooling methods for heatstroke is the fact that it is difficult to achieve enough power to see a difference between methods because there is a paucity of qualifying patients. As such, it is not surprising that many of the studies are observational case series utilizing one method or another. The best studies also tend to compare two similar techniques, and there is certainly a need for good studies comparing immersion therapy with the best evaporative techniques. The only paper that reviewed the literature regarding human reports and studies concluded that immersion in ice water was the most rapid way to cool patients, but this may be impractical in the clinical setting. In such a case with altered mental status, for example, evaporative cooling may be the preferred method of treatment.[68]

Medical Management

Dantrolene (Dantrium™ Norwich Eaton Pharmaceuticals)

Historically, the administration of Dantrolene Sodium for the treatment of both kinds of heat stroke has been a therapeutic option. Some scholars believe that heat stroke and both Neuromalignant Syndrome (NMS) and Malignant Hyperthermia (MH) can be grouped together as Thermic Stress Syndromes (TSS). While this point is still very controversial, it is not surprising that the known therapeutic treatment for the later two disorders became a source of research for heat stroke

Dantrolene attenuates the amount of calcium released from the sarcoplasmic reticulum into skeletal muscle. This reduces the amount of excitation-contraction coupling that can occur and subsequently inhibits skeletal muscle contraction. Heat is produced from the repetitive contraction of muscles, and as a muscle relaxant, dantrolene can blunt this response.

Dantrolene is not a benign drug, and there are numerous side effects associated with its administration. There are expected side effects such as muscular weakness and drowsiness.[76] However, the more serious ones could be catastrophic for a patient already dealing with multi-organ system dysfunction: Dantrolene can independently cause hepatic injury, and this is potentially in the face of a patient who could already be suffering from hepatic failure.[77] Furthermore, animal studies report negative inotropic effects in cardiac and skeletal muscle from the use of dantrolene.[78, 79]

There are very few studies which specifically look at the use of dantrolene as a therapeutic modality for heat stroke. Two early case reports form the 1980's revealed that dantrolene might have played a part in patients' recoveries.[80, 81] Animal studies have shown no benefit for treatment of heat stroke, but some studies have shown benefit in terms of cooling times (time to get core body below 39.5°C) in those pretreated with dantrolene.[82-85] Two human studies looking at dantrolene showed no benefit in terms of outcomes[34, 86] even though one of the two studies demonstrated a statistically significant decrease in cooling times in the group treated with dantrolene.[86]

The majority of authors who have reviewed the efficacy of dantrolene in heat stroke have concluded that there is no evidence to support its routine use in patient care.[68, 77, 87] It is safe to say that at this point the clinical utility of dantrolene should, at best, be reserved for refractory cases that might have evidence of associated malignant hyperthermia. There is evidence that using a prophylactic dose of 2-5 mg/kg might have therapeutic benefit, but the results are still mixed even in this case.[87]

Other Pharmacologic Options

Diazepam or another benzodiazepam might have therapeutic benefit in heat stroke patients. It can be helpful as an anxiolytic for patients with altered mental status, and can additionally be used for the treatment of seizures if they occur. While there is no

evidenced based literature to support its use, benzodiazepines and prochlorperazine can be considered to control the shivering response in patients undergoing immersion or evaporative cooling for heat stroke. This is done under the premise that shivering generates additional heat production which could decrease time to euthermia. This, however, has also not been elucidated in the literature. There is no literature to support the standard use of aspirin or acetaminophen in the treatment of heat stroke patients.

Cutting Edge / Controversies

There are a number of promising emerging therapies that concentrate on changes that occur at the molecular level following a hyperthermic insult. One example of this is the upregulation of heat shock proteins (HSP) following heat insult, which increases cellular protection against excessive heat exposure. Interestingly, there is evidence to suggest that pre-exposure to heat will upregulate the amount of circulating HSP's and thereby attenuate the body's response to heat stroke.[88] It has also been shown that pre-treating the body with oral glutamine might achieve the same response.[89] Additionally, there are over fifty genes not traditionally considered heat shock proteins which also could potentially play a therapeutic role in the management of heat stroke in the years to come.[90] Early studies utilizing naltrexone[91], more specifically mu-opoid receptor blockade[92], and aminoguianidine has also shown promise for attenuating the oxidative stress associated with heatstroke and decreasing energy depletion. This area of research is showing promising results which could alter they way we treat hyperthermic injury in the years to come.

Another potential therapy utilizes human umbilical cord blood cells. These are rich in hematopoetic stem cells and theoretically these cells can reconstitute lineages that are damaged by a number of varied insults in addition to providing enzymes of unclear importance in the systemic response to heatstroke. This has previously been shown in stroke research, but more recently has been demonstrated in the mitigation of heatstroke injury. Human umbilical cord blood cells have now been shown to reduce circulatory shock and cerebral ischemia in animal models providing a new area for future research.[93]

There is certainly work to be done in the realm of gene expression and immunomodulators. There are a multitude of gene expressions that appear to play a role in exert ional heat injury.[94] Following some difficulties with similar agents in the realm of sepsis therapy, we should have cautious optimism that any of these therapies will be available for bedside therapeutics anytime soon.

There are other treatments being studied for heatstroke that are of potential clinical benefit in the future. L-arginine is an amino acid used in the production of heat shock proteins and other mediators in the response to heat stress. Early studies have shown that by replenishing this amino acid the overall systemic response to heatstroke can potentially be attenuated and improve survival.[95] Furthermore, the attenuation of the production of nitric oxide synthase through lysine treatment has demonstrated a reduction in the shock response to heat stroke.[96]

Finally, there are a number of general experimental therapeutics which hold promise in the treatment of heatstroke. For one, there are early indicators that fluid replacement with colloid solutions could attenuate circulatory shock and cerebral ischemia and could become the preferred method of fluid resuscitation in heatstroke victims.[97] Also, early use of hyperbaric oxygen holds promise as a potential therapy for heatstroke.[98] In experimental models, it has been shown to decrease hypotension, the systemic response to heat insult, and cerebral ischemia.

Special Circumstances

Protective clothing

While not a regular topic in many reviews of heat related illnesses, the discussion of the special circumstances that exist with the use of protective clothing is nonetheless important in the age of terrorism. Emergency healthcare providers are increasingly involved in the oversight of individuals using protective clothing and increasingly likely to see the complications of its use. As discussed earlier, the clothing worn by individuals can have an appreciable effect on how individuals react to heat stress; however the use of protective clothing introduces several new considerations and factors. Several occupations use protective clothing to shield the individual from often extreme environments, i.e. a firefighter's hazardous materials suit and a soldier's nuclear biologic and chemical (NBC) protection gear. The protective gear is often heavy, bulky and of limited water vapor permeability. The system nearly or fully covers the body, including the head. This can

present the individual with an uncompensable heat stress (UHS) situation in which the body temperature will continue to rise resulting in heatstroke/death unless relieved of such stress. UHS is defined as the situation in which the rate of evaporative cooling is exceeded by the maximum evaporative capacity of the environment. Most of the heat illness literature addresses protective strategies and hazardous risk factors associated with heat illness in the context of a compensable heat stress (CHS) situation; there is increasing interest in the unique circumstances of UHS, demonstrating the limited applicability of previously documented modifiers of thermal stress in CHS situations.[18]

As presented previously, evaporative cooling is one of the primary mechanisms by which an individual is able to dissipate heat. Evaporative cooling is determined primarily by the difference in water vapor pressure at the body surface and the environment. In addition to the material's thermal resistance, all clothing produces a microclimate between the body surface and the material. Protective clothing, by design is of extremely limited permeability, producing a microclimate that is rapidly saturated by perspiration that greatly diminishes or virtually eliminates further evaporative cooling, contributing to UHS. UHS is not limited to the use of protective clothing and may be seen in any sufficiently humid environment that would severely limit evaporative cooling.

Protective clothing presents a significant factor to the generation of heat as well. Often bulky, heavy and of limiting ergonomics, protective clothing results in increase endogenous heat production. Three studies have shown that the use of NBC protective clothing results in a 13% to 18% increase in metabolic rate.[18, 99, 100] When VO2 was normalized for clothing weight in a treadmill study of 58 men and women wearing protective clothing with continuous mobility, no gender differences was noted.[99] A study of the Canadian Forces' NBC clothing demonstrated an individual could develop UHS during light exertion (VO2 <1L/min) in a warm environment (30°C 10% Relative Humidity) or with very light exercise (VO2 <0.5L/min) in a hot environment (40°C 30% Relative Humidity). Interestingly, in the same study it was demonstrated that protective clothing situations exist in which heat tolerance is governed primarily by the rate of heat production and not by environmental conditions.[18, 101]

Several potential modifiers of thermal stress during UHS have been evaluated. Similar to situations of CHS, hydration status prior to, as well as during exposure to UHS may significantly affect an individual's heat tolerance. Hypohydration (refers to state of hydration) of as little as 2.5%, during UHS has been consistently shown to impair physiological responses and tolerance regardless of aerobic fitness, exercise intensity or any physiological manipulations such as aerobic training and heat acclimation.[18] Likewise, dehydration (refers to dynamic loss of fluid) results in increasing heart rate, decreases in stroke volume, increases in core temperature, decreases in skin blood flow and increases in perceived effort.[102] However, fluid replacement while wearing protective clothing, under UHS, has been shown only to prolong exercise tolerance at light exercise intensities, and has been ineffective at higher intensities. Hyperhydration, by either water loading or glycerol ingestion provides no significant protective benefits.[18]

Strategies of heat acclimation as detailed previously, during times of CHS may produce 200-300% increases in work tolerance. However, several studies have demonstrated much more modest increases of 15-30% with use of protective clothing and UHS. Additionally it has recently come into question the transferability of hot-dry acclimation adaptations to the hot-wet environment inherent in protective clothing.[18]

Aerobic fitness level in UHS, as in CHS, seems to be associated with improved heat tolerance. However with UHS, a study at high exercise intensities indicates only a moderate trend, with benefits possibly limited by the already markedly elevated metabolic rate.[18] A recent cross-sectional study at lighter exercise intensities showed a larger increase in heat tolerance (110 vs. 88 min) in the highly fit compared to the moderately fit.[103] Several studies evaluating the effect of short term aerobic programs (2-8 wks) on heat tolerance in the previously unfit when protective clothing is worn have demonstrated limited benefit.[104-106] Ironically, it has also been proposed that as protective clothing restricts evaporative heat loss, and as increased sweat rate accompanies an increase in aerobic fitness, the aerobically fit may dehydrate faster in absence of oral hydration, although this has not been evaluated. It has also been proposed that heat tolerance for less fit individuals may be related more to the strain on the cardiovascular system in an attempt to dissipate heat and maintain arterial blood pressure, whereas the

Ten Pitfalls to Avoid

1. "He was still sweating so I treated him as having heat exhaustion."
The key differentiation between heat stroke and exertion is that of significant central nervous system dysfunction. Heat stroke victims, particularly the exertional form may still present diaphoretic.

2. "It was cold outside. How could the Hazardous-Materials provider have developed heat stroke?"
Protective clothing creates a significant barrier to evaporation which is the primary mechanism of heat transfer during most exertional situations. The use of protective clothing will often present the situation of an uncompensable heat stress with unique demands and concerns.

3. "We forgot to get a temperature on our altered mental status patient since it was not particularly hot outside."
A temperature must be obtained immediately on any patient with altered mental status, as heat stroke must always be in the differential. Early identification of heat stroke and initiation of aggressive cooling measures reduces both morbidity and mortality.

4. "I placed him in the cold water immersion tank for rapid cooling but could not then get an IV."
Establish IV access prior to cold water immersion as this method of cooling will present significant barriers to obtaining vascular access once initiated due to reflex vasoconstriction and shivering.

5. "That lady I diagnosed 2 days ago with a heat rash developed heat stroke!"
Conditions that cause anhidrosis over any significant portion of the body may place the already heat stressed individual at even greater risk for heat stroke. Patients must be educated about this increased risk and instructed to alter their behavior accordingly.

6. "The patient didn't feel particularly warm and the axillary temperature was only 102°F."
A core body temperature, esophageal, bladder or rectal must be obtained to accurately diagnose heat stroke as peripheral temperatures may underestimate the true magnitude of the condition. The core temperature must then be continuously monitored during aggressive cooling measures.

7. "I'm in good shape. I don't need to acclimate prior to my race in Arizona. Plus, I just don't have the time."
A high physical fitness level, while protective against heat illness, will not provide the advantageous physiologic adaptations that active acclimation will. Large protective adaptations will occur in only 7-14 days with daily exertion and heat exposure for 100 min/day. An acclimated athlete will exercise longer and at a high level of exertion than one that is not.

8. "I told the little league kids they only needed to drink when they were thirsty."
An involuntary dehydration of 2% or more of body weight may occur before a strong drinking response is observed. Oral intake, even when fluids are freely available and encouraged, rarely completely matches losses.

9.. "Today wasn't nearly as hot and humid as the preceding few days. Why are we seeing more heat related illnesses now?
There is evidence for a cumulative effect of heat stress in both classical and exertional heat stroke. Knowledge of the previous days heat stress is important in planning for the current day's level of exertion. Classical heatstroke typically develops over several days with a correlation to the rapidity in weather change more than the absolute level of heat stress.

10. "Our heat stroke victim has elevated troponins and concerning electrocardiographic changes. Cardiac catheterization isn't available, so we are considering thrombolytics."
Electrocardiographic changes and even troponin leaks are seen in patients with heat stroke. There are no reported cardiac catherizations studies showing vascular lesions in these patients. Treatment should be focused towards rapid temperature reduction.

increase in body heat content may be the greater limiting factor for more fit individuals.[18]

Individual characteristics including gender, oral contraceptive (OCP) use, body fat composition, age and circadian rhythm have all also been evaluated in the setting of UHS. When matched for body fat composition alone or in combination with VO2max, heat storage per unit of total mass and tolerance times while wearing protective clothing were similar between the sexes.[107] Though there is a biphasic rhythm in core temperature during the menstrual cycle with an approximately 0.4°C increase in basal body temperature during the luteal phase, during UHS, HR, and whole body sweat rate do not significantly differ, but there is an approximate 16% decrease in tolerance times. In the same study, oral contraceptive use reduced the menstrual variation in tolerance times to an approximate 12% decrease, although did not reach statistical significance.[108] Body fatness has also been associated with decreased heat tolerance while wearing protective clothing and performing light exercise. [18] Interestingly the normal oscillation in temperature by approximately 0.5°C from early morning to mid afternoon, does not affect heat tolerance times during UHS, but does result in a final higher core body temperature.[109] It is postulated by some that there is not an absolute core temperature that the body cannot tolerate but a given increase. This is however inconsistent with prior studies examining factors that also alter the basal body temperature such as the menstrual cycle. As such the complete mechanism is unclear.

For a more extensive and excellent overview of UHS please see the review by Cheung et al,[18] from which this section is heavily referenced, with further references to additional primary literature that is beyond the scope of this review.

Table 6: Risk by Wet Bulb Globe Temperature

- Low Risk = <64°F or <18°C
- Moderate Risk = 64-73°F or 18-23°C
- High Risk = 73-82°C or 23-28°C
- Hazardous = >82°F or >28°C

Adapted from references [13, 110]

Table 7: Athletic Hydration Guidelines

1. Pre-exercise hydration: 500-600 ml of fluid (preferably carbohydrate/electrolyte sports drink) consumed 2-3 hours before exercise; then consume 200-300 ml of fluid 10-20 minutes before exercise
2. Hydration during exercise: 200-300 ml of fluid (water or sports drink) should be consumed approximately every 10-20 minutes of exercise to minimize fluid losses.
3. Post-exercise hydration: approximately 500ml of fluid (sports drink) should be consumed for every pound of weight loss during exercise.

NATA guidelines 2000 [111]

Table 8: Guidelines for Returning to exercise after exertional Heat Stroke

- Physician clearance is necessary before returning to exercise. The athlete should avoid all exercise until completely asymptomatic and all laboratory tests are normal.
- Severity of the incident should dictate the length of recovery time.
- The athlete should avoid exercise for the minimum of 1 week after release from medical care.
- The athlete should cautiously begin a gradual return to physical activity to regain peak fitness and acclimatization under the supervision of a certified athletic trainer or other qualified health care professional. Type and length of exercise should be determined by the athlete's physician

From Inter-Association Task Force of Exertional Heat Illness Consensus Statement [61]

Disposition

The disposition of patients that develop a heat related illness can be variable. For heat stroke victims the only question is one of where in the hospital the patient should go. This is often dictated by hospital resources as well as the patients resulting complications and comorbidities. The need does exist however for guidance regarding the disposition of victims with less severe heat related illnesses. The athletic medical community probably contains the best documented recommendations with several guidelines offered for reference in the accompanying tables.

Table 6 provides a simple risk assessment tool for predicting heat illness. Wet bulb globe temperature (WBGT) is a commonly used standardized index that can be obtained from commercially available devices. The measure includes heat stress from ambient temperature, radiant heat and humidity.[13, 110] As rehydration is considered one of the most important factors in heat illness risk reduction, Table 7 provides easy to use hydration recommendations from the National Athletic Trainers Association. Finally, Table 8 provides recommendations for the victims of exertional heat stroke regarding returning to exercise. These guidelines were produced by an inter-

association task force comprised of representatives from wide-ranging organizations including, ACEP, American Academy of Pediatrics, American College of Sports Medicine, American Orthopedic Society of Sports Medicine, and Department of Defense.

Summary

This review attempts to generate an evidence-based approach for the treatment of heat injures. You now know there is no evidence for the routine use of pharmacologic therapy in the treatment of heat stroke as exemplified by the first case involving the fourteen month-old boy. In the second case, we have learned that exertional heat stroke can occur in the setting of varying environmental stresses, and there are ways to prevent such heat injury from occurring. Finally, there are methods such as wet bulb testing which can help planners better understand the effects heat could have on the event.

Whether in the emergency department, on the battlefield, or supporting a marathon, managing heat injuries is a complex and sometimes difficult task for the emergency physician. One must be able to recognize the varying severities of heat illness, and undertake the appropriate diagnostic workup and treatment. Understanding the physics behind heat transfer is helpful at both instituting the correct treatment of heat injuries, but also in planning for events where people could be at risk. As medical event planners, one must be aware that there are rehydration guidelines out there. One must recognize when it is crucial to keep an athlete from returning to his or her strenuous activity, and when it is reasonable to allow them to continue. Finally, it is important to recognize that heatstroke can be a fatal illness with mutisystem organ failure. As such, cast a wide net in the initial workup to ensure end organ liver, kidney, or cardiovascular damage is recognized. Understanding that both exertional and classic heatstroke can kill is a crucial point to remember-be cognizant during heat waves, and know when there are events occurring in the vicinity of your emergency department so you are ready for the "heat wave".

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CME Questions

81. A heat-related death is usually defined as all of the following except:
    a. exposure to hot weather
    b. the presence of perspiration on the body
    c. no alternative cause of hyperthermia

82. Conduction is the mechanism of heat exchange that:
    a. transfers energy or heat between a gas and liquid.
    b. is the heat exchange between two surfaces in direct contact.
    c. the transfer of heat by electromagnetic waves.
    d. the transfer of heat with the conversion of a liquid to a gas.

83. Heat cramps are best defined as:

a. fleeting painful spasms of the large voluntary muscles after strenuous exertion.
b. carpopedal spasms that result from hyperventilation in response to heat stress.
c. pain in the flanks following exertion during running or swimming.
d. pain with deep breathing following strenuous exertion.

84. All of these are defining components of heat stroke except:
a. a core body temperature of more than 105°F (40.5°C).
b. central nervous system dysfunction.
c. exclusion of CNS infections.
d. cessation of the sweating mechanism.

85. The geriatric population is more prone to:
a. exertional heat stroke.
b. classic heat stroke.
c. both. The elderly have an equal presence in both types of heat stroke.
d. neither. The elderly typically are not involved in heat injuries.

86. Risk factors for the development of exertional heat stroke include all except:
a. acclimatization.
b. sleep depreviation.
c. concominant drug use such as tricyclic antidepressants and ecstasy.
d. lack of physical fitness.

87. Current data suggests that having EMS personnel prepositioned at high risk events
a. increases the number of hospital transports for heat injuries.
b. decreases the total number of hospital transports for heat injuries.
c. does not impact the number of hospital transports for heat injuries.
d. increases the number of patients seeking medical assistance.

88. Medications that can contribute to heat injuries include all except:
a. diuretics
b. caffeine
c. amphetamines
d. aspirin
e. phenothiazines

89. The most common electrocardiographic finding in heat injured patients is:
a. right bundle branch block
b. atrial fibrillation
c. Q-T Prolongation
d. ST segment depression
e. supraventricular tachycardia

90. Common cardiovascular findings in heatstroke include all of the following except:
a. global hypokinesis on echocardiography
b. elevated serum cardiac markers such as CKMB and/or troponin I/E
c. ventricular fibrillation arrest
d. normal cardiac catheterizations following electrocardiogram and laboratory findings consistent with acute myocardial infarction

91. All of the following are likely laboratory findings in heatstroke except:
a. hypoglycemia
b. hypokalemia
c. hyopcalcemia
d. hypophosphatemia
e. hyponatremia

92. Common organ systems affected by heat injuries include all of the following except:
a. cardiovascular
b. renal
c. hepatic
d. all are potentially affected

93. All are techniques using evaporative and convective cooling except:
a. pouring tepid water over the patient and fanning the patient.
b. utilizing a body suit which sprays the patient and provides circulating warm air around the patient.
c. removing a patients clothing and pouring tepid water over the patient
d. placing ice bags in the axillae and groin of the patient

94. The most rapid form of cooling patients is most likely:
a. cold water immersion of the patient
b. ice packs in the axillae and groin
c. pouring tepid water over the patient
d. fanning the patient

95. Dantrolene
a. is recommended by most position statements for use in refractory heatstroke.
b. doesn't have evidence to support its regular use in refractory heatstroke.
c. has received a blackbox warning thereby negating its use in the emergency department.

d. should be given prophylactically to patients with a history of heatstroke prior to significant exertion.

96. Athletic hydration guidelines recommend that most athletes shoud:
    a. consume25 ml of fluid every 10-20 minutes of exercise to minimize fluid losses
    b. consume 200-300 ml of fluid every 10-20 minutes of exercise to minimize fluid losses
    c. consume 750-1000 ml of fluid every 10-20 minutes of exercise to minimize fluid losses
    d. consume 1500 ml of fluid every 10-20 minutes of exercise to minimize fluid losses

Coming in Future Issues

Pain Control • Seizures • Stroke • Swollen Extremity

Class Of Evidence Definitions

Each action in the clinical pathways section of *Emergency Medicine Practice* receives a score based on the following definitions.

Class I
- Always acceptable, safe
- Definitely useful
- Proven in both efficacy and effectiveness

Level of Evidence:
- One or more large prospective studies are present (with rare exceptions)
- High-quality meta-analyses
- Study results consistently positive and compelling

Class II
- Safe, acceptable
- Probably useful

Level of Evidence:
- Generally higher levels of evidence
- Non-randomized or retrospective studies: historic, cohort, or case-control studies
- Less robust RCTs
- Results consistently positive

Class III
- May be acceptable
- Possibly useful
- Considered optional or alternative treatments

Level of Evidence:
- Generally lower or intermediate levels of evidence
- Case series, animal studies, consensus panels
- Occasionally positive results

Indeterminate
- Continuing area of research
- No recommendations until further research

Level of Evidence:
- Evidence not available
- Higher studies in progress
- Results inconsistent, contradictory
- Results not compelling

Significantly modified from: The Emergency Cardiovascular Care Committees of the American Heart Association and representatives from the resuscitation councils of ILCOR: How to Develop Evidence-Based Guidelines for Emergency Cardiac Care: Quality of Evidence and Classes of Recommendations; also: Anonymous. Guidelines for cardiopulmonary resuscitation and emergency cardiac care. Emergency Cardiac Care Committee and Subcommittees, American Heart Association. Part IX. Ensuring effectiveness of community-wide emergency cardiac care. JAMA 1992;268(16):2289-2295.

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Date of Original Release: This issue of *Emergency Medicine Practice* was published June 30, 2006. **This activity is eligible for CME credit through June 30, 2009.** The latest review of this material was June 25, 2006.

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