Identification of Internal Risk Factors and Interventions to Prevent Exertional Heat Illnesses in Hikers: A Systematic Review

Sheri D. Erwin, FNP-C
Submitted in Partial Fulfillment of the Requirements
for the
Northern Arizona University
School of Nursing
Doctor of Nursing Practice Program

March 17, 2015

Abstract

Objective: To identify internal risk factors (e.g., caffeine and alcohol consumption, weight, medications, and medical conditions) and intervention strategies for prevention of exertional heat-related illnesses in hikers.

Methods: A systematic review was conducted using a predetermined list of MeSH headings to identify articles on exertional heat-related illnesses. CINHAL, MEDLINE, and PubMed databases were searched for articles published between 2009 and 2014. The studies were ranked using the Oxford Centre for Evidence-Based Medicine classification system. Studies were included if they had a level of evidence of 3 or higher or a grade of C or better.

Results: The initial search resulted in a total of 330 articles. After the application of the exclusion criteria and analysis using the Oxford Centre for Evidence-Based Medicine classification system, 38 studies and guidelines remained. The studies and guidelines indicated that various medications and medical conditions affect sweat production, core temperature and can reduce the amount of water in the body. Internal factors increase potential for exertional heat-related illnesses: caffeine consumption, alcohol intake, and being overweight. In addition, heat acclimatization is necessary regardless of fitness level.

Conclusion: To mitigate exertional heat-related illnesses related to medications, medical providers and dispensing pharmacists can assist patients with proper counseling regarding medications known to disrupt heat responses. Also, education of hikers about the effects of intermixing hiking activities with alcohol or caffeine may prevent or reduce the severity of exertional heat-related illnesses along with proper heat acclimatization.

Key words: heat illness, heat exhaustion, heat stroke, prevention, intervention

Identification of Internal Risk Factors and Interventions to Prevent Exertional Heat Illnesses in Hikers: A Systematic Review

In 2013, 49.4% of Americans participated in some type of outdoor recreation[1] which is the second highest percentage in the past five years. With more people participating in outdoor activities like hiking, it is important for them to be educated on the risk factors and prevention strategies to ensure a safe outcome. Identification of risk factors is not part of a person's usual preparation for a hike. However, hikers may be at risk for exertional heat illnesses (EHIs) associated with external risk factors, internal risk factors, or both.[2]

External or extrinsic risk factors for EHIs are those associated with the environment such as clothing; equipment; intensity of the activity; high temperature, humidity, sun exposure, or a combination of these; imbalance between work and rest, presence of shade, and water intake quantities and electrolyte types.[3] Internal or intrinsic risk factors for EHIs are those that are particular to the hiker such as level of alcohol or caffeine intake, heat acclimatization, weight, medications, and medical conditions.[4]

Heat-related illnesses range from minor to severe, ranging from heat cramps to heat stroke. Exercise-associated heat cramps cause involuntary, painful movements (spasms) of the skeletal muscle, which occur during or immediately following physical activity.[5] Possible causes include dehydration, electrolyte imbalance, neuromuscular fatigue or a combination of these. Heat syncope occurs when the blood vessels dilate in an effort to cool the body causing blood flow to the brain to be reduced.[6] Exercise induced heat exhaustion occurs when the heat overwhelms the body and the natural mechanism of cooling (sweating) is unable keep up with demands, also from sodium loss (hyponatremia), decreased energy, and or dehydration.[7] Exertional heat stroke is defined as a core temperature of 104 degrees Fahrenheit or higher. The body's temperature rises quickly and involves changes to the neurovascular system. This is

considered an emergency, which can be fatal if not treated promptly. The longer the person's body temperature remains above 104 degrees Fahrenheit the greater risk of morbidity and mortality.[6]

Exertional hyponatremia is an imbalance between water and salt, which leads to lower than normal sodium levels.[8] Symptoms of hyponatremia can be minor such as headache, irritability, and nausea, or severe such as convulsions, confusion, and muscle weakness. The normal concentration of sodium in the blood is 135 to 145 mEq/L. A person may experience a decrease in plasma sodium concentration between 125 to 135 mEq/L without having symptoms. Neurological symptoms such as respiratory arrest, coma, and seizures may develop at levels below 120 mEq/L.

The rate of incidence and severity of heat related illnesses increase as temperatures increases.[9] In 2013, the Grand Canyon National Park had 703 emergency medical services incidents; 62 (8.8%) of those were heat related. According the 2013 Grand Canyon National Park, Branch of Emergency Services Annual Report[10] the number of calls from hikers requesting assistance increased from 6.5 to 10.5 calls per 1000 hikers when temperatures exceed 95 degrees Fahrenheit, a 61.5% increase. From May to September the Grand Canyon averages 55 days of 95 to 100 degrees Fahrenheit and 30 days of 100 degrees Fahrenheit or higher.

The Centers for Disease Control (CDC) reported that approximately 2,480 people in the United States died from excessive heat exposure between 2006 and 2010.[11] The highest rate of deaths related to heat illness over a 35-year period occurred between 2005 to 2009 despite advancements in prevention, identification, and treatment of heat-related illness.[12] The Arizona Department of Health Services (ADHS) has reported that annually nearly 2,000 people seek emergency services for heat-related illness, and from 2000 to 2012, more than 1,500 deaths in

Arizona were related to heat illnesses.[13] In the Grand Canyon, 474 nonfatal heat-related illness cases were reported between 2004 and 2009.[14]

Cases of heat-related illness such as exertional hyponatremia have been reported among people participating in moderate exercise such as day hikes and short triathlons.[15] Most research and medical literature, guidelines, and educational programs for the management of heat-related illnesses focus on the elderly, workers, student athletes, or endurance athletes.[3, 16, 17] However, these studies typically do not describe the experience of hikers in depth.

In reviewing existing web sites, handouts, and guidelines on exertional heat illness prevention for hikers the main focus was on external risk factors with little focus on internal risk factors. Reports commonly sight that environmental factors contributing to heat related illness, but rarely discuss internal risk factors such as medications that may have contributed.[18] The purpose of this manuscript is to assist in the identification of internal risk factors and proper interventions to be used by hikers to prevent heat-related illnesses. This information may be used for revisions of existing educational materials, which focus heavily on external factors, leaving a crucial consideration unaddressed. Furthermore, the information obtained from this project can be applied to any outdoor exertional leisure activity.

Methods

This study is a systematic review of literature (i.e., case series, exploration or systematic literature reviews, and guidelines) published after 2009. With the addition of a few hand-searched articles published prior to 2009 with data still generally accepted within this field of study. The search focused on six areas of internal risk factors: medications, caffeine consumption, alcohol intake, obesity, heat acclimatization, and medical conditions. Medical Subject Headings (MeSH) were used to search 3 electronic databases: CINAHL Complete, MEDLINE, and PubMed. Searching these terms in isolation yields enormous results. The search

strategy combined one of the following: *internal risk factors*, *heat illness*, *exertional heat illness*, *heat exhaustion*, *heat stroke*, *heat syncope*, *hyperthermia* with one of the following: *medications*, *medical conditions*, *overweight*, *obesity*, *alcohol*, *caffeine*, and *acclimatization using* Boolean operator 'AND'. The studies selected for review included intervention studies, systematic reviews, guidelines. Study designs included were prospective, descriptive, randomized crossover, qualitative, and cohort.

A search for the term *heat-related illness* in the Wilderness Medical Society database produced one practice guideline. This guideline focuses on recognition, prevention, and treatment of heat-related illness in the wilderness for medical providers.[2] Sections within this guideline on internal and external risk factors are limited with general recommendations. The majority of the guideline focuses on the appropriate treatment options for heat-related illness in the field and hospital.

Literature was excluded if it was published before 2009 or written in a language other than English. Results were also excluded if they clearly conveyed opinion or if the outcomes or recommendations were unclear. The database search was supplemented by a hand search through the references of the articles meeting the inclusion and exclusion criteria. The studies were ranked with the Oxford Centre for Evidence-Based Medicine classification system. Only studies with a level of evidence of 3 or higher or a grade of C or better were included. The reporting of the review followed the PRISMA Statement and checklists.

Results

The initial search resulted in a total of 330 potential articles, which decreased to 158 after excluding articles published before 2009 and those in a language other than English. An additional 20 articles were identified through manually searching references of articles. Fifty-two articles were retained after reviewing the abstracts to determine whether a specific intervention

was identified and tested. After analysis using the Centre for Evidence-Based Medicine classification system, 38 studies and guidelines remained.

Medications

The presence of medications in the body can affect one's susceptibility to heat illness. Anticholinergic agents affect the body's ability to perspire, resulting in decreased heat loss,[19, 20] Medication with a higher anticholinergic activity combined with histamine H_1 antagonists, ganglionic blockers acting as nicotinic antagonists, tricyclic antidepressants, gastrointestinal and urinary antispasmodic medications, typical and atypical antipsychotic medications, bronchodilators, and anti-Parkinson anticholinergic medications decrease a person's ability to sweat.[19, 20, 21, 22, 23] Increasing serotonergic activity with serotonin 5-$HT_{1B/1D}$ receptor agonists and selective serotonin reuptake inhibitors can raise body temperature and potentially result in serotonin syndrome.[20, 21] Loop and thiazide diuretics reduce peripheral blood flow, resulting in decreased heat dissipation and increased sensitivity to heat due to excessive loss of water.[20, 22, 23] Alpha and beta agonists and decongestants cause vasoconstriction of the cutaneous blood vessels, helping to retain heat within the body.[20, 23] Central nervous system stimulants such as cocaine and amphetamines raise body temperature by interfering with the body's ability to regulate temperature, and catecholamines induce vasoconstriction in the cutaneous blood vessels to conserve heat within the body.[20, 21] If vasoconstriction, the inability to sweat, heat retention, or a combination of these scenarios exists, the body is unable to cool properly, increasing a person's potential for a heat-related illness. For more specific medication names and details about those used in this paragraph, see the Table.

Caffeine Consumption

Caffeine is an indirect sympathomimetic, which causes vasoconstriction and increased muscular activity from agitation—both of which elevate body temperature.[24] Ingestion of 9

mg/kg of caffeine during 30 minutes of exercise raises body temperature without individuals knowing; longer periods of time may begin to show the effect as peripheral blood flow decreases, causing an increase in water loss and decreased heat dissipation.[20, 22, 23, 25] The consumption of caffeine increases urine output and loss of sodium, chloride, and potassium.[26] Combining 6 mg of caffeine with a 6% carbohydrate-electrolyte solution increases core temperature.[26] As an example of the deleterious effects of caffeine, firefighters wearing a fire-protective ensemble and consuming 6 mg/kg of caffeine consumed more oxygen and had increased gastrointestinal temperature, resulting in greater physiological strain and placing the firefighters at increased risk of fatigue and illness.[27]

Alcohol Intake

Hydration status at the time of consumption determines alcohol's effect on urine output. Consuming alcohol containing 4% ethanol blunts the diuretic effect in dehydrated individuals.[28] However, in euhydrated individuals, urine output is increased.[28] Small doses of alcohol (0.5 ml/kg) decrease endurance performance due to increased cardiovascular strain.[29] Alcohol consumption significantly depresses the function of the myocardium, affecting left ventricular contractility.[30] The American College of Sports Medicine (ACSM) recommends refraining from alcohol consumption at least 48 hours before exercise due to the effect on exercise performance, resulting in detrimental effects on the cardiac and skeletal muscle systems.[31]

Obesity

Several studies have confirmed that obese and lean people have different outcomes in studies gauging body heat. Authors of a 1969 study,[32] found that obese people had a higher core temperature performing the same activities when compared with lean people. Adults who are overweight or obese compared with adults of average weight have a 3.5 times higher rate of fatal heatstroke.[33] This may be due to the lower thermal threshold to heat from the body's heat sensing

and dissipating abilities not operating properly in this population.[34] The US Army evaluated the incidence of heat-related illness in military recruits within the first 180 days of entering the military. They assessed their individual weight—categorized by whether they met the weight requirement or exceeded body fat standards—their 5-minute step test performance (pass or fail), and rates of heat-related illness.[35] Those who both met the weight requirement and passed the step test had lower rates of heat-related illness than recruits who either failed the step test or did not meet the weight standard.[35] Recruits who exceed the body fat standards had a 7.25% increased rate of heat-related illness compared with recruits who both passed the step test and met the weight standard.[36]

Heat Acclimatization

Hiking requires the activation of muscles to perform work, and in doing so the body produces heat. The author of a study in 2012,[37] found that untrained individuals have lower movement efficiency, contributing to greater heat storage than trained persons. It is common to exercise in intervals of intensity. A sudden increase in intensity results in increased heat production and requires more time for heat dissipation.[37] One researcher[37] recorded higher rectal temperatures in people participating in intermittent exercise patterns, with greater rates of heat accumulation in the untrained with no prior heat acclimatization individuals compared to the trained athlete. Most heat dissipation occurs via evaporation; sweat, high humidity, dehydration, or a combination of these can affect evaporation rates.[38] To achieve a reduction in heart rate, typically adults need to acclimatize 3 to 6 days.[39] Proper heat acclimatization aids in plasma volume increase, resulting in cardiovascular stability at a lower heart rate with increased stroke volume.[40]

Medical Conditions

The risk of heat-related illnesses is compounded by diabetes mellitus, cardiovascular

disease, or respiratory disease.[41] The rate of hospital admissions during heat waves is 30% greater for those with type 1 or type 2 diabetes mellitus, potentially due to delayed blood vessel dilation in the skin which results in decreased heat dissipation.[42] In another study,[43] participants with hypertension were found to have impaired heat transfer between the body core and skin compared with participants with normotension; this impairment resulted in hyperthermia in some instances. Meta-analysis findings indicated that people with respiratory diseases are at a greater risk of death during heat waves.[44]

Regarding the 3,442 deaths related to extreme heat exposure in the United States between 1999 and 2003, underlying causes were cardiovascular disease (67%), infection or psychiatric disorders (11%), endocrine, nutritional, or metabolic disease (3%), and other conditions with less than 3% being digestive, neurovascular, immunity, genitourinary disease, or neoplasms.[45] Renal and neurologic diseases can affect heat response. When blood flow in the renal system is decreased, the renin-angiotensin system responds by constricting the renal efferent tubules, which triggers antidiuretic hormone (ADH) secretion.[46] ADH causes the kidneys to decrease sodium excretion as a result of sodium lost in sweat.[46] Heat can aggravate neurological conditions such as multiple sclerosis and can increase cerebrovascular accidents due to increased blood viscosity.[46]

Discussion

Exertional heat-related illness reflects the human body's maladaptation to high humidity, ambient temperature, or both. Various forms of heat-related illness exist; however, the most severe is heat stroke, affecting the nervous system and potentially affecting multiple organs. Aside from environmental heat exposure, other factors contribute to heat-related illness. The presence of high environment temperature or physical activity—which both increase metabolic heat production—and a combination of certain medications, alcohol, caffeine, obesity, heat

acclimatization, and certain medical conditions can increase the potential for heat-related illness.

Medications can impair thermoregulation by decreasing peripheral blood flow, increasing water loss, inhibiting sweating, or raising body temperature. To mitigate heat-related illness related to medications, medical providers and dispensing pharmacists can assist patients with proper counseling about medications known to disrupt heat responses. Hikers can also benefit from limiting alcohol consumption to low-alcohol beverages and stopping 48 hours before their hike. Hikers should be cautioned to avoid caffeinated beverages due to associated increased physiological strain, elevation in body temperature, decreased peripheral blood flow, increased water loss, increased urination, and sodium loss.

Low fitness level, obesity, or both can increase a person's risk of heat-related illness, necessitating evaluation by a health care professional before participating in activities such as hiking. People who are overweight produce more internal body heat, increasing their risk of heat-related illness. Special considerations for hikers who are overweight include the following: duration of hike, time of day, and frequency of breaks to allow the body to cool. In addition, to minimize heat illness, hikers can reduce physiological strain and improve physical performance. Also, regardless of physical condition, hikers can benefit from partaking in heat acclimatization.[47] Complete heat acclimatization occurs after 10 to 14 days of cardiovascular endurance exercise, lasting 1 to 2 hours daily; however, 75% of adaptation occurs within 5 days with repeated heat exposure that is enough to elevate body temperature and induce profuse sweating.[48]

A large volume of medical conditions can effect susceptibility to heat-related illness. The affect on the body from the medical condition can cause temperature regulation issues. However, because of the time limitations for the study and the vast number of medical conditions that are potentially associated with heat-related illness, further research on medical conditions will be

pursued in a separate review.

Conclusion

Regarding heat-related illnesses, the proper identification and understanding of predisposing factors are critical to prevention. Areas of educational interventions that can be completed before hiking include teaching individuals about internal risk factors, signs and symptoms, and prevention strategies for heat-related illness. Enhancing awareness of internal risks and interventions has the potential to decrease the number of cases of heat-related illness in hikers. Related to the issue of internal risk factors for heat-related illness is the topic of optimal hydration of noncompetitive athletes during high heat or humidity while performing physical activities. This area of inquiry could enhance knowledge about risks to hikers and is a fertile area of research for future study.

References

1. Outdoor Foundation. Participation report 2014. http://www.outdoorfoundation.org/pdf/ResearchParticipation2014.pdf. Published February 1, 2014. Accessed January 28, 2015.
2. Lipman GS, Eifling KP, Ellis MA, Gaudio FG, Otten EM, Grissom CK. Wilderness medical society practice guidelines for the prevention and treatment of heat-related illness. *J Wilderness Med.* 2013;24(4):351–361. doi:10.1016/j.wem.2013.07.004.
3. National Athletic Trainers' Association. Inter-Association task force on exertional heat illnesses consent statement. http://www.nata.org/sites/default/files/Heat-Illness-Task-Force-Consensus-Statement.pdf. Published June 2003. Accessed February 24, 2015.
4. Coris EE, Ramirez AM, Van Durme DJ. Heat illness in athletics. *Sports Medicine*. 2004;31(4):9–16.
5. Schwellnus MP, Derman EW, Noakes TD. Aetiology of skeletal muscle 'cramps' during exercise: a novel hypothesis. *J Sports Sci.* 1997;15 (3):277–285.
6. Casa DJ, Roberts WO. Considerations for the medical staff in preventing, identifying and treating exertional heat illnesses. In: Armstrong LE, ed. *Exertional Heat Illnesses.* Champaign, IL: Human Kinetics; 2003.
7. Quinn E. Heat illness – heat exhaustion. http://sportsmedicine.about.com/cs/heatandcold/a/aa041404.htm. Published September 6, 2013. Accessed December 5, 2014.
8. Dugdale DC. Hyponatremia. Penn State Hershey Medical Center. http://pennstatehershey.adam.com/content.aspx?productId=117&pid=1&gid=000394. Published April 14, 2013. Accessed November 23, 2014.

9. The White House. 2014 The health impacts of climate change on Americans. http://www.whitehouse.gov/sites/default/files/docs/the_health_impacts_of_climate_change_on_americans_.pdf. Published June 1, 2014. Accessed November 13, 2014.
10. Grand Canyon National Park – Branch of Emergency Services. 2013 annual report: emergency medical services, search and rescue, structural fire, and preventive search & rescue. 2013 GCP Branch of Emer Svcs - Annual Report.pdf. Accessed August 3, 2014.
11. Centers for Disease Control and Prevention. Deaths attributed to heat, cold and other weather events in United States, 2006–2010. *Natl Health Stat Report*. 2014;76:1–16.
12. Casa DJ, Armstrong LE, Kenny GP, O'Connor FG, Huggins RA. Exertional heat stroke: new concepts regarding cause and care. *Curr Sports Med Rep.* 2012;11(3):115–123. doi:10.1249/JSR.0b013e31825615cc.
13. Arizona Department of Health Services. 2012 trends in morbidity and mortality from exposure to natural heat. http://www.azdhs.gov/plan/report/im/heat/trends-in-morbidity-and-mortality-from-exposure-to-excessive-natural-heat-in-az-2012.pdf. Published February 4, 201. Accessed August 11, 2014. Month day, year.
14. Noe BS, Choudhary E, Cheng-Dobson J, Wolkin AF, Newman SB. Exertional heat-related illnesses at the Grand Canyon National Park, 2004–2009. *Wilderness Environ Med*. 2013;24(4):422–428.
15. Shapiro SA, Ejaz AA, Osborne MD, Taylor WC. Moderate exercise-induced hyponatremia. *Clin J Sport Med.* 2006;16 (1):72–73.
16. Arizona Department of Health Services. Extreme weather and public health: heat safety. http://www.azdhs.gov/phs/oeh/extreme/heat/index.php. Accessed August 11, 2014.
17. Occupational Safety & Health Administration. Using the heat index: a guide for employers. United States Department of Labor.

https://www.osha.gov/SLTC/heatillness/heat_index/index.html. Accessed August 11, 2014.

18. Martinez M, Devenport L, Saussy J, Martinez J. Drug-associated heat stroke. *South Med J.* 2002;95(8):799-802.
19. Lechevallier N, Molimard M, Dartigues J, Fabrigoule C, Réglat A. Drugs with anticholinergic properties and cognitive performance in the elderly: results from the PAQUID Study. *Br J Clin Pharmacol*. 2005;59(2):143–151.
20. Lexicomp Online. http://online.lexi.com.ezproxy.mcphs.edu/lco/action/home. Accessed Nov 4, 2014.
21. Bohnert A, Prescott M, Vlahov D, Tardiff K, Galea S. Ambient temperature and risk of death from accidental drug overdose in New York City, 1990–2006. *Addiction*. 2010;105(6):1049–1054. doi:10.1111/j.1360-0443.2009.02887.x
22. Claremont, AD. Heat tolerance following diuretic induced dehydration. *Med Sci Sports.* 1976;8(4):239–243. http://www.ncbi.nlm.nih.gov/pubmed/1011962.
23. Glazer, J. Management of heatstroke and heat exhaustion. *Am Fam Physician.* 2005;71(11):2133–2140.
24. Vassallo S, Delaney K. Pharmacologic effects on thermoregulation: mechanisms of drug-related heatstroke. *Clin Toxicol*. 1989;27 (4-5):199–224.
25. Ely BR, Ely MR, Cheuvront SN. Marginal effects of a large caffeine dose on heat balance during exercise-heat stress. *Int J Sport Nutr Exerc Metab.* 2011;21(1):65–670.
26. Del Coso J, Estevez E, Mora-Rodriuez R. Caffeine during exercise in the heat: thermoregulation and fluid electrolyte balance. *Med Sci in Sports Exerc*. 2009:41(1):164–173. doi:10.1249/MSS.0b013e318184f45e.

27. Kellawan JM, Stuart-Hill LA, Petersen SR. The effects of caffeine during exercise in fire protective ensemble. *Ergonomics*, 2009;52(11):1445–1454. doi:10.1080/00140130903197453.
28. Hobson RM, Maughan RJ. Hydration status and the diuretic action of a small dose of alcohol. *Alcohol and Alcoholism*, 2010;45(1):366–373. doi:10.1093/alcalc/agq029.
29. Lecoultre V, Schutz Y. Effect of a small dose of alcohol on the endurance performance of trained cyclists. *Alcohol and Alcoholism*. 2009;44(3):278–283.
30. Lang RM, Borow KM, Neumann A, Feldman T. Adverse cardiac effects of acute alcohol ingestion in young adults. *Ann Intern Med.* 1985;102(6):742–747.
31. Kozier LP. Alcohol and athletic performance. American College of Sports Medicine. http://www.acsm.org/docs/current-comments/alcoholandathleticperformance.pdf?sfvrsn=5. Accessed December 27, 2014.
32. Bar-Or O, Lundegren HM, Buskirk ER. Heat tolerance of exercising obese and lean women. *J Appl Physiol.* 1969;26:403–409.
33. Henschel A. Obesity as an occupational hazard. *Can J Public Health.* 1967;58:491–493.
34. Herman RM, Brower JB, Stoddard DG, et al. Prevalence of somatic small fiber neuropathy in obesity. *Int J Obes (Lond),* 2007;31(2):226–235.
35. Bedno SA, Urban N, Boivin MR, Cowan DN. Fitness, obesity and risk of heat illness among army trainees. *Occup Med (Lond)*, 2014;64(6):461–467.
36. Bedno SA, Li Y, Han W, et al. Exertional heat illness among overweight U.S. Army recruits in basic training. *Aviation Space and Environmental Medicine,* 2010;81(2):107–111.
37. Mora-Rodriguez, R. Influence of aerobic fitness on thermoregulation during exercise in the Heat. *Exerc Sport Sci Rev*. 2012;40(2):79–87.

38. Adis International Limited. Heat, humidity and exercise can lead to heat illness in athletes. *Drug Therapy Perspectives.* 2005;21(3):18–30.
39. Armstrong LE, Maresh CM. The induction and decay of heat acclimatisation in trained athletes. *Sports Med.* 1991;12 (5):302–312.
40. Wendt D, van Loon LJ, Lichtenbelt WD. Thermoregulation during exercise in the heat: strategies for maintaining health and performance. *Sports Med.* 2007;37:669–682.
41. Kenny GP, Yardley J, Brown C, Sigal RJ, Jay O. Heat stress in older individuals and patients with common chronic diseases. *Canadian Medical Association Journal*, 2010: 182(10):1053–1060. doi:10.1503/cmaj.081050.
42. Semenza JC, McCullough JE, Flanders WD, et al. Excess hospital admissions during the July 1995 heat wave in Chicago. *Am J Prev Med.* 1999;16(4):269–277.
43. Kenney WL, Kamon E, Buskirk ER. Effect of mild essential hypertension on control of forearm blood flow during exercise in the heat. *J Appl Physiol.* 1984;56:930–935.
44. Bouchama A, Dehbi M, Mohamed G, et al. Prognostic factors in heat wave related deaths: a meta-analysis. *Arch Intern Med.* 2007;167:2170–2176.
45. Centers for Disease Control and Prevention. Heat-related deaths—United States, 1999–2003. *MMWR Morb Mortal Wkly Rep*. 2006. http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5529a2.htm. Published July 30, 2006. Accessed August 1, 2014.
46. O'Connor M, Kosatsky T, Rusimovic L. Systematic review: How efficacious and how practical are personal health protection measures recommended to reduce morbidity and mortality during heat episodes? http://www.ccnse.ca/sites/default/files/Heat_Protection_Advice_Feb_2008.pdf. Published February 28, 2008. Accessed December 15, 2014.

47. Molloy JM, Smith J, Pascoe DD. Effect of a 14-day high intensity exercise protocol on heat acclimation responses. *Int Sport Med J.* 2004;14(3):103–118..

48. Nunneley SA, Reardon MJ [2001]. Prevention of heat illness. In: Pandolf KB, Burr RE, eds. Medical aspects of harsh environments. Vol. 1. Washington, DC: Borden Institute, Office of The Surgeon General, AMEDD Center & School, U.S. Army. http://www.cs.amedd.army.mil/borden/Portlet.aspx?ID=eebb9338-2027-46d5-a5f2-f245e2019b6c. Accessed December 16, 2014.

Table. Medications That May Increase Risk of Heat-Related Illness

Class	Medication	Mechanism	Effect
Anticholinergic agent	Atropine Belladonna Benztropine Cyclopentolate Darifenacin Dicyclomine Fesoterodine Glycopyrrolate Homatropine Hyoscine Hyoscyamine Ipratropium Lupin Lupine Methscopolamine Oxybutynin Procyclidine Propantheline Scopolamine Derivatives Solifenacin Tiotropium Tolterodine Trihexyphenidyl Trimethobenzamide Trospium	Anticholinergic agents block the binding of acetylcholine at muscarinic receptors and inhibit parasympathetic nerve impulses.	Decreases sweating at sweat glands. Our body cools down temperature by dissipating heat through perspiration. Impaired sweating in the body results in decreased heat loss.
Histamine H_1 antagonist with higher potent anticholinergic activity	Chlorpheniramine Hydroxyzine Meclizine Oxomemazine Phenyltoloxamine Diphenhydramine[a] Doxylamine[a] Mequitazine[a] Pizotifen	Same as anticholinergic agent	Same as anticholinergic agent
Ganglionic blocker, acting as a nicotinic antagonist with higher potency of anticholinergic activity	Mecamylamine	Same as anticholinergic agent	Same as anticholinergic agent
Anti-Parkinsonian anticholinergics	Orphenadrine[a] Trihexyphenidyl[a]	Same as anticholinergic agent	Same as anticholinergic agent
Tricyclic antidepressants with higher potency of anticholinergic activity	Amitriptyline Amoxapine Clomipramine Dosulepin Doxepin Imipramine Maprotiline Protriptyline Trimipramine Desipramine[a] Nortriptyline[a]	Same as anticholinergic agent	Same as anticholinergic agent

	Opipramol[a]		

Table. Medications That May Increase Risk of Heat-Related Illness Continued

Anticholinergic agent/ gastrointestinal/urinary antispasmodics with higher potency of anticholinergic activity	Belladonna alkaloid Oxybutynin Tiemonium	Same as anticholinergic agent	Same as anticholinergic agent
Typical antipsychotic medication with higher potency of anticholinergic activity	Butyrophenone Chlorpromazine Flupenthixol Fluphenazine Haloperidol Molindone Perphenazine Phenothiazine Pimozide Prochlorperazine Thioridazine Thiothixene Thioxanthenes Zuclopenthixol	Same as anticholinergic agent	Same as anticholinergic agent
Atypical antipsychotic medication with higher potency of anticholinergic activity	Risperidone Quetiapine Aripiprazole Olanzapine	Same as anticholinergic agent	Same as anticholinergic agent
Anticholinergic agent/ bronchodilators with higher potency of anticholinergic activity	Ipratropium bromide Oxitropium bromide[a]	Same as anticholinergic agent	Same as anticholinergic agent
Serotonin 5-$HT_{1B/1D}$ receptor agonists	Almotriptan Eletriptan Frovatriptan Naratriptan Rizatriptan Sumatriptan Triptans Zolmitriptan	Serotonin agonists have been implicated in the development of serotonin syndrome with combination of SSRI.	Increased serotonergic activity in the body can raise body temperature in patients with serotonin syndrome.
SSRI	Citalopram Escitalopram Fluoxetine Fluvoxamine Paroxetine Sertraline Vilazodone	Serotonin agonists have been implicated in the development of serotonin syndrome with combination of SSRI.	Increased serotonergic activity in the body can raise body temperature in patients with serotonin syndrome.
Loop diuretic	Furosemide Bumetanide Torsemide	Inhibits reabsorption of Na^+ and Cl^- in the ascending loop of Henle and distal renal tubule. Thus, it can cause increased excretion of water, Na^+, Cl^-, Mg^{2+}, and Ca^{2+}.	Reduction in peripheral blood flow limits body heat dissipation. During exercise, diuretic could induce dehydration and increase heat sensitivity due to extreme water loss.

Table. Medications That May Increase Risk of Heat-Related Illness Continued

Thiazide diuretic	Hydrochlorothiazide Chlorthalidone Metolzaone Indapamide	Same as loop diuretic	Same as loop diuretic
Diuretic	Alcohol Caffeine	Same as loop diuretic	Same as loop diuretic
Alpha-1 agonist	Methoxamine Methylnorepinephrine Midodrine Oxymetazoline Metaraminol Phenylephrine	Alpha 1 agonists bind to alpha receptors on vessels, causing vasoconstriction	Vasoconstriction of the cutaneous blood vessels within the body would conserve heat in the body.
Alpha-agonist and beta-agonist decongestant	Ephedrine Norepinephrine Pseudoephedrine	Alpha-1 agonists bind to alpha receptors on vessels, and beta-1 agonists bind to beta receptors on blood vessels, causing vasoconstriction	Vasoconstriction of the cutaneous blood vessels within the body would conserve heat in the body.
Central nervous system stimulants	Amphetamine Methylphenidate Methamphetamine Cocaine MDMA Methylenedioxy PMA 4-MTA Heroin	Stimulants inhibit the reuptake and metabolism of catecholamine. Increased catecholamine can result in vasoconstriction.	Stimulants raise body temperature by interfering with the body's ability to regulate temperature. Catecholamine induces vasoconstriction in the cutaneous blood vessels causing conservation of heat in the body.

Abbreviation: 4-MTA, 4-Methythioamohetmne; MDMA, 3,4-methylenedioxy-methamohetamine; PMA, para-Methoxy amphetamine---; SSRI, Selective serotonin reuptake inhibitors.

[a] Medications have less anticholinergic activity