American Red Cross
Scientific Advisory Council

American Red Cross Scientific Advisory Council
Scientific Review
Exertional Heat Stroke

Questions to be addressed:

For adults and children with exertional heat stroke does cooling by one method compared with cooling by any other method practical to a first aid provider improve outcomes?

Introduction/Overview:

Previous reviews covered the spectrum of exertional heat illnesses, including heat cramps, heat exhaustion and heat stroke. While reaffirming earlier recommendations, this updated review is focused on exertional heat stroke. Extensive, in-depth content from earlier reviews of exertional heat illness can be found at the end of this document.

Search Strategy and Literature Search Performed

For this update, a search was conducted on June 9, 2022:

Search: heat-related illness* [ti] Filters: in the last 5 years

63 articles identified
60 articles excluded by title and abstract screening
3 included for full text review

3 articles selected for final inclusion.

The most recent search prior to this was in 2019, when a literature search was performed by the Red Cross Librarian using the following parameters:

Search (("Heat illness" OR "Heat cramps" OR "Heat exhaustion" OR "Heat syncope" OR "Heat stroke")) AND (first AID OR MANAGEMENT) Filters: Publication date from 2017/01/01 to 2019/04/02; English – 60 items

Search (hyperthermia) AND (exertional OR exercise-induced) Filters: Publication date from 2017/01/01 to 2019/04/02; English- 118 items

Search (((((("Heat illness" OR "Heat cramps" OR "Heat exhaustion" OR "Heat syncope" OR "Heat stroke")) AND (first AID OR MANAGEMENT)) AND ("2017/01/01"[PDat] : "2019/04/02"[PDat]) AND English[lang])) OR (((((Heat illness OR Heat cramps OR Heat exhaustion OR Heat syncope OR Heat stroke))) AND ((first AID) OR (MANAGEMENT)) AND (exertional OR exercise-induced)) AND ("2012/05/01"[PDat] : "2016/12/31"[PDat]) AND

English[lang])) OR (((hyperthermia) AND (exertional OR exercise induced)) AND ("2017/01/01"[PDat] : "2019/04/02"[PDat]) AND English[lang])) OR (((((Heat illness OR Heat cramps OR Heat exhaustion OR Heat syncope OR Heat stroke))) AND ((first AID) OR (MANAGEMENT)) AND (exertional OR exercise-induced)) AND ("2017/01/01"[PDat] : "2019/04/02"[PDat]) AND English[lang]) Filters: Publication date from 2017/01/01 to 2019/04/02; English- 178 items

("Heat illness" OR "Heat cramps" OR "Heat exhaustion" OR "Heat syncope" OR "Heat stroke") AND (first AID OR MANAGEMENT)
hyperthermia AND (exertional OR exercise-induced) 203 items

Animal studies were removed. Duplicates were removed.

203 total articles were reviewed by three investigators for content to include or exclude in answering the SAC question.

A total of 27 articles were included in the triennial review

Review Process and Literature Search of Evidence Since Last Approval Performed

Key Words Used

Search Conducted On: Thu Jun 09 14:43:06 2022

Search: heat-related illness* [ti] Filters: in the last 5 years

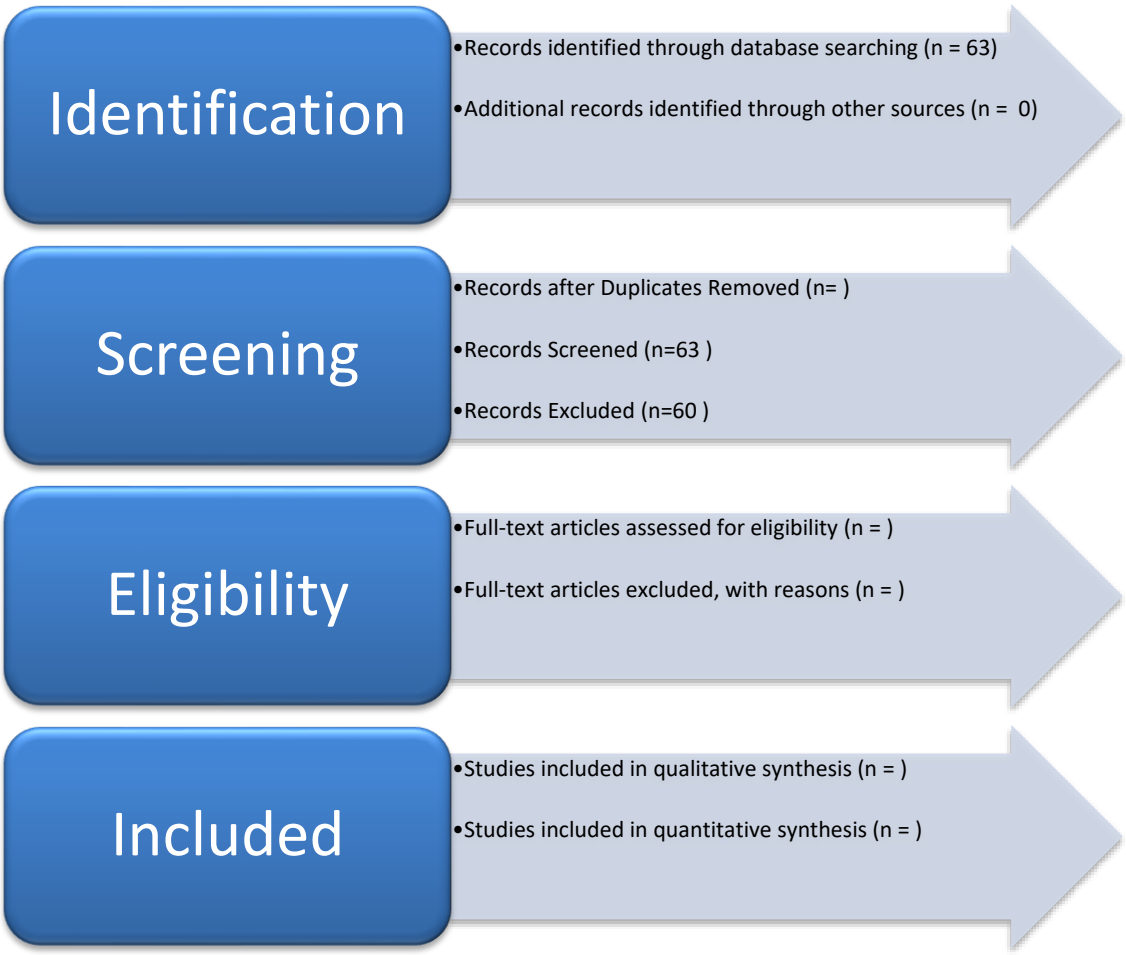
Inclusion Criteria (time period, type of articles and journals, language, methodology)
Exertional heat stroke, English language, all article types

Exclusion Criteria (only human studies, foreign language, etc.)

Limited to last three years, non-English language

Databases Searched and Additional Methods Used (references of articles, texts, contact with authors, etc.)

PubMed


Identification
•Records identified through database searching (n = 63)
•Additional records identified through other sources (n = 0)
Screening
•Records after Duplicates Removed (n=)
•Records Screened (n=63)
•Records Excluded (n=60)
Eligibility
•Full-text articles assessed for eligibility (n =)
•Full-text articles excluded, with reasons (n =)
Included
•Studies included in qualitative synthesis (n =)
•Studies included in quantitative synthesis (n =)

Scientific Foundation (Updated 2023):

An updated literature search on heat related illness only identified three articles for inclusion. These articles do not provide significant updates for the treatment of exertional heat illness. A systematic review and meta-analysis published by the ILCOR (Lin 2019) on first aid cooling techniques for heat stroke and exertional hyperthermia provides the most comprehensive recent review of this topic. The 2020 Red Cross TR included data from that ILCOR review and there are no studies published since that time that would significantly change Red Cross recommendations.

Gauer and Meyers published a review article in 2019 on heat related illness. This article summarizes the signs, symptoms and treatment of heat related illness, including heat stroke. Rapid cooling is suggested as a primary treatment and the article suggests that the most effective treatment modalities for heat stroke are cold water (46° to 57°F [8° to 14°C]) and ice water (35.6° to 41°F [2° to 5°C]) immersion, which result in cooling rates of 0.16 to 0.26°C per minute and 0.12 to 0.35°C per minute, respectively.

Mansor et al 2019 evaluated the threshold of thirst for prediction other symptoms of heat related illness. This was a retrospective survey of 340 outdoor community workers in Malaysiain March and April of 2016. Respondents were asked to recall if they experienced symptoms of heat related illness during the work day including tiredness, cramps, nausea, dizziness, thirst, vomiting, confusion, muscle weakness, heat sensations of the head or neck, chills and felling lightheaded. They were also asked to rate the severity of the symptoms. Three-hundred and twenty eight of 340 surveys were returned. Based on person-item map distribution, thirst was determined as the threshold item for preventative measures for moderate/severe heat related illness. While this is a low quality study, it emphasizes the need to pay attention to thirst as a marker of heat related illness.

A third study by Shimazaki et al in 2020 reported clinical characteristics, prognostic factors, and outcomes of heat-related illness in Japan. A total of 763 patients were enrolled in the study, with a median age 68 years (IQR 49-82 years) and median body temperature on admission of 38.2°C (IQR 36.8-39.8°C). A non-exertional cause was identified 56.9% of the time and exertional cause was 40.0%. Heat illness occurred indoors in 332 patients (43.5%), outdoors in 401 (52.5%) patients, and location was unknown in 30 (3.9%) patients. Causes of heat-related illness were daily activity in 429 (56.2%), office work in 5 (0.7%), physical work in 240 (31.5%), sports activity in 65 (8.5%), and unknown in 24 (3.1%) patients. Overall, 395/763 (51.8%) patients underwent active cooling therapy. In patients with a body temperature over 39°C on admission, 230 of 267 (86.0%) underwent active cooling, whereas in patients with a body temperature over 40°C on admission, 148 of 161 (91.9%) underwent active cooling. The overall median time from arrival to the start of active cooling was 9 (3–20) min. In the univariate analysis, time from arrival to start of cooling, time from arrival to reaching 38°C, and time from start of cooling to reaching 38°C did not predict mortality. Patients suffering non-exertional heatstroke were at higher risk for poor neurological outcome (OR 0.20, 95% CI 0.08–0.05, <0.01) The hospital mortality was 4.6%. Body temperature was not associated with mortality or poor neurological outcome.

Overview of Recommendation:

Only three articles were identified in this review potentially pertaining to the question. These studies do not provide significant new data, therefore, we choose to reaffirm the prior recommendations, however minor corrections were made in wording for clarification.

Specific Recommendations and Strength

Standards:

- Contact emergency medical services.
- Assess for and address life threats
- Assess for altered mental status and, if able, a core (e.g. rectal) temperature above 40° C, or >104° F.
- If present, begin immediate active cooling using whole body (neck down) water immersion (1-26° C, 33.8-78.8°F) until a rectal temperature of less than 39°C (102.2°F) is achieved or until mental status is improved.
- Where water immersion is not available or not practical, any other active cooling techniques that provides the most rapid cooling, such as using cool running water or sheets soaked in cold water, should be initiated.
- If no active technique is available, immediately begin cooling with a passive technique that provides the most rapid rate of cooling.
- Active cooling should be continued until there has been resolution of symptoms or for a reasonable amount of time, such as 15 minutes, as the benefit is more plausible than harm (Lin 2019).
- Transfer to the hospital while continuing to cool if necessary.

Guidelines: None

Options: None

Knowledge Gaps and Future Research

None provided

Implications for American Red Cross Programs

There are no new recommendations to change Red Cross programs.

Summary of Key Articles/Literature Found and Level of Evidence/Bibliography:

Last Name of First Author, Year Published: Gauer and Meyers 2019

Summary of Article: Gauer and Meyers published a review article in 2019 on heat related illness. This article summarizes the sign, symptoms and treatment of heat related illness, including heat stroke. Rapid cooling is suggested as a primary treatment and the article suggests that the most effective treatment modalities for heat stroke are cold water (46° to 57°F [8° to 14°C]) and ice water (35.6° to 41°F [2° to 5°C]) immersion, which result in cooling rates of 0.16 to 0.26°C per minute and 0.12 to 0.35°C per minute, respectively.

Methodology: Review Article
Bias Assessment (which tool is being used, if any):
Limitations: ☐Indirectness ☐Imprecision ☐Inconsistency
Key Results and Magnitude of Results:
Support, Neutral or Oppose Question: Support
Level of Evidence:
Certainty of Evidence: Why:

Last Name of First Author, Year Published: Mansor 2019

Summary of Article: Mansor et al 2019 evaluated the threshold of thirst for prediction other symptoms of heat related illness. This was a retrospective survey of 340 outdoor community workers in Malaysiain March and April of 2016. Respondents were asked to recall if they experienced symptoms of heat related illness during the work day including tiredness, cramps, nausea, dizziness, thirst, vomiting, confusion, muscle weakness, heat sensations of the head or neck, chills and felling lightheaded. They were also asked to rate the severity of the symptoms. Three-hundred and twenty eight of 340 surveys were returned. Based on person-item map distribution, thirst was determined as the threshold item for preventative measures for moderate/severe heat related illness. While this is a low quality study, it emphasizes the need to pay attention to thirst as a marker of heat related illness.

Methodology: Observational
Bias Assessment (which tool is being used, if any):
Limitations: ☒Indirectness ☐Imprecision ☐Inconsistency
Key Results and Magnitude of Results:
Support, Neutral or Oppose Question: Neutral
Level of Evidence:
Certainty of Evidence: Why:

Last Name of First Author, Year Published: Shimazaki 2020

Summary of Article: A third study by Shimazaki et al in 2020 reported clinical characteristics, prognostic factors, and outcomes of heat-related illness in Japan. A total of 763 patients were enrolled in the study, with a median age 68 years (IQR 49-82 years) and median body temperature on admission of 38.2°C (IQR 36.8-39.8°C). A non-exertional cause was identified 56.9% of the time and exertional cause was 40.0%. Heat illness occurred indoors in 332 patients (43.5%), outdoors in 401 (52.5%) patients, and location was unknown in 30 (3.9%) patients. Causes of heat-related illness were daily activity in 429 (56.2%), office work in 5 (0.7%), physical work in 240 (31.5%), sports activity in 65 (8.5%), and unknown in 24 (3.1%)

patients. Overall, 395/763 (51.8%) patients underwent active cooling therapy. In patients with a body temperature over 39°C on admission, 230 of 267 (86.0%) underwent active cooling, whereas in patients with a body temperature over 40°C on admission, 148 of 161 (91.9%) underwent active cooling. The overall median time from arrival to the start of active cooling was 9 (3–20) min. In the univariate analysis, time from arrival to start of cooling, time from arrival to reaching 38°C, and time from start of cooling to reaching 38°C did not predict mortality. Patients suffering non-exertional heatstroke were at higher risk for poor neurological outcome (OR 0.20, 95% CI 0.08–0.05, <0.01) The hospital mortality was 4.6%. Body temperature was not associated with mortality or poor neurological outcome.

Methodology: Observational

Bias Assessment (which tool is being used, if any):

Limitations: ☒Indirectness ☐Imprecision ☐Inconsistency

Key Results and Magnitude of Results:

Support, Neutral or Oppose Question: Neutral

Level of Evidence:

Certainty of Evidence: Why:

Level of Evidence	Definitions (See manuscript for full details)
Level 1a	**Experimental and Population based studies** - population based, randomized prospective studies or meta-analyses of multiple higher evidence studies with substantial effects
Level 1b	**Smaller Experimental and Epidemiological studies** - Large non-population based epidemiological studies or randomized prospective studies with smaller or less significant effects
Level 2a	**Prospective Observational Analytical** - Controlled, non-randomized, cohort studies
Level 2b	**Retrospective/Historical Observational Analytical** - non-randomized, cohort or case-control studies
Level 3a	**Large Descriptive studies** – Cross-section, Ecological, Case series, Case reports
Level 3b	**Small Descriptive studies** – Cross-section, Ecological, Case series, Case reports
Level 4	**Animal studies or mechanical model studies**
Level 5	**Peer-reviewed Articles** - state of the art articles, review articles, organizational statements or guidelines, editorials, or consensus statements
Level 6	**Non-peer reviewed published opinions -** such as textbook statements, official organizational publications, guidelines and policy statements which are not peer reviewed and consensus statements
Level 7	**Rational conjecture** (common sense); common practices accepted before evidence-based guidelines
Level 1-6E	**Extrapolations** from existing data collected for other purposes, theoretical analyses which is on-point with question being asked. Modifier E applied because extrapolated but ranked based on type of study.

REFERENCES

Gauer R, Meyers BK. Heat-Related Illnesses. Am Fam Physician. 2019 Apr 15;99(8):482-489. PMID: 30990296.

Mansor Z, Ismail NH, Rosnah I, Hashim JH. Thirst as the threshold symptom to prevent worsening heat-related illness. Med J Malaysia. 2019 Feb;74(1):1-7. PMID: 30846654.

Shimazaki J, Hifumi T, Shimizu K, Oda Y, Kanda J, Kondo Y, Shiraishi S, Takauji S, Hayashida K, Moriya T, Yagi M, Yamaguchi J, Yokota H, Yokobori S, Wakasugi M, Yaguchi A, Miyake Y. Clinical characteristics, prognostic factors, and outcomes of heat-related illness (Heatstroke Study 2017-2018). Acute Med Surg. 2020 Jun 16;7(1):e516. doi: 10.1002/ams2.516. PMID: 32551124; PMCID: PMC7298290.

American Red Cross

Scientific Advisory Council

ARC SAC SCIENTIFIC REVIEW
(Exertional Heat Illness)

Updated Scientific Foundation 2020:

There is **NO** new research that would support a change in the description of signs and symptoms of Exertional Heat Illness (EHI) including (1) muscle cramps, (2) exertional heat exhaustion, or exertional heat stroke. The current signs and symptoms and treatments for exertional heat illnesses are contained in Table 1.

Table 1. Signs and Symptoms, Treatment Recommendation and Return to Play for Exertional Heat Illness.

	Heat (Exercise Associated) Muscle Cramps	**Heat Syncope**	**Exertional Heat Exhaustion**	**Exertional Heat Stroke**
Core body temperature	Normal	Normal to mildly elevated	Elevated core body temperature (36-40 to 40.5 °C)	High core body Temperature (>40°C)
Signs of dehydration*, **	Evidence of dehydration	Evidence of dehydration	Evidence of dehydration	Severe dehydration
Symptoms	Acute, localized painful muscular cramps occurring in clusters while relaxing after activity due to dehydration and electrolyte depletion, thirst	Pale, sweaty skin, decreased pulse rate, collapsing in the heat, resulting in loss of consciousness (LOC),	Pallor, thirst, anorexia, generalized weakness, fainting, dizziness, headache, hyperventilation, nausea/vomiting, diarrhea, urge to defecate, persistent muscle cramps, decreased urine output, hyperventilation, tachycardia, sweaty skin, fatigue, decreased muscle coordination, decreased blood pressure, postural hypotension, tachypnea	Anhydrosis, flushed with hot dry skin, hot and sweaty skin, hyperventilation, evidence of shock and hypotension, tachypnea, tachycardia, Organ dysfunction (liver), (hepatic) (Hifumi 2018) Rhabdomyolysis (Koh 2018) Cardiac arrest (Ramirez 2018) Coagulation disorder (Hifumi 2018).
Neurologic symptoms	No neurologic Symptoms	Temporary neurologic dysfunction (e.g., AMS, vision or hearing deficits, weakness or tingling of the extremities) that likely resolves with lying supine and fluid intake, tunnel vision	Moderate neurologic dysfunction (e.g., confusion, agitation, psychosis, sleepiness, lethargy, paresthesias, incoordination)	Significant neurologic dysfunction (e.g., confusion, agitation, psychosis, sleepiness, lethargy, paresthesias, incoordination, unresponsiveness, encephalopathy), coma Seizure (Koh 2018)

Approved by ARC SAC January 2020

Treatment	Move to cool, shady area; firm gentle massage to cramp; encourage electrolyte drink oral intake	Move to cool, shady area; lay patient supine and elevate legs to restore central blood volume, encourage electrolyte drink oral intake (if able to swallow)	Move to cool, shady area, remove excessive clothing external cooling (fans, ice on neck, axilla, and groin, sponge baths), encourage electrolyte drink oral intake (if able to swallow), transport to the closest emergency department if symptoms persist,	Assess rectal temperature, immediate whole-body cold water immersion, focus on ABCs, call 911, and transport to the closest emergency department Alterative cooling Douse in cold water, tarp assisted cooling, rotating wet towel (Hosokawa, Nagata, & Hasegawa, 2019) WI (1–10°C) in various seated positions with at least legs and torso covered (Boehm 2018).
Return to play	When cramps are no longer uncomfortable	Mental status return to baseline and the victim able to ambulate without symptoms of dizziness	Cannot return to play	Cool to < 39°C within 30 mins of collapse (Hosokawa 2019) Cannot return to play

*Signs of dehydration include altered mental status, generalized weakness, headache, lightheadedness or dizziness, thirst, dry lips and/or tongue, paleness or coolness of the skin, tachycardia/tachypnea, or prolonged capillary refill.

**"Level of dehydration, the intensity of the exercise and the external environmental conditions determine the extent to which general physiological function is impaired. Dehydration and hyperthermia can elevate blood flow to heart, active muscles, and brain during low-intensity exercise. When exercise intensity is increased above moderate levels or when exercise duration is prolonged, brain, active muscle and systemic blood flow are gradually compromised, mechanistically associated with enhanced peripheral vasoconstrictor activity, suppressed venous return and cardiac filling that ultimately hinder cardiac output (Trangmar 2019)."

There is **NO** new research that would support a change to treatment recommendations for muscle cramps and exertional heat exhaustion.

A comprehensive systematic review and meta-analysis was conducted and published by the ILCOR first aid task force for first aid cooling techniques for heat stroke and exertional hyperthermia (Lin 2019) in 2019. Specifically, the first aid task force sought to answer the question, "Among adults and children (all ages) with heat stroke or exertional hyperthermia do any cooling techniques (or combination of techniques) appropriate for first aid compared to another cooling techniques (or combination of techniques) appropriate for first aid effect morality and rate of body temperature reduction (°C/min or °C/hr) (critical), organ dysfunction, adverse effects and hospital length of stay (important). The consensus on science examined the critical outcome of rate of body core reduction related to cold water immersion (14-15° C) for the torso, cold water immersion (10-17°C) of the hands and feet, colder water immersion (9-12°C) for the torso, ice water immersion (1-5°C) of the torso, evaporative cooling (mist and fan), ice sheets (3° C) vs towels soaked in ice water (14°C), commercial ice packs, fan alone, cold shower, hand cooling devices, cooling vests and jackets, and reflective blankets.

The ILCOR first aid task force recommendation for adults with exertional heat stroke are identified in table 2.

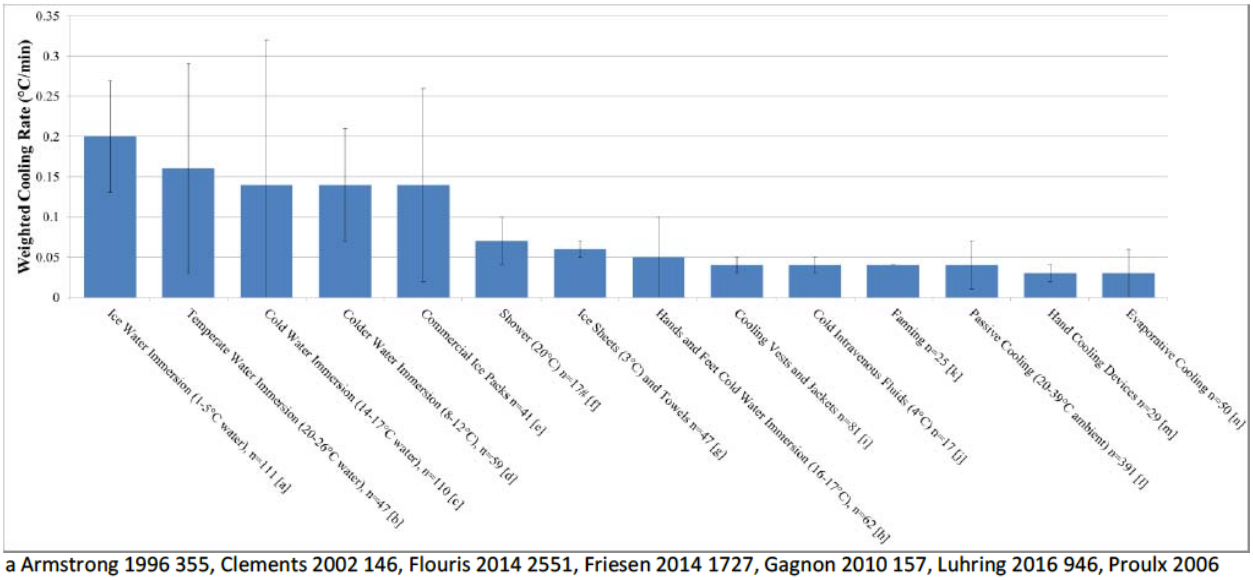
Cooling rates achieved with water immersion were faster than other active cooling interventions such as commercial ice packs, cold showers, evaporative cooking, ice sheets, and towels, fanning, evaporative cooling, cooling vest, and jackets (Figure 1).

For children with exertional heat stroke, no recommendation for or against any specific cooling technique compared with an alternative cooling technique was offered due to the lack of data.

Table 2. ILCOR CoSTR Treatment Recommendation for Exertional Heat Stroke (Lin 2019).

Recommendation	Statement	Grade
One	Immediate active cooling using whole body (neck down) water immersion (1-26° C, 33.8-78.8°C) until a core temperature of less than 39°C (102.2°F) is achieved.	Weak recommendation Very low certainty of evidence
Two	Where water immersion is NOT available, any other active cooling techniques be initiated.	Weak recommendation Very low certainty of evidence
Three	Immediate cooling using any active or passive technique available to care providers that provides the most rapid rate of cooling.	Weak recommendation Very low certainty of evidence

Figure 1. ILCOR CoSTR Weighted Mean Cooling Rates (°C/min) by Cooling Methods (Lin 2019).



a Armstrong 1996 355, Clements 2002 146, Flouris 2014 2551, Friesen 2014 1727, Gagnon 2010 157, Luhring 2016 946, Proulx 2006 434

b Caldwell 2018 512, Friesen 2014 1727, Lee 2012 655, Proulx 2006 434, Taylor 2008 1962

c Caldwell 2018 512, Clements 2002 146, DeMartini 2011 2065, Peiffer 2009 987, Peiffer 2010 461, Proulx 2003 1317, Taylor 2008 1962, Walker 2014 1159, Weiner 1980 507

d Clapp 2001 160, Halson 2008 331, Hosokawa 2017 347, Lee 2012 655, Nye 2017 294, Proulx 2006 434

e Kielblock 1986 378, Lissoway 2015 173, Sinclair 2009 1984

f Butts 2016 252

g Butts 2017 e1951, DeMartini 2011 2065, Nye 2017 294

h Barwood 2009 385, Carter 2007 109, Clapp 2001 160, DeMartini 2011 2065, Selkirk 2004 521, Zhang 2014 17

i Barwood 2009 385, Brade 2010 164, Lopez 2008 55, Maroni 2008 441, Smith 2018 413

j Morrison 2018 493, Sinclair 2009 1984

k Barwood 2009 385, DeMartini 2011 2065

l Adams 2016 936, Armstrong 1996 355, Barwood 2009 385, Brade 2010 164, Butts 2016 252, Butts 2017 e1951, Carter 2007 109, Clapp 2001 160, Clements 2002 146, DeMartini 2011 2065, Flouris 2014 2551, Gagnon 2010 157, Halson 2008 331, Hosokawa 2016 347, Kielblock 1986 378, Lissoway 2015 173, Lopez 2008 55, Luhring 2016 946, Maroni 2018 441, Peiffer 2009 987, Peiffer 2010 461, Pointon 2012 2483, Reynolds 2015 97, Sefton 2016 936, Selkirk 2004 521, Smith 2018 413, Taylor 2008 1962, Walker 2014 1159, Weiner 1980 507, Zhang 2009 283, Zhang 2014 17

m Adams 2016 936, Maroni 2018 441, Zhang 2009 283

n DeMartini 2011 2065, Sefton 2016 936, Sinclair 2009 1984, Kielblock 1986 378

The ILCOR task force also recognized that the optimal immersion time to reduce core temperature to below 39° C is unknow (Lin 2019). Thus, the task force recommended that even in the absence of core temperature measures, the use of water immersion, if available, should be continued until there has been resolution of symptoms or for a reasonable amount of time, such as 15 minutes, as the benefit is more plausible than harm (Lin 2019).

Core temperature cooling was found to be effective without removal of football uniform pads supporting a recommendation for immediate immersion in water before removal of sports equipment in athletes suffering exertional heat stroke (Miller 2018 1200). However, cooling while wearing equipment or uniforms may not be as effective if the hyperthermic person is wearing clothing or personal protective equipment, like firefighter turnout gear or Hazmat PPE which is designed to insulate.

All published studies and clinical reports used a core temperature measurement (eg, rectal, ingested pill, or esophageal) when assessing and cooling an individual's body temperature. This is consistent with evidence summary reported in ILCOR CoSTR on exertional heat exhaustion (Lin 2019). Ideally a core temperature (ie, rectal) should be obtained before, during, and following cold water immersion as peripheral temperature measurement (eg, tympanic, oral or axillary), while more readily available must be considered an unreliable indication of core temperature cooling (Casa 2015 990, Lin 2019).

Accurate measurement of temperature is not expected of a lay first aid provider. Signs and symptoms are similar to those of heat exhaustion with a key symptom the presence of *abnormal mental status in the context of exposure to heat*. When available and trained, assessing for exertional heat stroke using a rectal core temperature (40°C; <104°F) is recommended (Lin 2019). However, the absence of core rectal temperature measure should NEVER preclude initiation of whole-body cold-water immersion if available (Lin 2019).

Updated Scientific Foundation 2016:

1. New terminology in the literature is a more accurate description of our present understanding of heat illness. The review title is being changed from hyperthermia to exertional heat illness. Two of the three medical conditions addressed in this review, exercise associated muscle cramps and heat exhaustion, can occur without hyperthermia. In addition, hyperthermia is not a term used in first aid education nor is it consistent with current language from the National Athletic Trainers' Association (NATA) and the American College of Sports Medicine (ACSM). Commonly, first aid curricula label the topic "heat illness" and address exercise associated heat cramps, heat exhaustion and exertional heat stroke. The term 'heat cramps' has been changed to 'exercise associated muscle cramps' and the term 'heat stroke' to 'exertional heat stroke' to reflect current NATA and ACSM terminology.

2. There is no new research to suggest a need to change the previously described characteristic signs and symptoms of exertional heat illness.

3. There is research that suggests a change in the first aid treatment recommendations for exertional heat stroke. Cold water immersion, cold water on skin with fanning, or rotating towels/sheets wetted with cold water and placed on the trunk are much more efficacious that

isolated ice packs for reducing core body temperature. Ice packs will be classified as an option rather than a standard for the treatment of heat stroke.

4. Recommendations for treatment of exercise associated muscle cramps and exertional heat exhaustion no longer include intravenous fluids at the First Aid level.

2012 Scientific Foundation

NOTE: Due to the complexity of some of the commentary generated by this review, a table of contents is provided here.

Table of Contents

Question(s) to be addressed

Original 2009 Scientific Review Question:

(Copy from original document)

What are the current diagnostic criteria used to differentiate between the different types of hyperthermia (i.e., heat cramps, heat exhaustion, and heat stroke [exertional and classic]) and what are the current recommendations for managing these conditions?

PROPOSED REVISED QUESTION FOR TRIENNIAL REVIEW:

What are the current best methods for a first aid responder to recognize various types of heat-related illness and what are the current recommendations for managing these conditions?

RATIONALE: Hyperthermia is a physiologic condition defined as a core body temperature above a particular temperature, effectively any temperature above "normal" core body temperature, though, in the context of illness, 40ºC (104º F) is often cited as a temperature above which normal physiological functioning may be disrupted.

On review of the 2009 SR, the discussion of diagnosis and therapeutic intervention focused on the conditions noted in parentheses in the original question. Among these conditions, only heat stroke has been defined as being related to an elevated core body temperature. The other conditions are often grouped together with heat stroke under the term of "heat illnesses" or "heat-related illnesses," though they do not have hyperthermia as a part of either the pathophysiology or definitions commonly published. These terms were also used in the body of the 2009 SR to refer to the class of disorders being considered.

Thus, to avoid confusion, it is proposed to use the more global terms "heat illness" or "heat-related illnesses," as are used in the research medical literature and to address the disorders included in that class in the medical literature that are likely to benefit from an acute medical/first aid intervention. This will be further discussed in the section on search strategy and terms/definitions.

Additionally, due to a number of confusing points and controversies in the medical literature regarding the domain of heat-related illness, this review includes an updated review of the conditions being addressed. This is presented in Appendix A to preserve the brevity of the actual update presentation and statements. This appendix review of conditions is meant to provide complementary background information to that provided in the 2009 SR except for the discussion of heat cramps. For reasons elucidated in section on heat cramps in Appendix A below, a full review of the medical literature was undertaken and a new discussion developed for heat cramps. This revised discussion is presented in Appendix A which is intended to replace the discussion in the 2009 SR.

Review Process and Literature Search of Evidence since Last Approval Performed

(Describe process to determine if any new evidence available since last approval))

Review of and Comment on 2009 Scientific Review

The 2009 SR was reviewed in detail and most references related to statements having a bearing on the recommendations or on diagnostic features were reviewed to verify the foundation for the statements made in the SR. Many of the reference sources were found to be review or summation articles. Thus, most of these references were reviewed for the source of information that appeared to have been the basis for citation in the 2009 SR, particularly if the statement was relevant to underlying disease process, diagnosis or treatment. Many of these citations, in turn, referred to other review articles or textbook chapters. As much as practical (availability in libraries of textbook editions being cited and time to track down citations from before electronic versions, and, at times, in more obscure journals or ones that are now out of print), these secondary sources were also reviewed to determine if there was any experimental study behind the assertions and to assess the interpretations of statements made in citations. Additionally, many of these citations referenced newsletters and other "grey literature" sources, including "unpublished data." Among a core group of recent authors there was also a high tendency to cite review articles of which they were one of the authors and in which the foundation citations referred back to their own observational reports or "unpublished data."

For several reasons, there has been a marked increase in reports of various observations and studies of heat effects on athletic performance since the mid 1960s when carbohydrate-electrolyte rehydration solutions were developed and commercialized. There has also been a body of literature that has been expanding the knowledge and understanding of the effects of heat on the human body and of the pathophysiology of heat stroke. While there have not been dramatic changes in evidence-based knowledge regarding first aid treatment of the heat illnesses over the intervening time since the 2009 SR, there has been a further congealing of the knowledge gained from the on-going research efforts to better understand human interactions with heat stress with implications for potential future modifications of both first aid and definitive treatment, primarily for heat stroke. Much of this information is presented in Appendix A.

Review of medical literature for new publications on the topics.

2020 Review Process and Literature Search of Evidence

A literature search was performed by the Red Cross Librarian using the following parameters:

Search (("Heat illness" OR "Heat cramps" OR "Heat exhaustion" OR "Heat syncope" OR "Heat stroke")) AND (first AID OR MANAGEMENT) Filters: Publication date from 2017/01/01 to 2019/04/02; English – 60 items

Search (hyperthermia) AND (exertional OR exercise-induced) Filters: Publication date from 2017/01/01 to 2019/04/02; English- 118 items

Search (((((("Heat illness" OR "Heat cramps" OR "Heat exhaustion" OR "Heat syncope" OR "Heat stroke")) AND (first AID OR MANAGEMENT)) AND ("2017/01/01"[PDat] : "2019/04/02"[PDat]) AND English[lang])) OR (((((Heat illness OR Heat cramps OR Heat exhaustion OR Heat syncope OR Heat stroke))) AND ((first AID) OR (MANAGEMENT)) AND (exertional OR exercise-induced)) AND ("2012/05/01"[PDat] : "2016/12/31"[PDat]) AND English[lang])) OR (((hyperthermia) AND (exertional OR exercise induced)) AND ("2017/01/01"[PDat] : "2019/04/02"[PDat]) AND English[lang])) OR (((((Heat illness OR Heat cramps OR Heat exhaustion OR Heat syncope OR Heat stroke))) AND ((first AID) OR (MANAGEMENT)) AND (exertional OR exercise-induced)) AND ("2017/01/01"[PDat] : "2019/04/02"[PDat]) AND English[lang]) Filters: Publication date from 2017/01/01 to 2019/04/02; English- 178 items

("Heat illness" OR "Heat cramps" OR "Heat exhaustion" OR "Heat syncope" OR "Heat stroke") AND (first AID OR MANAGEMENT)
hyperthermia AND (exertional OR exercise-induced) 203 items

Animal studies were removed. Duplicates were removed.

203 total articles were reviewed by three investigators for content to include or exclude in answering the SAC question.

A total of 27 articles were included in the triennial review

Prior Development of Search Terms

Search terms used in the 2009 SR included:

- Heat illness,
- hyperthermia,
- body temperature regulation,
- heat exhaustion,
- heat stroke.

The topics discussed in the 2009 SR in terms of diagnosis and treatment were heat cramps, heat exhaustion and heat stroke. Given the proposed restatement of the question to address the larger segment of the class of heat-related illnesses, search strategies for this triennial review were developed based on the major disorders in that class. The class of heat-related illnesses has been defined somewhat differently by different authors from different domains interested in the topic. Conditions frequently listed as heat-related disorders or illnesses include:

- heat edema,
- heat rash,
- heat cramps,
- heat syncope,
- heat exhaustion and

- heat stroke.(Howe and Boden, 2007)

Among these disorders heat edema and heat rash will not be addressed in this review since they were not addressed in the 2009 SR. As a point of clarification with reference to the discussion in Appendix A, the medical disorders in this category would more correctly all be named as the general category; for example heat-related edema, etc. For simplicity, and in consistency with terminology used as keywords and title wording in medical literature, this discussion will maintain the terminology of the list above

Heat syncope was not included in the 2009 SR search strategies, though it was referred to in the discussion. It was incorporated as a search term for this review based on its presentation in a position statement from the National Athletic Trainers' Association (NATA) published in 2002, coupled with finding a positive response of citations to an initial search in PubMed and seeing it referred to in a number of articles cited in the 2009 SR.

Heat stroke was included to cover both exertional and classic, non-exertional heat stroke.

"Exertional hyponatremia," though presented in much of the sports medicine literature as a heat-related condition, was **not** used as a search term since this is a physiologic condition that occurs as a secondary phenomenon to inappropriate hydration activities. It will be briefly addressed in statements regarding treatment and in Appendix A.

Thus, the search term set for this review includes the general term heat illness as well as the specific disorder terms heat cramps, heat syncope, heat exhaustion and heat stroke.

In addition to the searches outlined above to directly seek any newer scientific information on heat illnesses, numerous other searches were conducted to clarify questions raised from the review of source material for the 2009 SR. These searches are not detailed here, though many of these sources will be cited in the discussion section and Appendix A of this review.

Previous Review Process and Literature Search of Evidence

Search process and results for all terms other than heat cramps
For all the topics except heat cramps, searches were restricted to January 1, 2009 through May 2012. Searches were limited to academic journal articles and English language. Search input structure used Boolean phrases combining the terms above into one search string ("heat illness" OR "heat cramps" OR "heat exhaustion" OR "Heat stroke" OR "heat syncope"). Two searches were performed crossing this string with "first aid" in one and "management" in the other using the Boolean operator "AND". The term "heat cramps" in quotations was included in these searches to cover all heat illnesses being considered and assuming that, in the limited time constraint it would not add many, if any, unrelated articles.

These searches produced "0" and 20 results respectively in PubMed. Review of the 20 results did not reveal any articles directly addressing treatment other than as review articles.

Searches were also performed in the databases CINAHL, SPORTDiscuss and Academic Search Premiere with the following overall results:

Search string / Database	CINAHL* SPORTDiscuss* Academic Search Premiere*	PubMed
Heat illness **OR** Heat cramps **OR** Heat exhaustion **OR** Heat syncope **OR** Heat stroke	758	207
AND First Aid	1	0
AND Management	757	20

*These databases were searched together through the EBSCO portal

Titles were reviewed of all citations retrieved in the two systems (965). Abstracts of seemingly relevant articles were then reviewed. From these a final total of 122 articles were fully reviewed for relevance. Many of the results in the databases searched via EBSCO were in non-peer reviewed magazines and trade publications.

Of these 122 articles, a number were general reviews of heat illnesses either as a class or of the individual disorders. These were scanned and any pertinent references retrieved, though none offered new scientific evidence for treatments beyond what was found in the database searches. Several policy and position statements were retained and reviewed in detail for both assessment of the positions of different organizations and for review of the scientific foundations upon which they based their positions to seek new leads not found on the literature search. Again, none of these articles led to any articles not already identified in the database searches.

Additionally, many of the citations from the original 2009 SR were reviewed with, again, pursuit, at times of citations from their references, largely to add contextual clarity and to seek any evidence-based foundations that had not been previously discovered.

Search process and results for heat cramps

Since the topic of heat cramps was being fully readdressed due to the issues identified with the references used in the 2009 SR, an additional set of searches were performed using just "heat cramp" and "heat cramps" with and without quotation marks as a search string to seek specifically any experimental studies on treatment. This search was undertaken in the same databases as the above search: PubMed and, via the EBSCO portal, CINAHL, SPORTDiscuss and Academic Search Premiere. Both search strings were entered with and without quotation marks.

In PubMed, in addition to using the four methods of posting the search strings, the Medical Subheading classification system, MeSH, was consulted to determine the placement of the strings as entry points. Heat cramps does not have the status of a MeSH term. It maps to "Heat Stress Disorders." The only individual heat stress disorders with MeSH status are "heat exhaustion" and "heat stroke," which has "sunstroke" as the only MeSH nested under it. Searches of PubMed with the string entered in its 4 forms are presented in the following table.

Search String	Number of results	
	All	Limit to Human
Heat cramp	4310	3125

Heat cramps	4321	3134
"Heat cramp"	5	3
"Heat cramps"	40	37
MeSH term "heat stress disorder"	3714	2725
Heat Cramps* limited to:		
Clinical Trials	172	152
Controlled Clinical trials	30	29
Systematic Reviews	41	38
Review	37	34
Journal Article	3962	2796

*Heat cramps without quotations chosen since it delivered the most results

From review of the first 200 titles returned in the searches above with no quotation marks, it was evident that many of the articles had, at best, very tangential relevance to the goal of the search. This is since the PubMed search engine searches for all results with either word in the title

The numbers of citations returned via the EBSCO portal are tabulated in the following table.

Search String	Number of citations
Heat cramp	120
Heat cramps	120
"Heat cramp"	7
"Heat cramps"	110
Combined with OR	120

Search strings were designated as TX All Text. General parameters and limitations placed on the search included using search mode as a Boolean/Phrase, Applying related words and searching within full text of articles. Limitation to "Scholarly(Peer-reviewed) Journals" was placed as a limitation. CINAHL was only limited to English and French. Academic Premiere was limited to English and French and periodicals. SPORTDiscus was limited to French and English and to journal articles. Combining the four searches with the OR operator, returned 120 citations, implying that the sets of the other searches under different rubrics were inclusive.

Of interest, with the noted limiters applied in the non-PubMed databases, the number of citations was very close to the results of a hand screen of a larger number of results with the broader terms. There was no electronic means to compare the results from the two database sets for completeness. This was not done formally on a hand review.

Reference list results

Review of the reference lists in review articles produced a number of relevant articles, particularly for the historical understanding of current treatment recommendations found in review articles. These results were not tabulated.

Literature Search Results

As noted above, the final list of articles for in-depth review for heat illness was 122, of which quite a few were general reviews.

References obtained that presented studies of treatment of heat illness, heat cramps, heat exhaustion, heat syncope or heat stroke are included in the following tables.

Each of the disorders commonly known as heat illnesses has some degree of either controversy around the defining factors or evolving understanding of the condition, understanding of which will make this review much more useful to the reader. Readers are, thus, referred to Appendix A at the end of this document for discussions of the disorders commonly called heat illnesses.

2020 Textual Summary of Recommendation for Revision, Reaffirmation or Retire

The question as formatted is not correctly formatted in PICOST format. The FA Subcouncil feels that the topic would be better address by breaking it up into individual questions that are more conducive to the PICOST format. We are requesting to **retire** the question in order to establish new questions around the topic of exertional heat illness as they arise.

Exercise Associated Muscle Cramps

Exercise-associated muscle cramps are muscle spasms, which can be intense and debilitating and occur typically in the legs, arms, and abdomen, presenting during or after exercise. The traditional and simplified term for this condition is "heat cramps" or "exertional heat cramps." The term exercise-associated muscle cramps reflect the understanding that these cramps, while possibly more common in hot and humid conditions, it is not directly related to elevated core body temperature.

Recommendations:

Standards

- None

Guidelines

We suggest interventions by first aid providers include:
(1) Rest. Stopping the activity associated with the cramping muscle(s).
(3) Icing to the affected muscle(s).
(2) Gentle stretching to the affected muscle(s).
(3) Massaging of the cramping muscle(s).
(4) Encouraging the victim to drink cool fluids (10°-15°C; 50°-59°F) is recommended, preferably containing carbohydrates and electrolytes (see ILCOR CoSTR recommendations).

(5) Exercise should not be resumed until all symptoms have resolved.

Options
- None

Exertional Heat Exhaustion

Exertional heat exhaustion is an inability to cope with heat stress and is caused by a combination of exercise-induced heat and fluid and electrolyte loss as sweat. Exertional heat exhaustion is characterized by fatigue, nausea and/or vomiting, loss of appetite, dehydration, exercise-associated heat cramps, dizziness with possible heat syncope, elevated heart and respiratory rate, and skin that is pale, cool and clammy, or slightly flushed. The patient may be weak and unable to stand but presents with normal mental status.

Accurate measurement of temperature is not expected of a lay first aid provider. If temperature measurement is available, the diagnostic criteria for exertional heat exhaustion is a rectal core temperature 40°C (<104°F).

Recommendations:

Standards
- None

Guidelines

We suggest interventions by first aid providers include:
(1) Removing from the hot, humid environment.
(2) Removing excess sporting equipment and clothing.
(3) Laying the victim in a cool place.
(4) Begin cooling with cold/cool water on the skin combined with fanning.
(5) Encouraging the victim to drink cool fluids (10°-15°C; 50°-59°F) is recommended, preferably containing carbohydrates and electrolytes (see ILCOR CoSTR recommendations).
(6) Exercise should not be resumed until all symptoms have resolved and victims' hydration status has returned to normal; often occurs within 24 h; same day return to play not advised.

If a person with suspected exertional heat exhaustion is unable to tolerate oral rehydration or develops any change in mental status, 9-1-1 should be called immediately.

Options
- None

Exertional Heat Stroke

In the spectrum of heat illness, heat stroke is the life-threatening emergency. Patients have exaggerated heat production and an inability to cool themselves.

The two main diagnostic criteria for exertional heat stroke are central nervous system dysfunction and a core body temperature greater than 40°C (104°F); however, cutaneous vasoconstriction may mean that a peripheral temperature measurement is inaccurately low (Walter 2018 153). A core temperature measurement (using a rectal thermometer) is required on any collapsed athlete. Rectal core temperature measurement is the only recommended method of obtaining a direct and accurate measurement of core body temperature. Other devices, such as oral, axillary, aural canal, tympanic, forehead sticker, and temporal artery thermometers, inaccurately assess the body temperature of an exercising person (Casa 2015 990, Walter 2018). Ingested thermometer pills must be taken in advance and are not typically available, and esophageal temperature probes require training to insert and may not be safe to attempt in a person with altered mental status.

However, if a suspected exertional heat stroke victim exhibits central nervous system dysfunction even though the rectal temperature is slightly lower (< 40° C; 104°F), it is reasonable to assume the victim is suffering from exertional heat stroke.

Accurate measurement of temperature is NOT expected of a lay first aid provider. Signs and symptoms are similar to those of heat exhaustion with a key symptom the presence of **abnormal mental status** in the context of exposure to heat. If an accurate measurement of temperature is available exertional heat stroke, diagnostic criteria is a core temperature > 40°C (104°F).

Immediate cooling of a suspected exertional heat stroke victim is of the utmost importance. Treatment delays are common during exertional heat stroke scenarios in athletes as reported in Miller Di Mango, and Katt (2018 1203). Athlete morbidity and mortality increase the longer the core remains elevated above the threshold for cell damage (ie, 40.5°C [105°F]) (Miller 2018 1203). In fact, reducing the core temperature to below 38.9°C within 60 minutes is associated with an improved survival (Walter 2018 154). Thus, the importance of initiating cold water immersion as quickly as possible after an exertional heat stroke assessment cannot be overstated (Miller 2018 1203).

Classic heat stroke is the entity typically seen in older adults during prolonged heat waves lasting several days and is not usually an illness that will be cared for by first aid providers. Treatment is similar to/the same as exertional heat stroke with rapid cooling.

Recommendations:

Standards
We suggest interventions by first aid providers include:

(1) Assess for life threats
(2) Assess core temperature (40° C; >104° F) if able and look for signs of central nervous system (CNS) dysfunction.
(3) Begin immediate active cooling using whole body (neck down) water immersion (1-26° C, 33.8-78.8°C) until a core temperature of less than 39°C (102.2°F) is achieved. Where water immersion is NOT available, any other active cooling techniques that provides the most rapid

cooling be initiated. If no active technique is available, immediately cooling with a passive technique that provides the most rapid rate of cooling.
(4) Contact 9-1-1.
(5) Active cooling should be continued until there has been resolution of symptoms or for a reasonable amount of time, such as 15 minutes, as the benefit is more plausible than harm (Lin 2019).
(6) Transfer to the hospital while continuing to cool if necessary.

Guidelines
- None

Options
- None

Updated References for 2020

Abdelmoety DA, El-Bakri NK, Almowalld WO, et al. Research article characteristics of heat illness during Hajj: A Cross-Sectional Study. *BioMed Research International*. February 2018:1-6. doi:10.1155/2018/5629474.

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Boehm KE, Miller KC. Does gender affect rectal temperature cooling rates? A critically appraised topic. *J Sport Rehab*. 2018 ahead of print doi: 10.1123/jsr.2018-0081

Brigham E, Brady J, Olympia RP. School nurses on the front lines of medicine: emergencies associated with sport and physical activities: part 1. *NASN School Nurse*. 2018;34(3):155-161. doi:10.1177/1942602X18819223.

Caldwell JN, van den Heuvel AMJ, Kerry P, Clark MJ, Peoples GE, Taylor NAS. A vascular mechanism to explain thermally mediated variations in deep body cooling rates during the immersion of profoundly hyperthermic individuals. *Experimental Physiology*. 2018;103:512–522. https://doi.org/10.1113/EP086760

Dunn RJ, Kim TY. Pediatric heat-related illness: recommendations for prevention and management. *Pediatr Emerg Med Pract*. 2017;14(8):1-20.

Hifumi T, Kondo Y, Shimizu K, Miyake Y. Heat stroke. *J Intensive Care*. 2018;6(1):30. doi:10.1186/s40560-018-0298-4.

Hosokawa Y, Nagata T, Hasegawa M. Inconsistency in the standard of care-toward evidence-based management of exertional heat stroke. *Front Physiol*. 2019;10:108.

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Koh YH. Case report heat stroke with status epilepticus secondary to posterior reversible encephalopathy syndrome (pres). *Case Reports in Critical Care*. June 2018:1-4. doi:10.1155/2018/3597474.

Miller KC, Di Mango TA, Katt GE. Cooling rates of hyperthermic humans wearing American football uniforms when cold-water immersion is delayed. *J Athl Train*. 2018;53(12):1200-1205. doi:10.4085/1062-6050-398-17.

Ramirez O, Malyshev Y, Sahni S. It's getting hot in here: a rare case of heat stroke in a young male. Cureus 2018;10(12): e3724. DOI 10.7759/cureus.3724

Smith M, Withnall R, Boulter M. An exertional heat illness triage tool for a jungle training environment. *J R Army Corps*. 2018;164:287-289.

Trangmar SJ, González-Alonso J. Heat, hydration and the human brain, heart and skeletal muscles. *Sports Med*. 2019;49(s1):69-85. doi:10.1007/s40279-018-1033-y.

Walter E, Steel K. Management of exertional heat stroke: a practical update for primary care physicians. *Br J Gen Pract*. 2018;68(668):153-154. doi:10.3399/bjgp18X695273.

Secondary References

Casa DJ, DeMartini JK, Bergeron MF, Csillan D, Eichner ER, Lopez RM, Ferrara MS, Miller KC, O'Connor F, Sawka MN, Yeargin SW. National Athletic Trainers' Association Position Statement: Exertional Heat Illnesses. *J Athl Train*. 2015 Sep;50(9):986-1000. doi: 10.4085/1062-6050-50.9.07. Erratum in: J Athl Train. 2017 Apr;52(4):401.

Godek SF, Morrison KE, Scullin G. Cold-water immersion cooling rates in football linemen and cross-country runners with exercise-induced hyperthermia. *J Athl Train*. 2017;52(10):902-909. doi:10.4085/1062-6050-52.7.08.

Lin S, Douma M, Aves T, Allan K, Bendal J, Berry D, Change WT, Hood NA, Singletary EM, Zideman D, Epstein J, on behalf of the international Liaison Committee on Resuscitation IILCOR) First Aid Task Force. First aid cooling techniques for heat stroke and exertional hyperthermia Consensus on Science and Treatment Recommendations [Internet] Brussels, Belgium: International Liaison Committee on Resuscitation (ILCOR) First Aid Task Force, 2019 Nov 2. Avalable from: http://ilcor.org

McDermott BP, Casa DJ, Ganio MS, et al. Acute whole-body cooling for exercise-induced hyperthermia: a systematic review. *J Athl Train*. 2009;44(1):84-93. doi:10.4085/1062-6050-44.1.84.

Miller KC, Hughes LE, Long BC, Adams WM, Casa DJ. Validity of core temperature measurements at 3 rectal depths during rest, exercise, cold-water immersion, and recovery. *J Athl Train*. 2017;52(4):332-338. doi:10.4085/1062-6050-52.2.10.

Poirier MP, Notley SR, Flouris AD, Kenny GP. Physical characteristics cannot be used to predict cooling time using cold-water immersion as a treatment for exertional hyperthermia. *Appl Physiol Nutr Metab*. 2018;43(8):857-860. doi:10.1139/apnm-2017-0619.

References for 2016

Author(s)	Full Citation	Summary of Article (provide a brief summary of what the article adds to this review)	Level of Evidence (Table Below)
Bergeron MF	Bergeron MF. Heat cramps during tennis: a case report. *Int J Sport Nutr.* Mar 1996;6(1):62-68	This is a case report of a 17 yo male tennis player with a history of cramps for whom Bergeron suggested ingesting a salt-containing drink during matches. The goal was not specifically to treat a bout of cramping, but to prevent cramping from occurring. Use of the proposed solution of a commercial carbohydrate and salt-containing liquid at prescribed amounts did prevent cramping. He did report one episode of the tennis player using a recommended salt solution to, apparently, abort cramping	3b/3bE
Brockbank EM	Brockbank EM. Miners' Cramp. *The British Medical Journal.* Jan 12 1929;1(3549):65-66	Brockbank presents a case report of a miner who developed cramping described as tetanic in nature commencing in the hands and, not infrequently, ascending to involve the upper back. He presents, including copy, two prior reports of miners suffering cramps involving exerted muscles and torso/abdominal muscles. In both his case and the experiences he presented, the cramping was resolved once the miners began consuming salted water during work as opposed to plain water. Brookbank does not offer any dosing information and there is no mention of acute treatment with salt solutions.	3bE
Davis CC	Davis CC. Salt treatment for miner's fatigue. *Journal of the American Medical Association.* 1924;83(26):2112	Reports, in a "correspondence" of an article in a non-medical journal that reported an experiment on a few miners reporting fatigue and cramps in which a group of an unspecified number were given a salt water solution to replace their normal daily ration of 2 quarts of water. 10 gm salt (2 teaspoons) was dissolved in 1 gallon water – described as a 0.25% solution). Six of the miners in the test group felt less fatigue and one stopped having cramps. One teaspoon salt was	2aE

		then added to each quart of drinking water used by the miners – no comment on results in the larger cohort.	
Ladell WSS	Ladell WSS. Heat Cramps. *The Lancet*. 1949;254(6584):836-839.	This is a report of a single heat/exertional-cramp-prone subject in whom cramping was induced in the legs with activity. Circulation in one leg was occluded with a blood pressure cuff, 162ml of 15% NaCl was injected into an arm vein over 3.5 min. Cramp induction techniques were started immediately. After 2 min they were no longer able to induce cramp in the unobstructed leg. The obstructed leg continued to cramp for 7 minutes when the tourniquet was removed by protocol. The cramping in the occluded leg resolved 2 minutes after the tourniquet was removed.	3b
Moss KN	Moss KN. Some Effects of High Air Temperatures and Muscular Exertion upon Colliers. *Proceedings of the Royal Society of London. Series B, Containing Papers of a Biological Character*. August 1, 1923 1923;95(666):181-200	Moss and colleagues chose 10 miners, some with a history of easy cramping and some without and had them consume drinking water with 10 grams of NaCl per gallon. They found that 2 cramp-prone miners stopped having cramps once ingesting the salt solution. Three other cramp-prone miners were fired before the actual experiment was started. Both miners remaining stopped having cramps once using the salt solution.	2aE
Oswald R	Oswald R. Saline Drink in Industrial Fatigue. *Lancet*. 1925;205(5313):1369-1370	Oswald reports the introduction of a saline drink to stokers in electric power plants with elimination of cramping after introduction. This is not acute treatment.	3bE
Talbott JH	Talbott JH, Michelsen J. Heat Cramps: A Clinical and Chemical Study. *J Clin Invest*. May 1933;12(3):533-549	This is a retrospective observational report of 5 workers on the Hoover Dam diagnosed as having heat cramps, though one may have been cardiac angina, treated with intravenous saline. Of note this is the only report to have detailed clinical progress information on the acute (within a few hours) response of patients to the intervention.	3b
Talbott JH	Talbott JH. Heat Cramps. *Medicine*.1935;14(3):323-376	This is the first review of the topic of heat cramps. Talbott reviews some of the reports noted above as well as others. He reviews biochemical abnormalities as they could be studied at the time and as his team had done in regards to laborers building the Hoover Dam and in a steel mill in Youngstown, Pennsylvania. He also reviews a number of apparent contributing risk factors. He comments on other authors' reports of the use of saline, administered orally, by enemas, by clysis and by intravenous. His personal data came from 5 cases of heat cramp at the Hoover dam site and 34 cases from the steel mill. He reports the resolution of cramps in all patients in his series before the end of the first 1 liter infusion. Of note, he reports that,	3b

		when the patients were able to take salt by mouth, milk (NV) or salt tablets (PA) were used for further replenishment. Patients treated with salt tablets were given one 1gm tablet every hour until 15 tablets had been administered with no report of gastro-intestinal symptoms. Talbott also reported various salt solutions that had been used (these are presented in App A: Heat Cramp Treatment)	
Thrower, R	Thrower R. Heat Cramp. *The British Medical Journal.* 1928;1(3508):546.	Thrower reports experience in a population of "engine-room staff of a modern motor vessel" who were experiencing both exhaustion and cramps "analogous to fireman's cramps." He reported not using oatmeal water, "which is often recommended", but addressed the problem with "addition of salt in small amounts to the mess drinking water, as has been suggested by various writers, seemed to prove efficacious."	3bE

Author(s)	Full Citation	Summary of Article (provide a brief summary of what the article adds to this review)	Level of Evidence (Table Below)
Amorim FT, Yamada PM, Robergs RA, Schneider SM	Amorim FT, Yamada PM, Robergs RA, Schneider SM. Palm cooling does not reduce heat strain during exercise in a hot, dry environment. Applied Physiology, Nutrition & Metabolism. 2010;35(4):480-489	Comparison of cooling device held in hands, hand and forearm immersion in cool water and use of a cool-water perfused vest to slow heat accumulation in adults exercising in elevated heat stress conditions and wearing summer military clothing with backpacks. Only the vest slowed heat accumulation. This small study adds to literature suggesting that for cooling, the amount of body surface area subjected to cooling is important.	2aE
Barwood MJ, Davey S, House JR, Tipton MJ	Barwood MJ, Davey S, House JR, Tipton MJ. Post-exercise cooling techniques in hot, humid conditions. Eur J Appl Physiol. Nov 2009;107(4):385-396	This study had a within-participant repeated measures design in which participants completed self-paced exercise on a treadmill in hot [31.20 (0.20)oC] and humid [70.00 (1.90)% RH] conditions until they reached a rectal temperature of 38.5°C. They then received one of five post-exercise cooling techniques or completed a control session for 15-min (COOL 1). At the end of COOL1 participants recommenced self-paced exercise until Tc again reached 38.5oC. They then completed a 30-min period of post-exercise cooling using the same cooling intervention as COOL1, but with and without the addition of face fanning. Cooling techniques compared were whole body fan (WBF), phase change garments (PCG), air cooled garments (ACG), hand immersion (HI), and liquid cooled garments (LCG). Whole body fan (subject seated 1.2m in front of a large fan blowing air at 3.5-3.8 m/sec over all parts of the	2a

		body except the head, which was isolated to separately study the effect of face fanning). WBF was best followed by HI. PCG, LCG and ACG were not statistically significantly different from Control (subject seated in same room for appointed times with no other intervention)	
Casa DJ, Kenny GP, Taylor NA	Casa DJ, Kenny GP, Taylor NA. Immersion treatment for exertional hyperthermia: cold or temperate water? Med Sci Sports Exerc. Jul 2010;42(7):1246-1252	This is a dual review of contrasting opinions regarding the ideal temperature for performing cold water immersion cooling of persons with elevated core temperatures associated with exercise in heat stress. Casa and Kenny support water at 2^{o}C monitored with rectal temperature while Taylor makes the argument for water at 24-26 ^{o}C with monitoring done with an esophageal probe.	5
Hagiwara S, Iwasaka H, Shingu C, Matsumoto S, Uchida T, Noguchi T	Hagiwara S, Iwasaka H, Shingu C, Matsumoto S, Uchida T, Noguchi T. High-dose antithrombin III prevents heat stroke by attenuating systemic inflammation in rats. Inflamm Res. Jul 2010;59(7):511-518	"Anticoagulants, such as antithrombin III (AT III), inhibit inflammation resulting from various causes. As heat stroke is a severe inflammatory response disease, we hypothesized that AT III would inhibit inflammation and prevent heat stress-induced acute heat stroke. While 80% of rats died within 10 h after heat stress, 30% of rats pretreated with AT III (250 U/kg) died in the same time frame." Pathological changes in lungs and liver were much less in the AT III pre-treated rats. "Given our findings, it is possible that AT III might have therapeutic benefit for patients with heat stroke. In line with this, AT III has low toxicity and has been approved for treatment of systemic inflammatory diseases."	4E
Hagiwara S, Iwasaka H, Goto K, et al	Hagiwara S, Iwasaka H, Goto K, et al. Recombinant thrombomodulin prevents heatstroke by inhibition of high-mobility group box 1 protein in sera of rats. Shock. Oct 2010;34(4):402-406.	The protein C anticoagulant system inhibits inflammation resulting from various causes. Thrombomodulin (TM) [approved for treatment of disseminated intravascular coagulopathy in Japan], a widely expressed glycoprotein originally identified in vascular endothelium, is an important cofactor in the protein C anticoagulant system. We tested the hypothesis that TM could prevent acute inflammation induced by heat stress in a rodent model. TM exhibited a strong anti-inflammatory effect. TM represents a potential therapeutic agent for heatstroke prevention or management in patients.	4E
Hagiwara S, Iwasaka H, Shingu C, et al	Hagiwara S, Iwasaka H, Shingu C, et al. Danaparoid sodium attenuates the effects of heat stress. J Surg Res. Vol 171. United States: 2011 Elsevier Inc; 2011:762-768.	"Anticoagulants, such as danaparoid sodium (DA), [similar to low molecular weight heparin] inhibit various types of inflammation. In rats pretreated with DA, induction of cytokines (interleukin [IL]-1b, IL-6, and tumor necrosis factor [TNF]-a), nitric oxide (NO), and high mobility group box 1 (HMGB1) protein were reduced compared with saline-treated rats.	4E

		Histologic changes observed in lung, liver, and small intestine tissue samples of saline-treated rats were attenuated in DA-treated rats. Moreover, DA pretreatment improved survival in our rat model of heat stress-induced acute inflammation."	
Hee-Nee P, Rupeng M, Lee VJ, Chua WC, Seet B	Hee-Nee P, Rupeng M, Lee VJ, Chua WC, Seet B. Treatment of exertional heat injuries with portable body cooling unit in a mass endurance event. American Journal of Emergency Medicine. 2010;28(2):246-248.	This is a case series report of using a military-style, portable chamber with 2 trolley spaces with misting tubing arrayed above them and a fan set to blow over patients on the trolleys. The authors report 3 cases of heat stroke (defined as marked alteration in neurologic function such as delirium, coma, or convulsions and rectal T> 40^{o}C) and 4 cases of heat exhaustion (mild alterations in neurologic function such as giddiness, and irritability) treated with an average core temperature drop of 0.14^{o}C/min. They propose misting with a fan as an alternative to immersion to facilitate performing other clinical interventions on critically ill patients.	3b
Hong JY, Lai YC, Chang CY, Chang SC, Tang GJ	Hong JY, Lai YC, Chang CY, Chang SC, Tang GJ. Successful treatment of severe heatstroke with therapeutic hypothermia by a noninvasive external cooling system. Ann Emerg Med. 2012;59(6):491-493.	This is a case report relating a well-documented case of heat stroke (Tre 42.7°C (108.9°F)) with multi-organ failure in which therapeutic hypothermia to 33°C (91.4°F) was induced with a non-invasive external cooling system and maintained for 24 hrs until physiologic parameters stabilized. The patient was then rewarmed and recovered with no sequelae. The concept being tested was that of therapeutic hypothermia as has been shown to be neuro-protective in post cardiac arrest situations.	3b
Hostler, D	Hostler, D., Reis, S.E., Bednez, J.C., Kerin, S. & Suyama, J. Comparison of active cooling devices with passive cooling for rehabilitation of firefighters performing exercise in thermal protective clothing: a report from the Fireground Rehab Evaluation (FIRE) trial. Prehosp Emerg Care. 2010:14, 300-309	This is a within group comparison of cooling rate with subjects mimicking the heat stress of firefighters by exercising while dressed in standard firefighter gear including SCBA , hood and mask. Six different cooling methods practical for use during a firefighter rest period prior to returning to fight a fire were evaluated: forearm arm immersion in cold water, hand enclosure in iced cooling device, fan with ambient air, IV cold saline, ice-water infused cooling vest and no intervention No statistical difference was found in the cooling rates of the various interventions. This study simply demonstrates more options for cooling.	2a
Marchbank T, Davison G, Oakes JR, et al.	Marchbank T, Davison G, Oakes JR, et al. The nutriceutical bovine colostrum truncates the increase in gut permeability caused by	Heavy exercise causes gut symptoms and, in extreme cases, "heat stroke" partially due to increased intestinal permeability of luminal toxins. We examined bovine colostrum, a natural source of growth factors, as a potential moderator of such effects. Twelve volunteers	1bE

	heavy exercise in athletes. Am J Physiol Gastrointest Liver Physiol. 2011;300(3):G477-484.	completed a 14 day double-blind, placebo-controlled, crossover protocol prior to standardized exercise. In both study arms, exercise increased blood lactate, heart rate, core temperature (mean 1.4°C rise) by similar amounts. Gut hormone profiles were similar in both. Intestinal permeability in the placebo arm increased 2.5-fold following exercise (0.38 ± 0.012 baseline, to 0.92 ±0.014, P < 0.01), whereas colostrum truncated rise by 80% (0.38 ± 0.012 baseline to 0.49 ± 0.017) following exercise.	
McDermott BP, Casa DJ, Ganio MS, et al.	McDermott BP, Casa DJ, Ganio MS, et al. Acute whole-body cooling for exercise-induced hyperthermia: a systematic review. *J Athl Train.* Jan-Feb 2009;44(1):84-93.	***Data Sources:*** During April 2007, we searched MEDLINE, EMBASE, Scopus, SportDiscus, CINAHL, and Cochrane Reviews databases as well as ProQuest for theses and dissertations to identify research studies evaluating whole-body cooling treatments without limits. ***Conclusions:*** After an extensive and critical review of the available research on whole-body cooling for the treatment of exertional hyperthermia, we concluded that ice-water immersion provides the most efficient cooling. Further research comparing whole-body cooling modalities is needed to Identify other acceptable means. When ice-water immersion is not possible, continual dousing with water combined with fanning the patient is an alternative method until more advanced cooling means can be used. Until future investigators identify other acceptable whole-body cooling modalities for exercise-induced hyperthermia, ice-water immersion and cold-water immersion are the methods proven to have the fastest cooling rates.	5(E)
Sinclair WH, Rudzki SJ, Leicht AS, Fogarty AL, Winter SK, Patterson MJ	Sinclair WH, Rudzki SJ, Leicht AS, Fogarty AL, Winter SK, Patterson MJ. Efficacy of field treatments to reduce body core temperature in hyperthermic subjects. Med Sci Sports Exerc. Nov 2009;41(11):1984-1990.	Eleven healthy active male volunteers performed an intermittent walk–run (2 min at 6 km/hr and 4 min at 10 km/hr) protocol conducted within a climate-controlled chamber (34.2 ± 0.5°C and 62.3 ± 3.1% relative humidity) until Tc was 40°C on 3 occasions. They were then cooled during a 40-min period using three different methods: ice packs to the neck, axillae, and groin (ICE); water spray and fan (FAN); and 2 L of chilled (20oC) intravenous saline administered during a 20-min period (IV). Rate of decrease in Tc, cardiovascular responses, and any incidence of reported adverse effects were investigated. Trials were presented in a counterbalanced order. Results: Rate of Tc reduction during the first 20 min of cooling was greater for FAN compared	2aE

		with ICE (0.09 ± 0.02°C/min vs 0.07 ± 0.02 ° C/min, P >0.05), whereas IV did not differ with the other trials (0.08 ± 0.01 ° C/min, P > 0.05). Three participants complained of numbness or paresthesia in their arm or hand during administration of the chilled saline, although these symptoms resolved within 5 min of ceasing the infusion. Conclusions: All three cooling techniques reduced Tc and would be suitable for first aid application in a field setting during transportation to adequate medical facilities. Chilled IV saline did not produce any contraindications, providing a suitable alternative for Tc cooling.	
Sithinamsuwan	Sithinamsuwan P, Piyavechviratana K, Kitthaweesin T, et al. Exertional heatstroke: early recognition and outcome with aggressive combined cooling--a 12-year experience. Mil Med. May 2009;174(5):496-502	This retrospective record review reports on 12 years of experience in the Thai army with patients admitted to the ICU with a diagnosis of heat stroke. Patients were treated with a variety of external cooling techniques (e.g. cold packs or ice slush in the groin and axillary regions in 27 patients (96.4%), wetting and fanning in 23 patients (82.1%). cool water aerosol in 20 patients (71.4%). cooling blanket in 9 patients (32.1%), and ice bath in 1 patient (3.6%). No patients achieved the of a core temperature < 38oC within 30 min. Median *(? Why reported vs mean*) cooling time to achieve the goal in survivors was 3 hrs. vs 18 hrs in non-survivors. They observed that "patients who took longer than 3 hours to cool to 38°C had significantly more DIC and nearly twice as high a percentage of poor outcome (dead and neurologic sequelae) as patients who cooled within 3 hours."	3b
Yue H, Zhou F, Liu H, et al.	Yue H, Zhou F, Liu H, et al. Fatal exertional heat stroke successfully treated with cold hemofiltration: a case report. Am J Emerg Med. 2009;27(6):751 e751-752	Case report of a 22-year-old man with syncope, convulsion, profuse sweating, and no blood pressure after running 4.8 km for 20 minutes in military training. Initial Tre 42.2°C with ambient air temperature of 32°C and the humidity 60%. He received conventional antishock management and was sent to the emergency department. The patient had no significant medical history. On admission, the comatose patient manifested respiratory dysfunction, hypoxemia, and heart dysfunction. His rectal temperature was 40.6°C He was refractory to external cooling methods (cold gastric lavage, ice packs, ice cap, ice blanket). At 3.5 hrs with worsening renal function, hemofiltration was started with an initial filtrate	3b(E)

		temperature of 28°C for 2.5 hours and 35°C thereafter. Patient Tre decreased to 38°C in 2 hours and remained at less than 37.5. [The authors state that they maintained hemofiltration for 10 days, but do not state specifically at what temperature the patient was maintained during that time.] The patient was discharged after 16 days with only mild renal and liver dysfunction.	
Zhou F, Song Q, Peng Z, et al	Zhou F, Song Q, Peng Z, et al. Effects of continuous venous-venous hemofiltration on heat stroke patients: a retrospective study. *J Trauma*. Dec 2011;71(6):1562-1568	**Methods:** A total of 16 patients with HS were retrospectively analyzed. All patients were treated by continuous venous-venous hemofiltration (CVVH) for at least 96 hours, and CVVH was initiated with replacement fluid between 25°C and 30°C for 2 hours to 2.5 hours, and 36°C thereafter. The vital signs were monitored and blood samples were collected during CVVH to measure serum urea, creatinine, myoglobin, creatine kinase, and total bilirubin. **Results:** All patients survived. The core temperature of the patients decreased from 41.3±0.2°C to 38.7±0.1°C after 2 hours and to 36.7±0.1°C after 5 hours during CVVH ($p < 0.05$). Compared with values before starting CVVH, there were remarkable improvements in mean arterial blood pressure, heart rate, and oxygenation index ($p <0.05$). The serum creatinine, urea, myoglobin, and creatine kinase decreased significantly ($p <0.05$), while the bilirubinemia had no obvious decline ($p >0.05$). The scores of APACHE II and arterial lactate had also obvious decline ($p <0.05$). The hemodynamic variables were stabilized during CVVH, and no obvious side effects related to CVVH were found. **Conclusions:** CVVH is safe and feasible in the treatment of patients with HS by lowering core temperature, removal of myoglobin, support of multiorgan function, and modulating systemic inflammatory response syndrome (SIRS). The impact of CVVH on patient outcome, however, still needs proof by larger randomized controlled trials.	2a(E)

Adverse Outcomes from Treatment for Heat Stroke

Author(s)	Full Citation	Summary of Article (provide a brief summary of what the article adds to this review)	Level of Evidence (Using table below)

Makranz C, Heled Y, Moran DS	Makranz C, Heled Y, Moran DS. Hypothermia following exertional heat stroke treatment. Eur J Appl Physiol. Sep 2011;111(9):2359-2362.	This is a case report of a soldier who collapsed while exerting in heat and was treated as heat stroke empirically with cold water splashing on site. His T_R was 40°C after 5 min splashing. This was continued at a clinic until he began to shiver when T_R was recorded as 33 °C. He was covered with blankets and transferred. While en route he awoke to normal consciousness. Mild rhabdomyolysis was identified at the hospital which may have been from exertion or elevated core temperature.	3b
Tobalem M, Modarressi A, Elias B, Harder Y, Pittet B.	Tobalem M, Modarressi A, Elias B, Harder Y, Pittet B. Frostbite complicating therapeutic surface cooling after heat stroke. Intensive Care Med. 2010 Sep;36(9):1614-5.	This is a case report of a young woman found unconscious in a sauna who was treated with towels immersed in ice bags for 20 min followed by cold water-soaked towels on her lower torso and thighs. She developed 2nd and 3rd degree skin tissue changes consistent with cold injury/frostbite in the areas of ice bag contact.	3b

NOTE: Studies denoted with (E) were so marked since, though they addressed acute cooling for heat stroke, they were studying techniques not currently available in a first aid setting. They were included to reinforce the importance of continued cooling once patients arrive at a hospital.

Level of Evidence Table

Level of Evidence	Definitions (See manuscript for full details)
Level 1a	**Experimental and Population based studies -** population based, randomized prospective studies or meta-analyses of multiple higher evidence studies with substantial effects
Level 1b	**Smaller Experimental and Epidemiological studies -** Large non-population based epidemiological studies or randomized prospective studies with smaller or less significant effects
Level 2a	**Prospective Observational Analytical** - Controlled, non-randomized, cohort studies
Level 2b	**Retrospective/Historical Observational Analytical** - non-randomized, cohort or case-control studies
Level 3a	**Large Descriptive studies** – Cross-section, Ecological, Case series, Case reports
Level 3b	**Small Descriptive studies** – Cross-section, Ecological, Case series, Case reports
Level 4	**Animal studies or mechanical model studies**
Level 5	**Peer-reviewed Review Articles** - state of the art articles, review articles, organizational statements or guidelines, editorials, or consensus statements
Level 6	**Non-peer-reviewed published revies and opinions -** such as textbook statements, official organizational publications, guidelines and policy statements which are not peer reviewed and consensus statements

Level 7	**Rational conjecture** (common sense); common practices accepted before evidence-based guidelines
Level 1-6E	**Extrapolations** from existing data collected for other purposes, theoretical analyses which are on-point with question being asked. Modifier E applied because extrapolated but ranked based on type of study.

Updated Scientific Foundation

(Please provide a summary of the science from the last approval and of any new evidence. If new evidence exists please comment whether this would support or alter the previously approved statement)

Heat Cramps

Exercise-associated muscle cramps are muscle spasms, which can be intense and debilitating and occur typically in the legs, arms, and abdomen. The traditional and popular term for this condition is heat cramps. The term 'exercise-associated muscle cramps' – updated for 2016 - reflect the understanding that these cramps, while possibly more common in hot and humid conditions, are not directly related to an elevated body temperature.

The exhaustive 2012 review of the literature below includes provides a backdrop to the various forms of attempted treatment over the year.

Based on the review of the 2009 SR and of the literature cited for that review, the literature review for heat cramps was extended to a full review of the literature available in the databases noted earlier in this report.

Most of the following articles are from the early to mid 20th century when the phenomenon of heat cramps was identified as an industrial disorder. They do, however, represent the foundations for both description of the phenomenon of heat cramps and the basis for treatment. The more recent articles have been associated with the development of commercially available carbohydrate/electrolyte "sports drinks" and assessment of their applicability for treating and preventing adverse events associated with exertion that produces sweating and, hence, water and salt loss. Of note,

The articles are presented in chronological order to help the reader appreciate the value of the older literature.

Moss (1923)

In a report on various effects of the high air temperature in mines on colliers (miners), Moss reported finding scanty urine production and low chloride content of a miner known to suffer from diffuse cramps which led to developing a prospective uncontrolled before and after trial of use of a solution of "10 grams of sodium chloride in a gallon of water." Ten (10) miners "suffers and non-sufferers of good and poor physique" were selected to receive the salt solution to see whether it decreased their tendency to cramp. Of the seven cases reported, only 2 of those who had been initially enrolled who were noted as suffering from cramps prior to the intervention were available for follow-up. The others were fired for poor performance. Both of these miners reported cessation of cramping during the 3 month follow-up period. It is not clear whether that meant it took three months for cessation or if they had immediate cessation that continued throughout the three month follow-up period, though the latter seems more realistic. Though not an experiment specifically studying the treatment of acute cramps with salt, this study

reinforces the relevance of salt to the heat-effort-associated cramping process. (Moss, 1923)

Davis (1924)

In a correspondence to the Journal of the American Medical Association, Davis reports an experiment initially reported in the non-medical journal "Colliery Guardian, a leading English coal journal." In this experiment "a few" miners were selected to receive a "0.25%" salt solution containing 10 grams/gallon (2 teaspoons salt/2-quart drinking bottle carried by the miners each day) primarily to treat fatigue. Six miners reported decreased fatigue. One miner reported resolution of leg cramps. The report does not specify how many miners were in the experimental group, nor does it report if the five miners with resolution of fatigue also suffered from cramps. Thus, though the reported study was set up as a prospective uncontrolled intervention trial, the reporting leads to some lack of clarity on the significance of the results. Due to the faults in design, though set up as a prospective interventional experiment, the evidence presented is more in line with a case report, thus a level of evidence of 3b.(Davis, 1924)

Oswald (1925)

In a letter to the editor of the Lancet, Oswald reports a case series intervention among stokers working for a gas company in which he introduced a drinking solution made from a stock solution containing 120 gm potassium chloride and 180 gm sodium chloride per liter of water of which 2.5 liters was added to 213.3 liters water to make the final drinking solution. He reported that cramp was "eliminated" following introduction of the solution. This is not a report of an acute treatment of an active cramp. It does, however, reinforce the value of added salt.(Oswald, 1925)

Thrower (1928)

In a letter to the editor of the British Medical Journal, Thrower reports adding "small amounts" of salt to mess drinking water on board a "modern motor vessel" where engine room crew had been experiencing diffuse muscle cramping. He reported this to "prove quite efficacious" without further specifying. (Thrower, 1928)

Brockbank (1929)

Brockbank presents a case report of his own of a miner who developed cramping and two previously presented cases, all of which had resolution of cramping once they began consuming salted water during work. He does not offer any information on dosing.(Brockbank, 1929)

Talbott (1933)

This is a convenience sample observational report of cases of diffuse cramping among workers building the Hoover Dam in the Nevada desert. The report is largely of the biochemical evaluation of the workers who were incapacitated enough to have been brought to the hospital. Five individual cases were presented

in detail with personal histories as a part of examining predisposing factors for these workers compared to the many who did not experience cramps. All victims of cramps were treated with intravenous 0.9% saline solution. Talbott relates the rapid cessation of cramping in most subjects with ability to return to work the next day.(Talbott and Michelsen, 1933);

Talbott (1935)

This is the first apparent review of the topic of heat cramps. Talbott reviews some of the earlier reports included here as well as others. He reviews biochemical abnormalities as they could be studied at the time and as his team had done in regards to laborers building the Hoover Dam and in a steel mill in Youngstown, Pennsylvania. He also reviews a number of apparent contributing risk factors. He comments on other authors' reports of the use of saline, administered orally, by enemas, by clysis and by intravenous. He comments on the differential diagnosis from non-heat-related exertional cramps and concludes from his data and other reports that the likely pathological physiology underlying the cramping tendency is from a combination loss of water and salt (sodium chloride, NaCl). He reviewed specifically theories of carbohydrate metabolism disturbance as related to the pathogenesis of heat cramps presenting data to argue against such an association. He particularly noted that administration of dextrose or adrenaline to patients in his series from Hoover Dam and Youngstown with mild to moderate cramps worsened.

Intervention	#	Result
Rest in bed and food	12	"rapid and satisfactory" recovery from "mild"cramps
Hot packs	3	"In each patient cramps continued from one and a half to six hours."
Calcium chloride and calcium gluconate in varying doses between 2 to 5 grams	3	No "therapeutic benefit"
Sodium Bicarbonate 3.5 to 7.0 grams IV	4	"In each patient cramps could be induced afterwards."
Dextrose	5	"In all of these the persistence of cramps after giving dextrose necessitated subsequent administration of saline to
Normal saline IV	?	All 5 cramp patients in Hoover Dam series and unspecified number in Youngstown series. "600 to 1000cc were given iv the first 6 hours and repeated if the patient were markedly dehydrated. After the first few hours the patients were generally able to begin taking salt by mouth."

Of note, Talbott reports that, when the patients were able to take salt by mouth, milk (NV) or salt tablets (PA) were used for further replenishment. Patients treated with salt tablets were given one 1gm tablet every hour until 15 tablets had been administered with no report of gastro-intestinal symptoms.(Talbott, 1935)

Ladell (1949)

This is a single subject within subject temporal comparison study of the effect of intravenous saline on leg cramps produced with an exercise protocol. The male subject was chosen on the basis of a history of developing cramps when exercising in heat. For this experiment, he exercised a hot environment until he developed calf

and thigh cramps. Circulation in one leg was occluded with a blood pressure cuff and 162ml of 15% NaCl was injected into an arm vein over 3.5 min. Cramp induction techniques were started immediately. After 2 min cramp could no longer be induced in the unobstructed leg. The obstructed leg continued to cramp for 7 minutes when the tourniquet was removed by protocol. The cramping in the occluded leg resolved 2 minutes after the tourniquet was removed. This study, though only in one case, supports the concepts that saline depletion is a significant factor in the development of heat cramps and that the cramping tendency can be resolved relatively quickly with saline administration. Although IV administration is outside the scope of practice of the majority of first responders, this article does support the value of salt replacement in the acute treatment of heat cramps.(Ladell, 1949)

Bergeron (1996)

This is a single case report of a 17 yo male nationally-ranked tennis player with a history of primarily leg cramps when playing or practicing for longer periods in warm or hot environments. He had also experienced cramps associated with playing basketball in a warm setting. He came to a tennis training center in southern Florida for evaluation. It was found that he ate a low sodium diet due to his father having hypertension. On evaluation his salt loss in sweat was deemed to be slightly higher than that observed by Bergeron in a previous observational study of salt loss in a group of tennis players. Bergeron recommended that he increase his daily dietary sodium intake, that he hydrate more prior to practice or play in the heat and that he drink a specified amount of a commercial carbohydrate-electrolyte sports drink, which he names twice in the report, at changeovers in practice and play and that he carry a small packet containing approximately ½ teaspoon table salt to be consumed in approximately 0.5 L water at the earliest sign of impending cramps (the subject had reported often having twitching in the affected muscles for around 30 minutes prior to onset of full cramping). He notes that the sodium content of this mixture (102.6 mmol/L = 2358mg/L = 23.58mg/dl) is about 5 times the concentration of that in the named sports drink. He references prior work by himself and two other authors in which they measured sweat and sodium loss in tennis players exerting in heat. He reports that once this player followed his recommendations, he stopped suffering from cramps when playing or practicing in heat. In addition, he recounts one episode a year later in which the same player was again in southern Florida for training and play when he noted that on the first day of training when he had not yet acclimated to the heat, he noted twitching during a practice match. He mixed the solution suggested above and began consuming it. The twitching disappeared and he was able to finish a full match "for several more hours." Despite the advice noted above, approximately 3 weeks later, in very humid conditions with ambient temperature reported >35^{o}C, the player developed cramps during a match and defaulted. His dietary intake and use of the on-court salt solution at that time was not recorded. Bergeron does report, however, that he then advised that the player drink a mixture of 0.5tsp salt in "20-24 oz" water (unclear why he switches to ounces from metric) in the evening and after breakfast. He reports that the player decided to make the mixture 0.5tsp salt in 8-10oz of a named commercial vegetable juice which he

reported to contain 620mg Na per 8 oz. The player reportedly consumed this mixture each evening and morning during 6 more weeks of training and competition in Florida under similar meteorological conditions without further cramping incidents.

This report has been presented in some detail since it is very frequently referenced in subsequent recent literature such as guidelines and general reviews of heat illness as the primary citation for statements regarding use of salt to both treat and prevent heat cramps. It is also frequently cited for the formulation of adding 0.5 tsp salt to water or to a commercial sports drink for treatment or prevention of heat cramps. As Bergeron implied in the article, his recommendations for salt replacement were based on a prior study of losses incurred by persons playing tennis in the heat, not by experimental studies.(Bergeron, 1996)

Exertional Heat Exhaustion

Exercise-associated muscle cramps are muscle spasms, which can be intense and debilitating and occur typically in the legs, arms, and abdomen. The traditional and popular term for this condition is heat cramps. The term exercise-associated muscle cramps reflect the understanding that these cramps, while possibly more common in hot and humid conditions, are not directly related to an elevated body temperature. Accurate measurement of temperature is not expected of a lay first aid provider. If temperature measurement is available heat exhaustion diagnostic criteria is a core temperature <104°F (40°C).

No literature was identified specifically addressing treating the phenomenon of heat exhaustion. Please refer to the discussion in Appendix A.

Heat Stroke

In the spectrum of heat illness, heat stroke is the life-threatening emergency. Patients have exaggerated heat production and an inability to cool themselves. The practical and key field assessment is to recognize *altered mental status in the context of heat stress.*

Classic heat stroke is an entity typically seen in older adults during heat waves lasting several days, and is not commonly an illness that will be cared for by first aid providers. Treatment is similar to/the same as exertional heat stroke with rapid cooling.

Accurate measurement of temperature is not expected of a lay first aid provider. Signs and symptoms are similar to those of heat exhaustion with a key symptom the presence of *abnormal mental status in the context of exposure to heat*. If accurate measurement of temperature is available exertional heat stroke diagnostic criteria is a core temperature >104.9°F (40.5°C).

Articles summarized and reviewed from the 2012 review and up to 2016 relate to treatment of persons experiencing significant change in mental status (delirium, coma, seizure) and rectal temperature of 40.5ºC or greater, the most widely quoted clinical diagnostic criteria for heat stroke. Human experimental studies cited here do not induce heat stroke in subjects, but do address methods of cooling human subjects in whom body temperature has been elevated through exercise or exercise combined with other methods of raising body temperature. (A more in-depth discussion of heat stroke as a disorder is presented in Appendix A.) Various articles

discussing the physiological derangements in heat stroke re-affirmed the value of rapid decrease in body temperature in a setting in which heat stroke is suspected, even if core temperature cannot be measured directly. Additionally, with the evolving understanding of the underlying pathophysiological phenomena that occur in persons who become severely ill after exposure to elevated heat stress, rapid evacuation to hospital-level medical care is critical in conjunction with continued cooling.

Various, relatively simply applied methods of cooling have been discussed in the literature, particularly in relation to use at sporting events. Authors have debated the optimal temperature for water to be used for an immersion treatment with the person being cooled placed into the water at varying depths. While, as noted in the 2009 SR, immersion in iced water at a temperature of 2ºC to 4ºC (35.6ºF to 39.2ºF) has been recommended for athletes with a question of elevated core temperature, a water bath at that temperature is not likely to be available in many settings where a person may be deemed as a concern for incipient heat stroke.

Amorim

This sequential comparison trial involved 10 artificially heat-acclimate subjects exercising in heat stress until rectal temperature was either 38.5ºC in the first trial or 39.0ºC in the second trial. Each subject performed the two exercise sessions with a 40 min cooling period between them using each of four methods for cooling: a hand-held device, a hydraulic cooling vest, hand immersion in cool water or no cooling. Active cooling techniques were used during the activity as well as during the cooling period. Only the vest slowed heat accumulation.

This small study adds to literature suggesting that for cooling, the amount of body surface area subjected to cooling is important.(Amorim et al., 2010)

Barwood

This study had a within-participant repeated measures design in which participants completed self-paced exercise on a treadmill in hot (31ºC) and humid (70% RH) conditions until they reached a rectal temperature of 38.5ºC. They then received one of five post-exercise cooling techniques or completed a control session for 15-min (COOL 1). At the end of COOL1 participants recommenced self-paced exercise until T_R again reached 38.5 ºC. They then completed a 30-min period of post-exercise cooling using the same cooling intervention as COOL1, but with and without the addition of face fanning. Cooling techniques compared were whole body fan (WBF), phase change garments (PCG), air cooled garments (ACG), hand immersion (HI), and liquid cooled garments (LCG). Whole body fan (subject seated 1.2m in front of a large fan blowing air at 3.5-3.8 m/sec over all parts of the body except the head, which was isolated to separately study the effect of face fanning). WBF was best at cooling followed by HI. PCG, LCG and ACG were not statistically significantly different from Control (subject seated in same room for appointed times with no other intervention).

This article reaffirms the value of evaporative cooling, the same as the natural cooling based on perspiring with evaporation. The hand-immersion technique is one that has been promoted for persons who incur a significant heat load while in

clothing that cannot be removed easily and who must continue with exertion in a heat stress environment such as fire fighters and football players. Although this article does not directly address cooling of victims of heat stroke or persons with core temperatures elevated to the ranges of heat stroke (≥40.5ºC), it still demonstrates the potential value of different cooling techniques. For example, a football player or fire fighter who collapses with a question of heat stroke could have cooling treatment started with applying cold compresses to exposed body parts while the uniform is being removed in order to begin some cooling as quickly as possible. The article does not, though support substitution of these cooling techniques for immersion.(Barwood et al., 2009)

Casa, Kenney & Taylor (2010)

This article is a dual review formatted as a "Contrasting Perspectives" discussing optimal water temperature for cooling of persons with elevated core body temperature and suspected of developing or being at risk to develop heat stroke. Casa and Kenney provide the prevailing view that cooling be performed optimally with 2ºC water based on studies and field experiences using rectal temperatures to diagnose and monitor persons. Taylor argues firstly that water at temperatures of 24–26-C "will be equally fast, less hazardous, and more comfortable," and secondly that esophageal temperature is a better reflection of the temperature of critical organs since the esophagus, at the level where esophageal temperatures are typically measured, has closer physical proximity to core blood supply than does the rectum, which, at the usual level of temperature sensing, is imbedded among muscles of the lower pelvis. He posits that, since rectal temperature has been shown to change more slowly than esophageal temperature, it is more suited to either steady-state core temperature approximation or for situations with slow changes, whereas esophageal temperature monitoring tracks more closely more rapid changes in "core" temperature, the temperature of blood closest to vital organs. Additionally, Taylor offers the challenge that immersion of hyperthermic persons in colder water will lead to more skin and superficial subcutaneous vasoconstriction, thus decreasing the available vascular volume for heat exchange with the body interior and that it carries an elevated risk of "cold shock" with autonomic reactions that may provoke cardiac dysrhythmias.

Casa and Kenney argue that even with a rapid fall in esophageal temperature, there is likely a significant amount of heat still present in organ tissues, thus leading to a false sense of adequate total body cooling if one is only using esophageal temperature to determine an endpoint for cooling. Casa cites field experiences using ice water for cooling runners who have collapsed at road races without apparent adverse effects from the cooling technique. Taylor largely relies on laboratory experience with subjects whose core (esophageal) temperature was elevated with a combination of exercise in a hot environment and conductive heat application with a water jacket vest.

Casa makes the additional argument that relying on rectal temperatures is much more practical in the field, thus arguing that rectal temperature should be used for studies, while Taylor makes the argument that ice water is not always available and

ambient temperature water is likely adequate for cooling rapidly enough to avoid setting off the fully cascade of heat stroke pathophysiology. Taylor's study that he cites was performed using a circulating water bath in which subjects were immersed up to the clavicles. On-site water immersion cooling systems used at most sporting events are shallow, often children's wading pools, in which full immersion is not possible. Taylor does make the good point, though, that with any immersion, the cooling effect will be augmented by circulating the water to constantly replace the warmed water closest to the skin with cooler water.

The major value of this dual review lies in referring to the articles that are cited to see that cooling rates in Taylor's study are reasonably rapid, implying that any water temperature below body temperature will cool, though the lack of comparison to evaporative techniques and the lack of any study directly comparing rectal and esophageal temperatures in the same population are shortcomings in the literature and this review.(Casa et al., 2010)

Hagiwara (2010a)

This animal comparative trila was designed to assess whether pre-treatment of rats with Antithrombin (AT) III would protect them from the effects of various inflammatory molecules released in response to heat stress. AT III is an anticoagulant with anti-inflammatory properties that function through undefined mechanisms. Rats were either pre-treated with AT III or received no intervention prior to heat stress. Before and after blood analyses were performed. The mortality in the group without pretreatment with AT III was 80% and 30% in the treated group. Inflammatory markers were significantly less elevated in the treated rats.

Although this was an animal study, it represents the future directions of research in seeking treatments for heat stroke. In light of rapid advances in innovative treatments of SIRS, this article mostly should encourage first aid providers to move potential heat stroke victims to the hospital as quickly as possible. (Hagiwara et al., 2010b)

Hagiwara (2010b)

In this study, rats were pre-treated with thrombomodulin, a protein with anticoagulant and anti-inflammatory properties, or saline. The rats were then subjected to passive heat stress (42ºC for 30 min). They reported that 80% of rats not treated with TM died while only 20% of treated rats died. In addition, hematologic studies revealed less elevation of levels of various inflammatory cytokines and other pro-inflammatory molecules.

As with the prior study, this one likely portends future treatments for heat stroke victims, though studies into the effectiveness of thrombomodulin following heat stress and onset of signs of heat stroke are needed to better demonstrate a therapeutic effect.(Hagiwara et al., 2010a)

Hagiwara (2011)

This article is the third in a series from the same laboratory in which danaproid, an anticoagulant with known action to suppress certain mediators of inflammation, was given to rats as a pre-treatment prior to exposing the rats to heat stress adequate to likely be fatal. As in the other trials, the results were positive with a statistically significant reduction in the levels of several major inflammatory mediators and, once again, 80% mortality in the saline treated, heat stressed rats by 10 hours following heat stress and 20% mortality in the rats treated with danaproid. Danaproid is the only one of the three molecules evaluated that is currently in clinical use.(Hagiwara et al., 2011)

Hee-Nee

This is a descriptive report from Singapore of deployment of a mobile "body cooling unit" to a mass endurance event with 72,000 runners participating in a ½ marathon in 30ºC ambient temperature with 85% relative humidity. Diagnostic criteria were based on a Singapore Air Force Medical Corps Preventive Medicine Directive. Heatstroke included (a) a rectal temperature greater than 40°C and (b) marked alteration in neurologic function such as delirium, coma, or convulsions. Casualties with (a) a rectal temperature greater than 38.5°C, (b) mild alterations in neurologic function such as giddiness, and irritability were treated as for heat exhaustion. Any cases presenting to the medical team and meeting these criteria were treated in the unit. The unit is in a 20-foot long side-expandable modified shipping container with 2 beds, an overhead water misting system and fans directed at the beds. They used water at room temperature, adhering to the controversial position that colder water will impede cooling due to superficial vasoconstriction and shivering muscle activity generating more heat. They also used 39ºC rectal temperature as the cut-off to stop cooling.

They reported having 7 persons present who met the above criteria, including 3 who met the heat stroke criteria and were hypotensive. Of these, one was markedly hypotensive (BP on presentation 63/20) and was intubated and resuscitated with intravenous fluids. His temperature was lowered from a presenting temperature of 41.9ºC to 39ºC over 30 minutes when he was transferred to hospital where he developed a full systemic inflammatory response syndrome (SIRS) with multi-organ dysfunction (MOD), though he had complete recovery by 10 days. All but one of the other patients cooled in either 15 or 20 minutes except one who cooled in 5 minutes.

This descriptive study reinforces the concept of early cooling for heat illness with systemic signs and symptoms and preparation in the face of events with known risk. It is of interest that there were only 7 people meeting treatment criteria among 72,000 participants with the meteorological conditions described. It is also of interest that this group adhered to the controversial, and somewhat disproven, position that cold water is counterproductive in terms of cooling.(Hee-Nee et al., 2010)

Hong

This article is a case report of a 22yo, previously healthy man performing military exercises in 33°C (91.4°F) (humidity not specified) and collapsed with a body temperature of 42.7°C (108.9°F) on arrival in the hospital an signs of impending multi-organ failure. In addition to standard heatstroke cooling to 38-39°C (100.4-102.2°F), he was cooled further to 33°C (91.4°F), based on the evidence of the neuro-protective effect in persons resuscitated from cardiac arrest, a condition associated with similar inflammatory pathophysiology to heat stroke. He was maintained at that temperature for 24 hours, at which time he had become hemodynamically stable. He was extubated the next day and discharged 2 weeks post admission. At one year follow up, he had no apparent residual ill effects.

Although this is only a case report and should, thus, not be a basis for a change in practice, it is presented here for two points: First, it demonstrates that future heat stroke treatment advances are likely to come from research into the broader area of multi-organ dysfunction; and, secondly, it demonstrates that cooling persons beyond the standard recommended temperature of 38-38.5°C (100.4-101.3°F) may not cause harm. (Hong et al., 2012) `

Hostler

This technique comparison trial examined, in a laboratory setting, several commercially-marked methods for firefighters to cool during prescribed rest periods while fighting fires. Eighteen (18) subjects, (14 males, 4 females) were studied with each method. There were 13 firefighters and 5 "fit" university student volunteers. Subjects exercised in a heated (35ºC, no statement of humidity level) laboratory, walking on a treadmill at various inclines while dressed in full fire-protection clothing with a helmet, mask and air cylinder on their backs, all intended to simulate actual firefighting exertion. Subjects exercised in two sessions for evaluation of each cooling technique. Each session was terminated by either time (50 min) or one of several subject-dependent variables (1) respiratory rate > 60 breaths per min, 2) heart rate exceeded age predicted maximum (220-age) + 10 bpm, 3) core temperature > 39.5° C, 4) unsteady gait making it unsafe to continue treadmill exercise, or 5) subject request). The subjects were undressed, weighed nude, redressed, hydrated with water equivalent to weight loss and then subjected to one of the cooling methods. Cooling methods are listed:

- Passive cooling in a room maintained at 24.0 ± 1.4°C;
- An intravenous infusion of cold (4°C) normal saline equivalent volume to weight- assessed fluid loss minus 50ml;
- Reclining in semi-fowler position;
- A forearm and hand immersion device marketed to the fire service;
- A cooling fan;
- An ice-water perfused hand cooling device that applies slight vacuum distal to the wrist filled with ice water just prior to each test;
- An ice-water perfused cooling vest (empty mass = 0.6 kg) filled with ice water just prior to each test and worn during the rehab period.

Each subject was cooled with each method to a target temperature of 37.5ºC, specified by the institutional review board, which generally came prior to the end of the National Fire Protection Association standard recovery time period. Following the recovery period, subjects were re-weighed, re-dressed and subjected to a second exercise period with the same protocol as the first. Subjects were undressed and discharged from the study following the second exercise session.

It was noted that arm cooling differed in their study compared to other studies which had shown a higher effect. They speculated that this may have been due to having used a smaller reservoir and not having used a circulating water bath in their study. Subjects reported significant discomfort in the arm and shoulder of the arm receiving the cold IV saline infusion.(Hostler et al., 2010)

Makranz

This is an observational case report from a series of 3 cases of hypothermia associated with treating Isreali soldiers for suspected heat stroke with splashing water on them and fanning. Only one case was presented due to missing data in the other cases. (Makranz et al., 2011)(Makranz et al., 2011)(Makranz et al., 2011)(Makranz et al., 2011)(Makranz et al., 2011)(Makranz et al., 2011)(Makranz et al., 2011)(Makranz et al., 2011)(Makranz et al., 2011) The case reported was of a recruit who collapsed at 17.5 km of a 21km march in environmental temperature of 14ºC (57ºF) and 50% relative humidity. An initial rectal temperature was not recorded, but heat stroke treatment was initiated upon collapse with undressing and splashing with 80L of 16ºC water, warmer than ambient temperature. His rectal temperature was reported as 40ºC 5 minutes later. He was evacuated to a clinic where "cool water cooling" continued (exact technique was not specified) until he began to shiver, at which point (40 min following collapse), his rectal temperature was recorded as 33ºC. This report brings to attention two significant issues. First, exertional heat stroke can occur in relatively cool environments with a moderate degree of exertion. Second, cooling a person with water in a cooler environment may lead to much more rapid cooling than expected based on experience in or recommendations for hotter environments.

Marchbank

This is a double-blinded, placebo-controlled, crossover protocol trial of the protective effect of cow colostrum on human intestinal integrity in subjects subjected to exercise in elevated heat stress experiencing a mean 1.4ºC rectal temperature rise. Intestinal permeability was assessed by 5 hour urinary lactulose-to-rhamnose ratios. This study grew out of work demonstrating an in-vitro effect of colostrum (the milk produced by females during the first few days following giving birth, known to be rich in a variety of immunoglobulins and cytokines (Playford et al., 2000)). This same group had already done work showing a protective effect in animals and humans against intestinal damage caused by non-steroidal anti-inflammatory medications (NSAIDs). Subjects exercised for 20 min on a treadmill at 80% VO_2 max (80% of predetermined maximal exercise capacity for each individual – protocol chosen from prior work demonstrating adequacy to

increase gut permeability and to raise core temperature approximately 1.5-2.0ºC). Evaluation of bowel leakiness and intestinal demonstrated an approximate 80% decrease in bowel permeability associated with consuming colostrum prior to exercise. In a series of associated *in vitro* evaluations colostrum was demonstrated to protect intestinal epithelial cells from heat-induced damage in association with decreases in certain proteins known to be associated with cell damage and elevations in others known to be protective in other cell stresses such as hypoxia and NSAIDs.

Colostrum is available on the open market and is already being used by athletes to improve performance and recovery during high intensity training. Thus, though not at this time a specific treatment for persons deemed to be at high risk of developing SIRS associated with elevated heat stress with or without exertion, this study further supports the relationship among elevated core temperature, exertion and intestinal leakiness.

Not only might the future hold better treatments, but also possibly improved methods to decrease the risks of heat stroke in anticipation of activity in heat stress environments.

McDermott

The athletic trainer authors performed a literature review in April 2007 with unlimited date ranges including several electronic databases to seek articles reporting research on methods of cooling persons with elevated core body temperature following exertion. They eventually identified 7 articles describing either laboratory or field comparisons of cooling methods. None of the articles had any blinding or placebo treatments due to the nature of the interventions. Of the articles that included cold/ice water immersion, it was shown to have the fastest cooling rate. The next most effective, in terms of ºC/min was dousing with water and fanning.

The following table summarizes studies reviewed by McDermott:

Author	Method	ºC/min
(Armstrong et al., 1996)	Immersion of torso & upper legs in 1-3 ºC water	0.20
	Wet towels over same body area as immersion – no fanning	0.11
(Clements et al., 2002)	Water immersion shoulders to hips 5.15 or 14.03ºC	0.16
	Mock immersion (ambient air) 28.8 ºC	0.11
(Kielblock et al., 1986)	Supine on stretcher (25-27 ºC air temp)	0.027
	Ice packs at neck, groin & axillae	0.028
	24-28 ice packs covering body	0.034
	Waer splashed on body with fanning @ 0.5 m/sec	0.035
	Ice packs water splashed on body with fanning @ 0.5m/sec	0.036

(Proulx et al., 2003)	Cold water immersion to neck	
	2 ºC	0.35
	8 ºC	0.19
	14 ºC	0.15
	20 ºC	0.19
(Scott et al., 2004)	Cold water immersion to clavicles in circulated 7 ºC water	0.129
(Wyndham et al., 1959)	Kneeling in empty immersion tub with fanning 0.61 ºC m/sec	0.076
	Kneeling in empty immersion tub with fanning with water sprayed on body	0.073
	Sitting on stool room air at 21 ºC	0.066
	Kneeling in empty tub with water splashed on for initial 3 minutes	0.050
	Water immersion to neck 14.4 ºC	0.044
	Sitting on stool in air 32.2 ºC	0.040
(Clapp et al., 2001)	Sitting in shade (no air temp given)	0.11
	Cold-water torso only immersion 10 ºC	0.25
	Cold-water immersion of only hands and feet 10ºC	0.16

Sinclair

This prospective non-controlled comparison trial was designed to study cooling techniques that are less cumbersome than ice water (2ºC) immersion which has been presented as the most rapid method to cool potential heat stroke victims. 11 healthy athletic males exercised in heat with a goal of reaching a core (ingested pill thermometer) temperature of 40ºC. Five subjects were unable to exercise long enough to achieve the target temperature, stopping due to exhaustion in the heated chamber. Although they did not reach target temperature, their core temperatures ranged from 39.5-39.9 ºC and they were maintained as subjects. Each subject exercised 3 different times 72-96 hours apart and underwent as different cooling technique following each exercise period. The cooling techniques were ice packs to the neck, axillae, and groin (ICE); total body ambient heat chamber temperature (~32ºC) water spray (508 ± 108ml) repeated every 5 min and continuous 8.4-3.5m/s (head to foot) air flow fan (FAN); and 2 L of chilled (20ºC) intravenous saline administered during a 20-min period (IV).
Cooling treatments were undertaken for 40 minutes based on the time to infuse the 2 liters of saline and allowing 15 minutes for complete mixing in the circulation. The other cooling techniques were applied for 40 minutes as well.

The cooling rates reported showed the most rapid cooling in the first 10 minutes of treatment (a 5 minute lag time occurred from finishing the exercise to starting cooling to weigh the subjects – average temperatures continued to rise during that time). Over the first 20 minutes cooling with FAN (0.09 ± 0.02ºC) was statistically significantly ($p<0.05$) faster than ICE (0.07 ± 0.03ºC). IV cooling during the same 20 minute time period was 0.08 ± 0.01ºC, not statistically significantly different.

At the end of the 40 minute test period, though all three modalities had cooled 0.06 ± 0.01ºC.

Although cold water cooling has been demonstrated to lead to the fastest cooling rates for hyperthermic persons, it is not always practical. Thus, this study helps classify other options as to their relative benefit.(Sinclair et al., 2009)

Sithinamsuwan

This report is a retrospective chart review over 12 years of patients admitted with a diagnosis of heat stroke based on a history of strenuous exercise and heat exposure, evidence of CNS dysfunction (seizures or altered sensorium [disorientation, delirium, and coma]) and Tc > 40.0°C or documented evidence of cooling before the first recorded temperature. A variety of cooling techniques had been used. Only 5 patients were cooled below 38ºC within 30 minutes with cooling times extending out to more than 18 hours. Additionally, 27 of the 28 cases cited were reported to have been experiencing low grade fever for several days prior to presentation to the hospital. Twenty-five of the 28 patients were military recruits. Survivors overall were cooled to 38ºC within less time (1.75-6 hrs) than non-survivors (12-24 hrs).

Although this report covers 12 years with varying cooling techniques, once again the urgency to cool persons suspected of heat stroke is demonstrated. Although not directly evaluated, it is of interest that 27 of the patients had reported to colleagues having had a low grade temperature for several days prior to hospital presentation. The association of prior infections with heat stroke has been made in other reviews as well.(Sithinamsuwan et al., 2009)

Yue

Yue presents a single patient case report of a man who collapsed during exertion in heat with an on-site rectal temperature of 42.2°C who failed to respond to initial cooling techniques (cold gastric lavage, ice packs, ice cap, ice blanket). He was then started on hemofiltration, a treatment usually used in intensive care units for persons with renal failure in which the blood is passed out of the body through tubing in a bath of liquid to remove normal chemicals excreted in the urine. The temperature of this bath can be regulated. In this case the temperature was lowered to 28ºC initially with the patient's Tc lowering to 38 ºC in 2 hours.

Although this case report relates use of techniques that are beyond the scope of first-aid, it does relate alternative techniques available in the hospital setting, implying that, not only is it critical to begin cooling on-site as quickly as possible, but transport should also not be delayed in case the victim is not responding quickly to out-of-hospital cooling techniques. Additionally, reporting to the Emergency Department what cooling techniques have been used and for how long may help the staff make decisions to move to more aggressive invasive cooling techniques with minimal delay.(Yue et al., 2009)

Zhou

Zhou and colleagues performed a retrospective chart review of patients who had been admitted with a diagnosis of heat stroke and treated with Continuous Venous-Venous Hemofiltration (CVVH) in which they used it to both cool patients and to filter out myoglobin and cytokines following the logic of the heat stroke syndrome having components of rhabdomyolysis, diffuse inflammatory reaction and coagulopathy associated with elevated blood levels of cytokines. They reported 15 males 18 to 28 yo and one 17 yo female diagnosed with heat stroke (though they only give pretreatment temperatures of 40.8-42.1ºC and "strenuous physical exercises of different degrees in temperate or hot climates" and a distribution of ancillary signs "15 (93.75%) experienced dizziness and anhydrosis, 14 (87.5%) headache, and 13 (81.25%) alteration of consciousness or possible coma" as diagnostic criteria). They used a serum creatinine kinase level >5,000U/L as diagnostic for rhabdomyolysis and the RIFLE criteria from an international consensus group of renal and critical care specialists to define acute renal failure.

They concluded that CVVH appeared to have a beneficial effect as a "pre-emptive" treatment in heat stroke, though they cited a number of limitations in the study. They did not, however, cite as a limitation the fact that the diagnosis of heat stroke among their presenting patients was not standardized. Thus, it is not known whether any particular patient may have improved just as well with less invasive techniques.(Zhou et al., 2011)

While the articles summarized here do not specifically report on first aid treatments for heat stroke, they do lend additional understanding of the value of rapid cooling through whatever mechanism may be at hand.

Textual Summary of Recommendation for Revision, Reaffirmation or Retire

(Please explain basis for recommendation)

Much of the literature from the past 20 years regarding out-of-hospital treatment of what are termed heat illnesses has come from the sports medicine literature. For several reasons such as relatively low incidence of severe disorders, there are no well-constructed clinical trials of treatments. Reviews and guidelines statements from organizations such as the American College of Sports Medicine and the National Athletic Trainers Association (2016) have treatment statements that are often not supported with citations to prospective trials.

Heat Cramps

This textual summary of recommendations for treatment of heat cramps is based on the literature presented in the preceding sections of search results and updated scientific evidence. Since this is part of a revision of the 2009SR, no reference will be made to any recommendations put forward there. Please refer to Appendix A for discussion related to the revision foundations and process.

Despite a literature debate outlined in Appendix A section "Debate on cramps: types, causes and treatment," the evidence appears quite strong from literature dating back through the 20th century that one type of cramp experienced in association with exertion in elevated heat stress has as a fundamental distinguishing feature from any other cramp the water and salt loss experienced in such exertion.(Talbott, 1935), (Ladell, 1949), (Bergeron, 2008) Heat cramps have been described throughout this body of literature as presenting in a spectrum from isolated cramps in muscles being exerted ((Talbott, 1935), (Bergeron, 1996)) to diffuse cramps involving abdominal and facial muscles ((Edsall, 1904),(Moss, 1923), (Brockbank, 1929)).

Heat cramps have been deemed "mild" when they only involved the muscles being exerted, but which responded in a timely fashion to rehydration with a salt-containing fluid, and as severe when there is diffuse cramping including muscle groups not directly being maximally exerted. Although one group of authors has proposed that exertion/exercise associated muscle cramps (EAMC) that are not linked to salt and water deficits may also occur during exertion in heat ((Schwellnus, 2009, Sulzer et al., 2005)), it is difficult to know if they were, in fact, observing a different phenomenon since they did not perform any trial of salt/water solutions to assess effect and since, older studies reported workers with mild cramping in heat that did not require acute medical treatment but that did not recur once rehydration fluids were salted.(Brockbank, 1929)

Treatment for simple cramps of muscles being exerted has been accepted to be gentle stretching combined with massaging the muscle, in addition to cessation of the offending activity, usually a decision made immediately by the cramp sufferer. Stretching has been demonstrated in one small study to specifically interrupt the cramping contractions.(Bertolasi et al., 1993) Some authors have suggested either heat or ice application to assist with resolution of both simple exertional cramp and heat cramp, though no reference could be found through a PubMed search.(Bergeron, 2008), (Eichner, 2008), (Coris et al., 2004) Some early authors describing heat cramps specifically commented that it was impossible to stretch out the affected muscles.

Considering the empirical experience of most persons that stretching and massaging helps to relieve cramps, based on rational conjecture, these two interventions seem to be reasonable first line treatment attempts for isolated muscle cramps occurring in association with exposure to elevated heat stress despite no experimental evidence regarding their efficacy in that setting.

Commentaries on diffuse cramps associated with exertion in elevated heat stress environments from early in the 20th century related cessation of cramping among workers when salt and water solutions for hydration replaced water alone.(Davis, 1924), (Thrower, 1928), (Oswald, 1925) Later authors have presented case reports or small case series reporting resolution of diffuse cramping temporally associated with salt and water replacement either intravenously (Talbott, 1935)or orally (McCance, 1936). Additional reports have documented resolution of localized cramps occurring in association with exertion in elevated heat stress in temporal relation to intravenous (Ladell, 1949) or oral (Bergeron, 1996) salt and water. No literature was found from 2012 back to the beginning of the 20th century in which either blinded comparisons of salt solutions at different concentrations had been compared with each other or with plain water or other solutions specifically for treating actively cramping persons.

Thus, although the evidence is strongly supportive of salt and water solutions having positive therapeutic effect on what are known as heat cramps, since the evidence is based almost solely on case reports or case series without any prospective controlled trials, it seems reasonable to propose salt solutions as a guideline rather than a standard. This recommendation also takes into account the difficulty in differentiating isolated cramps clinically between heat cramps and simple exertional cramps.

Some authors have reported specific use of carbohydrate and electrolyte solutions for treatment of heat cramps(Bergeron, 1996), though it has been demonstrated that treatment of heat cramps with dextrose is not beneficial (Talbott, 1935). Other authors have promoted the addition of carbohydrate to a salt-containing hydration fluid to restore glycogen stores in exerting athletes to(Casa et al., 2000), a goal unrelated to treatment of cramps. Thus, there does not appear to be a basis for recommending specific use of a carbohydrate-containing liquid for rehydration to treat heat cramps.

For presentation of and comment on the various suggested salt solutions and dosing schedules that have been proposed by various authors, the reader is referred to the section on treatment in Appendix A. .

Heat Exhaustion

The 2009SR did not offer specific standards, guidelines or options for treatment of persons suffering from heat exhaustion. It simply affirmed, without citing them, that then-current first aid recommendations were consistent with then-current literature. Current recommendations of the American Red Cross were not reviewed as a part of the process for this review.

In all of medicine, developing optimal treatment for conditions depends on having as precise a physiologic definition of the disorder as possible. One recent review authored by career heat illness researchers and focused on athletes noted that there is little clinical difference between persons reaching a point of exhaustion, defined as the inability to continue physical activity, in cool versus heat-stressed conditions.(Armstrong et al., 2007) The authors continued to note that the inability of a person to continue exerting in either setting is likely based on a combination of physiological conditions including depletion of energy reserves, dehydration, muscle fatigue, psychological fatigue and others. Researchers at the Thermal & Mountain Medicine Division of

the US Army Research Institute of Environmental Medicine reviewed experimental studies of the effect of heat and hydration on subjects exerting at varying levels of their maximum capability have demonstrated that inability to continue to exercise at the set level occurs earlier with higher heat stress and with hypohydration.(Sawka et al., 2001) As presented in the 2009SR and elaborated upon in Appendix A, various authors have presented a multitude of signs and symptoms associated with exhaustion while exerting in elevated heat stress settings.

Persons experiencing exhaustion will begin treatment spontaneously by the nature of the phenomenon in that they will cease physical activity. This may be all that is needed for treatment. In experimental studies that have relied on exhaustion as the end point for a specific experiment, subjects may only have a rest period prior to engaging in another episode of exhaustion.{McLellan, 2004 #2321}

Thus, a first treatment for the person experiencing heat exhaustion, defined as difficulty or inability to continue exerting would be to physically assist them such that they are not further exerting themselves. This performs two functions. By avoiding activity the internally generated heat stress from muscular metabolic activity will be lowered. If the exhaustion is due to depletion of energy stores, it reduces demands, allowing more energy stores to be directed to the brain and other vital organs.

Without laboratory analysis or more specific field information on the person exhibiting exhaustion, such as pre and post weights, it is impossible to accurately determine whether dehydration or electrolyte imbalance are contributing to the condition. In the setting of exhaustion in an elevated heat stress setting where the victim is likely to have been perspiring heavily, voluntary hydration with salt-containing fluids has a physiologically-based rationale. Use of intravenous saline for hydration, if available, might be considered. Such a decision should be based on more specific clinical assessment of pulse, blood pressure and other parameters of dehydration as in any setting and by a person trained to make such assessments and treatment decisions. Any person treated in the field for heat exhaustion with intravenous hydration should have evaluation by a trained professional prior to being released on their own.

A team of prominent heat/exercise researchers reported in a review that there is no evidence that heat stroke is preceded by less severe heat-associated disorders.(Casa et al., 2005) Despite this review articles continue to caution that untreated heat exhaustion may progress to heat stroke.{Howe, 2007 #2228}

Based on the information presented in Appendix A on both heat exhaustion and heat stroke, the primary task confronting a rescuer responding to assist a person who has seemingly unintentionally interrupted physical in a setting of elevated heat stress is ruling out heat stroke. The most reliable method to rule out incipient heat stroke is to measure core/rectal temperature. If rectal temperature evaluation is not possible, the person experiencing symptoms should be assumed to be at high risk for developing heat stroke, particularly if there are any changes in mental status, including minor changes such as irritability, and whole body cooling should be instituted along with rehydration with a salt-containing liquid orally, if tolerated, otherwise intravenously.{Casa, 2005 #1013} Furthermore, if mental status does not return to normal within a few minutes of cooling or if it degrades, the person should be transported as rapidly as possible to a hospital without interruption of cooling activity. The concept of a lucid interval has been documented in which persons with, sometimes markedly, elevated core temperatures were,

apparently either acting normally or manifesting relatively subtle changes in behavior and went on to develop heat stroke.{Casa, 2005 #1013}, {Schnirring, 2010 #2320}

Heat Stroke

This discussion presents information largely published in reference to exertional heat stroke; however, the treatment principles are the same for exertional and non-exertional heat stroke. The 2009SR cited seminal studies demonstrating rapid cooling of athletes with elevated core temperatures with the use of cold water immersion or cold water application with fanning. McDermott performed a literature review in April 2007, finding 7 studies of both convenience samples of runners at races and experimental heating protocols and a number of case reports and case series that demonstrated ice water immersion, either up to the clavicles or of the torso and upper thighs, provided the most rapid cooling

None of the literature found since 2009 refutes those conclusions. Several studies or case reports since the latest references in the 2009SR examine alternative cooling techniques since cold water immersion may not always be available as a first aid intervention. Several representative cooling techniques proposed by different authors since McDermott's review are presented in table 1.

Table 1: Representative Cooling Rates with Different Techniques: reports since McDermott

Author	Yr	Subjects	Technique	Cooling rate
Hee-Nee	2010	7 Male & female participants in 21Km footrace	Continuous total body ambient (28-34°C) water misting combined with fan (speed not specified) – cooled to different final temperatures	**0.09-0.18**°C/min (avg 0.14°C/min)
Hostler	2010	18 male & female volunteers exercised in firefighter gear simulating firefighting work-rest cycle	Forearm and hand immersion device (14.3 ± 2.7°C water)	**0.05** ± 0.03°C/min
			Fan blowing ambient air	**0.04** ± 0.02°C/min
			Ice-water perfused wetted hand cooling device which includes a wrist cuff and vacuum on the hand	**0.04** ± 0.02°C/min
			IV 4°C normal saline	**0.06** ± 0.06°C/min
			Semi-Fowler's rest in 24°C room no fan	**0.05** ± 0.03°C/min
			Ice-water perfused wetted cooling vest	**0.04** ± 0.02°C/min
Sinclair	2009	11 male volunteers exercised to target temp in heat chamber	Total body ambient temp (~32°C) water spray (508 ± 108ml) every 5 min and continuous 8.4-3.5m/s (head to foot) air flow fan	**0.09** ± 0.02°C/min (during 20 min)
			Ice packs to axillae, groins & posterior neck	**0.07**±0 ± 0.03°C/min (during 20 min)
			2 liters IV saline over 20 min	**0.08** ± 0.01°C/min (during 20 min)
Taylor	2008	8 male volunteers exercised to 39.5°C(esophageal)	Resting supine in air-conditioned room (20–22°C) All cooling methods done to T_{es} 37.5°C	**0.07**±0.01°C
			Cold (14°C) water immersion to chin	**0.18**±0.04°C/min
			Temperate (26°C) water immersion to chin	**0.10**±0.02°C/min

(Armstrong et al., 1996, Hee-Nee et al., 2010), (Hostler et al., 2010), (Sinclair et al., 2009), (Taylor et al., 2008)

No more recent studies revealed any methods more effective than either whole-body immersion as reported by McDermott. This technique is not practical for first aid. The two next most effective cooling techniques appear to be immersion of torso and upper thighs in near freezing water (Armstrong) and continuous ambient temperature misting with a fan (Hee-Nee).

Taylor presented the concept of immersion in tepid water to avoid any skin vasoconstriction, citing concern that it may decrease heat loss, or lead to shivering, for the concern that it may produce more heat. He reported results monitoring esophageal, auditory canal and rectal temperatures. He promoted the use of esophageal temperature as the most reflective of true core temperature based on it being the closest to the central circulation. Using esophageal temperature, his results showed tepid water to cool faster than ice water. Although that may be the case, rectal temperature is more practical and used most frequently in clinical situations and research. For these reasons the rectal temperature results from Taylor's report will be used for comparison here. Several authors have participated in this discussion of where to ideally measure core temperature which is beyond the scope of this review. ((Saltin and Hermansen, 1966), (Robinson et al., 1998), (Lefrant et al., 2003), (Gagnon et al., 2010b))

Among these cooling techniques reported above, the principle of misting the entire body and blowing air across the moist body to increase evaporation appears to be the most effective that would be adaptable to a wide variety of first aid situations.

Although the pathophysiology of advanced heat stroke, whether associated with exertion or not, has been identified to be a systemic inflammatory response leading to multi-organ dysfunction (MOD) or multi-organ failure (MOF), the primary concern for first aid providers is early identification of persons near the entry point in the pathophysiologic downward spiral. Early diagnosis is dependent on history and clinical examination since there are no laboratory examinations specific to heat stroke. The presenting history may simply be someone exposed to elevated heat stress, whether from ambient temperature, physical exertion or a combination. The presenting clinical status may be collapse with some stage of delirium or coma.

Collapse and altered mental status, however, may occur in persons experiencing elevated heat stress without progressing to heat stroke despite not being treated with cooling.(Wyndham et al., 1968) Reports of non-exertional/classic heat stroke also report patients with changes in mental status, though not so consistently loss of consciousness, as an initial identifying clinical characteristic.(Misset et al., 2006)

Recommendations for initial treatment by lowering core temperature as rapidly as possible (ideally less than 30 min from time of collapse or identification of elevated core temperature with associated symptoms suggestive of significant organ dysfunction – see discussion of diagnostic criteria in Appendix A) to below 39ºC (102.2°F) have not changed. Discussion has ensued regarding optimal target core temperature at which to stop cooling due to concerns of inducing hypothermia. A recent study by Gagnon(Gagnon et al., 2010a) to experimentally look at the risk of hypothermia following cooling with an exit temperature of 38.6 ºC as recommended by Proulx (Proulx et al., 2006) based on calculations demonstrated a mean nadir esophageal temperature of 36.7ºC (range 35.36–38.06ºC) with a mean rectal temperature nadir of 37.1ºC. Removing subjects at a rectal temperature of 37.5ºC was associated with a mean esophageal temperature nadir of 35.7ºC and mean rectal temperature nadir of 36.4ºC, both at the edges of defining temperatures of hypothermia (32-34 ºC).

Based on the pathophysiological similarities between advanced heat stroke and the sepsis syndrome, physicians treating patients in intensive care units have been successfully invoking more aggressive cooling to levels of therapeutic hypothermia (32ºC [89.6ºF]) as an organ-protection strategy.(Yue et al., 2009), (Hong et al., 2012) While this sort of treatment is currently reserved for in-hospital and , to date, reports are only individual case reports, the logic may have relevance in the field. Therapeutic hypothermia to ~32ºC has been reported to offer protection to the brain from the effects of hypoxia in victims of ventricular fibrillation cardiac arrest.(Peberdy et al., 2010) Since the local biochemical reactions are similar in sepsis and post hypoxemia reperfusion, tissue cooling beyond normo-thermia is speculated to have similar protective effects in persons experiencing hyperthermia associated with collapse following exertion in elevated heat stress.(Hong et al., 2012)

Makranz reported the case of an Isreali military recruit who collapsed while exerting in an environmental temperature of 14ºC (57ºF) and 50% relative humidity with an unrecorded initial rectal temperature, but for whom heat stroke treatment was initiated upon collapse with undressing and splashing water that was warmer than ambient temperature on him and fanning. (Makranz et al., 2011) Rectal temperature was reported as 40ºC 5 minutes later. "Cool water cooling" was continued (exact technique was not specified) at a clinic until he began to shiver, at which point (40 min following collapse), his rectal temperature was recorded as 33ºC. This report brings to attention two significant issues. First, exertional heat stroke can occur in relatively cool environments with a likely confluence of other risk factors. Secondly, active cooling techniques advocated in the literature are predicated on taking place in a warm to hot environment and may need to be adjusted with cooler ambient temperatures. Despite this case having been presented as a precaution for close monitoring of temperature when cooling, this patient was cooled to within one degree Celsius of the target temperature (32°C to 34°C (89.6°F to 93.2°F) used commonly for therapeutic hypothermia in post-cardiac arrest situations.(Peberdy et al., 2010)

Tobalem and colleagues presented a case of an "apparently healthy" young woman found unconscious in a sauna with an initially recorded (not stated how long after discovery) tympanic temperature of 41.9ºC (107.4ºF).(Tobalem et al., 2010) She was also hypotensive with a blood pressure of 80/60. Initial treatment consisted of application of towels soaked with ice packs for 20 minutes followed by cold wet blankets for 40 minutes over the lower abdomen and upper thighs. At that point her rectal temperature was 38ºC (100.4ºF) and her blood pressure was improved. She, however, developed 2nd and 3rd degree tissue damage in spotty areas where she had been treated with the cold applications. This case was felt to demonstrate the risk of aggressive surface cooling with hypotension associated with heat injury since the skin circulation may already be compromised to the point that the cold leads to ischemic and cold tissue damage.

An increasing number of persons suffering heat stroke in monitored settings such as sports training, sports events and military training has highlighted the role of event organizers and medical monitors as determinants of survival. Reviews of military and sports-associated fatal cases of heat stroke have demonstrated frequent delays in optimal treatment for a variety of reasons: commonly, misdiagnosis due to either not obtaining a rectal temperature or to underestimating the implications of changes in mental status.(Casa et al., 2012) Additionally, whenever possible either avoidance of creating predisposing individual physiologic conditions or screening for them and trying to avoid them prior to exertional events or heat stress exposure

should decrease the incidence. A list of such predisposing factors is presented in the Appendix A discussion of heat stroke.

The increasing understanding of heat stroke as a "severe inflammatory response disease" is leading researchers to explore other cross-over treatments than cooling. Hagiwara has looked at the effect of anti-inflammatory molecules and anti-coagulants that are known to have anti-inflammatory properties. He and colleagues demonstrated that anti-thrombin III , danaproid sodium and recombinant thrombomodulin all have an attenuating effect in rats exposed to adequate heat stress to produce lethal heat stroke in untreated animals.(Hagiwara et al., 2010a), (Hagiwara et al., 2010b), (Hagiwara et al., 2011) While no human studies have been published, these frontiers suggest that additional tissue-protective treatments for heat stroke may become available in the not-too-distant future, initially in hospitals, though, ultimately, potentially, in field settings.

Marchbank and colleagues reported a protective effect to the increased intestinal permeability seen with increased heat and/or extreme, prolonged physical activity with pre-stress ingestion of cow colostrum.(Marchbank et al., 2011) Colostrum is a substance secreted by mammary glands of female mammals during the first few days following giving birth. It is known to be rich in growth factors and cytokines as reviewed by Playford. (Playford et al., 2000) Not only might the future hold better treatments, but also possibly improved methods to decrease the risks of heat stroke in anticipation of activity in heat stress environments.

Exertional Hyponatremia

As noted above in relation to the NATA heat illnesses classification, exertional hyponatremia will not be reviewed in detail. This is a disorder related to persons consuming liquids in high quantities that are lower in sodium content than blood and body fluids. The condition was more common some years ago in association with endurance events and advice to drink large quantities of fluids to avoid dehydration regardless of level of thirst. Further discussion of optimal hydration techniques during exertion is beyond the scope of this review.

Hyponatremia can be fatal, thus it is an important consideration in any discussion of use of fluids for replacing sweat losses. There are a number of factors that may have an influence on the sensitivity of a person to developing hyponatremia.

- Use of diuretic medications (fluid pills)
- Following a low sodium diet
- Individual variation in amount sweating
- Sweat sodium content (known to vary by persons and state of acclimatization)

Persons engaged in exertion in heat stress environments or exposed to high heat stress environmental conditions where sweating may be profuse, should be attentive to the potential to lose significant amounts of body fluid. Drinking large amounts of fluids low in sodium content should be avoided for fluid replacement. Specific sodium concentrations in fluids for consumption in settings of high sweating have not been agreed upon in the medical literature.

Since this topic was not one of the heat disorders for which a literature search was undertaken there are no final recommendations in terms of Standards, Guidelines or Options.

Standards, Guidelines and Options

NOTE: The user of these standards, guidelines and options is strongly encouraged to read the discussion of the clinical entities in Appendix A due to the importance of making the correct diagnosis prior to application of the treatment interventions in this section.

Exercise Associated Heat Cramps

Standards

None

Guidelines

- Rest. Stop the activity that is associated with the cramping muscles.
- Massage of the cramping muscle
- Gentle stretching
- Hydration with a salt and water-containing liquid by mouth if tolerated,

Options

None

Exertional Heat Exhaustion

Standards

- Begin cooling the victim by
  - Removing him or her from the hot environment
  - Remove excess clothing
  - Begin cooling with cold/cool water on skin combined with fanning
- Begin oral rehydration with electrolyte-containing solutions
- If a person with suspected heat exhaustion is unable to tolerate oral rehydration or develops any change in mental status, 9-1-1 should be called immediately.

Guidelines

None

Options

None

Exertional Heat Stroke

Standards

- Contact 9-1-1 immediately
- Begin immediate and aggressive cooling of the victim
  - Remove from hot environment
  - Remove excess clothing

    - Begin cooling with as cold as is available water immersion, cold water on skin with fanning, or rotating towels/sheets wetted with as cold water and placed on the trunk
- Transfer to hospital while continuing to cool

Guidelines

None

Options

If cold water immersion, cold water on the skin combined with fanning or rotating wet cold sheets/towels are not available, then ice packs, ideally multiple ice packs, may be applied to the trunk (axilla and groin areas) while awaiting arrival of EMS and transfer to a hospital.

Appendix A – Terminology, Definitions and Human Temperature Physiology

Core Body Temperature

Core body temperature is a critical factor in the discussion of heat illnesses. The exact definition is a controversial topic in the scientific literature and its definition is frequently not the same among authors.

The body is made up of elements with various capacities to store and produce heat: bone, solid internal organs in the torso and abdomen, brain, muscles, blood. Thus, on a true sense of body temperature, there is no one temperature for all tissues. The central heat regulating mechanism is in the hypothalamus, deep in the brain, which is influenced by neural input from temperature sensors in both deep tissues and skin as well as local blood temperature. (Boulant, 2011 (First published in print 1996)) Thus, blood temperature at the hypothalamus is taken by some researchers to be the true core body temperature. For practical technical reasons body temperature is measured at other sites in clinical assessment. Simultaneously recorded temperatures differ slightly among those measured 10cm (4inches) internal to anal sphincter (rectal), under the tongue, in the ear (tympanic), under the arm (axillary), in the esophagus at the level of the heart, or on the forehead or temple skin by patch or hand held scanner.(Casa et al., 2007) Despite these differences, all these sites demonstrate that body temperature ranges between 36-38ºC (96.8-100.4ºF) in situations where the body is not performing either compensatory heat dissipation or heat generation activity.(Saltin and Hermansen, 1966), (Casa et al., 2007)

Esophageal temperature is often taken as providing the closest minimally-invasive temperature to deep internal organ temperature which is assumed to be represented by pulmonary artery or right atrial blood temperature obtained with central intravenous probes.(Lefrant et al., 2003) Although esophageal and rectal temperatures closely approximate each other in a steady state, it has been demonstrated that esophageal temperature tends to change more rapidly than rectal temperature during active and passive heating and cooling.(Gagnon et al., 2010b) Authors have speculated as to whether this is due to the heat stored in the muscles and other tissues surrounding the rectum versus the esophageal probe being adjacent to the central blood vessels that will be filled with constantly changing mixed blood from the different vascular beds (muscles, skin, brain, abdomen and lungs) .

Measurement of temperature in the ear (aural/ tympanic), in the mouth (sublingual), in the axilla (axillary), on the skin (forehead) and with instruments designed to estimate temporal artery temperature have all been shown to demonstrate lower temperature than rectal measurement with increasing difference as rectal temperature rises.(Casa et al., 2007) (Ganio et al., 2009) Thus, these sites are not recommended for assessment of persons at risk for heat stroke. Rectal temperature has been used for the majority of research on exercise in heat stress settings. Rectal temperature, preferably obtained at least 4 cm (approximately 1.5 inches) above the anal opening is referenced most commonly as the standard for clinical evaluation of persons with a question of heat stroke, particularly in the out-of-hospital setting since placement of esophageal probes is impractical.

Heat Stress

Heat stress refers to environmental conditions that stimulate the body to engage in active mechanisms to dissipate heat that may be produced internally via cellular activity or absorbed from the external environmental.(Sawka et al., 2011) It is expressed by metrics defined by calculations incorporating environmental factors such as ambient temperature, humidity, wind, dew point and cloud cover. Different countries and different research and regulatory bodies use differing metrics to determine a degree of heat stress.

Related terms of importance in the domain of heat-related illness include:

The Heat Index is the official United States (US) heat metric adopted by the US National Weather Service (NWS), a division of the National Oceanographic and Atmospheric Administration (NOAA) in the United States. It incorporates ambient temperature in the shade and relative humidity (the ratio of the partial pressure of water vapor in the air currently to the partial pressure of water vapor at the same temperature if the air were fully saturated with water vapor – the point at which one would see mist forming). In addition to these meteorological factors, the formula incorporates factors for presumed clothing, body activity and other parameters.(Rothfusz, 1990) The resulting number is expressed as "effective" or "perceived" temperature in degrees Fahrenheit.

Wet Bulb Globe Temperature (WBGT) is another method of expressing environmental heat load, developed by the United States Marine Corps.(Budd, 2008) This metric incorporates air temperature in the shade, effects of wind, evaporation and sun radiation, thus accounting for the various methods by which a *resting* body can gain and dissipate excess heat.(US Army, 2003) This method of assessing the environmental factors related to heat stress is often used by the military, sports managers and in industrial managers and their advisory bodies for developing guidelines regarding exposure. The military has developed a flag system which is often referred to in other guidances regarding activity in heat.

Category	WBGT °F	WBGT °C	Flag Color
1	<= 79.9	<= 26.6	White
2	80-84.9	26.7-29.3	Green
3	85-87.9	29.4-31.0	Yellow
4	88-89.9	31.1-32.1	Red
5	=> 90	=> 32.2	Black

The Occupational Health and Safety Administration (OSHA) has promulgated a work/rest regimen for workers wearing normal clothing which uses an adjusted temperature calculation to approximate the WBGT.(Occupational Health and Safety Administration, 2011) This is more completely presented with calculation formulas in an OSHA Technical Manual chapter.(Occupational Health and Safety Administration, 1999)

Compensable heat stress refers to situations in which the body's cooling mechanisms are able to maintain core temperature at a level that allows continued functioning at whatever activity in which the person is engaged.(Sawka et al., 2011)

Uncompensable heat stress refers to situations in which the body's cooling mechanisms are unable to dissipate body heat build-up, whether the heat load comes from internal metabolic activity or external, environmental heat sources. The inability to compensate may either be due

to internal factors such as the effect of medications or other alterations in the body's natural cooling mechanisms that impede optimal functioning or to external factors such as elevated environmental temperature or humidity. The elevation of core temperature leads to one of three outcomes: the person involuntarily stops whatever physical exertion, regardless of how minimal, they are engaged in due to what is termed heat exhaustion; the person voluntarily removes themselves from the heat stress either by decreasing physical activity or undertaking some other cooling behavior; the core temperature continues to rise, and leading, in conjunction with any other predisposing factors, to development of elements of the syndrome of heat stroke. (Sawka et al., 2011)

Heat strain

Heat strain refers to the physiological consequences of heat stress such as elevated body temperature and physiological mechanisms engaged for cooling since these involve additional metabolic activity/strain. (Sawka et al., 2011)

Heat Acclimatization/Acclimaton

It has been demonstrated that both the performance and endurance of athletes and workers under elevated heat stress improves over time with the maximum effect occurring at some point between 3 to 10 days. (Goldman, 2001) Acclimatization is represented physiologically by increased sweat production for a similar level of activity and heat stress, but with lower sweat sodium content.(Allan and Wilson, 1971), (Chinevere et al., 2008) Acclimatized persons also tend to have cooler skin as long as the environmental temperature is cooler than the core body temperature, thus creating more of a gradient from the core to the exterior.(Lorenzo and Minson, 2010)

By convention, the sports medicine literature uses acclimatization in referring to persons adjusting to an elevated heat stress environment during personal life activities while acclimation is used to refer to conditioning to heat under artificial conditions, either experimental protocols or hot chambers used in preparing for competition in heat.

Heat illness (Heat-related illness)

The terms heat illnesses and heat-related illnesses have been developed to refer to physiological derangements that have a strong association with exposure to elevated levels of heat stress, whether environmental or exertional. One author has proposed a new paradigm in which only heat stroke would be termed a heat illness since that is the only one of the disorders in which elevated core body temperature appears to be a primary pathological factor.(Noakes, 2008) Although Noakes has published widely on sports in elevated heat stress environments, this proposal has not been picked up by the remainder of the heat illness research community based on Medline not demonstrating any citations to this article.

One of the primary difficulties in developing medical guidelines for management of any abnormal condition is to first arrive at a clear definition of the pathologic condition being considered in both molecular and clinical terminology that allows it to be differentiated from other phenomena that may have similar associated circumstances, symptoms or findings on examination (including laboratory or other examination beyond an unaided physical examination) in case there may be differences in treatment or risk of advance to more serious conditions. This is particularly important in the setting of first response were the information available may be limited to the history of an event, interrogation and examination of the victim and observation of the environmental circumstances.

Cramps, syncope, exhaustion are all abnormal physiologic phenomena or conditions that are found to occur in multiple settings other than exposure to elevated heat stress. Thus, the first question that must be asked is whether there is a fundamentally different pathology (physiologic abnormality) present in these conditions (cramps, syncope, exhaustion and hyponatremia) when they happen in settings of elevated heat stress that would lead to a different treatment. Heat stroke is the only one of the "heat related illnesses" in which an elevation of body temperature has been implicated in the clinical and pathophysiologic definition of the phenomenon.

An associated question arises of whether these named phenomena are distinct "disorders" or simply clinical stages along a continuum that has been set in motion once any one of the disorders appears. If there is no unifying pathological process related to heat stress, then it does not make biological sense that there would be a direct pathological progression among the disorders. Answering this question will have relevance to development of response actions on the part of first aid providers.

Since the goal of a discussion of these entities is to provide guidance for training first responders to both recognize and institute interventions to minimize the adverse health effects of situations that put humans at risk of death or disability, it is important to keep the primary focus on diagnostic features and interventions readily available without advanced technologies. Despite a diagnostic and treatment focus on individuals already suffering from a condition, equipping first responders with the understanding of risks and how to mitigate the conditions is also important for preventing further harm to current victims and to others.

On a practical level, when addressing conditions such as heat illnesses where the pathological conditions are preventable and are directly associated with a human-environmental interaction that is modifiable, it is of critical value to teach the principles of the underlying interaction to allow for creative solutions to decreasing risk for humans confronted with elevated heat stress situations.

On-going research in the domain of heat-related illnesses has expanded the understanding since publication of the 2009 SR. The 2009 SR presents a fundamental discussion of epidemiology that will not be re-presented or expanded upon here. This review will, present discussions of these listed disorders focused on assisting with arriving at a clinical, non or minimal laboratory-based diagnose

Heat Cramps (Exertion-related Muscle Cramps)

This discussion is intended to replace the presentation in the 2009SR.

Many of the references cited in the 2009SR for both the discussion of signs and symptoms and for treatment were reviews that either cited other reviews or textbook chapters for justification for statements or had no citation. A table is presented in Appendix C that maps the references for a table of treatments presented in the 2009SR demonstrating the lack of experimental evidence for various treatments proposed for cramps.

This section presents a clinical and pathophysiological discussion intended to help the reader better understand the entity in order to make the most accurate diagnostic decision to guide therapeutic interventions.

Clinical description of heat cramps

Over 100 years ago, reports appeared in the medical literature of cramps experienced by workers in different hot (often cited up to 110ºF to 115ºF), humid environments such as coal-burning ship or train engine rooms (stokers' cramps or firemen's cramps), deep-shaft coal mines (miners' cramps) or sugar cane fields (cane-cutters' cramps). (Welsh, 1909) Many of the references cited in this discussion will seem "old." This is partly due to the fact that many of the fundamental clinical characteristics of heat cramps as well as enduring treatment principles were established in literature from the first half of the 20th century. Medical literature discussion of heat cramps was limited primarily to the domains of industrial medicine until World War II when more military literature appeared, primarily in the British medical literature. The medical literature discussion of heat cramps in civilian populations appears in the mid-1990s with Bergeron's presentation of his experience treating a tennis player who suffered from disabling cramps when playing or practicing in higher heat stress conditions.(Bergeron, 1996)

The cramps described in the early literature were characterized as diffuse, often involving muscles not directly engaged in strenuous activity, particularly abdominal muscles.(Welsh, 1909), (Talbott, 1935)The involved muscles have been described both as cramping of the entire muscle and as only involving various bundles within the muscle.(Talbott, 1935), (Bergeron, 1996) Early descriptions of workers in steel mills, coal mines and as stokers for steam engines noted a combination of premonitory muscle twitching/fasciculation with individual muscle bundles contracting and relaxing prior to involvement of the entire muscle. Once the entire muscle was involved the contraction was described as extremely strong and painful. These contractions were described as often spontaneously relaxing after 3 to 5 minutes. The muscles were described as remaining very sensitive to initiation of cramping with stimuli such as a light breeze, moving bed covers or jostling of the bed on which the victim was resting setting of further cramps. Fasciculations of bundles were described also as continuing, but not being painful unless advancing to a total muscle cramp.(Welsh, 1909), (Edsall, 1904), (Talbott, 1935), (Hubbard and Armstrong, 1989), (Bergeron, 2003)

Cataloguing signs and symptoms is helpful for differentiating disorders. In this case, the primary disorder from which heat cramps need to be differentiated is exertional exercise-associated muscle cramp (EAMC). EAMCs are generally considered cramps of specific muscle groups that have been over exerted either in a sustained contraction or through repetitive contraction and which have no relation to heat stress or fluid and electrolyte balance.(Schwellnus, 2009), (Bergeron, 2008), (Eichner, 2007) Difficulty in differentiating the two may arise when a person is exerting in a setting of elevated heat stress since that does not preclude developing muscle/action-specific/isolated cramps.

The 2009 SR presented a table of signs and symptoms for heat cramps, reproduced here:

Signs	Symptoms
• Decreased water intake (thirst) • Loss of 2% body water (sweating) • Loss of electrolytes (e.g., sodium and chlorine) • Palpable muscle spasm • Tachycardia	• Fatigue • Intense pain • Thirst

- Dehydration

A number of the elements in this table are not what would typically be thought of medically as "signs" and "symptoms." Additionally, although they are phenomena that may be associated with heat cramping, they are not specific to heat cramps compared to exercise associated muscle cramps (EAMC), making them of little value in differentiating clinically between the two entities. Based on the literature reviewed for this revision, the only two differentiating clinical features between exercise/effort-associated muscle cramping (EAMC) and heat cramps are the diffuse nature of heat cramps and visible fasciculations of diffuse muscles prior to onset of cramping.(Welsh, 1909), (Talbott, 1935)

The first report in the literature that proposed a set of diagnostic criteria, and which is still frequently cited, was from Talbott, who proposed 5 criteria based on study of 5 cases(Talbott and Michelsen, 1933):

- Exposure to a high temperature at work.
- Rapid loss of salt in the sweat, that is not replaced.
- Painful muscle cramps.
- Diminished concentration of chloride* and base in the blood and likewise in the body tissues.
- Rapid amelioration of symptoms after therapy.

*At the time of Talbott's writing, chloride was used in laboratory testing to reflect sodium chloride levels. Only the first three of these criteria would be available to a first aid provider.

Talbott did not provide a detailed description of the presenting features as had earlier authors noted above. Additionally, his criteria include criteria that would not be available to a first responder.

Several other factors have been noted as associated and potentially creating a higher risk for heat cramps.

- History of less than 7 to 14 days exposure to similar activity levels in similar environmental conditions (lack of acclimatization – it has been demonstrated that sweat salt concentration decreases as persons become acclimatized, while sweat volumes increase(Chinevere et al., 2008))
- History of low salt consumption in diet
- History of taking diuretic medications

Despite awareness of these additional associated features, the clinical descriptions provided by the earlier authors noted above provide the most rapid differentiation between the two entities of EAMC and heat cramps.

Table 2: Heat Cramps vs Exercise-Associated Muscle Cramps: Clinical Differentiating Features

	Heat Cramps	Exercise-Associated Muscle Cramps
Clinical Findings	• Cramps in muscles not directly over exerted (e.g. arms, thorax, abdomen)	• Cramps in muscles directly exerted – e.g. calves in runners

	• "Wandering" muscle bundle contractions in muscles not directly involved in excess exertion (e.g. arms, face, abdomen) – described as looking like a "bag of worms"	
Additional features (available to first aid providers)	• Prior history of similar diffuse cramping with exertion in elevated heat stress • Recent (<7d) onset of activity with elevated heat stress • Heavy perspiration • Salt-restricted diet • Diuretic use • Lack of salt in fluids consumed while exerting	• None

Pathophysiology of Heat Cramps

Since the early articles of the 20th century, the mechanism for heat cramps has been debated. Early proposals were that it was based on "water poisoning" a condition that was not well documented from a physiological basis, but would most closely equate to what would now be classified as hyponatremia from excess consumption of free water (water without anything dissolved in it, particularly salt – sodium chloride - NaCl).(Haldane, 1928), (Brockbank, 1929) Empirical decisions, based on realizing that sweat contains NaCl, to replace plain water with salted water for workers in hot, humid settings with a history of diffuse body cramping was repeatedly reported to resolve the cramping as well as to be associated with less fatigue.(Brockbank, 1929), (Oswald, 1925), (Talbott and Michelsen, 1933),

McCance presented a quasi-experimental design study supporting the apparent importance of salt in the development of these diffuse cramps. He and two other volunteers were subjected to passive heat exposure on repeated days in a heated tent without salt supplementation and with elimination in their diets. Diffuse cramping developed that was provoked with slight movements. Although he does not report specifically the time frame for resolution of the cramping tendency once salt was reintroduced, he does report significant improvement in ability to forcefully use muscles as in climbing stairs within a few hours.(McCance, 1936)

Ladell reported direct evidence of a role of salt in heat cramps by inducing cramping in a subject with exertion in elevated heat stress then occluding blood flow to one leg and injecting a saline solution designed to replace the calculated saline loss in the experimental exercise into the unoccluded general circulation. The injection was done over 3.5 min. Cramping resolved in 2 minutes in the leg with unoccluded circulation. Cramps were still present 7 minutes after injection in the occluded leg, but resolved within 2 minutes of removal of the occlusion. (Ladell, 1949)

Bergeron presented a case report of a young tennis player who experienced repeated cramping, though not as diffuse as in earlier reports of workers and military personnel, that was eliminated

by increasing salt intake prior to and during play in elevated heat stress settings.(Bergeron, 1996) His patient also reported arresting the progression from premonitory muscle twitching that began during play to cramps by acute ingestion of salted water. Following ingestion of a salted drinking solution he was able to return to play in the same match without adverse effects. This article has become a keystone article, being cited repeatedly as "proof" that salt loss is the primary physiological basis for heat cramps. The athlete reported in this article had been on a low salt diet in his home due to a household member having hypertension.

Bergeron and other more contemporary authors have anecdotally reported rapid resolution of cramping in athletes following intravenous administration of normal saline (0.9% NaCl) without carbohydrate (dextrose).(Bergeron, 2007), (Stone et al., 2003)

Schwellnus and colleagues have challenged the concept of water and sodium loss being the foundation for developing cramping in muscles that are exerted in heat.(Schwellnus et al., 1997) He cites cases of persons experiencing muscle cramping isolated to the muscles being exerted and finding no evidence on blood analysis of a sodium deficit. He does not report any subjects with diffuse cramping, the clinical picture from throughout the literature addressing heat cramps of "severe" cramping. The body of literature regarding heat cramping has consistently referred to severe and mild cramping, identifying mild as cramping limited to muscle groups actively engaged in strenuous activity. There does not seem to be any clinically evident distinction, other than, perhaps, premonitory fasciculations, between mild, focal heat cramping that will respond to salt and water replacement and focal solely exertion-based cramping. The literature discussion of salt solutions having an effect on focal cramping has either been in regards to groups of workers changing hydration fluids and eliminating focal cramping or case reports. The recent literature discussion has been clouded by reference to heat/exertion-associated cramps as Exercise Associated Muscle Cramps (EAMC) in recent reviews of heat illness.(Armstrong et al., 2007) EAMC has, in other settings been used as a term to refer specifically to muscle cramps **not** associated with elevated heat stress or water and electrolyte disturbances.(Bergeron, 2008) This review has, based on the large number of reports of populations of workers who stopped experiencing both focal and generalized cramps while working in hot environments upon changing to salted water for rehydration, ascribed to the concept that there is, at least, a type of cramp that is associated with fluid and electrolyte imbalance.

Heat Cramps as Precursor to Heat Stroke

Much literature distributed to the public (CDC/NIOSH, NOAA/NWS, as the primary sources for "authenticated" information), including instructor material from American Red Cross, speaks of "heat cramps" as being a part of a continuum toward heat stroke. There is no literature demonstrating a pathophysiologic continuum from developing cramps to developing heat stroke. Elevated core body temperature is not cited in the literature as a diagnostic feature of heat cramping. Additionally, there are clear reports of athletes and workers suffering heat cramps and continuing play or work in the same conditions once the cramps have resolved, usually in association with drinking salted fluids, without developing heat stroke.(Bergeron, 2007), (Stofan et al., 2005), (Talbott and Michelsen, 1933)

Despite there being no evidence of a direct pathophysiological continuum between heat cramps and heat stroke, someone suffering from heat cramps in association with high volumes of sweating and continuing to exert themselves even with the cramps in a particularly high heat stress setting, particularly if they do not replenish fluid losses with a salt-containing liquid, may

have an increased risk of developing heat stroke. (see the section in this appendix on heat stroke for more discussion regarding the relationship between hypohydration and heat stroke risk)

Heat Cramp Treatment

As with any medical condition, the goal of research in treatment is to find the most specific intervention for the pathophysiologic process involved with the least risk to the affected person. Although the exact pathophysiologic mechanisms underlying various cramping experiences occurring during exertion in an elevated heat stress setting have not been fully elucidated, the number of case reports and case series reporting both rapid resolution and resolution over several hours of cramping in relation to administration of salt and water imply that these are reasonable therapeutic interventions.(see citations in Heat Cramps section of "Textual Summary of Recommendations for Revision, Reaffirmation or Retire" above. Additionally, again based on the numerous case reports and case series, there does not appear to be significant risk of harm from treatment with oral salt administration to the person suffering cramps.

Issues related to 2009 SR

The 2009 SR included a table of treatment recommendations for heat cramps. (Reproduced in Appendix C) The references cited for that table are review articles, most of which also used review articles or textbook chapters as foundation for their recommendations. A number of the recommendations in review articles did not have any reference or cited foundation for the recommendation. A few of the second tier references appeared to be actual studies, though observational rather than experimental in design. These were retrieved, when possible, via electronic or local library resources as available to this reviewer. This reviewer did not generally pursue the reference trail beyond the second layer due to increasing difficulty with access to the articles cited and lack of access to most of the editions of textbooks cited.

While there has been some literature debate regarding the pathophysiological basis for cramping isolated to exerting muscles in persons exerting in heat stress, the literature does seem to support a role of sodium in diffuse body cramping in persons exerting in elevated heat stress. As with many disorders, there is a strong argument to be made for prevention that seems possible through attention to dietary salt/sodium intake during times of expected increased sweating.(Bergeron, 2003),

Table 3: Heat Cramp Treatment Options from various authors

(see Appendix C for more in-depth discussion of some of the replacement fluid recommendations in this table.)

Treatment	Basis
Massage and Stretching	These are standard cramp therapy. This was noted in several reviews, but no studies were found and no reviews had references to any studies To the contrary, several of the early literature reports noted the inability to either physically stretch the affected muscles due to the force of the cramp or the lack of therapeutic effect to terminate the cramping following stretching as specific characteristics of what became known as heat cramps.(Moss, 1923), (Talbott, 1935)

Various concentration salt and water solutions	
16 to 20 ounces of a Sports drink plus ½ teaspoon salt to be consumed as quickly as possible.	Anecdotal report by Bergeron based on his calculations of presumed salt loss. (Bergeron, 1996)
Hypertonic intravenous saline (15%)	162ml injected to one subject with cramps and one leg occluded by a tourniquet.(Ladell, 1949)
Intravenous "normal" saline = 0.9% NaCl/water	Talbott provided 3 cases at the end of a review article on heat cramps relating the response to different treatments. In one case cramps resolved following approximately 200cc of intravenous saline. (Talbott, 1935) Bergeron also mentions without, evidentiary support, use of IV Saline as having been successful in resolving cramps in a timely fashion for tennis players and American football players.

Only two of the various references identified in the literature searches conducted for this review which documented a positive effect on cramping related acute response to treatment. Talbott reported workers with cramps experiencing relief by the time they had received one infusion of normal saline intravenously, between 4-6 hours after presentation. (Talbott and Michelsen, 1933) Bergeron reported acute relief of pre-cramp fibrillation in a single subject who consumed ½ teaspoon of table salt in approximately 1 pint (473bml) water.(Bergeron, 1996)

Various authors have proposed different solutions of salt for rehydration. (Table 5)

To facilitate discussion of salt and sodium in relation to treatment of heat cramps, some relations are presented here:

Table 4: Reference guide of Salt and Sodium equivalents

Salt Dose	NaCl	mg Na^+	mmol Na^+	mEq Na^+
1 Gram table salt	1 Gm NaCl	390 mg Na^+	17.1 mmol Na^+	17.1 mEq Na^+
1 teaspoon salt	≈6 Gm NaCl	≈2,400 mg Na^+	≈104 mmol Na^+	≈104 mEq Na^+

Table 5: Salt Content of Various Rehydration Solutions Noted in Heat Illness Literature

Year	Author(s)	Proposed salt solution	mEq/L*
1923	Moss	10 grams sodium chloride in 1 gallon (=3.78 L) water (Moss, 1923) (10 Gm salt = 171 mEq Na, thus 171mEq/3.785L = 45mEq/L)	45
1924	Davis	Trial solution: "0.25% made from 10gm per gallon of water" Daily use solution: 1 teaspoon salt to 2 quarts water (daily ration in the mine) (Davis, 1924) (Trial Solution: 45mEq/L Daily use formula: 12 gm salt/1 gal = 12gm/3.785L = 54mEq Na/L)	 45 54
1925	Oswald	180 gm sodium chloride per liter of water of which 2.5 liters was added to 213.3 liters water to make the final drinking solution (Oswald, 1925) Solution ≈ 36mEq Na/L.	36

1928	Thrower	"Addition of salt in small amounts to the mess drinking water" but no specified quantities.(Thrower, 1928)	
1929	Brockbank	No dosing information, simply statement of "salt solutions" for consumption during work. There is no mention of acute treatment with salt solutions.(Brockbank, 1929)	
1933	Talbot	Intravenous saline.(Talbott and Michelsen, 1933) Of note, this is the only report found to have detailed clinical progress information on the acute (within a few hours) response of patients to the intervention.	154
1935	Talbott	Normal saline (0.9%NaCl) intravenously Salt tablets - one 1gm tablet every hour until 15 tablets had been administered (Talbott, 1935) = 256 mEq Na^+ total, but no concentration since accompanying water volume not specified	154
1949	Ladell	Intravenous hypertonic NaCL (162ml of 15% NaCl over 3.5 minutes = 415 mEq total Na^+ given). After 2 min no longer able to induce cramp.(Ladell, 1949)	N/A
1996	Bergeron	Mixture of 0.5 tsp table salt in 500ml water aborted apparent impending cramps in cramp-prone individual. Bergeron notes that "the [Na*] of this mixture is 102.6 mmol/L = mEq/L (about 5 times the [Na*] of" the commercial sport drink he named.(Bergeron, 1996) 1 tsp salt (NaCl) = 6 Gm = 104 mEq Na	104
2003	Bergeron	Anecdotal statement in an article that intravenous normal saline frequently allows players of American football suffering cramps to return to play in the same game, implying an immediate	154

*The calculation to a mEq/L for the solutions is to allow comparison among the various proposed solutions and with normal blood Na as usually expressed in laboratory results (note that, for Na, SI units mmol/L have the same numeric value as mEq/L)

For comparison Sodium content of two leading sports drinks, the World Health Organization's recommended rehydration fluid and intravenous normal/0.9% saline are presented with the normal range for human serum sodium content.

Table 6: Sodium Content of Some Exemplary Commercial and Other Rehydration Fluids Compared to Human Serum

Solution	Sodium Concentration	mEq/L
Gatorade®†	450mg Na/L = 19.6 mEq Na/L http://www.pepsicobeveragefacts.com/infobycategory.php?pc=brand.1043.1002&t=1026&s=20&i=ntrtn	19.6
Powerade®†	225 mg Na/L = 9.8 mEq/L http://www.powerade.co.nz/hydration/products/why-drink-a-sports-drink-over-water	9.8
WHO Rehyd	75 mEq Na/L http://apps.who.int/medicinedocs/en/d/Js4950e/2.4.html#Js4950e.2.4	75
Normal Saline	Intravenous fluid 0.9% NaCl = 9Gm NaCl/Liter = (9 Gm X 17.1 mEq/Gm)/L= 153.9mEq/L	154
Human serum Na^+	135-145mEq/L	140

†Representative numbers from core product – other products in each brand have different amounts

Salt tablets

The 2009 SR addresses the use of salt tablets in the discussion: "However, salt tablets are not indicated because gastric irritation can occur (A. Dreyer & M. Kulesa, 2002) (LOE 5) and should be prescribed by a physician. If salt tablets are used (1 g of NaCl per tablet), the tablets should be taken with plenty of fluid (eg, 3 crushed and dissolved tablets to 1 liter of water)." The statements offer unclear guidance. The cited article by Dreyer and Kulesa is a review article published in an orthopedic nursing magazine, not a peer-reviewed journal, that. That article references a Centers for Disease Control website on Heat Cramps under the Extreme Heat domain for the recommendation to not use salt tablets.(Dreyer and Kulesa, 2002) The current CDC site on Extreme Heat does not have any statement regarding salt tablets. The other reference in Dreyer's review for the statement is from a textbook to which access was not available for this current review/revision.

Searches of PubMed for ("salt tablets" AND complications) and ("salt tablets" AND "adverse effects") did not return any citations of relevance. A search for ("salt tablets") alone, however returned several citations of studies in which subjects were given salt tablets to either restore electrolytes or to prevent ill effects of electrolyte loss with sweating, but with no mention in the articles of adverse effects.(Waters et al., 2005), (Tzemos et al., 2008) Several of the authors cited in this review who have written about industrial settings and resolution of cramping in association with changing from water only rehydration to salt have cited the use of 1 Gm salt tablets. Those authors did not specify an amount of water to be consumed with the tablets or a dosing schedule for the tablets.

Statements of concern were noted in several non-scientific, primarily endurance sports forums identified through general Internet searches performed with Google® search engine using the same search strings as used in PubMed. The concern brought up in these forums relates to unmonitored use of salt tablets, potentially in excess, as with endurance athletes using multiple tablets during the course of an event or taking multiple tablets at one time, that may lead to acute side-effects such as stomach cramps and vomiting.

A report on optimal delivery method for supplying salt to industrial workers commented that the use of "pure sodium chloride tablets," of unspecified strength, was "frequently" associated with nausea unless large amounts (quantity not specified) of water were given as well.(Stewart, 1945) Subjects ingesting 3 Gm of salt in tablet form every hour over 3 hours along with drinking water in quantities estimated equivalent to sweat loss while marching outdoors during an experiment on the effect of salt ingestion during exercise in hot environments reported "gastrointestinal uneasiness" and demonstrated worse heart rate and rectal temperature than subjects who only drank water. (Pitts et al., 1944) Ingestion of extremely large amounts of a very hypertonic salt solution has been associated with unintentional death in a case report of a young woman undergoing a prescribed exorcism.(Ofran et al., 2004)

All of these reports seem to indicate that 1Gm salt tablets may be used as long as they are accompanied by "adequate" amounts of water. Based on the various reports of use of salt tablets in clinical or research settings cited in the accompanying table, "adequate" seems to be in the range of 250 to 500cc (1 to 2 pints; 16 to 32 oz) water with one salt tablet, though there is likely significant individual variation in tolerance without GI upset.

Salt tablets are not standardized in dose. All the literature cited in this review refers to 1 Gm tablets. One on-line sports supplement vendor's salt tablets are reported to contain 215 mg Na per tablet, approximately ½ what would be in a 1 Gm tablet. (Saltstick.com: http://www.saltstick.com/products/sscaps/cfeatures.htm) One salt tablet such as this would provide the sodium equivalent to approximately two cups (400ml ≈1pint =16 oz = slightly less than ½ liter) of most of the sports drinks and of milk.

Dietary intake

Several of the early reports of heat-related whole-body cramping noted an observed correlation between level of dietary salt intake and propensity for cramping.(Talbott, 1935, {Brockbank, 1929 #1941) In a review of fluid consumption in the workplace, Parmeggiani reviewed case reports and case series from various work settings of decreasing or eliminating the incidence of heat cramps in workers who adjusted their dietary sodium intake and avoided rehydrating with plain water while working.(Parmeggiani, 1958) Bergeron has anecdotally reported that tennis players, who are particularly prone to heat/sweating-related cramps having been able to avoid them in multi-day tournaments or when training in the elevated heat stress conditions immediately preceding a match by increasing dietary sodium intake.(Bergeron, 2003)

Heat Exhaustion

The following discussion of heat exhaustion is intended to be complementary to the general presentation provided in the 2009 Scientific Review.

Exhaustion is an imprecise term, thus leading to lack of precision in the definition of heat exhaustion. The most direct definition is that of a person not being able to continue physical effort without, necessarily, collapsing.{Armstrong, 2007 #1152} Even in the setting of a person collapsing without loss of consciousness, there would be great subjectivity in terms of impetus and volition to make further effort. For example, the person who runs a race and collapses at some point from "exhaustion" may still be able to quickly get up and move if a sudden threat to safety or life were to manifest.

A broad set of symptoms and signs have been attributed to heat exhaustion in several heat disorder reviews in the sports medicine literature. (Table 7) Similar symptom sets have been reported in various occupations such as mining.(Donoghue, 2004)

Table 7: Heat exhaustion symptoms and signs noted in two example review articles

Symptoms	Signs	Author
Anxiety Confusion Cutaneous flushing Hypotension Oliguria Pyrexia Tachycardia Vomiting	Anorexia Dizziness Fatigue and malaise Headache Nausea Visual disturbances Weakness	Glazer JL. Management of heatstroke and heat exhaustion. *Am Fam Physician.* Jun 1 2005;71(11):2133-2140.
Normal or elevated body-core temperature Dehydration Dizziness Lightheadedness		Binkley HM, Beckett J, Casa DJ, Kleiner DM, Plummer PE. National Athletic Trainers' Association Position

Syncope Headache Nausea Anorexia Diarrhea Decreased urine output Persistent muscle cramps Pallor Profuse sweating Chills Cool, clammy skin Intestinal cramps Urge to defecate Weakness Hyperventilation	Statement: Exertional Heat Illnesses. J Athl Train. Sep 2002;37(3):329-343.

None of these signs or symptoms is specific to heat exhaustion. Many could also be associated with exhaustion from any cause without involvement of elevated heat stress, with heat stroke or with a variety of other disorders having nothing to do with exhaustion. These signs and symptoms would likely appear in various combinations and in varying orders from person to person and depend on the setting. Initial postulations to classify heat associated exhaustion into salt- or water-depleted categories (Leithead, 1964)have not been substantiated by more recent observations(Armstrong et al., 1988). To date no syndromic classification of heat exhaustion based on sensitivity and specificity of the validated studies of the signs and symptoms has been developed.(Becker and Stewart, 2011)

Exhaustion in the sense of inability to move a muscle despite as great a conscious, volitional command a person may give may be based on a number of factors such as lack of further energy sources for muscular activity, overall fitness level for the physical activity undertaken, or mental/emotional volition to persevere. Clinically, heat exhaustion does not seem to appear different from physical exhaustion at any temperature. Physical collapse is not a necessary component, though it may occur.

A number of these symptoms and signs overlap with those reported among persons ultimately diagnosed with heat stroke. The differentiating criteria for heat stroke as opposed to heat exhaustion are usually cited as more severe alterations in mental status (marked delirium, seizures, coma) with, by convention, a core body temperature $\geq$40.5ºC (different authors use temperatures from 39.5 to 41 ºC as their defining criterion for heat stroke). (Bergeron et al., 2011), (Armstrong et al., 2007), (Binkley et al., 2002)

Despite inconsistencies in studies and subject selection that preclude defining a universal set of criteria for exhaustion, elevating ambient temperature and increasing levels of dehydration have been shown in a laboratory setting to lower the amount of work output necessary to produce "exhaustion."(Sawka et al., 1992) The point of exhaustion while performing exercise at approximately 70% of their maximum capacity came significantly faster for 8 cyclists at 30.5ºC (51.7 min) than at 10ºC (93 min), both with 70% relative humidity.(Galloway and Maughan, 1997) Maximum core temperatures associated with subjects stopping effort reported in studies are often in the range from 38.5 to mid/high 39ºC.(Lind, 2010 (Initially published 1971)), (Nielsen et al., 1993) Despite these observations, highly conditioned and heat acclimatized athletes have been reported to exert to core temperatures between 41 and 42ºC without apparent ill effects.(Pugh et al., 1967), (Maron et al., 1977) Additionally, endurance athletes have been

found in field observations to have better-than-usual performance times despite both dehydration, based on body weight loss, and elevated temperatures.{Noakes, 2006 #418}

Theories regarding the underlying cause for inability to persist with exertion in the heat have invoked salt and water depletion (Leithead, 1964), cardiovascular factors and the effect of elevated core body temperature on CNS functioning(Casa et al., 2005). More detailed assessment of body temperature has suggested that a cooler skin temperature may allow subjects to exert beyond the point they would have stopped with a warmer skin temperature due to increased ability to transfer core heat to the environment, as long as environmental temperature is lower than skin temperature.(Sawka et al., 2012) Hypohydration is postulated to exacerbate this effect since the body is then dually challenged in efforts to cool since the lack of volume makes it harder to supply both the dilated skin vasculature needed for cooling and the dilated muscular circulation needed to sustain effort.(Sawka et al., 2012), (Kenefick et al., 2010) This phenomenon does not, however, answer the question of what physiologic mechanism leads to decreasing ability of individuals to sustain a level of function.

As long as the body can continue to shed heat, it has been shown that elevated core temperatures can be tolerated for quite long periods of time, particularly in acclimatized persons.(Wyndham et al., 1968) In that same study of experienced, highly acclimatized South African miners who were maintained in an elevated heat environment for hours at varying temperatures, many demonstrated psychological aberrancies with persistent elevated core temperatures including aggressivity, crying and lassitude. None developed heat stroke or needed external cooling and none had to be removed from the experimental environment before planned termination of a session.(Wyndham et al., 1968)

The fact that some persons can function with core temperatures higher than 40.5ºC without developing heat stroke or exhaustion suggests that there is not a direct continuum from heat exhaustion to heat stroke based solely on body core temperature. This is further elucidated in the discussion of heat stroke below. Despite this, given the clinical association between core temperature elevated above 40 to 40.5ºC and heat stroke, prudence would suggest that when faced with a person in an elevated heat stress situation exhibiting mental functioning changes and found to have a core temperature in this range, cooling procedures should be undertaken without delay.(Roberts, 2007a)

One recent study demonstrates one of the difficulties with the literature on the topic of heat illnesses and heat exhaustion, in particular. Donoghue presented a prospective case series of miners reportedly experiencing heat exhaustion.{Donoghue, 2000 #911} He performed hematologic and biochemical analyses as well as a non-random treatment option of oral or intravenous fluids reporting that intravenous fluids led to a more rapid recovery. He did not time the difference in recovery nor did he correlate the difference in recovery times to the biochemical abnormalities or symptom complexes of the individual subjects. Additionally, and of greater relevance for generalizability of his data, he did not use inability to continue physical exertion as the clinical inclusion criterion. He used inclusion criteria of “considerable heat exposure” along with one or more of headache, dizziness, fatigue, nausea, vomiting, transient loss of consciousness starting after beginning work without any other evident alternative basis for the symptoms. Only 2 of the 106 identified cases suffered transient loss of consciousness. The initial population from which cases were drawn included any miner who “requested treatment from the mine’s medical center.” This study has been cited in the American College of Sports

Medicine Position Stand on Exertional Heat Illness in Training and Competition as a foundation for the recommendation that intravenous fluids may lead to more rapid recovery from heat exhaustion which is defined in the position paper as "the inability to continue to exercise."{Armstrong, 2007 #1152} This does not seem appropriate since the inclusion criteria for the study were not the same as the concept for which it is being cited as support.

Complicating the picture even more is the clinical reality that a person who collapses at any level of physical exertion at any heat stress level must be evaluated for the full range of possible reasons for collapse such as dehydration, internal bleeding or myocardial dysfunction.

Exercise Associated Collapse (EAC)

Exercise associated collapse is a term that was developed to assist with building a classification and reaction matrix for evaluation of participants in endurance sports events who collapse where any one of a number of conditions may be the ultimate diagnosis.(Roberts, 2007a) It is not a specific condition, nor does it particularly imply collapse related to exertion in settings of elevated heat stress. It is meant to address heat stroke, heat exhaustion, hypothermia and fatigue. It does, however, offer the reminder that evaluation of persons who collapse during exertion must begin with assessment for the most serious possibilities.

Heat Syncope and Allied Disorders

Different authors in the sports medicine literature refer to conditions such as heat syncope and heat associated postural hypotension in relation to persons who collapse while exerting in a setting of elevated heat stress with no evidence of severe, life threatening causes and either no loss of consciousness or rapid return of normal mental function once in a supine position. (Anley et al., 2011), (Binkley et al., 2002) Syncope is defined as a sudden, transient loss of consciousness and postural tone. Syncope is based on sudden loss of vascular tone from an alteration in the balance of sympathetic and parasympathetic autonomic nervous system messages to the heart and vascular system resulting in a dilation of peripheral blood vessels and a drop in blood pressure without a compensatory increase in heart rate or force of heart beat to maintain adequate blood flow to the brain to maintain consciousness. There may me a paradoxical slowing of heart rate below the person's baseline heart rate. Return of consciousness in syncope occurs rapidly when the person experiencing it is placed in a horizontal body position, thus re-establishing adequate cerebral blood flow for consciousness. Since numerous other medical conditions may lead to sudden loss of consciousness and postural tone, syncope is a diagnosis of exclusion, meaning that more serious conditions must be considered first, particularly if the person does not regain consciousness rapidly once in a horizontal position or if they exhibit other evidence of another, more serious medical or traumatic condition. Thus, the most significant importance of rapidly evaluating a person experiencing sudden loss of consciousness and postural control in the setting of elevated heat stress is consideration of the onset of the heat stroke syndrome as the cause for the collapse.

Heat associated postural hypotension, as it is used in the literature is a term encompassing both collapse without loss of consciousness and syncope with no evidence of other more severe causes. Both of these conditions are thought to be related to varying degrees of hypohydration and alterations in the lower extremity vascular tone related to exercising or stopping exercise. (Anley et al., 2011), (Binkley et al., 2002) The relation with stopping exercise has been proposed based on observations of endurance runners when a runner stops and the leg muscles are no longer contracting in the constant rhythmic manner of running, thus, likely, allowing blood to pool in the legs. Since most endurance athletes lose overall fluids during competition, based on

body weight losses representing fluid loss, the postulation is that some athletes are more sensitive to the relatively sudden fluid shift when the legs abruptly stop the pumping action associated with running.

Cardiac arrest or dysrhythmia must be considered in all persons who collapse during athletic activities regardless of age. Ventricular tachycardia or fibrillation associated with hypertrophic cardiomyopathy is the number one cause for sudden death in young persons engaged in athletic activities.(Gersh et al., 2011) Additionally, with increasing numbers of middle-age adults participating in athletic challenges of all sorts, cardiac causes of collapse with loss of consciousness should be the first consideration of a first aid responder.

The peripheral vasodilatation that occurs as a part of normal cooling mechanisms in heat may be enough in some non-exercising persons with limited or altered cardiac reserve or with hypovolemia for reasons other than exercise to cause either syncope and/or, if there is a predisposition related to underlying heart disease, dysrhythmias. Thus, regardless of the degree of apparent heat stress, including physical exertion, any person who collapses with loss of consciousness should first be evaluated following general CPR response guidelines.

Only after cardiac causes have been ruled out, can one progress with an assessment for possible heat-related illnesses such as heat exhaustion, onset of heat stroke or other medical conditions outside the scope of this discussion.

Heat Stroke

Heat Stroke was known for centuries as "sun stroke." It was not until the middle of the 20th century that the term "heat stroke" was adopted for the phenomenon of people suffering collapse, severe physiological dysfunctions and death related to exposure to heat or exertion in heat. Epidemiologically, as reviewed in the 2009 SR, heat stroke is generally categorized as exertional or non-exertional, also referred to as "classic." Heat stroke has been largely defined by retrospective clinical assessments as a syndrome of marked mental status changes, typically listed as delirium, coma or seizures accompanied by elevation of core body temperature, variably cited as above 40 to 41ºC. The following discussion is presented since, much like in the transition of terminology from sun stroke to heat stroke, current understanding of the pathophysiologic processes involved is leading to new understanding regarding treatment and prevention with implications for first responders.

Starting in the 1960s researchers began to realize there was great similarity of the pathophysiology of severe heat stroke with or without ultimate death with sepsis, severe systemic infection, and some patients who experienced severe trauma with hypotension.(Knochel et al., 1961), (Knochel, 1975), (Bouchama et al., 1991), (Bone et al., 1992), (Bouchama and Knochel, 2002) Study of sepsis and trauma reactions had demonstrated that activation of inflammatory responses and the blood clotting system which spiraled out of control was the pathophysiologic basis for the ultimate organ failure leading to death. The clinical course of patients with severe heat stroke was seen to be very similar to, if not the same as that seen in these settings with liberation into the blood of various inflammatory mediators leading to a constellation of pathological inflammatory reactions grouped together under the term systemic inflammatory response syndrome (SIRS).(Bouchama, 1999), (Bouchama and Knochel, 2002), (Sawka et al., 2011) The out of control inflammatory reactions of SIRS leads to multi-organ dysfunction syndrome (MODS) including cardiac, hepatic, renal, pancreatic, hematologic and neurologic

dysfunctions seen in sepsis, trauma and severe, advanced states of what is termed heat stroke.(Bouchama et al., 1991)

Endotoxin, a lipopolysaccharide component of cell walls of gram negative bacteria inhabiting the intestines of all mammals, is the primary element that sets off the inflammatory and organ damage cascade in gram-negative sepsis. It is implicated as a precipitant of SIRS in trauma and other settings of marked or prolonged hypotension that may lead to a "leaky gut" syndrome based on ischemia (lack of adequate oxygen for normal metabolism) from inadequate blood flow to the intestines.(Andreasen et al., 2008) Studies into the similarities between the clinical syndromes seen in heat stroke and sepsis have led to finding elevated levels of endotoxin in the blood of human heat stroke victims and animals in whom heat stroke has been induced.(Bouchama et al., 1991), (Leon and Helwig, 2010b)

In-vitro studies of intestinal epithelial cell cultures have demonstrated that the normal junction between cells (the tight junction) does break down in a time and temperature dependent manner with temperatures between 37-41oC (98.6-104^{o}F).(Dokladny et al., 2006) Human studies have also demonstrated increased intestinal permeability associated with both strenuous exercise alone(van Nieuwenhoven et al., 2004) and in heat stress settings(Marchbank et al., 2011).

Animal studies have demonstrated evidence of intestinal and liver cell damage with induced hyperthermia.(Hall et al., 1999) The liver is the first line of cleansing defense against endotoxin that does leak into the circulation. Animal studies have also demonstrated that pre-treatment with antibiotics that are not absorbed, but are active against gram negative bacteria, and desensitization to endotoxin both lead to greater heat tolerance in induced hyperthermia in animal models.{DuBose, 1983 #1401}, (Gathiram et al., 1987) These studies support the development of a "leaky gut syndrome" and the potential role of endotoxin as significant initiating factors in the SIRS associated with heat stroke.

Physiological studies of response to heat and exercise have demonstrated that in both situations, the increased demand for blood to muscles and skin is partially met by diversion of the intestinal and other abdominal organs' circulation, the splanchnic circulation, to meet the demands from the exerting muscles and dilating skin circulation.(Rowell, 1974), (Rowell, 1983), (Kenney and Ho, 1995), (Perko et al., 1998) This diversion favors increased intestinal wall permeability in two manners. Firstly, as less blood exchanges in the intestinal circulation the capability to transfer heat away from the intestines is diminished, which may lead to adequate elevation of intestinal mucosa temperature to induce tight junction leakiness based on temperature-dependent molecular changes.(Dokladny et al., 2006) Secondly, at some point the demands for blood flow to the exerting muscles and to the dilated skin circulation can lead to low enough flow of oxygenated blood in the splanchnic circulation to compromise the metabolic activities of the intestines necessary to maintain the integrity of the tight junctions.(van Wijck et al., 2011) Hypohydration has been shown to exacerbate bowel leakiness in exercising humans.(Lambert et al., 2008)

Increased non-selective permeability of the tight junction to molecules of comparable size to endotoxin has been demonstrated with elevation of intestinal temperature in exerting human subjects.(Lambert, 2008), (Pals et al., 1997) Runners completing endurance races have also been found to have elevated endotoxin levels in the general circulation.(Brock-Utne et al., 1988), (Camus et al., 1997) An other piece of circumstantial evidence is the high incidence of marathon runners who experience intestinal symptoms, though the epidemiology in relation to other

aspects of heat stroke and the underlying pathophysiology of these symptoms are not well understood at the time of this writing. (Jeukendrup et al., 2000) Lambert(Lambert, 2009) and Zuhl(Zuhl et al., 2012) have recently reviewed many of the relevant aspects of these relationships. Marathon runners are also known to experience lower intestinal bleeding to the extent of severe hemorrhage in some.(Heer et al., 1987), (Beaumont and Teare, 1991) Endoscopic findings suggest this may be due to ischemia of the bowel mucosa. (Schwartz et al., 1990)

Clinical Definition of Heat Stroke for Early Detection

Clinical definitions of heat stroke over the past 50+ years cite two findings as defining the syndrome: markedly altered mental status such as delirium, coma or seizures and a rectal temperature of at least 40.0 to 41.5ºC (104 to 106.7ºF) depending on author. Shibolet presented one of the most complete, though small, series of patients with apparent exertional heat illness classified as heat stroke in which more complete "modern" advanced clinical and laboratory evaluation was performed.(Shibolet et al., 1967) Shibolet used entry diagnostic criteria "during exertion of sudden collapse and loss of consciousness, sometimes preceded by brief irrational behavior." He noted that seizures, though common among persons more severely affected, as defined by persistent unconsciousness and evidence at presentation of coagulopathy, occurred at presentation in only one of six patients who seized in his series of 36 patients. Shibolet also made the point that very little was known of the premonitory states of patients suffering heat stroke since the more severe cases died. Among the less severe cases in his series, however, patients reported marked thirst, dizziness and sudden increase in sweating. Additionally, persons who have been found to meet the temperature criteria have been noted to manifest only mild alterations in mental status with changes such as irritability.{Casa, 2005 #1013}

Hyperthermia

Elevated temperature can be a significant factor in creating cell damage in *in vitro* laboratory tests, but an exact temperature at which cell damage will begin to occur in humans has not been established. Several threads of research demonstrate that well-hydrated, resting humans can survive core body temperatures up to 42ºC (108ºF) for a at lease one hour without serious or lasting adverse reactions.(Bynum et al., 1978) Both athletes and human exercise experimental subjects have been documented to function without adverse effects at core body temperatures as high as 41.5 ºC (106.7 ºF). (Robinson, 1963), (Pugh et al., 1967), (Byrne et al., 2006) These findings imply that other factors than core body temperature are important in the process of precipitating heat-associated SIRS.

To further complicate the discussion regarding whether it is the core body temperature that defines heat stroke are studies of whole body hyperthermia for cancer treatment. Hyperthermia has been explored for cancer treatment since the late 1800s. More recent work has demonstrated whole-body hyperthermia to have a positive effect in certain resistant cancers. The protocols use a target core temperature of around 41.8ºC (107.2ºF) maintained for an hour, following which patients are allowed to cool by removing from the heat source and any added insulation with no active cooling intervention. (Robins et al., 1985), (Atmaca et al., 2009) Multiple reports document no events of heat stroke. The only adjunct treatment that would likely have a protective effect in these hyperthermic settings is that patients received intravenous saline or dextrose and saline during the treatments. Maintenance of a well-hydrated and resting state may

both contribute to the body's ability to tolerate these core temperatures in this clinical setting. One technique of heating involves immersing the person in warmed paraffin, thus a setting in which the body cannot cool by evaporation of sweat.

Mental status

Most frequently the literature refers to "severe" changes in mental status, often citing the presence of delirium, coma or seizures as differentiating heat stroke from heat exhaustion, which has been associated with "minor" mental status changes such as confusion or irritability. One retrospective descriptive chart review study of a ten-year experience in an Israeli hospital that identified 32 patients with a diagnosis of exertional heat stroke did not utilize the criteria noted above, but did identify 4 patients who presented in coma and 2 with seizures. Fifteen patients were identified as having presented with variations of "confusion, disorientation" or "psychomotor agitation."(Zeller et al., 2011) This study exemplifies the difficulty non-standard diagnostic criteria presents in analyzing the literature related to heat disorders.

As noted above in the discussion of Heat Exhaustion, changes in behavior, which may be indistinguishable from early stages of delirium, are also associated with exhaustion that may not proceed to heat stroke. Since persons who reach exhaustion effectively begin at least one treatment method for potential heat stroke simply by stopping any activity and the associated muscular production of heat, there is no good way to precisely decide that they are not actually in a physiological state that may go on to heat stroke *if* they had not stopped activity or *if* they have other associated conditions that would predispose to developing a SIRS of "severe" heat stroke. Even when a person stops heavy physical activity, heat production and transfer to the core from heated muscles does not stop immediately. There may be a continued increase, albeit small, in core temperature in the first few minutes following cessation of muscle activity.

Factors Influencing Risk of Developing Heat Stroke

As noted in the above discussion regarding the pathophysiology of heat stroke and the imprecisions of clinical signs, the question has been addressed of what other factors than environmental heat and exertion my contribute to individual susceptibility. Knowledge of these additional risk factors will likely be of use for assisting persons who are not in obvious severe distress; for example, hot with delirium or coma.

Minard proposed a useful methodology for classifying and evaluating the presence of potential predisposing factors which was summarized and referenced in a presentation of a series of heat stroke cases occurring among Israeli army recruits. (Rav-Acha et al., 2004) Minard proposed three groups of predisposing factors: individual physiologic limiting factors; environmental factors; training organization factors. Knowledge of these factors may assist in recognizing a person with questionable signs of early heat stroke as being at elevated risk. A detailed discussion of these factors is beyond the scope of this review. However, several of the more important factors are presented in the following table with a brief comment on the manner in which they influence the risk of developing heat stroke.

Table 8: Predisposing Factors for Heat Stroke

Factor	Influence
Dehydration	Since the primary cooling mechanism in settings of heat stress and exertion is sweating (Stolwijk and Hardy, 1971) which requires dilated

	skin blood vessels, if persons are inadequately hydrated, the body will have difficulty supplying the skin, exerting muscles and internal organs. This may also lead to bowel ischemia with associated endotoxin leakage as discussed in the text.(Leon and Helwig, 2010a)
Acclimatization	As persons spend time in elevated heat stress environments, adaptation mechanisms occur such as increased volume of sweating for similar activity with decreased salt content of sweat.(Allan and Wilson, 1971)
Obesity	Obesity is associated with elevated levels of pro-inflammatory cytokines that may decrease the threshold for setting in motion a SIRS related to heat stress.(Vendrell et al., 2004)
Physical Fitness	The relationship is not fully defined, but is speculated to possibly relate to decreased levels of inflammatory proteins associated with physical fitness.(Pedersen and Hoffman-Goetz, 2000), (Pedersen, 2006)
Recent or current systemic or local infectious illness	Shibolet reported one case of severe heat stroke with a pyrexic illness one week prior to suffering fatal heat stroke and two victims with diarrhea for 2 days prior to heat stroke.(Shibolet et al., 1967) One series of 28 cases of EHS 14% had a history of URI for a few days prior to the episode of exertion.(Sithinamsuwan et al., 2009) One case report of a military study subject with irritated, open foot blister that became cellulitic demonstrating increased body temperature rise from same exertion compared to day without blister.(Carter et al., 2007)
Lack of sleep	Review of military cases has shown several with association of lack of sleep in the day or two prior to exertion to be associated with heatstroke.(Shibolet et al., 1967), (Rav-Acha et al., 2004) Unfortunately, in the case reports, no information was given regarding sleep status of those participants in the activity who did not experience heat stroke. Sleep loss has been shown to be associated with increased inflammatory signaling.(Irwin et al., 2008)

Fluids Treatment in Impending Heatstroke

An analysis of patient records from victims of what was diagnosed as heat stroke in relation to a heat wave in France in 2003 revealed that many of the patients were either hyponatremic or hypernatremic.(Misset et al., 2006) The long term outcome was much worse for those who were hypernatremic. There is no reliable clinical, non-laboratory way to differentiate hypo and hypernatremia. This information suggests that any oral rehydration given to persons who seem at high risk of developing non-exertional heat stroke should not include liquids with sodium concentrations higher than normal blood concentrations. Normal blood serum sodium concentration is approximately 140±5 mEq/L which equates to slightly less than 1.5 teaspoons (9 grams) table salt (NaCl) dissolved in 1 liter water (154 mEq Na/L). See section on rehydration fluid suggestions in discussion of heat cramps above for more information on rehydration liquids.

Clinical Decisions in Potential Heat Stroke

These complicated and intertwined pathophysiological interactions that have been identified and implicated in heat stroke do not, unfortunately help greatly either with on-site clinical determination of which person with some degree of weakness and/or mild alteration in mental functioning might be in the early enough stages of heat stroke where cessation of activity, cooling and oral rehydration will resolve the situation or how to recognize those cases of persons collapsing while exerting in heat who need not only immediate cooling, but transfer to a higher level of care.

Considering the articles retrieved since the 2009SR regarding innovative therapies directed at aborting development of a SIRS, early initiation of cooling and transport to hospital level care with continued cooling of persons suspected of developing heat stroke should not be delayed. It is far better to err on the side of caution by transporting some persons who may not be "over the edge" into developing a SIRS.

Exercise Associated Hyponatremia

This is a fully preventable disorder that arises in settings of elevated sweating and consuming high volumes of lower in sodium content than normal blood concentrations, effectively disproportionately replacing the water and not the salt lost in sweat. Sports drinks are hypotonic to serum; that is, they have a lower concentration of sodium than serum.(see Table 5 above) Thus, consumption replaces water disproportionately to sodium. Concern has been raised as to whether marketing messages from the sport drink industry may have contributed to the incidence of hyponatremia associated with endurance sports events.(Noakes and Speedy, 2006), (Winger et al., 2011) Noakes's assessment of the situation has been challenged in a lively debate of letters to the editor of the British Journal of Sports Medicine.(Murray, 2007), (Noakes and Speedy, 2007b), (Roberts, 2007b), (Noakes and Speedy, 2007c), (Epstein and Cohen-Sivan, 2007), (Noakes and Speedy, 2007a) Further discussion of this important topic is beyond the scope of this review.

Appendix B – Temperature Equivalents

Since the majority of the scientific literature refers to body temperatures in Celsius/centigrade temperatures were cited in Celsius in the discussion above. Since the Fahrenheit scale is still more commonly used by the general public in the US, this appendix is simply a listing of several temperatures used in the discussion above in Celsius and Fahrenheit.

^{o}C	^{o}T	Comments
37	98.6	"Normal" body core temperature
40.0	104	
40.5	104.9	Commonly cited as criterion for heat stroke
41	105.8	
41.5	106.7	

Appendix C – 2009 SR Therapeutic recommendations and evidence

The 2009 SR presented a table of proposed therapeutic interventions for heat cramps. The reverences for these were largely review articles. Within these review articles, when there were citations in support of statements, they, frequently, referred to another review article or textbook chapter. Subsequent review of these citations revealed often another layer of review articles or textbooks. A table is presented here charting these relationships.

Table 9: 2009 SR Cramp treatment table reference expansion

2009 SR Statement	References cited in 2009SR	Reference Statements	Source Citations
Discontinue all activity and sit in a cool environment.	Coris EE, Ramirez AM, Van Durme DJ. Heat illness in athletes: the dangerous combination of heat, humidity and exercise. *Sports Med.* 2004;34(1):9-16. *Review article*	Stretch, ice massage, oral fluids (No mention of sitting in cool environment)	No citation
	Dreyer AR, Kulesa MG. Hot Topic: Hyperthermia-related Disorders. *Orthopaedic Nursing* 2002 21 (1):45-53. *Review article*	Cessation of activity, mild cooling, oral hydration with an electrolyte solution, icing affected muscles.	- CDC website on heat illness – same statements as in 1988 NIOSH bulletin – No citation in either for recommendations - Rich, B. (1996). Environmental concerns: Heat. In R. Sallis & F. Massimino (Eds.), Essentials of sports medicine (pp. 349- 356). St.Louis: Mosby (Reference not pursued due to being a book not available to this reviewer and low likelihood that a book would report initial research findings.)
	Griffin LY. Emergency preparedness: things to consider before the game starts. *Instructional course lectures.* 2006;55:677-686. *Review article*	Rest and stretch the affected muscle, Drink sports drinks to help replace fluids and sodium.	Table reprinted "with permission" from Gatorade Sports Medicine Institute tip sheet 2002

Rehydrate using water (may add 1/8–1/4 teaspoon of table salt to 10-16 oz of fluids or bullion broth) or a commercial electrolyte solutions (Sports Drinks – 16 to 20 ounces) (sic)	Armstrong LE, Casa DJ, Millard-Stafford M, Moran DS, Pyne SW, Roberts WO. American College of Sports Medicine position stand. Exertional heat illness during training and competition. *Med Sci Sports Exerc.* Mar 2007;39(3):556-572. *Review article*	oral NaCl ingestion in fluids or foods (i.e., 1/8–1/4 teaspoon of table salt added to 300–500 mL of fluids or sports drink, 1–2 salt tablets with 300–500 mL of fluid, bullion broth, or salty snacks).	No citation
	Binkley HM, Beckett J, Casa DJ, Kleiner DM, Plummer PE. National Athletic Trainers' Association Position Statement: Exertional Heat Illnesses. *J Athl Train.* Sep 2002;37(3):329-343. *Review article*	replace lost fluids with sodium-containing fluids,	No citation
		A high-sodium sports product may be added to the rehydration beverage to prevent or relieve cramping in athletes who lose large amounts of sodium in their sweat.19	19. 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. This source was reviewed and presented no experimental evidence
		A simple salted fluid consists of two 10-grain salt tablets dissolved in 1 L (34 oz) of water.	No citation

		Intravenous fluids may be required if nausea or vomiting limits oral fluid intake; these must be ordered by a physician. 6,7,52,90,91	**6**. Rich B. Environmental concerns: heat. In: Sallis RE, Massimino F, eds.*Essentials of Sports Medicine.* St Louis, MO: Mosby Year Book; 1997:129–133. (Reference not pursued) **7**. Casa DJ. Exercise in the heat, II: critical concepts in rehydration, exertional heat illnesses, and maximizing athletic performance. *J Athl Train.* 1999;34:253–262. (salt tablets in water (2 10-grain salt tablets dissolved in 1 L of water) or intravenous saline if nausea and vomiting are present. – referenced to Hubbard RW, Armstrong LE. Hyperthermia: New Thoughts on an Old Problem. The Physcian and Sportsmedicine. 1989;17(6) which has no citation, but stated as if from personal experience.) **52**. Casa DJ, Armstrong LE, Hillman SK, et al. National Athletic Trainers' Association position statement: fluid replacement for athletes. *J Athl Train.* 2000;35:212–224. (Recommends transport to hospital if athlete unable to tolerate oral rehydration so may receive IV – references his article noted next) **90.** Casa DJ, Maresh CM, Armstrong LE, et al. Intravenous versus oral rehydration during a brief period: responses to subsequent exercise in the heat. *Med Sci Sports Exerc.* 2000;32:124–133. (This article is a physiological study of subjects artificially rendered dehydrated and observation of exercise performance. It does not address the use of IV fluids as a back-up treatment for cramping.) **91.** Noakes T. Failure to thermoregulate. In: Sutton J, Thompson M, Torode M, eds. *Exercise and Thermoregulation.* Sydney, Australia: The University of Sydney; 1995:37. (Book – not pursued)
	Wexler RK. Evaluation and treatment of heat-related illnesses. *Am Fam Physician.* Jun 1 2002;65(11):2307-2314. *Review article*	Liberal intake of water is recommended, but this may induce hyponatremia if lost salt is not replaced Commercial electrolyte solutions may help to prevent excessive salt loss,	11. Birrer RB. Heat stroke: don't wait for the classic signs. Emerg Med 1996;28:52. Emergency Medicine is a non-peer reviewed publication. The article was not retrieved to check references.

		and a homemade formula of 1 tsp salt in 500mL of water may also be used.[11]	
May add 0.5 teaspoon (3 g) of salt to the sports drink.	Bergeron MF. Exertional heat cramps: recovery and return to play. J Sport Rehabil. Aug *2007;16(3):190-196.*	No data - No Citation	
Prolonged stretch with the muscle groups at full length.	Armstrong LE, Casa DJ, Millard-Stafford M, Moran DS, Pyne SW, Roberts WO. American College of Sports Medicine position stand. Exertional heat illness during training and competition. Med Sci Sports Exerc. Mar 2007;39(3):556-572. *Review article*	EAMC responds well to rest, prolonged stretch with the muscle groups at full length,	**NOTE:** Armstrong used the designation EAMC throughout this document in reference to heat cramps. A distinction has been made between the two entities in other literature. This is discussed in the text of Appendix A.
	Dreyer AR, Kulesa MG. Hot Topic: Hyperthermia-related Disorders. *Orthopaedic Nursing* 2002 21 (1):45-53. *Review article*	Gentle stretching *before* exercise can prevent heat cramps. (italics added)	Review article - No specific citation for this statement – section referenced to - CDC website on heat illness – same statements as in 1988 NIOSH bulletin – No citation in either for recommendations - Rich, B. (1996). Environmental concerns: Heat. In R. Sallis & F. Massimino (Eds.), Essentials of sports medicine (pp. 349- 356). St.Louis: Mosby (Reference not pursued)
	Wexler RK. Evaluation and treatment of heat-related illnesses. *Am Fam Physician.* Jun 1 2002;65(11):2307-2314. *Review article*	Stretching the affected muscles and maintaining good hydration are important.	
Apply an ice application, either crushed ice or ice massage	Coris EE, Ramirez AM, Van Durme DJ. Heat illness in athletes: the dangerous combination of heat, humidity and exercise. *Sports Med.* 2004;34(1):9-16. *Review article*	Stretch, ice massage, oral fluids	Review article – no citation

	Dreyer AR, Kulesa MG. Hot Topic: Hyperthermia-related Disorders. *Orthopaedic Nursing* 2002 21 (1):45-53. *Review article*	icing affected muscles	- CDC website on heat illness – same statements as in 1988 NIOSH bulletin – No citation in either for recommendations - Rich, B. (1996). Environmental concerns: Heat. In R. Sallis & F. Massimino (Eds.), Essentials of sports medicine (pp. 349- 356). St.Louis: Mosby (Reference not pursued)
Eat a well- balanced meal to ensure adequate consumption of electrolyte. If inadequate access to meals, or meals are not eaten regularly is a common occurrence, consider adding sodium chloride (salt) at meal time.	Bergeron MF. Exertional heat cramps: recovery and return to play. J Sport Rehabil. Aug *2007;16(3):190-196.*	This is not applicable to a first-aid intervention.	
Do not return to strenuous activity for a few hours after the cramps subside, because further exertion may lead to heat exhaustion or heat stroke.	D Dreyer AR, Kulesa MG. Hot Topic: Hyperthermia-related Disorders. *Orthopaedic Nursing* 2002 21 (1):45-53. *Review article*	- CDC website on heat illness – same statements as in 1988 NIOSH bulletin (No citation in either for recommendations) - Rich, B. (1996). Environmental concerns: Heat. In R. Sallis & F. Massimino (Eds.), Essentials of sports medicine (pp. 349- 356). St.Louis: Mosby (Reference not pursued)	**NOTE**: The second part of this recommendation – the precaution regarding progression to heat exhaustion or heat stroke is not supported by reported experience of athletes returning to play in the same session without progression.

Seek medical attention for heat cramps if they do not subside in 1 hour or spread to other parts of the body.	No Citation	**NOTE:** Though this seems like a reasonable recommendation, there is no data to support the 1 hour time frame versus some other parameter. Additionally, by definition, heat cramps are diffuse.	

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