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Confronting heatstroke: Understanding, preventing and treating a deadly condition

Dujrath Somboonviboon, Pattanapol Aramareerak, Amornchai Lertamornpong, Kunchit Piyavechviratana

Division of Pulmonary and Critical care Medicine, Phramongkutklao Hospital, Bangkok, Thailand, 10400

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Corresponding author:

Dujrath Somboonviboon
Division of Pulmonary and Critical care Medicine, Phramongkutklao Hospital, Bangkok, Thailand, 10400
Tel: (+66) 27-639-3319
E-mail: Dujrath@gmail.com

ABSTRACT:

Heatstroke is a potentially fatal condition that occurs when the body's thermoregulatory responses are overwhelmed by excessive heat. This review provides an overview of heatstroke, discussing risk factors, pathophysiology, and clinical presentation. Emphasis is placed on the importance of early recognition, prompt diagnosis, rapid cooling, and various cooling strategies, along with organ-supportive care, to improve patient outcomes. Additionally, the review underscores the need for increased awareness and public health initiatives to prevent and manage this life-threatening condition.

Keywords: Heatstroke; Heat-related illness; Hyperthermia; Exertional; Cooling therapy

INTRODUCTION

Heatstroke is a life-threatening condition within the spectrum of heat-related illnesses, progressing from heat exhaustion. It is clinically diagnosed by elevated core temperature greater than 40 degrees Celsius (°C) accompanied by central nervous system dysfunction, which can include seizures and altered consciousness ranging from confusion to coma [1]. Heatstroke is generally characterized as either classic or exertional, depending on its cause. Classic heatstroke results from passive exposure to severe environmental heat, while exertional heatstroke is associated with strenuous physical activity. Despite their different causes, both types occur due to the body's failure to dissipate excessive heat.

Classic heatstroke, also referred to as non-exertional heatstroke, usually occurs among vulnerable individuals such as chronically ill persons, children and elderly people who cannot care for themselves. Elderly individuals, in particular, have an impaired ability to adjust physiologically to heat stress and dissipate heat [2]. Additionally, children, left unattended in parked vehicles can suffer fatal consequences within a few hours. [2]

Exertional heatstroke is directly related to strenuous physical activity in hot and humid environments and can occur among healthy individuals, such as athletes during sporting events, soldiers in military training, agricultural workers, or firefighters in certain situations [3].

Climate change and global warming are causing an increase in average temperatures and increasing the frequency of heat-related illness [4]. This rise in temperature presents a significant public health challenge, emphasizing the need for early recognition, prompt and effective management to combat the increasing incidence of heatstroke.

RISK FACTORS

Several factors contribute to the development of heatstroke, including environmental factors, host factors, and predisposing medications, as shown in Table 1 [2,3,5-7].

PATHOPHYSIOLOGY

Thermoregulation is a body process controlled by the anterior hypothalamus to maintain a body temperature of 37 °C. Mechanisms for dissipating body heat include evaporation, radiation, convection, and conduction [8,9] (Figure 1). When body temperature rises, peripheral and hypothalamic heat receptors signal the hypothalamic thermoregulatory center. This response increases the delivery of heated blood to the body surface, reducing visceral perfusion, particularly in the intestines and kidneys. Meanwhile, active sympathetic cutaneous vasodilatation initiates thermal sweating, especially if the surrounding air is not saturated with water [1,8,10]. Thus, dehydration impairs thermoregulation. An elevated blood temperature also leads to tachycardia, increases cardiac output, and raises minute ventilation.

Heatstroke occurs when the body's thermoregulatory responses are overwhelmed by excessive heat loads. The body's heat dissipation becomes compromised, causing core body temperature to continue rising, which leads to a direct cytotoxic effect and an inflammatory response, resulting in multiorgan failure [2]. The release of cytokines and the high-mobility group box 1 protein (HMGB1), which are endogenous molecules, causes excessive activation of leukocytes and endothelial cells, leading to systemic inflammatory reactions [2]. Due to this inflammatory response, heatstroke is considered 'a form of hyperthermia linked to a systemic inflammatory response, resulting in a syndrome of multiorgan dysfunction where encephalopathy is the predominant feature' [1].

KEY MESSAGES:

- Heatstroke is a critical medical emergency and diagnosed by clinical presentation of the triad of hyperthermia, neurological symptoms, and history of heat exposure.
- Early diagnosis, along with rapid cooling and supportive care, is crucial for improving patient outcomes.

Heatstroke-induced decreases in intestinal blood flow cause gastrointestinal ischemia, leading to increased cell wall permeability. Consequently, endotoxins leak from the intestinal mucosa to the systemic circulation, along with interleukin (IL)-1 or IL-6 proteins moving from the muscles to the systemic circulation [10].

CLINICAL PRESENTATIONS

Patients with heatstroke typically present with a constellation of symptoms, including hyperthermia, altered mental status, confusion, nausea, vomiting, headache, and signs of multiorgan failure (Figure 2).

DIAGNOSIS

The diagnosis of heatstroke is clinically based on the triad of hyperthermia, defined as a core body temperature greater than 40 °C, neurologic dysfunction, and recent exposure to a hot environment (in the classic form) or physical activity (in the exertional form) or both [2].

Table 1. Risk factors of heatstroke.

Environmental factors	Host factors	Medications or substance
<ul style="list-style-type: none"> • High temperatures • High humidity • Heatwaves • Lack of access to water • Long duration of heat exposure • Lack of heat acclimatization • Unventilated and non-air-conditioned living space • Inappropriate clothing • Over motivation, under peer and coach pressure 	<ul style="list-style-type: none"> • Older age • Prepubertal children • Undomiciled • At-risk occupations (outdoor workers, soldiers, firefighters) • Obesity • Impaired cognitive function (dementia, Parkinson's disease, Psychotic disease) • Comorbidities (Diabetes mellitus, cardiovascular disease, pulmonary illness, sweat gland dysfunction or skin disorders) • Concurrent infections • Pre-existing dehydration • Poor physical condition (sedentary lifestyle, low physical fitness levels) • Sleep deprivation • Previous episode of heat illness 	<p>Medications</p> <ul style="list-style-type: none"> • Anticholinergics • Antipsychotics • Benzodiazepines • Beta-blockers • Calcium-channel blockers • Diuretics • Laxatives • Lithium • Tricyclic antidepressants • Serotonin-reuptake inhibitors • Thyroid medication <p>Substance/Drugs</p> <ul style="list-style-type: none"> • Cocaine, heroin, amphetamines, amphetamine-like agents, alcohol

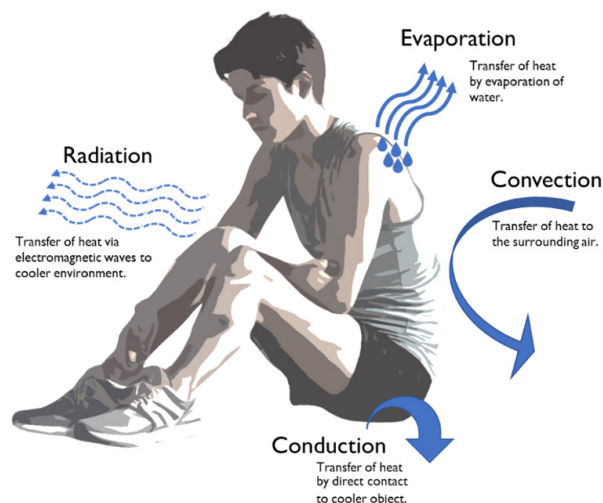


Figure 1. Mechanisms of body heat dissipation including evaporation, convection, conduction and radiation.

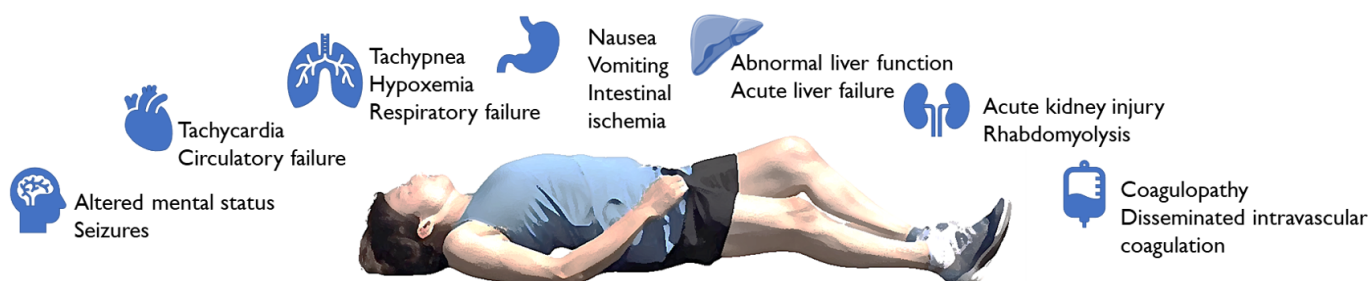


Figure 2. Clinical presentation of multiorgan failure in heatstroke.

Differential diagnosis

Other systemic diseases that present with similar symptoms of fever and neurological dysfunction, such as meningitis, encephalitis, intoxication, and any metabolic syndrome (e.g., neuroleptic malignant syndrome, serotonin syndrome, thyroid storm, or pheochromocytoma crisis), should also be considered [2]. However, delaying heatstroke treatment increases morbidity and mortality. Therefore, these other diseases should be considered after initiating cooling management and ruling out heatstroke.

MANAGEMENT

There is limited high-quality direct evidence regarding management of heatstroke, with most data based on observational studies, case series, or case reports. Optimal treatment of heatstroke involves immediate rapid cooling and supportive care, including fluid resuscitation and organ support in an intensive care unit (ICU) setting. Therefore, patients with heatstroke should receive prompt initiation of cooling and multidisciplinary ICU care [7].

Cooling therapy

Treatment begins with maintaining the airway, breathing, and circulation, followed immediately by rapid cooling. Regardless of the classification, rapid cooling should com-

mence promptly and continue during transfer. Effective dissipation of heat relies on the rapid transfer of heat from the core to the skin and then to the external environment. The aim of therapeutic cooling techniques is to facilitate this transfer without compromising blood flow from the core to the skin. This is achieved by increasing the temperature gradient between the skin and the environment through conduction, enhancing the gradient of water vapor pressure via evaporation, and increasing the velocity of the surrounding air over the skin through convection [1,11]. Cooling therapy can be broadly classified into conventional and modern techniques, as detailed in Table 2. The selection of cooling methods should be based on the availability of devices and resources at the healthcare facility. The cooling rates associated with each technique are illustrated in Figure 3A [7].

Conventional cooling techniques are categorized as conduction, evaporation, and convection based on these heat dissipation principles. Conductive cooling techniques involve direct contact of cooler objects with the skin, including ice or cold-water immersion, ice sheets, tarp-assisted cooling oscillation (TACO), cooling blankets, and ice packs applied to the neck, groin, and axillae. Evaporation and convection techniques rely on the principle that water converts to gas, consuming heat. To accelerate evaporation, water is sprayed and air is blown over it [2,11].

Table 2. Cooling methods for heatstroke.

Conventional cooling methods	Modern cooling methods
Conduction <ul style="list-style-type: none"> • Ice or cold-water immersion • Tarp-assisted cooling oscillation (TACO) • Ice sheets • Ice or cold packs applied to neck, groin and axillae • Cooling blanket Evaporation and convection <ul style="list-style-type: none"> • Spraying water and blowing air Others <ul style="list-style-type: none"> • Cold fluid infusion • Cold water gastric lavage • A three-way foley catheter bladder irrigation. 	<ul style="list-style-type: none"> • Closed circuit endovascular cooling catheter • Automated surface cooling device • Extracorporeal circulation cooling system

Cold fluid infusions (4°C) have been widely used and are associated with more rapid cooling; however, the rate is insufficient to be considered as a primary cooling strategy. Therefore, cold intravenous (IV) fluid can be considered an adjunct to other external cooling methods, particularly in patients requiring fluid replacement. Cold-water irrigation of a nasogastric tube or bladder is not routinely recommended, as these methods result in only minor reductions in core temperature and require significant time from medical staff [7]. Thus, these methods may be employed only to supplement other cooling techniques if the core temperature is not decreasing at the desired rate.

Modern cooling devices, such as closed-circuit endovascular cooling and surface cooling devices, have been utilized in post-cardiac arrest care. These devices can also be employed to treat patients with both classic and exertional heatstroke by accelerating cooling and improving patient comfort. However, further studies are needed to assess their efficacy [11,12]. The ideal time frame for cooling is within 30 minutes, with an initial target temperature between 38 and 39 °C [7,13]. Taking over 60 minutes to reach the target temperature is associated with adverse outcomes and mortality [14].

For exertional heatstroke, cooling rates of greater than 0.15°C per minute are desirable and are associated with reduced mortality [15]. Ice-cold water immersion has been used as the gold standard for achieving this target cooling rate in exertional heatstroke [16]. A recent study demonstrated that ice sheets (bed sheets soaked in ice water) or TACO can be an effective alternative for treating exertional heatstroke when cold water immersion is not available [17,18].

In elderly patients with classic heatstroke, the treatment of choice involves the use of a cold fluid infusion, the application of ice packs, cold packs, or wet gauze. Although these methods are less efficient than ice or cold-water immersion, they are better tolerated by vulnerable patients [2].

The role of medications in decreasing core temperature is minimal. Dantrolene is used to manage malignant hyperthermia, but its effects on temperature control in heatstroke have been mixed and did not demonstrate an improvement in clinical outcomes in previous studies

[19,20]. Antipyretics, including nonsteroidal anti-inflammatory drugs and acetaminophen, are ineffective in heatstroke and also increase risks for kidney and hepatic injury [7].

SUPPORTIVE THERAPY

Despite cooling management, most heatstroke patients develop multiorgan failure and require ICU admission.

Temperature management

The optimal temperature target after initial cooling is unclear. It is generally suggested to maintain normothermia, with a body temperature between 36.5 and 37.5 °C. Temperatures above 37.5 °C tend to reduce survival in critically ill non-infective patients, with a significant decrease in survival seen above 38.5 °C [5]. During cooling management, patients may experience shivering and agitation. Thus, sedation with benzodiazepines is suggested regarding a theoretical benefit in blunting the shivering reflex and reducing oxygen consumption [5,21].

Fluid management

In heatstroke, blood flow redistribution to the skin, along with vasodilatation, can decrease preload and impair perfusion. Additionally, heatstroke is also often associated with hypovolemia due to dehydration and excessive sweating. Therefore, circulatory failure is common, making appropriate volume management vital [7]. Aggressive fluid administration is indicated when rhabdomyolysis is suspected. However, caution is warranted with large fluid amounts in cases with signs of right-sided heart failure, pulmonary edema, or acute respiratory distress syndrome (ARDS). Thus, fluid management should be carefully monitored and adjusted using dynamic fluid assessment. Crystalloids, especially normal saline, are preferred for fluid resuscitation in heatstroke patients due to the potential development of hyponatremia and hypochloremia from sweat loss [7,22].

Treatment of complications

Treatment of complications in heatstroke, including multiorgan failure (Figure 3B), involves managing con-

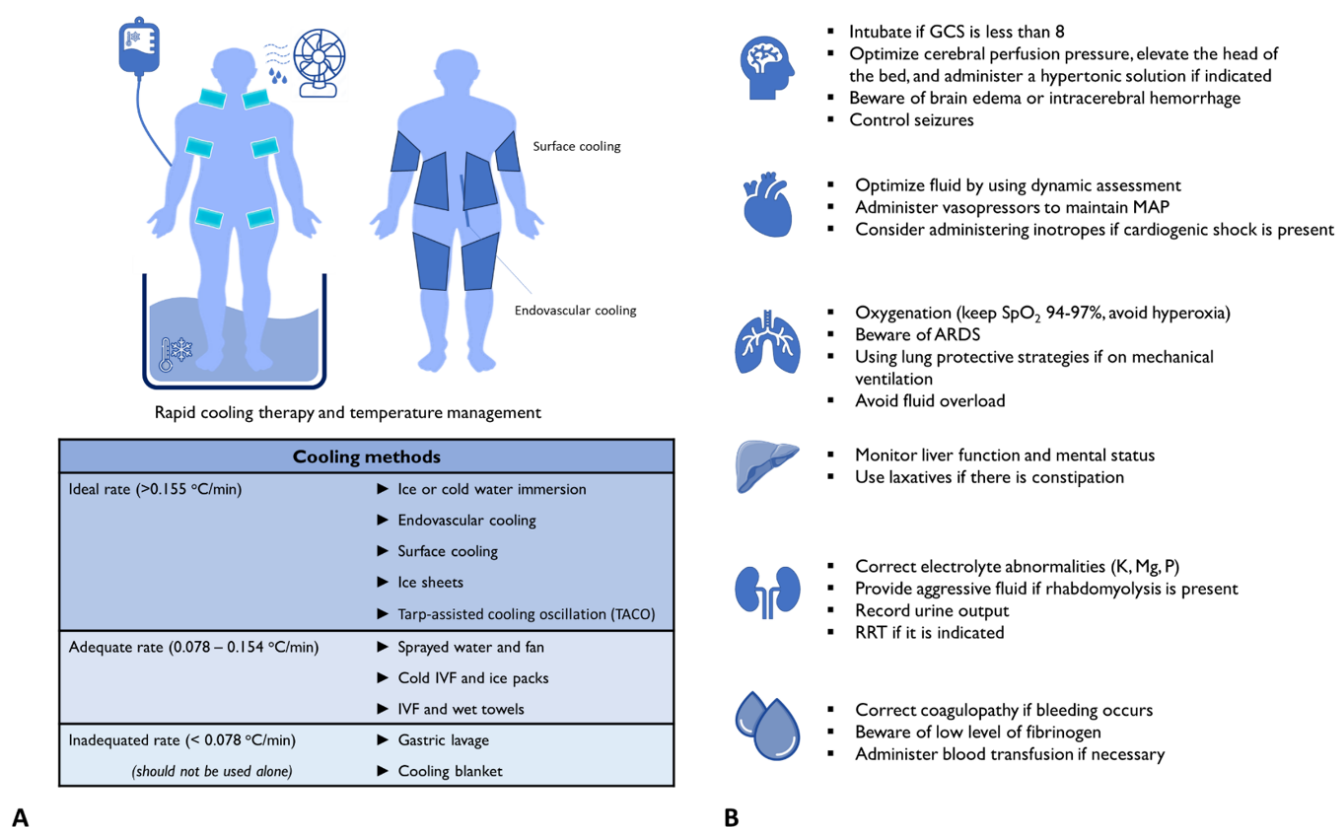


Figure 3. Management in heatstroke involves immediate rapid cooling (A) and supportive care and organ support (B) in an intensive care unit (ICU) setting. **Abbreviations:** ARDS: Acute Respiratory Distress Syndrome; GCS: Glasgow coma scale; IVF: Intravenous fluid; K: Potassium; MAP: Mean arterial pressure; Mg: Magnesium; P: Phosphate; RRT: Renal Replacement Therapy; SpO_2 : Saturation Pulse Oximetry.

ditions such as seizures, increased intracranial pressure, shock, ARDS, acute kidney injury, liver dysfunction, disseminated intravascular coagulation, and coagulopathy. Similar to other critical conditions like trauma or sepsis, these complications require intensive care with a multidisciplinary approach [5,7,12].

PREVENTION

During the summer, clinicians should identify vulnerable patients and inform them and their caregivers of the potential risks. On extremely hot days, they should counsel them on recognizing high-risk heat conditions and the signs and symptoms of heat-related illnesses, providing clear instructions on how to reduce risk and when to seek medical attention [13].

Heat acclimatization, which is a hot environment adaptation, allows people to work safely at levels of heat that were previously intolerable. This process usually takes several weeks with enhancement of cardiovascular system, increased renin-angiotensin-aldosterone activity, salt conservation by kidneys and sweat glands, a rise in glomerular filtration rate, and expansion of plasma volume [1]. In higher-risk heat conditions, practices and sports events should be scheduled at cooler times of the day and allow for more rest breaks [13].

Improving public awareness and education on heatstroke prevention and management can reduce the incidence and severity of heat-related illness.

FUTURE DIRECTION

Future research and innovation in the prevention, diagnosis, and management of heat stroke are essential to improve patient outcomes. Advancing technologies and strategies for early detection and effective treatment are needed to better protect at-risk populations. Furthermore, developing comprehensive public health policies that address heatstroke prevention will be vital in safeguarding against both exertional and classic heatstroke.

CONCLUSION

Heatstroke, whether classic or exertional, is a severe condition requiring immediate medical attention. Rapid diagnosis and prompt initiation of cooling and supportive care are crucial.

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