

Review Article

An analysis of heat-related illnesses in children due to immoderate temperatures

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ABSTRACT

Soaring temperatures, as a result of climate change, is impacting all beings across the globe. This has led to multiple illnesses and emergency room visits, during extreme temperatures, especially summers. The most vulnerable to scorching heat are infants, children and adolescents along with the elderly. Heat-related illnesses (HRIs) may range from minor forms, such as prickly heat, to severe, life-threatening conditions such as heatstroke. Pediatricians need to be aware of the varying physiologies and behaviors the children might present as a result of HRI and predisposing factors that may put them further at risk. Although the pathophysiology of HRI is understood, the scope of pharmacotherapy to treat them is limited. Currently, prevention is the best course of action against HRIs. Thus, the escalating average temperatures and challenges, posed by climate change, demand a review of the existing preventive and treatment strategies for HRIs. This article hence, attempts to compile the different kinds of HRIs along with their pathophysiology, causes, and detection and how they can be prevented and treated among children.

Keywords: Heat-related illnesses, children, athletics, acclimatization, heat

Unprecedented amounts of heat exposure are being caused by climate change, which is raising average world temperatures and intensifying, prolonging, and causing recurring extreme heat events [1]. The last seven years have been the hottest on record, and recent high-heat events in Europe (2022), India (2022), and the Pacific Northwest of the United States (2021) have all been significantly exacerbated or caused by climate change [2]. Over one-third of all warm-season heat-related deaths worldwide are linked to climate change, and the mortality rate from heat-related causes has increased by 54%, among those over 65, in the last 20 years [3,4].

The majority of the world is predicted to experience frequent extreme heat events in the upcoming decades [5] due to our current trajectory of global greenhouse gas emissions, which is expected to warm the planet by 2°C over preindustrial temperatures by midcentury. Previously, once-in-10-year, heat waves were projected to occur more than 5 times as frequently, and once-in-50-year events almost 14 times as frequently [6]. Increased global health costs and significant economic losses are already a result of high temperatures and heat waves [1].

Humans use behavioral and autonomic processes, such as sweating and vasodilation, to thermoregulate, keeping their internal body temperature around 37°C. An internal heat load is produced by metabolic activity, while exogenous heat from the surroundings increases the overall heat burden that needs to be controlled. Higher humidity levels, which are factored into the heat index, make it more difficult to dissipate heat. The human body's capacity to regulate its temperature may be overtaxed or stressed under extreme heat loads brought on by external heat, internal heat, or both. This can lead to a variety of heat-related disorders. Heat exhaustion, heat syncope, heat edema, cramps, and heat rash are examples of non-life-threatening disorders. Heat stroke, which results from a rise in body temperature above a critical threshold, is a serious condition.

According to the American Academy of Paediatrics Committee on Environmental Health [9], children are defined as humans under the age of 18, with infants being those under the age of one year. Children's vulnerability to heat waves may be heightened by the following differences between them and adults:

Access this article online

Received – 10th May 2024Initial Review – 25th May 2024Accepted – 10th June 2024

DOI: 10.32677/ijch.v11i5.4691

Quick Response Code



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(1) Physiological modality: children's bodies have a higher surface area-to-mass ratio and less developed thermoregulatory mechanisms than adults', which permits the body to absorb more heat and cold from the surroundings [10]. (2) Metabolic modality: children may be more susceptible to heat waves due to their greater metabolic rates [11]. (3) Cardiovascular modality: children's cardiac output is lower than adults' at a given exercise level (12). Furthermore, compared to adults, children, particularly newborns, have a lower cardiac index, which may lead to varying physiologic responses to heat waves.

(4) Behavior modality: Children may be more exposed to the outdoors at certain developmental stages if they spend more time outside and engage in more physically demanding activities than adults [13]. (5) Self-care ability modality: newborns and young children under two years old, in particular, are unable to care for themselves and must rely on others to keep them safe from dangerous situations [14]. (6) Life expectancy modality: a longer amount of time to experience the delayed negative health effects of exposure to intense heat is also provided by a higher predicted future life expectancy [15,16].

The frequency of heat-related illnesses and injuries (HRI) is rising as the earth warms [17]. Children make up nearly half (47.6%) of the population of people with HRI [17]. First of all the most prevalent types of heat-related illness in youngsters are found in teenagers who exercise and in kids who are left alone in cars or other very warm places. Pediatricians need to provide guardians with effective advice on how to avoid dehydration and heat-related illnesses. When prevention fails, it is critical to identify and treat HRI as soon as possible.

This review, thus, attempts to highlight the various kinds of HRIs, their symptoms, and management along with certain precautions that can prevent HRIs in children.

Heat-Related Illnesses – Terminologies

The term '**Heat-related illness**' (HRI) describes a wide range of clinical conditions brought on by exposure to extreme heat in the environment and the body's incapacity to control its temperature. Heat rash and heat stress are examples of mild presentations, while heat stroke is a severe one. Be aware that each person has a different heat tolerance. The impact of heat on an individual is dependent on a number of elements, such as general health, overall conditioning, hydration status, and capacity to acclimatize, or gradually adjust to, changes in temperature. Following are various kinds of HRIs –

Heat rash and prickly heat, medically termed as miliaria, is often seen during humid and high temperature seasons, in infants. The rash may appear as papular, vesicular, or erythematous and is brought on by a blockage of the eccrine sweat glands [18]. It is benign, self-limiting, and may be

pruritic. Supportive loose clothing should be worn and without restriction, and overheating should be avoided [17].

Heat edema, a minor variant of HRI, causes swelling in the hands, feet, and other dependent areas. Vasodilation and venous pooling cause it to happen in people who are not acclimated to their surroundings [18]. Children can also get heat edema, albeit it is more frequent among the elderly. The patient's body temperature is normal, and neither renal disease nor heart failure are the cause of the disorder. Compression stockings, elevation, and relocating to a colder location are supporting measures [17].

Heat cramps are caused by skeletal muscular spasms that happen uncontrollably during or after strenuous physical activity [19,20]. The phrase "heat cramps" is misleading because cramps are not caused by the heat per se; rather, high-intensity physical activity in cold weather—such as hockey or swimming—is linked to cramps. *Muscle cramps* related to exercise is a more accurate description. Only the muscular groups that are actively engaged in exercise are typically affected by the excruciating spasms [19]. Usually, they affect dehydrated, under conditioned or inadequately acclimated athletes [21]. A history of muscle cramps or prior injuries to the muscle, tendon, or ligament; excessive perspiration; dehydration; or inadequate sodium intake prior to or during activity are risk factors [20]. Static stretching, drinking, and rest are supporting measures [18-20].

Heat syncope is associated with venous pooling and vasodilation. It is an orthostatic event that results in a momentary loss of consciousness and is typically experienced by people who stand for extended periods of time or move around a lot in a warm atmosphere [19]. Although it may not be the primary cause of the occurrence, heat exposure may have a role. Body temperature is normal, just as it is with heat edema. Patients should be transferred to a cooler location and kept supine until their vital signs return to normal and their dizziness subsides. It is important to check the patient's level of hydration when giving them oral or intravenous fluids [17].

Heat stress is a mild form of HRI. It describes the sensation of physical strain and discomfort brought on by being in the heat or in a warm environment. Usually, the symptoms are not too severe, and the core temperature stays within normal limits [17].

Heat exhaustion, sometimes referred to as heat injury, is a mild sickness characterized by a rise in core temperature (98.6°F to 104°F [37°C to 40°C]). Its symptoms include headaches, dizziness, vomiting, thirst, and syncope [18]. Dehydration and profuse perspiration are also common. It is probable that the patient's vital signs will show hypotension and tachycardia. The absence of end-organ injury or malfunction of the central nervous system (CNS) is a crucial aspect of this clinical condition [20]. If CNS symptoms occur, they are modest and go away fast with rest and cooling.

Examples of these symptoms are headache and moderate disorientation [17]. Reducing physical activity, taking off extra clothing and equipment, moving to a cooler location, and hydrating with oral or intravenous fluids are the steps involved in treating heat exhaustion [17].

Heat stroke is the most serious type of HRI, which is brought on by a breakdown in the thermoregulatory system. A core temperature of more than 104°F (>40°C) combined with CNS dysfunction with known heat exposure and/or vigorous exercise is considered a life-threatening condition. Coma, delirium, agitation, and confusion are some of the CNS disorders associated with heat stroke [23].

Pathophysiology and Acclimatization

The anterior hypothalamus controls body temperature, which is kept between 97.7°F and 99.5°F (36.5°C and 37.5°C) [19]. The body switches from heat storage to heat dissipation when the core temperature rises (due to exertion or exposure to outside heat) [21]. The body can thermoregulate through a number of mechanisms, but when the outside temperature rises, these mechanisms become less efficient. Heat radiation from the body to the outside world only happens when the outside temperature is lower than the interior temperature. Conduction is the direct movement of heat from a warmer (the body) to a cooler surface, whereas convection is the transfer of heat from the body to cooler air (gas). Thus, evaporation serves as the main thermoregulation mechanism as the ambient temperature rises [21]. Heat evaporation and cooling are made possible by vaporization of sweat at the skin's surface. As the body's core temperature rises, physiological changes take place. Vasodilation causes an increase in heart rate, stroke volume, and cardiac output.

The warm blood flows to the skin's periphery, facilitating the formation and evaporation of sweat [21]. Visceral perfusion decreases when blood flows from the center to the periphery, especially in the kidneys and stomach [24]. The body's ability to adapt is reduced if heat exposure is severe or persistent. An animal's heat exposure period and core body temperature are represented by the Critical Thermal Maximum (CTM). For one to eight hours, the CTM in humans is considered to be between 106.9°F and 107.6°F (41.6°C and 42°C) [25]. Extended heat beyond the CTM can result in a hazardous chain reaction that includes multisystem organ failure, ischemia, and possibly even death. High cardiac output, as the body tries to cool, can lead to cardiogenic shock and cardiac failure. Due to hypovolemia (related to profuse sweating and insensible losses) and vasodilation (as part of the thermoregulatory process), hypotension frequently develops. Changes occur equally on vascular and cellular levels due to prolonged exposure to high temperatures, resulting in intravascular coagulation and activation of various cytokines and inflammatory pathways respectively, leading to apoptosis and protein denaturation eventually [24,26].

Clinicians should be aware of how age and development affect the thermoregulatory mechanism since hyperthermia has the potential to be fatal. Recent research refutes the notion that young athletes are more prone to heat injury from a physiological perspective, and instead suggests that they are just as capable of good thermoregulation during exercise as their adult counterparts [27]. Adults, who frequently have more cardiovascular disease and comorbidities that worsen HRI outcomes, typically have a higher risk of HRI than children. However, children differ from adults in terms of physiology and development, when it comes to thermoregulation. Compared to adults, children and adolescents require more time to acclimatize to a warm atmosphere.

The process of adjusting to a change in humidity and/or temperature is called *Acclimatization*. Increased sweat production, decreased electrolyte losses in sweat, increased skin blood flow during exercise, larger stroke volume, larger plasma volume, increased aldosterone production with decreased urine sodium excretion, and a decreased temperature threshold to start sweating are some of the physiological changes that take place during the acclimatization period [19,21]. In warm conditions, student-athletes should be given 10 to 14 days to adjust to new physical training. In addition, it is believed that infants and young children lack the developmental capacity to modify their behavior in reaction to overheating (e.g., drink water, take off seat belts or clothing, change locations), and thus special care must be taken during periods of extreme heat [28,29].

Causes of Heat-Related Illnesses

1. **Etiology:** Heat exposure is the main cause of heat stroke. Heat stroke can be further classified into two categories based on the type of exposure: *exertional heat stroke* and *nonexertional (classic) heat stroke*. When there is no extreme physical activity involved, exposure to high environmental temperatures can lead to **non-exertional heat stroke**. Young children and the elderly are more at risk, hence it is most frequently observed in these age groups during heat waves or other extreme heat events. A child left alone in a car (vehicular heat stroke) or residing in a home without climate control or central air conditioning are common examples of these situations [30].

Air conditioning has been demonstrated to be protective during periods of excessive heat and is linked to a lower risk of heat-related mortality [31]. In the last 20 years, there have been, on an average, 37 deaths annually in the US from vehicular heat stroke, making it a prevalent occurrence among the pediatric population. 87% of the children who died from vehicular heat stroke were under the age of 3 years [32]. A study of 171 vehicular heat stroke deaths revealed that

youngsters left in the vehicle (73%) or playing in the vehicle (27%) led to fatalities commonly [33]. The most frequent occurrence is when a parent leaves their child in the car unintentionally after forgetting that they are in the back. This could occur when a parent deviates from their regular schedule [34]. **Exertional heat stroke**, as opposed to nonexertional heat stroke, is more common among athletes and happens during extended, intense exercise.

Also susceptible to it include those who enlist in the armed forces, work in public safety, or perform hard labor in warm climates while wearing bulky protection gear or uniforms. Over 9,000 high school players annually seek treatment for exertional heat illnesses [35]. Among athletes, football players are most susceptible to exertional heat stroke [35]. An average

Table 1 - Reasons why children are more prone to HRIs

1. Greater surface area to body mass ratio than adults
2. Production of more metabolic heat per kilogram of body weight
3. Slower rate of sweating than adults
4. Temperature when sweating starts is higher
5. Lower cardiac output at a given metabolic rate than adults
6. Rate of acclimatization is slower
7. Thirst response is blunted compared with adults
8. Hypohydration affects children more than adults

Table 2 - Medical conditions susceptible to HRIs

1. Excessive fluid loss
 - Febrile state
 - Gastrointestinal illness
 - Diabetes insipidus
 - Diabetes mellitus
2. Suboptimal sweating
 - Obesity
 - Spina bifida
 - Cystic fibrosis
 - Sweating insufficiency syndrome
3. Excessive sweating
 - Congenital heart defects
 - Hyperthyroidism
4. Diminished thirst/intake
 - Mental retardation
 - Young children
5. Hypothalamic dysfunction
 - Anorexia nervosa
 - Recent episode of heat illness

(Adapted from the Committee on Sports Medicine and Fitness, American Academy of Pediatrics) [38]

of two high school football players per year passed away from exertional heat stroke between 1995 and 2010. Although athletes can be impacted by exertional heat sickness in colder months as well, August is the month when it happens most frequently [35-37].

2. **Risk factors and Medical Conditions:** Children are more prone to heat illness than adults for many reasons summarized in [Table 1] [38-41]. Many common medical conditions in children may place them at increased risk for heat illness [Table 2].

Detection of Heat-Related Illnesses

1. **Differential diagnosis:** The physician must recognise and differentiate between several causes of hyperthermia. Fever as a manifestation of hyperthermia is frequent in the pediatric population. A fever is a typical physiological reaction that results in an increase in body temperature due to an illness or inflammation. The brain's major thermoregulatory centers regulate the reaction, and in a neurologically normal host, the temperature rises, although it typically doesn't rise above 105.8°F (41°C). There may or may not be additional symptoms of infection, disease, or inflammation along with a fever. Malignant hyperthermia and neuroleptic malignant syndrome are less frequent causes of hyperthermia. Patients using antipsychotic drugs may experience an unusual and potentially fatal reaction called neuroleptic malignant syndrome. In the context of exposure to dopaminergic drugs, it is characterized by the clinical triad of muscle rigidity, altered mental status, and hyperthermia. A hereditary disorder known as malignant hyperthermia develops in those who are vulnerable to inhalational anesthetics and/or succinylcholine exposure. It responds to dantrolene treatment and is characterized by heat and stiff skeletal muscles [17].
2. **Diagnosis:** Heat exhaustion and heat stroke are clinical diagnoses, both defined by hyperthermia after heat exposure, as elaborated in [Figure 1]. Exertional and non-exertional heat stroke victims typically have comparable clinical characteristics, regardless of the kind of exposure; however, end-organ damage may also be observed in heat stroke victims. The CNS symptoms can start as moderate disorientation but can progress to more severe forms (such as delirium, seizures, encephalopathy, and coma) and become more noticeable as the core temperature rises above 105.8°F (>41°C). It is crucial to bear in mind that in cases when cooling measures have already been implemented, the core temperature upon presentation to medical treatment may be lower than 104°F (<40°C). Thus, even in cases when a patient's core temperature is below 104°F (<40°C), heat stroke should still be considered a differential diagnosis for individuals with appropriate exposure and clinical presentation [17,18].

Patients with classic or nonexertional heat stroke will present with hot, dry skin as a result of persistent dysregulation of the thermoregulatory system [19]. Patients suffering from exertional heat stroke, on the other hand, would have clammy, chilly skin or might be hot and sweaty if they had just finished a vigorous workout.

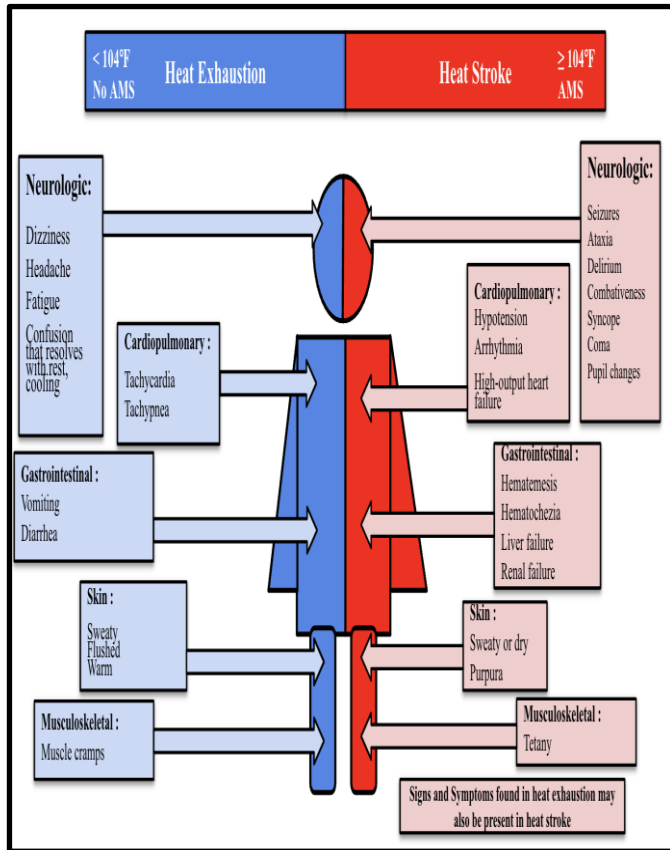


Figure 1 – Clinical findings of Heat Exhaustion versus Heat Stroke {AMS – altered mental state}

3. **Prognosis:** Patients suffering from heat stroke, who can maintain sufficient cardiac output to satisfy increased circulatory demand, have a good prognosis. In heatstroke, three main prognostic categories have been established [42]. Patients with extended coma, coagulation problems, renal failure, severe hypotension, and delayed seizures have a significant risk of death. Poor prognostic indicators include core body temperature greater than 41.1°C and early, high liver transaminase levels (serum glutamic oxaloacetic transaminase greater than 1,000 within 24 hours). Individuals who regain consciousness within 4–10 hours may see a decline in their renal and hepatic function over the course of 3–5 days, followed by an improvement. In particular, ataxia or cerebellar disease, as well as difficulties in thermoregulation, are neurologic sequelae that may persist in some people even after recovery. Individuals experiencing a reduction in consciousness for less than three hours typically make a full recovery [43].

Precautions

When it's hot outside, common sense can help prevent a lot of ailments linked to the heat. On very hot and humid days, kids should be kept inside and under air conditioning as much as possible. If they must go out, they ought to dress comfortably, in light colored clothing and wear a hat. Using umbrellas as a parasol to protect young children from the sun could be beneficial. Because they are more susceptible, infants and toddlers rely on their guardians to keep them cool during the summer. Infants shouldn't be overdressed; they should feel comfortable wearing the same amount of layers as their parents. Young children and infants should never be left unsupervised in cars. In a few minutes, the temperature inside a vehicle, exposed to the sun, can rise to 49°C to 60°C (120°F to 140°F) from 30°C to 40°C (86°F to 104°F) outside [23]. Hot tubs, saunas, steam rooms, and whirlpool baths pose a risk to children as well.

Since water is a great conductor, heat is transferred to unsupervised children quickly. When starting a rigorous exercise programme or returning from a trip to a warmer area, children should gradually acclimate to hot temperatures. They should also avoid exercising in the hottest portion of the day, which is late morning through afternoon [38]. When starting a strenuous training or performance programme in the sweltering summer, young athletes (or marching band members) should be advised to start out with a lesser amount and duration of activity and acclimatize gradually over a period of 10 to 14 days. Athletic event planners and coaches should be aware of local weather changes and make appropriate plans accordingly. Relative humidity, sun radiation, and air temperature should be taken into consideration when engaging in strenuous exercise for more than fifteen minutes. The climatic heat stress is sufficient to cause heat-related disease at Wet Bulb Globe Temperature (WBGT) more than 24°C (75°F). The American Academy of Paediatrics advises against participating in any sports with WBGT higher than 29°C (85°F).

Youngsters should have plenty of fluids before exercising. Since high-osmolar fluids, such as sodas and high-sugar drinks, might promote water loss, they should refrain from consuming them. The best are electrolyte or water solutions. Periodic drinking should be enforced during physical exercise (150 mL of cold water or flavored salted beverage every 20 minutes for a 40-kg youngster, 250 mL for a 60-kg adolescent). Because of their high sodium chloride content and potential for stomach distress, salt replacement tablets are not advised [44]. According to preliminary research, children and teenagers with cystic fibrosis can tolerate fluids during hot activity, and electrolyte solutions with a high salt content (50 mmol/L or higher) may be able to increase thirst [45,46]. To allow for evaporation, only one layer of light-colored, absorbent, and lightweight clothes should be worn during exercise. Clothing soaked in sweat needs to be replaced regularly [43].

Prevention

1. **Non-exertional Heat Stroke Prevention:** Pediatricians need to be prepared to make patients and families aware of the risks associated with prolonged exposure to heat. Families should be provided with basic counseling regarding proper clothing and covering (bundling) as the weather changes, especially for infants and children with special needs who are unable to adjust their behavior in response to extreme heat or overheating. During times of high heat and humidity, special needs children and newborns may experience higher insensible losses, necessitating the supplementation of extra fluids (human milk, tube feeds, free water, etc.). Therefore, extra attention should be paid to hydration status during these seasons. Numerous preventative techniques are available for classic heat stroke and vehicle-related HRI. To prevent entrapment, guardians should be instructed to never leave their child unsupervised in a car and to keep the doors locked while not in use [32].
2. **Exertional Heat Stroke Prevention:** Several regulatory organizations have created policy statements to direct education, management, and prevention of exertional heat stroke in athletes, including the American Academy of Paediatrics, the National Collegiate Athletic Association, and the National Athletic Trainers Association [18,26]. Pediatricians, coaches, sports directors, athletes, and caretakers should all be knowledgeable about the warning signs and symptoms of HRI and how to avoid these potentially fatal illnesses [18].

Screening - All athletes should have a preparticipation history and physical examination performed before beginning any sports activity to rule out any medical issues or prescription drugs that could put them at risk for HRI. *Acclimatization* - In one to two weeks, athletes should raise their exercise level to acclimatize to the warmer conditions. *Sports Equipment and Clothing* - Sportswear should be light-colored, airy, and loose-fitting for athletes [16]. Clothing soaked in sweat needs to be taken off right away [19]. *Hydration* - It is important to remind athletes to drink enough water before, during, and after physical activity [18]. *Scheduling* - Practices should be moved to early mornings and evenings when the weather is exceptionally hot. *Preparation* - Athletic events should have access to medical supplies and tools for quick cooling, such as rectal thermometers, ice towels, and cold-water tubs [18].

Treatment and Complications

Heat stroke needs to be identified quickly and treated seriously. Treatment is summarized in [Table 3]. Prioritizing the patient's airway, breathing, and circulation following life-support guidelines is the initial step in resuscitation (depending on the presenting site, emergency medical services

may need to be activated simultaneously). After addressing the airway, breathing, and circulation, the next step should be to measure the core temperature and start cooling the patient. The gold standard for measuring body temperature at the core is a rectal thermometer [18,47].

Table 3 - Treatment Strategy for HRIs

A. Prehospital care
Assess the airway, breathing, and circulation
Measure core body temperature {rectal}
Remove clothing and athletic equipment
If older child/adolescent - Cold water immersion (if available); Cover head and neck with wet towel
If infants, young children, or cold-water immersion is not available - Evaporative cooling with wet towels or sheets and high flow fan
Assess temperature and vital signs every 3-5 minutes
B. Emergency Department care
Assess the airway, breathing, circulation and neurologic disability
<ul style="list-style-type: none"> - Consider intubation if unable to protect airway - Consider benzodiazepines to combat seizures or excessive shivering
Measure core body temperature {rectal}
Remove clothing and athletic equipment
Apply a cardiorespiratory monitor and rectal or esophageal temperature probe
Establish vascular access, evaluate for associated complications
Evaporative cooling with wet towels or sheets, high flow fan, and cooling blankets
Normal saline bolus (at room temperature)
Assess temperature and vital signs every 3-5 minutes
Continue cooling until the core temperature is $\leq 102^{\circ}\text{F}$
Expert management of end-organ damage and complications

Table 4 - Complications due to HRIs

- High output cardiac failures
- Pulmonary edema
- Rhabdomyolysis
- Acute renal illness
- Hepatocellular necrosis
- Disseminated intravascular coagulation
- Cerebral edema

Rectal thermometers should always be used in conjunction with external commercial thermometers that measure body temperature. Initiate hospital transfer (if the physician is present on site, then it is up to their discretion) temperature tympanically, orally, or temporally. These thermometers are not accurate enough to measure core temperature [17]. As soon as heat stroke is detected, cooling must start [47]. Restoring blood flow from the periphery to the core and lowering body temperature by lowering the body's hypermetabolic state are the two goals of cooling [18]. The patient's age and the available resources may have an impact on the cooling technique.

After cooling has begun and the airway, breathing, and circulation have been attended to, secondary therapy includes assessing the patient's electrolyte and hydration levels and identifying and treating any heat stroke consequences. Urine output measurements can be performed continuously and accurately with the use of an indwelling bladder catheter [19]. No particular drugs are advised for the treatment of heat stroke. Pharmacotherapy should be evaluated on a case-by-case basis to manage the problems resulting from heat stroke. Benzodiazepines, for instance, may be used to regulate the shivering response and to stop seizures, which could be a heat stroke complication [19].

Complications of heat illness are listed in [Table 4]. Hemostasis, hematuria, gastrointestinal bleeding, and conjunctival hemorrhage are indicators of poor prognosis [41]. Most often, cardiopulmonary collapse results in death.

CONCLUSION

A child in good health may rarely get HRIs. Pediatricians and emergency room personnel should be aware of the risks that immoderate temperatures pose to their patients. While prevention is better than cure, effective treatment depends on early identification of the range of HRIs and timely initiation of the proper care.

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Funding: None; Conflicts of Interest: None Stated.

How to cite this article: Agrawal A, Agrawal R. An analysis of heat-related illnesses in children due to immoderate temperatures. *Indian J Child Health.* 2024; 11(5):38-45.