CLINICAL PRACTICE

FOSSIL-FUEL POLLUTION AND CLIMATE CHANGE
Caren G. Solomon, M.D., M.P.H., *Editor*

Treatment and Prevention of Heat-Related Illness

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This Journal *feature begins with a case vignette highlighting a common clinical problem. Evidence supporting various strategies is then presented, followed by a review of formal guidelines, when they exist. The article ends with the authors' clinical recommendations.*

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A 71-year-old man with a history of coronary artery disease, congestive heart failure, and schizoaffective disorder presents to the emergency department with confusion. On the day of presentation, he was seen walking near his apartment complex in a busy urban area and was later found collapsed outside his building. The local heat index (accounting for temperature and relative humidity) is 105°F (40.6°C). On arrival in the emergency department, he is conscious but confused. His heart rate is 130 beats per minute, blood pressure 100/70 mm Hg, respiratory rate 28 breaths per minute, rectal temperature 40.5°C, and oxygen saturation 90% while he is receiving oxygen at a rate of 3 liters per minute through a nasal cannula. He opens his eyes to voice and can state his name. He is able to move his arms and legs and has no focal neurologic deficits. His skin is hot and dry to the touch. His medications include furosemide, risperidone, and carvedilol. The patient lives alone in a top-floor apartment without air conditioning. How should this heat-related illness be treated, and how could it have been prevented?

THE CLINICAL PROBLEM

Climate change is causing a global increase in average temperatures and increasing the frequency, duration, and intensity of extreme heat events,[1] resulting in unprecedented levels of heat exposure. The past 7 years have been the hottest on record,[1] and climate change either caused or dramatically worsened[2] recent extreme heat events in Europe (2022),[3] India (2022),[4] and the Pacific Northwest of the United States (2021).[5] In the past 20 years, there has been a 54% increase in heat-related mortality among persons older than 65 years of age,[6] and more than one third of all global warm-season heat-related deaths are attributable to climate change.[7] On our current global greenhouse gas emissions trajectory, with warming of 2°C over preindustrial temperatures expected by midcentury, most of the world is expected to encounter frequent extreme heat events in the coming decades[8]; formerly once-in-10-years heat waves are projected to occur more than 5 times as frequently and once-in-50-years events almost 14 times as frequently.[2] Elevated global temperatures and heat waves are already increasing the global health burden and causing substantial economic loss.[1]

Humans thermoregulate through behavioral and autonomic mechanisms (e.g., vasodilation and sweating) to maintain a core internal temperature of approximately 37°C. Metabolic activity generates an internal heat load, and exogenous heat from

KEY CLINICAL POINTS

TREATMENT AND PREVENTION OF HEAT-RELATED ILLNESS

- Climate change is causing increasingly frequent and severe heat waves, resulting in increases in the incidence of heat-related illness and exacerbations of heat-sensitive conditions.
- The risk of heat-related illness is driven by heat exposure (ambient and internally generated heat from exertion), individual susceptibility (influenced by age, pregnancy status, and coexisting conditions), and sociocultural factors (including environmental racism, poverty, lack of social cohesion, lack of access to health care, and limited worker protections).
- Heat-related illnesses range from mild to life-threatening, and heat exposure exacerbates many common health conditions, including cardiac, respiratory, and kidney diseases.
- Without prompt recognition and treatment, heat stroke has high associated mortality. Treatment includes rapid cooling, rehydration, and management of potential end-organ damage.
- Heat-related illness is preventable. Clinicians have a role in identifying patients at risk, providing counseling regarding signs and symptoms, and recommending strategies for reducing risk.

the environment adds to the total heat burden that must be managed; higher humidity levels (which are taken into account in the heat index) exacerbate the challenges of dissipating heat. Under heavy heat loads resulting from exogenous heat, endogenous heat, or both, the thermoregulatory ability of the human body may become strained or overwhelmed, which can result in a spectrum of heat-related illnesses. These illnesses range from non–life-threatening conditions (heat exhaustion, heat syncope, heat edema, heat cramps, and heat rash) to life-threatening heat stroke resulting from an increase in body temperature above a dangerous threshold (Table 1).

Heat stroke, the most serious heat-related illness, is subcategorized as "classic" or "exertional"; the former is typically observed in patients with preexisting conditions and the latter primarily in healthy persons who exceed thermoregulatory boundaries owing to increased metabolic heat generation from performing demanding physical tasks, often but not necessarily in conjunction with exposure to high ambient temperature. Both conditions lead to a similar cascade of physiologic abnormalities caused by a failure to dissipate excessive body heat, including a decrease in central venous pressure, the onset of cellular and organ dysfunction, injury to the gastrointestinal tract and resulting endotoxemia, triggering of a systemic inflammatory response, and elevation of the core body temperature.[12]

Heat stroke is a medical emergency that requires rapid recognition and treatment to prevent permanent complications and death; mortality from classic heat stroke approaches 80% and, for exertional heatstroke, 33% in the absence of prompt treatment.[10,13] The hallmark of heat stroke is the combination of central nervous system dysfunction and a core body temperature of greater than 40°C.[14]

Beyond traditionally recognized heat-related illnesses such as those that are the focus here, many diseases are "heat sensitive," meaning that they are exacerbated or triggered by exposure to heat. Multiple studies have shown increases in the occurrence and exacerbations of a wide range of conditions during periods of high temperature,[15-17] including ischemic heart disease, cardiac dysrhythmias, ischemic stroke, asthma and chronic obstructive pulmonary disease, respiratory tract infections, hyperglycemia, kidney failure, neuropsychiatric disorders (e.g., psychosis, suicides, homicides, anxiety, and depression), and adverse birth outcomes, such as preterm delivery and small-for-gestational-age infants.[18]

The risk of heat-related illness results from a combination of individual susceptibility, endogenous and exogenous heat exposure, and sociocultural factors that affect the ability to adapt (Fig. 1). Older persons (>65 years of age), young children, infants, pregnant women, persons with preexisting medical conditions (including obesity) or disabilities, outdoor workers, and athletes are at increased risk,[19] as are persons living in lower-income households and some communities of color.[20]

Individual exposure to heat-related risks varies according to geography, occupation (e.g., agricultural work, construction work, delivery driving), social isolation, and time spent outdoors or in areas that amplify heat, such as urban heat islands and areas with less green space.[19] Urban heat islands are areas of densely built infrastructure, which absorbs and then re-emits heat from

Table 1. Spectrum of Heat-Related Illnesses and Their Treatment.*

Heat-Related Illness	Description[9]	Treatment[10,11]
Severe illness		
Heat stroke	A multisystem, life-threatening illness characterized by elevation of the core body temperature (to >40°C) and CNS dysfunction Classic heat stroke: most often occurs among older persons with compromised behavioral and physiological compensatory responses to heat exposure Exertional heat stroke: most often occurs among healthy persons during extreme physical exertion, which results in excessive metabolic heat generation, often but not always with concomitant ambient heat exposure	Move patient to cool environment; manage airway, breathing, and circulation; administer rapid cooling with cold-water or ice-water immersion or other means; administer intravenous rehydration; and evacuate to emergency department after on-site cooling is performed. ICU admission is warranted for management of end-organ sequelae.
Moderate illness		
Heat exhaustion	Profound fatigue, weakness, nausea, headache, or dizziness (or a combination of these symptoms) resulting from a decrease in body water content or blood volume due to water or salt depletion from heat exposure; mild elevation (<40°C) in body temperature may be present, but no altered mental status	Remove patient from heat; treat with rest in supine position, evaporative cooling, and intravenous or oral rehydration; monitor mental status. Delayed response to treatment warrants further evaluation.
Mild illness		
Heat syncope	Brief loss of consciousness due to vasodilation and pooling of blood in the limbs as a result of physiological compensation to heat exposure	Remove patient from heat and treat with rest in supine position, passive cooling, and oral or intravenous rehydration. Prolonged recovery or a medical history or physical examination arousing concern for a cardiac cause if the patient has cardiac risk factors should prompt further evaluation.
Heat edema	Swelling of the limbs caused by peripheral vasodilation and interstitial pooling resulting from physiological compensation in response to heat exposure	Remove patient from heat and elevate the legs. Diuretic agents are not indicated.
Heat cramps	Painful muscle spasms in the abdomen, arms, or legs during or after activity in the heat, which often occur when excessive amounts of salt are lost during sweating from physical exertion	Remove patient from heat, treat with rest, oral electrolytes, and fluid repletion.
Heat rash	An inflammatory disorder of the epidermis that results from blockage of sweat glands; may be followed by superimposed bacterial soft-tissue infection.	Remove patient's clothing; treat with evaporative cooling and glucocorticoid and antibacterial creams as needed, but avoid topical emollients; monitor for cellulitis. Advise patients to avoid hot environments and to wear loose clothing.

* CNS denotes central nervous system, and ICU intensive care unit.

the sun, resulting in "islands" of higher temperatures; temperatures in these areas can be 1° to 7°F (0.6° to 3.9°C) hotter, on average, than outlying areas and have much higher nighttime temperatures, as a result of re-radiation of heat from the surrounding environment. In the United States, the residents of urban heat islands are disproportionately low-income Black communities and other underrepresented racial and ethnic groups because of historically racist zoning practices (i.e., "redlining").[21]

In many communities, climate change is increasing the frequency, duration, and severity of extreme heat hazards, resulting in larger and longer population exposures; meanwhile, adaptation measures, especially among the most vulnerable communities and persons, are not keeping pace.[1] Although early-warning systems and other public health measures undertaken during heat waves may provide some protection, there is emerging evidence that, at least in some regions, most deaths due to heat may occur outside of traditionally defined heat waves. For example, the evaluation of the Heatwave Plan for England concluded that more than 90% of deaths in many parts of the country have been occurring outside of heat-wave alert periods.[22] A similar study across 22 U.S. states showed that a heat-attributable health burden starts to occur at moderately hot heat-index values, which in some regions are below alert ranges.[23]

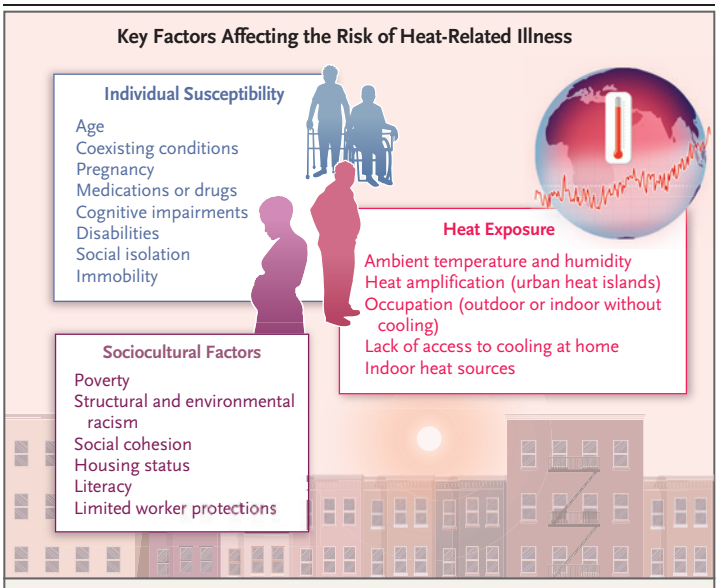

Figure 1. Factors Affecting the Risk of Heat-Related Illness.

STRATEGIES AND EVIDENCE

CLINICAL PRESENTATION

The clinical manifestations of heat-related illness vary according to severity (Table 1). Heat stroke is characterized by the triad of hyperthermia, neurologic abnormalities, and recent exposure to hot weather (classic), physical exertion (exertional), or both.[12] Tachycardia, tachypnea, and hypotension are common. Sweating is typical of exertional heat stroke, whereas in cases of classic heat stroke, the skin is often hot and dry.[12] A change in mental status (e.g., confusion or delirium) best differentiates heat stroke from heat exhaustion and other milder forms of heat-related illness.[24] Early manifestations include behavioral changes, confusion, delirium, dizziness, weakness, agitation, combativeness, slurred speech, nausea, and vomiting.[25] Seizures and sphincter incontinence may occur in severe cases.[26] Heat stroke characteristically manifests in three phases: a hyperthermic–neurologic acute phase, a hematologic–enzymatic phase (characterized by inflammation and coagulopathy and peaking at 24 to 48 hours after onset), and a late hepatic–renal phase (characterized by organ failure and occurring 96 hours or longer after onset), all of which have been well described elsewhere.[12]

EVALUATION AND DIAGNOSIS

Heat-related illness may occur in the absence of a heat wave, and a high index of suspicion is warranted in the context of suggestive symptoms. The initial evaluation should include prompt assessment of the patient's preceding heat exposure and exertion (on the basis of history obtained from emergency medical services personnel, the patient, or other sources) and measurement of the core temperature, recognizing that this may have decreased by the time of assessment. Important historical information includes the patient's occupation, degree of preceding physical exertion, home environment, coexisting conditions, and use of medications or other drugs that may increase the risk of heat-related illness (Table 2). The presenting symptoms of heat stroke can mimic many other illnesses, including sepsis, ischemic stroke, and toxicologic or endocrinologic emergencies, particularly if the core body temperature is not measured.[12] These other conditions must be considered, but treatment for heat stroke should not be delayed, because rapid intervention

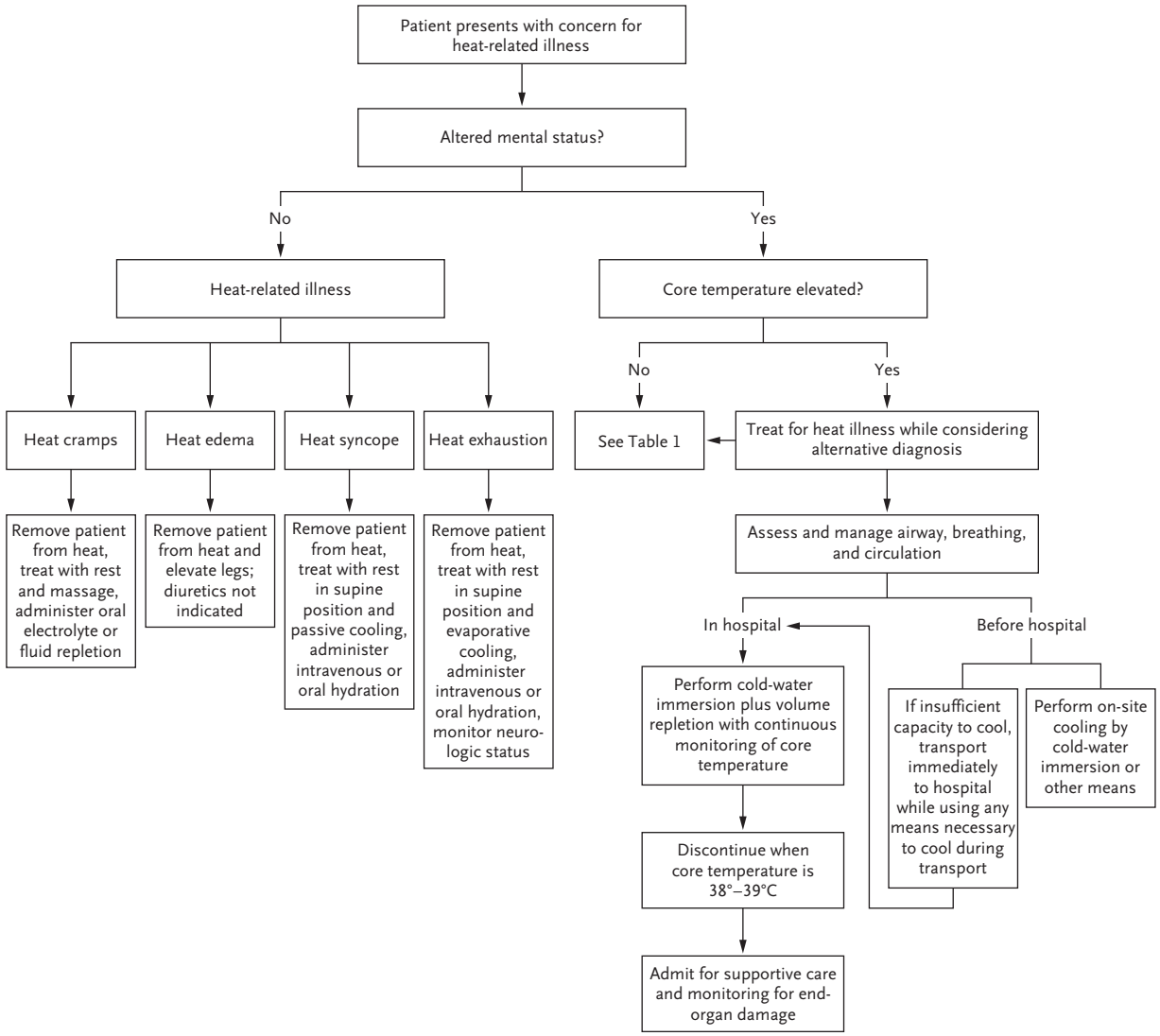

Figure 2. Algorithm for the Diagnosis and Management of Heat-Related Illness.

If cold-water immersion is not feasible, consider the use of intravascular cooling devices; a three-way Foley catheter for bladder irrigation; infusion of chilled fluids; placement of ice packs to axilla, groin, and neck; or misting of the patient with water and directly fanning. These methods may also be used to augment cold-water immersion if the core temperature is not decreasing at a rate of 0.20° to 0.35°C per minute.

is paramount to prevent serious complications and death.[29] Routine assessment of patients presenting with presumed heat stroke includes a complete blood count, complete metabolic panel, urinalysis, urine drug screen, prothrombin time and partial thromboplastin time, creatine kinase level, an electrocardiogram, and a chest radiograph if signs of respiratory involvement are present.

MANAGEMENT

Mild-to-Moderate Heat-Related Illness

Evidence to inform the treatment of mild or moderate heat-related illness is limited. Society-based and expert guidelines, largely based on clinical experience and observational studies, are summarized in Table 1, and an algorithm for the treatment of heat-related conditions is pro-

Table 2. Medications and Drugs with Potential to Increase Risk of Heat-Related Illness.*

Agent	Mechanism[27]
Alcohol	May reduce alertness and affect judgment and perception of heat; exacerbates dehydration and affects vasodilation and cardiac contractility
Amphetamines	May increase metabolic heat production
Anticholinergics	May decrease sweat production
Antihistamines	May cause peripheral vasoconstriction, limiting radiative cooling
Antipsychotics	Interferes with hypothalamic thermoregulation
Benzodiazepines	May reduce alertness and affect judgment and perception of heat
Beta-blockers	Decreases heart rate and contractility
Calcium-channel blockers	Decreases cardiac contractility and compromises vascular compensatory mechanisms
Diuretics	May increase risk of dehydration and hypovolemia
Illicit drugs (e.g., cocaine, heroin, phencyclidine, and MDMA)	May increase metabolic heat production and reduce alertness and judgment
Laxatives	May increase risk of dehydration and hypovolemia
Lithium	May reduce alertness and affect judgment and perception of heat and lead to nephrogenic diabetes insipidus; levels may rise to dangerous levels and cause kidney injury in the context of dehydration
Serotonin-reuptake inhibitors	May interfere with hypothalamic thermoregulation
Thyroid agonists	May increase metabolic heat production
Tricyclic antidepressants	May cause peripheral vasoconstriction, thereby limiting radiative cooling, and may affect central thermoregulation
Weight-loss supplements that may increase metabolic rate (e.g., carnitine and green tea extract)	May increase metabolic heat production

* This list of medications (based on information from Pryor et al.[28]) and mechanisms is not comprehensive. MDMA denotes 3,4-methylenedioxymethamphetamine.

vided in Figure 2. Heat exhaustion exists on a continuum with heat stroke, and its treatment is dictated by the severity of symptoms. Mild cases can be managed with passive cooling and rehydration, whereas moderate cases typically warrant active management with convective cooling (i.e., with the use of fans), infusion of cold fluids, and close monitoring.[10]

Heat Stroke

For patients with heat stroke, treatment begins with maintaining the airway, breathing, and circulation, immediately followed by rapid cooling. Because delays in cooling are associated with worse outcomes, initial management is focused on rapidly reducing the core body temperature to 38° to 39°C, ideally within 30 minutes after presentation.[30] The most effective cooling methods are cold-water immersion and ice-water immersion[31]; a crossover study found no difference in cooling rates between these methods.[32] A rapid rate of cooling, ideally 0.20° to 0.35°C per minute, with continuous monitoring of the core temperature, is safe and has been associated with a better prognosis than slower cooling in observational studies.[12] In settings outside the hospital, where immersion is not available, a cooling rate of 0.10°C per minute can be achieved by pouring copious amounts of water over the victim and fanning.[33] If airway compromise, ongoing cardiopulmonary resuscitation, or resource availability prevents cold-water immersion, treatment involves a mixture of evaporative and conductive cooling methods, including infusion of cold fluids; application of ice packs to the neck, groin, and axillae; and fanning.[12] Intravascular cooling can also be used.[13] Monitoring of the core temperature throughout the cooling process is imperative,

Table 3. Prevention Strategies for the General Population and for Specific Groups.*

Risk Group	Strategy
General population	Identify heat-vulnerable patients. Alert patients and caregivers to potential heat risks. Provide counseling regarding signs and symptoms of heat-related illness (e.g., excessive sweating or cessation of sweating, thirst, myalgias, confusion)[27,38] Provide counseling regarding how to reduce risks and when to seek medical attention.[39] Provide education regarding medications that may increase heat risk.[27] Provide counseling about ensuring access to cooling when needed, including the appropriateness of fans as a cooling strategy[40] and access to mechanical air conditioning at home or at a nearby site, where available. Review emergency plans in the event of a power outage.[41] Engage social work and related services as needed to assist in reducing risks, including arrangement of safety checks. Become familiar with local heat-risk thresholds and monitor risk levels[42] (in the United States, information can be obtained through a free OSHA application[37]).
Athletes	Educate administrators, coaches, stakeholders, athletes, staff, and spectators about the risks and manifestations of heat-related illness.[43] Encourage acclimatization in advance of substantial heat exposure.[10] Provide counseling regarding when to schedule practices and events and exercise-modification strategies appropriate for the region.[43] Support event organizers in planning and preparedness activities.[43]
Outdoor workers	Identify heat-vulnerable patients who work outdoors.[44-47] Explore potential barriers to reducing heat risk and formulate strategies to address these barriers, including drinking water, resting, or removing extra clothing or equipment.[45] Discuss whether outreach to the patient's employer about the reduction of heat risks might be beneficial. Inform patients of relevant local worker protections and standards.[48]

* OSHA denotes Occupational Safety and Health Administration.

with a goal of reaching normothermia. It is recommended that cooling measures be taken before and during transport to the hospital whenever possible.[34]

Antipyretic agents should not be used; they are ineffective in patients with heat stroke and may aggravate coagulopathy and end-organ damage.[10] Dantrolene has been associated with reduced cooling time but not with improved rates of recovery; it is not used to treat heat stroke in practice.[35] Benzodiazepines may be used to control agitation, discomfort, and shivering.

Patients who are successfully cooled and survive the hyperthermic–neurologic phase are at high risk for progression to the hematologic–enzymatic and late hepatic–renal phases. These patients are best treated in an intensive care setting with a multidisciplinary team.[13]

RISK REDUCTION

Because evidence from randomized trials is limited,[36] strategies to prevent heat-related illness are guided largely by clinical experience and observational data. These data support the benefits of screening for risk and of the use of behavioral interventions, particularly those targeted to susceptible persons and their caregivers, athletes, and outdoor workers. Table 3 outlines strategies for risk reduction.

Expert guidelines recommend that before the warm season, clinicians should identify heat-vulnerable patients (Fig. 1) and alert them and their caregivers to their potential risks, noting that a single day of extreme heat poses a threat; counsel them about the identification of high-risk heat conditions (Fig. S1 in the Supplementary Appendix, available with the full text of this article at NEJM.org) and the signs and symptoms of heat-related illness; and provide clear instructions about how to reduce risks and when to seek medical attention.[27,38] A randomized trial of a preventive-messages tool for older adults in Australia showed significant uptake of behavioral strategies and a 63% lower risk of self-reported heat stress among those who received the intervention than among those who did not.[36] General guidance to reduce risk includes keeping living spaces cool with fans, air conditioning, or misting (with the caveat that fans are likely to be ineffective at temperatures >99°F [>37.2°C] and

may be detrimental in dry conditions[40]), locating cooling centers or other accessible places with cooling, limiting physical activity, increasing water intake, wearing lightweight clothing, self-dousing and taking cool showers, and monitoring for symptoms, including frequent safety checks from caregivers.[39]

Athletes and persons who manage athletic practices and events should be counseled that heat acclimatization, which involves short periods (1 to 2 hours) of heat-exposed exertion each day over a period of 10 to 14 days, has been shown to increase the ability of the body to tolerate and dissipate heat.[10] In higher-risk heat conditions, practices and events should be scheduled at cooler times of the day and allow for more rest breaks.[43] Clinicians can refer to region-specific exercise-modification tables for additional guidance[43] and should encourage organizers of sporting events to have trained personnel on site and the capacity to provide cold-water immersion if needed.[43]

Preventive actions are challenging for many workers who perform heavy labor in hot conditions.[44] Outdoor workers often have little control over their work environment and activities, which complicates normal behavioral responses to heat.[45] According to data from the Centers for Disease Control and Prevention, crop workers die from heat stroke at a rate nearly 20 times that of U.S. civilian workers overall; most fatalities occur among adults 30 to 54 years of age, with a majority of victims being foreign-born workers.[46] Factors contributing to the high risk of heat-related illness in persons who work outdoors include direct exposure to heat (indoor and outdoor), extreme physical exertion, heat-trapping protective work clothing, and job insecurity.[47] Despite convincing evidence of the negative health effects of increased workplace heat, there is no dedicated U.S. standard that specifically addresses occupational heat exposure, although there are efforts under way to create one,[48] and certain states (e.g., California and Washington) have standards and regulations in place.

GUIDELINES

The Wilderness Medical Society and American College of Sports Medicine have published guidelines on the prevention and treatment of heat-related illness.[10,43] The National Association of Emergency Medical Service Physicians has a consensus statement on the prehospital recognition and management of exertional heat stroke.[34] All guidelines stress the importance of rapid cooling for persons with heat stroke, recommend cold-water immersion as first-line therapy, and advocate for the initiation of cooling by any means available while the patient is still in the field, followed by transportation to a medical facility. Our recommendations align with these guidelines.

AREAS OF UNCERTAINTY

High-quality studies to identify the temperature of water in which to immerse a patient are lacking, although observational studies suggest that cooling rates are similar with cold water and ice water.[32] Expert consensus supports discontinuing cooling when the core temperature reaches 38° to 39°C, after which the body temperature typically continues to decline to normal; however, this recommendation has not been rigorously studied, and isolated case reports have described favorable outcomes with therapeutic hypothermia.[49]

Further study of medications to treat heat stroke and improvements in the identification of persons at high risk for heat-related illness are warranted. Randomized trials involving persons in high-risk groups are needed to evaluate the benefits of screening and of behavioral and other interventions (such as provision of air cooling in homes and congregate living settings and referral to cooling centers). Ongoing research is evaluating the effects of public health measures such as heat-wave alerts and heat early-warning systems on the burden of heat-related disease; research to date has shown inconsistent results.[50]

CONCLUSIONS AND RECOMMENDATIONS

The 71-year-old man described in the vignette presents with confusion and hyperthermia in the context of a high ambient temperature, making heat stroke the likely diagnosis. Risk factors include his living alone on the top floor of a building without air conditioning and his use of medications that can compromise thermoregulation. Treatment should involve rapid cooling followed by diagnostic evaluation and management of complications such as aspiration pneumonia, as well as monitoring in an intensive care unit. Subsequent preventive strategies are needed,

and, if instituted earlier, might have averted the current illness. These strategies should include clinical screening before the warm season, tailored recommendations that take into account the patient's coexisting conditions and medications, and involvement of a multidisciplinary team to aid in improving the safety of his home environment. In addition to broad-based public health measures aimed at reducing risks, rapid action to reduce greenhouse gas emissions is needed to prevent further increases in morbidity and mortality due to heat exposure.

Disclosure forms provided by the authors are available with the full text of this article at NEJM.org.

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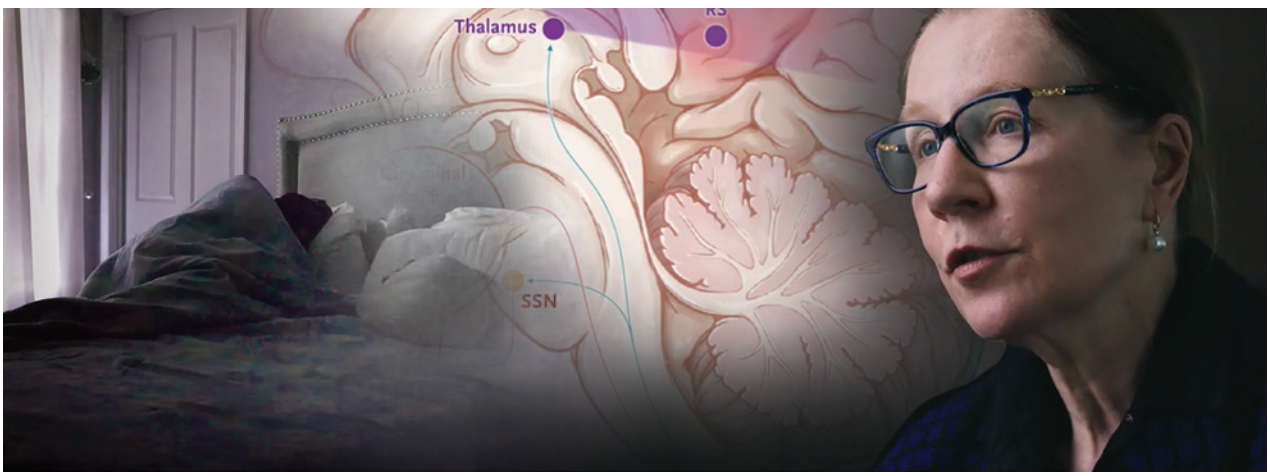
Double Take Video **Migraines — Treatment and Preventive Therapies**



Focusing on acute and preventive therapies for migraines, this video discusses pathophysiology and provides practical treatment information for this common condition.