

Occupational Heat Stress and Kidney Health: From Farms to Factories



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Millions of workers around the world are exposed to high temperatures, intense physical activity, and lax labor practices that do not allow for sufficient rehydration breaks. The extent and consequences of heat exposure in different occupational settings, countries, and cultural contexts is not well studied. We conducted an in-depth review to examine the known effects of occupational heat stress on the kidney. We also examined methods of heat-stress assessment, strategies for prevention and mitigation, and the economic consequences of occupational heat stress. Our descriptive review summarizes emerging evidence that extreme occupational heat stress combined with chronic dehydration may contribute to the development of CKD and ultimately kidney failure. Rising global temperatures, coupled with decreasing access to clean drinking water, may exacerbate the effects of heat exposure in both outdoor and indoor workers who are exposed to chronic heat stress and recurrent dehydration. These changes create an urgent need for health researchers and industry to identify work practices that contribute to heat-stress nephropathy, and to test targeted, robust prevention and mitigation strategies. Preventing occupational heat stress presents a great challenge for a concerted multidisciplinary effort from employers, health authorities, engineers, researchers, and governments.

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Until recently, chronic kidney disease (CKD) was thought to be primarily a consequence of other chronic conditions such as diabetes mellitus and hypertension. Acute kidney injury (AKI), and especially recurrent episodes of AKI, have now also been shown to be associated with CKD.¹ In the past few years, environmental and occupational factors have also been associated with CKD, especially in so-called CKD hotspots, which are defined as countries, regions, or ethnicities with a higher than average incidence of CKD.² CKD of unknown etiology (CKDu) has become a newly categorized condition, a diagnosis of exclusion, made when a patient fulfills the Kidney Disease Improving Global Outcomes (KDIGO) CKD

criteria without evidence of a recognized cause such as diabetes, hypertension, genetic disease, or glomerulonephritis.³ The incidence of CKDu is higher in most CKD hotspots, such as Sri Lanka, India (state of Andhra Pradesh), Pakistan, and Egypt, and coastal zones of Nicaragua, El Salvador, and Costa Rica. The causal relationship of environmental and occupational factors and CKDu has not been clearly delineated. However, study of CKDu has been recognized by the ISN as a global research priority.⁴

Approximately 40% of the world's population lives in a climate zone where the normal daytime temperatures exceed 30°C most of the year. In these regions, many workers have physically demanding jobs, are paid by output, lack employment alternatives and health insurance, and live in substandard housing, all of which can independently increase the risk for heat-related morbidity and mortality.^{5,6} As the frequency of hot days and heat waves is expected to increase globally over the coming decades,⁷ the risk of heat-related illnesses and injuries is also expected to rise.^{8–10}

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The threat of excessive occupational heat exposure and its consequences, although also present in developed countries and in formal working sectors, is particularly high in tropical, low-to-middle-income countries where large informal sectors of workers exist, often operating in hot, densely populated environments with high physical workloads and scant safety regulations.^{8,11} The lack of representation of these workers in the social security systems, as well as not being able to count on organized public health systems in these countries, make community-based prevalence studies highly necessary to address this topic.

Occupational heat exposure may affect both outdoor and indoor workers who perform activities in hot environments, such as near furnaces, ovens, and boilers.¹² There is limited research on the effects of chronic indoor occupational heat stress on the kidney health and function. As such, we conducted an in-depth descriptive review of the known effects of indoor occupational heat stress on kidney function. We also examined methods of heat-stress assessment, strategies for prevention and mitigation, and the economic consequences of occupational heat stress.

Heat Stress

Heat stress is considered to be the sum of the heat generated in the body (metabolic heat), plus the heat gained from the environment (environmental heat), minus the heat lost from the body to the environment.¹³ Environmental and metabolic heat stress result in physiological responses (heat strain) to promote the

transfer of heat from the body back to the environment to maintain core body temperature.¹⁴ The body's heat balance is determined by 6 fundamental factors: 4 climatic (air temperature, radiant temperature, humidity, and air movement) and 2 nonclimatic (clothing and the metabolic heat produced during physical activities).⁸ Heat dissipation occurs through dry heat loss (radiation and convection) and evaporative heat loss (sweating) (Figure 1).¹⁵ Heat stress results in heat-related occupational illnesses, injuries, and reduced productivity, when sweat evaporation is insufficient, and other physiological changes cannot prevent the core body temperature from rising.¹³ If temperature rises beyond 39°C, heat stroke may occur, with eventual failure of the central nervous thermoregulatory system.^{16,17}

Heat stress often occurs in conjunction with dehydration, and manifests as a range of heat-related symptoms such as fatigue, headache, muscle cramps, weakness, dizziness, nausea, vomiting, tachycardia, hyperventilation, ataxia, hypotension, syncope, and transient alteration in mental status.¹⁸ The occurrence of heat-related illnesses in an individual or among a group of workers in a hot environment represents "sentinel health events," which indicate that heat control measures, medical screening, or environmental monitoring measures may be inadequate.¹⁹ Individual tolerance to heat stress is variable, and is affected by acclimation, pre-existing disease, clothing, age, gender, level of physical activity, and body size.^{20,21}

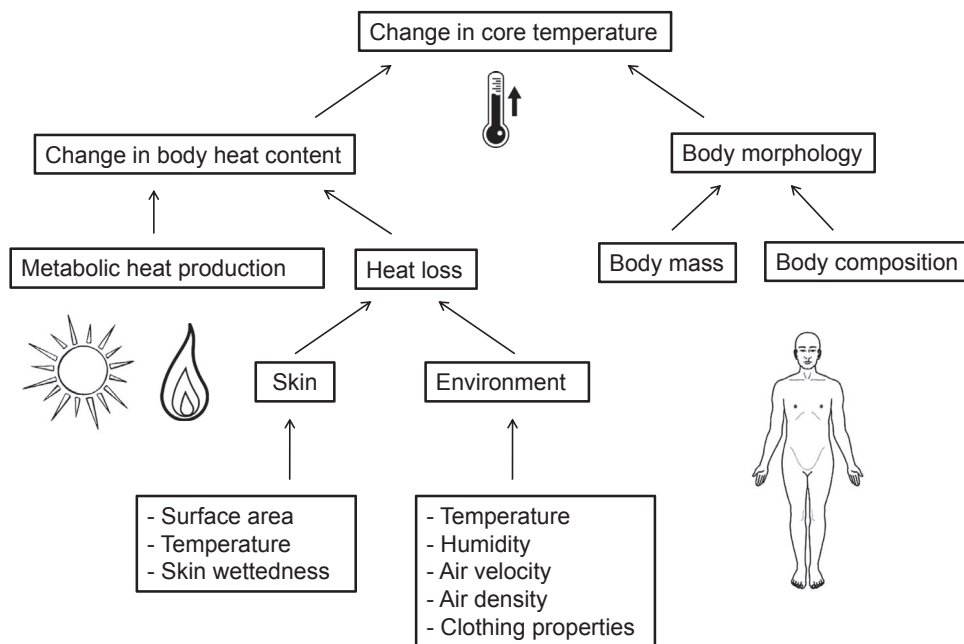


Figure 1. Biophysical factors affecting the change in core temperature during exercise and environmental heat exposure. Reprinted from *Anatomic Neuroscience*, Volume 196, Cramer MN, Jay O. Biophysical aspects of human thermoregulation during heat stress. Pages 3–13, Copyright © 2016, with permission from Elsevier.²⁰

Heat Stress Assessment

International agencies responsible for preventing the health risk of occupational heat stress have formulated heat stress standards and guidelines that specify upper limits of safe heat exposure.²² In 1982, the International Organization for Standardization (ISO) established the WetBulb Globe Temperature (WBGT) as an international standard for safe heat exposure, as it accounts for the combined effects of air temperature, solar radiation, humidity, and wind speed and provides reference values for work–rest regimens in jobs at different work intensities. For example, at a WBGT threshold of 30°C combined with a heavy work load, a 25% work to 75% rest ratio per hour is recommended.²³ Ideally, a WBGT or individual environmental factor profile should be established for each exposed work area. This would then guide engineering controls and work practices.¹³

Another ISO-recommended index is the Predicted Heat Strain index (PHS).²⁴ In contrast to WBGT, PHS is a method (based on human body heat balance equations that account for all 6 factors involved in heat transfer) for predicting both sweat rate and internal core temperature resulting from heat stress.²⁵ When the pre-established criteria are met, the exposure time is calculated and recommended as a maximum work time.²⁶

Both indices have characteristics that limit their use in all settings. For example, WBGT requires specific and expensive equipment, and although it is appropriate for initial assessment, it is not practical for day-to-day monitoring.^{26,27} Also, neither the WBGT nor the PHS methods are valid for the assessment of rapidly changing environments and short exposure durations.²⁸ Alternatively, when continuing assessment is required, the American National Institute for Occupational Safety and Health (NIOSH) recommends the use of the heat index system, which combines both air temperature and relative humidity into a single value that indicates the apparent temperature. Risk levels were established and vary from caution (fatigue is possible with prolonged exposure and activity) to extremely dangerous (heat stroke is imminent).¹³

In a recent review, Gao *et al.* stated that future heat-stress assessment tools (in the context of climate change) should be validated for use in high-risk climate zones and should be interpretable, translatable, acceptable and accessible. These tools should also take individual vulnerabilities into consideration, be appropriate for both hot–dry and hot–humid environmental conditions, and allow for a wide range of clothing adjustments.²⁵

Unfortunately, occupational guidelines for heat stress are not universally implemented, and there are

numerous examples of workplace temperatures exceeding maximum thresholds in outdoor and also indoor activities.^{29–33} In India, a study of nearly 400 measurements of heat stress over a 4-year period, within 8 units of an automotive industry, found that 28% of workers were at risk for health impairment related to heat stress.³⁰ Heat stress can also occur in cooler climates. Chen *et al.* studied 55 subjects in winter, when the outdoor temperature was between 14° and 18°C, and found that the temperatures near furnaces in a steel plant ranged from 35.5° to 46.5°C.³⁴ Heat exposure may be further exacerbated in workers wearing semipermeable or impermeable protective clothing, which can severely impede heat exchange through evaporation.³⁵ This may lead some workers to remove their protective clothing and increase their risk for workplace injury.³⁶

Mesoamerican Nephropathy and Other Regional Nephropathies Potentially Linked to Heat Stress

Since the late 1990s, many studies have documented a startling excess of CKD in Central America and Southern Mexico, a phenomenon termed Mesoamerican nephropathy.^{37–41} Rates of CKD in these regions are nearly 9 times higher than in age-matched populations in the United States. El Salvador currently has the highest mortality rate from kidney disease in the world.⁴² The highest rates of CKD are observed among sugarcane workers in the hottest Pacific lowlands of Nicaragua and El Salvador, where the prevalence of CKD is 18% compared with 1% in communities at higher, cooler elevations.⁴² Scientists initially suspected that pesticides used in sugarcane production might be implicated in this epidemic. However, when kidney function was compared between groups of lowland and highland sugarcane workers, the lowland workers were 10 times more likely to demonstrate elevated serum creatinine.³⁹ Sugarcane harvesting typically involves 4 to 12 hours of uninterrupted intense physical exertion, in temperatures that range on average between 34° to 42°C.^{27,43–46} Fields are usually burned the night before harvesting, and workers entering this heated environment quickly becoming coated in soot, which further impedes cooling. Although workers can take water breaks, payment is based on the amount of cane cut, and several studies have shown that workers exhibit signs of dehydration.^{27,43–46}

A similar phenomenon of chronic kidney disease of unknown origin (CKDu) has been documented in the North Central Province of Sri Lanka and in the coastal region of Andhra Pradesh in India. CKDu was first recognized in the 1990s and is currently thought to

affect more than 100,000 individuals.^{47,48} Both Meso-american nephropathy and CKDu in different regions disproportionately affect younger male agricultural workers, and both conditions appear to develop in the absence of traditional risk factors such as hypertension and diabetes.^{3,49} Patients present with elevated serum creatinine, low-grade or no proteinuria, and no known cause of kidney disease. In case-series studies of sugarcane and agricultural workers in Nicaragua and El Salvador, kidney biopsies show evidence of glomerulosclerosis, glomerular hypertrophy, signs of chronic glomerular ischemia, and mild-to-moderate chronic tubulointerstitial damage.^{42,50–52} Initial theories advanced to explain these epidemics have included exposure to contaminated drinking water or alcohol, heavy metals, pesticides, or infectious agents such as leptospirosis. However, evidence to date supporting these theories is inconsistent.^{40,53,54}

The Heat-Stress Hypothesis

Although dehydration has not traditionally been considered a risk factor for CKD, dehydration is well known to adversely affect kidney function. Dehydration increases urinary concentration (due to vasopressin activation) secondary to an increase in serum osmolarity due to the loss of body water. It is also associated with renal vasoconstriction, but with initial relative maintenance of glomerular filtration rate (GFR). If the volume depletion is severe or prolonged, the GFR subsequently falls. This insult to the kidney was initially thought to be completely reversible with hydration, unless ischemia resulted in acute kidney

injury (AKI).⁵⁵ However, there is now evidence that chronic or repeated episodes of heat stress accompanied by water and solute loss (by dehydration or volume depletion) can cause repeated subclinical ischemic kidney injury, which over time may lead to permanent kidney damage and CKD (Figure 2).^{40,56} These repeated episodes of injury, which can be combined with some acute clinical episode,⁵⁷ eventually result in abnormal repair mechanisms,⁴⁸ leading to renal fibrosis, vascular rarefaction, and glomerulosclerosis.⁵⁸

Glaser *et al.* detailed the potential pathological mechanisms by which repeated heat stress and dehydration, coupled with overexertion, may lead to low-grade or overt rhabdomyolysis, hyperosmolarity, hyperthermia, and extracellular volume depletion. These processes can result in several mechanisms that cause AKI, including the direct effects of vasopressin on renal tubules, endogenous fructose metabolism in the proximal tubule via the fructokinase system, the development of uricosuria and urate crystal formation, hypokalemia-induced renal vasoconstriction and injury, and a generalized reduction in renal blood flow exacerbating ischemic damage.⁴⁸

Other authors have hypothesized that the nephrotoxic effect of heat stress and dehydration may be compounded by rehydrating with high-fructose-containing drinks. Work in mice provides compelling evidence that recurrent dehydration can induce renal injury by a polyol-fructokinase mechanism.^{54,59,60} In addition, AKI caused by chronic dehydration and heat stress may be aggravated by

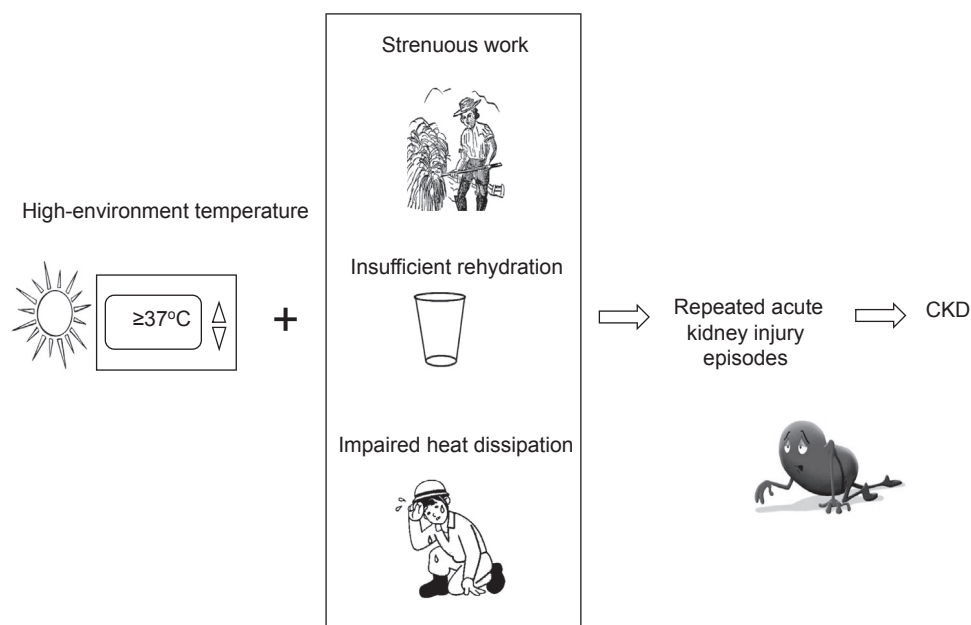


Figure 2. Environmental and exposure factors associated with chronic kidney disease (CKD).

other exposures that may occur simultaneously with the use of potentially nephrotoxic drugs, such as nonsteroidal anti-inflammatory agents, rhabdomyolysis due to extreme labor, illegal alcohol, pesticides and other agrochemicals, heavy metals, and toxic pollutants.^{4,61} Key occupational, personal, socio-economic, and climate factors that may interact to increase the risk of CKDu are summarized in Figure 3.

Many scientists now believe that heat-stress nephropathy, resulting from extreme occupational heat stress and repeated dehydration, is central in the pathophysiology of Mesoamerican nephropathy, and this may hold true for CKDu in other CKDu hot-spots.^{27,40,45,46,48,56,62} Whether heat stress causes CKD directly or in combination with other factors is an intriguing hypothesis; however, it remains unproved.^{47,48,63,64}

The First International Research Workshop on Mesoamerican Nephropathy issued several recommendations for future studies to better understand this unique form of CKDu. These included the following: measuring workload, heat stress, water and solute loss among workers; quantifying nephrotoxic agents in drinking water and food; and measuring biomarkers of AKI in workers before and after shifts.⁴⁰

Occupational Heat Stress and Kidney Health in Indoor Workers

Although the relationship between occupational heat stress and kidney health in outdoor workers has been more fully explored, data on indoor workers is almost entirely absent. Millions of indoor workers may be at risk, particularly those working near furnaces, ovens, smelters, and boilers in kitchens, steel plants, foundries, automobile industries, and glass manufacturing units. Two recent reports from India seem to be the first to address this issue. Both were cross-sectional studies and assessed simple urinary kidney health markers. A total of 94 kitchen workers in northern India were subjected to an average workplace temperature of 38°C with 67% humidity. Workers had a high urinary specific gravity, and 85% had an albumin-to-creatinine ratio > 30 mg/dl.⁶⁵ Another study of 312 female workers in southern India examined 3 occupational sectors associated with hot environments: agricultural field work, brick making, and steel manufacturing. In this study, 71% of workers had exposures above the recommended limit (defined using WBGT), with the highest exposure among steel workers (90% of participants). At the steel workers' site, the maximum WBGT was 41.7°C, and a greater percentage of women had a urine specific gravity

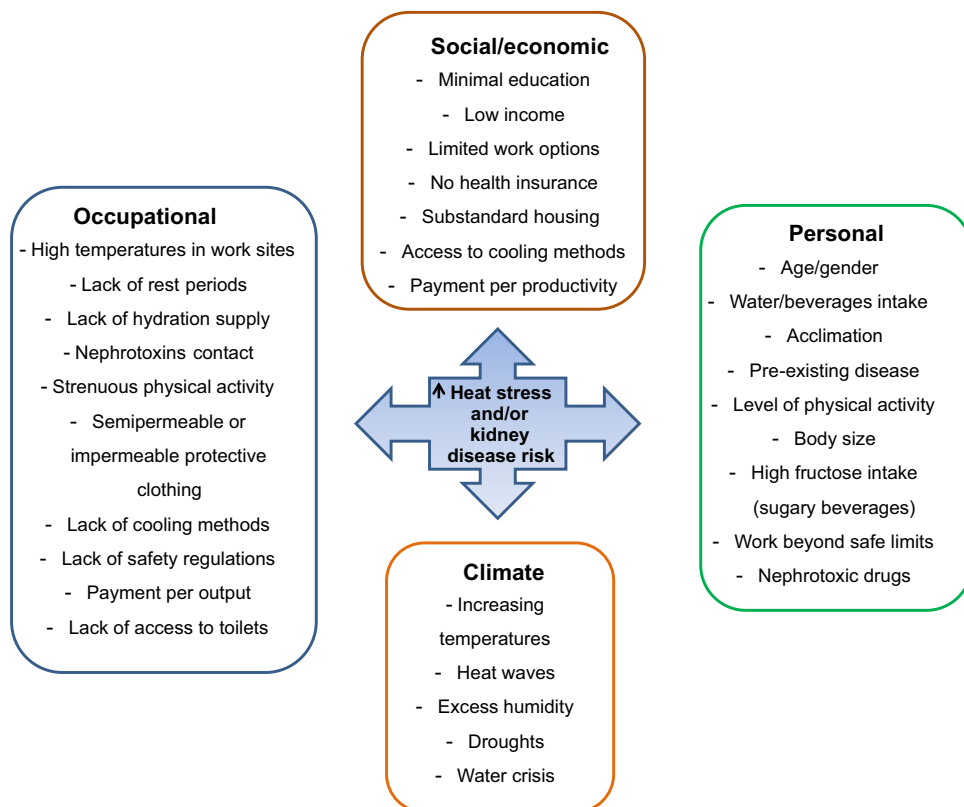


Figure 3. Occupational, personal, socioeconomic, and climate factors that may interact to increase the risk of heat stress and/or kidney disease.

> 1.020, indicating dehydration. Among all participants, 87% reported excessive sweating and thirst during work shifts. Another finding was that 64% of participants lacked access to toilet facilities while working, and a significant association was observed between high-heat exposures, inadequate toilet facilities, self-reported adverse heat-related symptoms, and prevalence of genitourinary issues. Lack of access to toilets led some women to drink less to avoid urination, which may further compromise adequate hydration and further increase the potential risk of kidney disease.³²

Epidemiological studies have shown that populations exposed to chronic dehydration, high ambient temperatures, and intensive physical activity have a higher incidence and prevalence of kidney stones.^{66–69} Furthermore, increased water intake is known to be the most effective therapeutic measure to prevent the recurrence of stones.⁶⁶ By increasing renal clearance, a high water intake can decrease the supersaturation of sodium, urea, and osmoles.^{70–72} Recent research has also shown that individuals who develop kidney stones were twice as likely to develop end-stage kidney disease in the subsequent decade, although the absolute increase in risk was small.⁷³ There is some evidence that occupational heat stress increases the risk for kidney stones in indoor workers. In a study of male steel workers, those exposed to occupational temperatures exceeding 45°C were 9 times more likely to develop kidney stones compared with those working in areas at room temperature (8.0% vs. 0.9%).⁷⁴ Similarly, in a study of machinists at a glass plant in Italy, the prevalence of kidney stones was significantly higher among machinists working in the hottest areas (8.5%) compared with machinists working in areas of normal temperature (2.4%).⁷⁵ It is worth mentioning that predictions based on a climate model of intermediate severity warming indicate a climate-related increase of 1.6 to 2.2 million lifetime cases of nephrolithiasis by 2050 only in the United States, representing up to a 30% increase in some climate divisions.⁶⁷

Prevention and Mitigation Strategies

Occupational health and safety guidelines have been developed to protect workers, yet many workers are denied this right.¹² Even with enforced guidelines and recommendations for work modification, highly motivated individuals often exert themselves beyond safe thermal limits, sometimes resulting in serious health consequences.⁷⁶ As well, the social norms or culture of an institution affect these practices. In workers with a low socioeconomic status, payment per output or fear of losing employment can drive individuals to work beyond safe thermal limits.²⁹ Concerning labor

violations among farm workers in the Central American sugar sector were observed by an independent nonprofit organization, which conducted a risk analysis based on interviews. They found evidence of recruitment abuses, child labor, restrictions on workers' right to freedom of association, gender-based discrimination, wage and working hours' violations, inhumane living conditions, and threats to workers' health and safety, such as lacked access to sufficient food, potable water, breaks, and shade while working. They also observed that pain killers were also provided by the companies for workers to meet the rigorous physical demands of their jobs.⁷⁷

Maintaining adequate hydration may be the single most important intervention in the management of workers exposed to heat stress.¹² However, even if water is readily available, men working in the heat have been shown to drink less than they lose through sweating.¹⁴ In fact, it is well documented that workers performing activities in hot environments often not only become dehydrated on the job but workers may also start the workday with a fluid deficit.^{78–81}

Also, as mentioned by Kenefick *et al.*, employers have not always promoted drinking, as this would require more rest breaks and thus decrease employee productivity.⁷⁸

Guidelines recommend weight monitoring and replacing fluids frequently when exposed to heat stress, such as 1 cup (250 ml) every 20 minutes or according to weight loss when working in warm environments.¹³ Weight monitoring was also proposed in CKDu prevention as being the least expensive, most feasible means of assessing changes in hydration status.⁴⁰

The first-morning urine concentration has been considered as a reliable marker for hydration status, but its values can provide misleading information if obtained during rehydration periods.⁸² Thus, urine specific gravity measured by dipstick can be used to identify workers who are dehydrated before starting their activities. Urine visual assessment charts can also be implemented as a training tool to demonstrate the concept of color change between the urine of a well-hydrated worker and that of a dehydrated worker.¹³

An interesting and simple tool for self-monitoring day-to-day fluid intake adequacy, using first-morning measures of body weight, thirst perception, and urine color, was proposed by Chevront and Kenefick.⁸³ However, the effectiveness of this method has not been tested in chronically dehydrated subjects.

Better education for workers in hot environments is clearly needed to communicate the risks associated with heat exposure and dehydration. Workers should be trained to recognize the signs of heat illness⁸⁴ and to

practice appropriate prevention by hydrating regularly during working hours and afterward.¹² It is more likely that sustaining hydration will maintain worker productivity sufficiently to offset any work breaks, particularly during hot weather. In addition, the decrease in health care costs associated with possibly reducing accidents or illnesses in the workplace could further help offset the small decline in productivity from rest breaks.⁷⁸ Besides constant environmental monitoring to establish work/rest cycles, appropriate work conditions and interventions to alleviate heat strain must also include ready access to toilet facilities, appropriate clothing, and personal cooling techniques (Figure 4).^{11,32} Furthermore, development of acclimation procedures, hazard communications, early warning systems, surveillance, and increased emphasis on prevention can be useful tools.⁸⁵ Even though self-paced or regulated work/rest cycles can be essential in some occupations to control heat exposure, it is vital that workers be appropriately compensated for the work that they perform and not be penalized for environmental constraints, as income and livelihood are pervasive motivating factors that can drive workers to ignore psychophysiological indicators of heat strain.⁸⁴ Heat exposure can be extreme during sugarcane cutting, and to maintain safety, workers should limit work activities to as short as 15 minutes per hour during part of the day.²⁹ However, there are reports that these workers cut up to 12 tons a day during harvest months to secure higher income.⁴⁵

Identifying high-risk individuals would allow a more targeted strategy of risk reduction. Unfortunately, there are limited tests in heat-related occupations that specifically assess an applicant’s capacity to undertake physical work in hot environments.²² Most tests do not evaluate kidney health. There are reports

from Mesoamerican countries that some sugarcane employers are requiring potential employees to demonstrate a normal serum creatinine as a condition of employment. Detection of CKD in either existing or new hires may protect against the development and progression of CKD. However, it can also result in loss of employment, and importantly, health benefits in areas that are not able to provide adequate treatment or alternative sufficient income.

Low-cost measures that reduce thermal stress without compromising performance and productivity are more likely to be accepted by workers and employers. A recent intervention package designed to reduce risk among sugarcane workers appeared to be effective. This intervention study was led by the Worker Health and Efficiency Program (WE Program) a growing multi-stakeholder partnership with representatives from civil society, academia, private companies, and governments.²⁷ It was tested in a 60-person cutting group, which was provided water supplied in individual backpacks, mobile shaded rest areas, and scheduled rest periods. Ergonomically improved machetes and efficiency strategies were also implemented. Post intervention, there was a 25% increase in self-reported water consumption, a significant decrease in symptoms associated with heat stress and dehydration, a 43% increase in individual daily production, and less adverse impacts on kidney function both across a day and across an entire harvest. The authors concluded that with proper attention to work practices, good employee health and productivity can both be achieved.^{86,87}

The Economic Impact of Occupational Heat Stress

There are other consequences of working in hot environments. A natural reaction to heat is to reduce

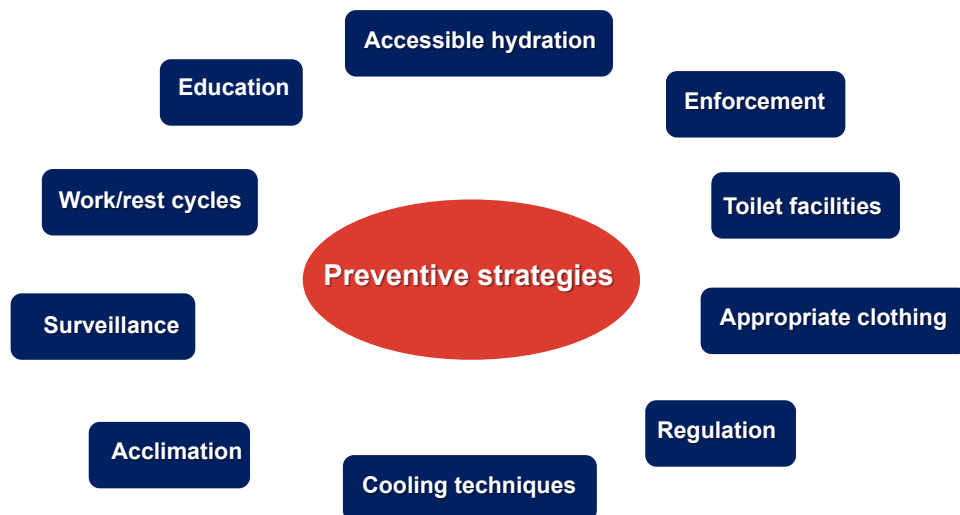


Figure 4. Preventive strategies against occupational heat stress.

activity to lower the body's internal heat production. This results in lower productivity, which in the long term affects individual, local, and national economic productivity affecting developing countries disproportionately, as most of these already are located in warm climates.^{12,88} The general working population is also increasingly older, more sedentary, and less fit, with a higher prevalence of chronic disease and medication use.⁸⁹ This combination of personal risk factors reduces the thermal tolerance of the average worker and increases that individual's susceptibility to heat-related illness.⁹⁰ Increased hospitalization during heat waves are reported in many countries. Chinese data highlight a 4.5% increase in hospitalization with every 1°C increase in mean daily temperature above 29°C,⁹¹ with similar reports in Australia,⁹² Canada,⁹³ and the United States.⁹⁴

In a study of Thai industrial workers in 2009, 60% reported loss of working capacity during heat, and about 20% were more vulnerable to heat illnesses during summer months.⁹⁵ According to Dunne *et al.*, heat stress has impaired global labor capacity by up to 10% in recent decades. This is predicted to double by the summer of 2020.⁹⁶ The economic consequences of this work force reduction are marked, with estimated net costs of USD \$2.4 trillion by 2030 attributed to heat-related reductions in work productivity alone.⁹⁷

Adequate water intake, both in quantity and in quality, is essential to maintaining proper hydration. Higher temperatures and changes in extreme weather conditions are projected to affect availability and distribution of rainfall, snowmelt, river flows, and groundwater, and further deteriorate water quality with a significant increase in cost to access safe water.⁹⁸

CKD requires very expensive treatment, in its late stages when renal replacement therapy is necessary to maintain life.⁹⁹ As mentioned by the ISN position statement on CKDu, this condition typically affects poor agricultural communities, affecting large numbers of working-age adults. Thus, the individual, social, and economic impact is already very high. For those without access to renal replacement therapies, CKDu leads to death, and even when renal replacement therapy is available, the condition imposes a formidable challenge to local health systems.¹⁰⁰

Taking all these factors into account, the burden in health, economic, and social costs to treat both acute and chronic effects of heat stress exacerbated by climate change are almost immeasurable.

Conclusion

Millions of workers around the world are exposed to chronic heat stress and recurrent dehydration that

may increase their risk for CKD and ultimately kidney failure. Currently, the prevalence and extent of excessive heat exposure in different occupational settings, countries, and cultural contexts is not well studied. This has resulted in a near universal failure to implement effective guidelines and mitigation strategies.¹⁰¹ Rising global temperatures coupled with decreasing access to clean drinking water may exacerbate the effects of occupational heat exposure in tropical countries, where many workers are exposed to high temperatures, intense physical activity, and lax labor practices that do not allow for sufficient rehydration breaks.¹⁰² There is an urgent need for health researchers to identify work practices that contribute to heat-stress nephropathy, and to test targeted, robust prevention strategies. Similarly, validation of and funding for more sensitive biomarkers of disease would allow early detection and an opportunity to try to slow disease progression.³ Preventing occupational heat stress is especially important in developing countries and will require a concerted multidisciplinary effort from engineers, employers, health authorities, researchers, and governments.

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