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Some chronic disease medications found to impair the body's cooling ability

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Medications to treat various chronic diseases may hinder the body's ability to lose heat and regulate its core temperature to optimal levels. The loss of effective thermoregulation has implications for elderly

people receiving treatment for illnesses like cancer, cardiovascular, Parkinson's disease/dementia and diabetes, particularly during hot weather, according to a review by a team of scientists from various institutions in Singapore.

The group, led by Associate Professor Jason Lee from the Human Potential Translational Research Programme at the Yong Loo Lin School of Medicine, National University of Singapore (NUS Medicine), identified and reviewed relevant research papers using keyword searches on databases such as PubMed and Google Scholar.

These papers studied the associations and effects of medications on thermoregulation. The review findings were presented in a topical manner, focusing on medication classes used to treat commonly diagnosed chronic conditions (e.g., diabetes, cardiovascular disease, neurodegenerative disease, and cancer).

The study is published in *Pharmacological Reviews*.

The findings show that medications used to treat common chronic conditions, like blood thinners, blood pressure drugs, Parkinson's disease/Alzheimer's medications, and some chemotherapy drugs, can make it harder for the human body to handle hot weather by reducing its ability to sweat or increase blood flow to the skin.

Lead author and second-year Ph.D. candidate from the Human Potential Translational Research Programme Mr. Jericho Wee said, "Rising global temperatures caused by climate change pose a significant health concern for clinical patients reliant on long-term medications and health care. Increasingly, we will continue to see more elderly patients, many who have multiple health conditions and are taking different types of medication concurrently to manage their chronic diseases, compounding the risk of heat-related illness and dehydration."

"Understanding how each medication impacts thermoregulation, in the face of warmer environments, is the crucial first step to predicting the possible health outcomes when multiple medications are taken concurrently."

While previous reviews have highlighted the impacts of medications on heat, the scope of those reviews did not present the evidence in the context of the chronic diseases and aging.

The team's narrative review presents the evidence in the context of high ambient temperatures and their impact on chronic disease sufferers who are on long-term and life-long medication.

Senior author Assoc Prof Jason Lee said, "This review emphasizes the importance of studying the mechanisms of altered thermoregulation in individuals with diabetes and other cardiometabolic conditions to prevent heat-induced conditions. This is most relevant in Singapore and many other countries, where we have rapidly aging populations and rising ambient temperatures."

"Pharmacological and thermal physiologists should focus transdisciplinary efforts on this area of research to refine and enhance safe medication prescription guidelines to preserve the health of people who need these medications, even in hot weather."

Assoc Prof Melvin Leow, the review's co-author and Senior Consultant Endocrinologist at Tan Tock Seng Hospital said, "Physicians are often unaware of the potential harms certain drugs may cause by compromising the body's thermoregulatory control mechanisms. This is an especially important area to delve into as those with chronic diseases and older adults are susceptible to adverse health outcomes in the heat, due to their reduced thermoregulatory capacity."

"It is timely and prudent that scientists and doctors collaborate even closer in this important field that cuts across a wide range of medical disciplines."

The findings, in brief:

Cancer

Patients on certain cancer medications have reported symptoms of hot flushes, such as inappropriate sweat responses and an increase in core temperature which affects quality of life. Exercise and improved fitness levels have been shown to reduce the frequency of hot flushes and improve thermoregulatory responses in other chronic conditions such as diabetes, and it remains a crucial component in maintaining the nervous and cardiovascular functions of cancer patients. However, bodily impairments and limitations caused by chemotherapy and medications may limit their ability to exercise, which perpetuates a cycle of loss in exercise capacity that is crucial to their recovery.

Cardiovascular disease

Patients who have cardiovascular diseases, such as coronary heart disease, stroke and heart failure, are more vulnerable to high heat exposure because their hearts will be working harder to deliver blood to the skin and working muscles to maintain core temperature at an optimal level while maintaining work output. Anti-platelet medications, such as aspirin and clopidogrel, are usually taken to prevent blood clots from forming in the blood vessels, that could lead to stroke or heart disease.

Yet, these anti-platelet medications may increase core temperature, whether at rest or during exercise. These medications also reduce skin blood flow and suppress sweat responses, which means thermoregulatory

responses would be less sensitive to accumulated heat, and delay in cooling itself down, which could lead to heat stroke.

Used for multiple cardiovascular conditions, such as ischemic heart disease, high blood pressure, and heart failure, beta-blockers can reduce skin blood flow during heat stress by reducing blood pressure and facilitating additional constriction of skin blood vessels. However, the findings of the effects of beta-blockers on sweat responses remain mixed, with some studies showing no changes in sweating, while others demonstrate reduced sweating.

As such, greater research efforts are needed to understand how different types of beta-blockers may impact sweating.

Some studies have highlighted that the type of beta-blocker is an additional consideration. For example, non-selective beta-blockers like propranolol, widely prescribed at the population level, can result in greater impairments in thermoregulation than selective-beta-blockers that only target cardiac or peripheral tissues. Hence, non-selective beta-blockers could predispose patients to greater heat strain and heat-related illness.

Diabetes

Insulin, which is typically used to reduce high blood sugar, or hyperglycemia, in patients with type 1 diabetes, has been shown to impair the ability of the body to regulate heat properly. It also increases metabolic heat production at rest and during exercise, which can be fatal to the body when the accumulated heat cannot be dissipated quickly.

For patients with type 2 diabetes who consumed metformin to manage their condition, nearly 30% of patients experience diarrhea and nausea when they are first prescribed the medication. If the fluid loss cannot be

sufficiently replaced, patients, especially the elderly, are at a higher risk of dehydration, which may result in greater cardiovascular strain during exertional heat stress.

Neurocognitive diseases

Due to an internal imbalance in dopamine and acetylcholine levels, patients with neuropsychiatric diseases such as Parkinson's and Alzheimer's disease experience thermoregulatory dysfunction when their body is unable to control its temperature. However, the medications to manage these neurological conditions have been known to alter the brain's control of thermoregulation and thermoregulatory responses, such as sweating and cutaneous vasodilation, which could result in both hyperthermia and hypothermia.

Anticholinergics and cholinesterase inhibitors are prescribed to improve motor and cognitive symptoms in the brain for Parkinson's Disease patients. However, these agents also alter the dopamine and acetylcholine levels, likely inducing changes in the central thermoregulatory drive that affects the central processing and integration of thermal information and numbs the instinctive responses to heat stress, while driving up the body's core temperature. This could lead to an increased risk of developing heat-related illnesses.

Dopamine replacement agents and dopamine agonists are usually prescribed to those with Parkinson's disease to increase dopamine levels to help in movement and coordination. While highly effective, these agents have been observed to significantly influence thermoregulation and impair sweat responses which are crucial for heat dissipation. It is important that the dosage of these agents is appropriately adjusted to minimize the onset of severe after-effects.

More information: Jericho Wee et al, Effects of medications on heat

loss capacity in chronic disease patients: health implications amidst global warming, *Pharmacological Reviews* (2023). DOI: 10.1124/pharmrev.122.000782