Multiple sclerosis and thermoregulatory dysfunction

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Multiple sclerosis is a demyelinating disease of the central nervous system, characterized by a relapsing and remitting or, alternatively, by a steady and continuous course of dysfunction. The hallmark of the disease is heterogeneity. How the disease presents itself depends on the exact location and total accumulation of lesions and on the impact of demyelination on nerve conduction. Conduction maybe be enhanced, producing positive symptoms like tic douloureux, paresthesiae, or tingling, or conduction may be diminished, producing negative symptoms like blindness and palsy (7, 8). Diminished conduction may be total or partial, with decreases in the maximum of frequency or velocity of conduction. During remission, which may last months or years, symptoms improve as inflammation subsides, sodium channels migrate into the bare axon, remyelination of the denuded site occurs, and, ultimately, conduction resumes through the lesion sites. The deficit may also become permanent as axons degenerate (9). During shorter periods lasting hours or days, symptoms may also worsen, as conduction through old lesions fluctuates; conduction is “highly insecure” and subject to inflammatory factors like nitric oxide and temperature changes (5, 8).

Heat worsens and cooling improves negative symptoms of multiple sclerosis, sometimes dramatically so. The underlying mechanism relates to the influence of temperature on sodium channels and on current necessary for depolarization of the axon. Increases in temperature diminish the depolarizing current, whereas decreases in temperature have the opposite effect (8). Sensitivity can be extreme, and very small changes can have profound effects. Heating, for example by radiation from the sun, can turn a limping gait into no gait at all. Alternatively, hot air from a hair dryer can turn a hopeful morning into an exhausting one. Cooling, on the other hand, by sitting in a cool bath or shower, can turn the “disease off” (at least for a little while) and give an individual back the freedom for exercise or work.

As you might expect, the impact of the disease on the thermoregulatory system takes a myriad of forms, depending on lesion location and severity. With any location and lesion load, however, the impact of the disease depends on body temperature, worsening as activity is diminished in more and more demyelinated axons. In addition, thermoregulatory impact is worsened by lack of physical fitness and lowered blood volume. The individual may be suddenly overcome. Getting into a hot bath may seem a great way to relax, but then suddenly the individual with multiple sclerosis is too weak to get out. Triggering such a collapse of the thermoregulatory system explains sudden deaths associated with sun exposure (1).

This editorial has been prepared to provide insight gained from living with multiple sclerosis and its heat-related symptoms and from working many years as a research physiologist. Discussions focus on three areas where further research may have important implications to those living and coping with the disease: thermoregulatory failure, the cranial radiator, and exercise-induced heat.

Thermoregulatory system. Recently, one study has assessed the thermoregulatory center and its impact on multiple sclerosis (3). In this study of a single subject with a history of multiple sclerosis and thermoregulatory dysfunction, temperature thresholds were calculated as the core temperature was slowly warmed to sweating and again as the core temperature was gradually cooled to vasoconstriction and shivering. It was found that the sweating threshold was a full 1°C higher than normal and the vasoconstriction threshold was 2°C below normal, making the calculated sweating-to-vasoconstriction range four times the normal amount. The shivering threshold was also lower than normal (31.8°C), making the vasoconstriction-to-shivering range more than twice the normal amount. Providing such information may sound academic and simplistic; however, this may be an important point to those with multiple sclerosis, altering them to the extent of dysfunction, and to others like caretakers and insurance companies, alerting them to the hazards of increased body temperature and the need for cooling devices.
Cranial radiator. The brain is one of the most metabolically active tissues, generating large amounts of heat. Dissipating this heat as well as heat absorbed from the environment has been a major evolutionary hurdle, one that was necessary to overcome for the continued development of the brain and the evolution of humans. Simply put, the brain, like the automobile engine, could not increase in size without the simultaneous development of an adequate cooling system. The brain was constrained and could only develop in parallel to its “cranial radiator” (2). However, for many with multiple sclerosis, the cranial radiator is simply not adequate.

The evolution of emissary veins solved this problem and removed any restraint on brain development. According to this theory, a vascular network in the scalp and face developed with veins draining through emissary veins in the skull joining the meningeal veins and sinuses of the dura mater. From the dura, venous blood drains to veins within the brain, thereby removing heat from the brain. With heat stress, the venous plexus on the face and scalp dilate, promoting heat loss by conduction. In addition, secretomotor pathways activate sweating, further cooling the blood by evaporation. Thus venous blood, the temperature of which is lowered by conduction and evaporation, percolates back to cool the brain (2).

Lucy, an Australopithecus afranensis, had not yet developed a cranial radiator. As a result, her brain size remained small and her wanderings were limited to the cool jungles. However, as the network of veins and holes evolved, thermal constraints were released and the brain began to increase in size. With an adequate “cranial radiator,” early humans were also free of the forest. Many individuals with multiple sclerosis have inadequate cranial radiators (2) and have been restricted in their movements to the air-conditioned indoors.

Exercise-induced heat. The final area where research could make a difference is exercise. The first report that vision deteriorated with exercise came in 1890 by the German ophthalmologist Uhthoff. Loss of vision was linked to block of the optic nerve and was associated with exercise and increases in body temperature (6). Subsequently, this phenomenon was expanded to include other negative symptoms as well, setting the stage for the long-standing recommendation given to many individuals with multiple sclerosis: “avoid exercise.” However, there is no doubt that exercise programs are beneficial and for a number of reasons; besides the obvious ones, such as improved strength and reduced body fat, there are more subtle ones, such as diminished anger and depression (4).

There is a simple solution to this dilemma, made clear when I was swimming at a local recreational pool. I routinely swam 300–400 yards before fatigue limited my performance. At the end of the swims, getting to the shower without tripping was a serious concern. However, one day the heater broke. Water temperature fell 2–3°C per day, and with each day I felt stronger, faster, and more flexible. My distance swimming also increased. I was not alone. Picking up my daughter from her swim practice, I discovered that the heater in her pool had also broken: while the young swim team members balked at jumping in, one senior club member rejoiced. He, as you might have guessed, had multiple sclerosis. In both cases, we had come across the solution: using cool water temperatures to offset Uhthoff’s phenomenon. These observations by themselves mean little, but a recent study confirms this simple solution (10). Further confirmation of these findings is important because keeping in good physical health is the best preventative treatment that can be offered to individuals with multiple sclerosis and the best advice for long-term, cost-effective care.

Multiple sclerosis may someday be prevented or cured. However, today’s research designed to find a cure or cause offers little solace to the 2.5 million people with the disease. These individuals must accept their disability and manage their symptoms. However, these symptoms would be easier to manage if those with the disease and others understood more about thermoregulation and its impact on multiple sclerosis.

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REFERENCES