Invited Review: Aging and human temperature regulation

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Kenney, W. Larry, and Thayne A. Munce. Invited Review: Aging and human temperature regulation. J Appl Physiol 95: 2598–2603, 2003; 10.1152/japplphysiol.00202.2003.—This mini-review focuses on the effects of aging on human temperature regulation. Although comprehensive reviews have been published on this topic (Kenney WL. Exercise and Sport Sciences Reviews, Baltimore: Williams & Wilkins, 1997, p. 41–76; Pandolf KB. Exp Aging Res 17: 189–204, 1991; Van Someren Ed, Raymann RJ, Scherder EJ, Daanen HA, and Swaab DF. Ageing Res Rev 1: 721–778, 2002; and Young AJ. Exp Aging Res 17: 205–213, 1991), this mini-review concisely summarizes the present state of knowledge about human temperature regulation and aging in thermoneutral conditions, as well as during hypo- and hyperthermic challenges. First, we discuss age-related effects on baseline body core temperature and phasing rhythms of the circadian temperature cycle. We then examine the altered physiological responses to cold stress that result from aging, including attenuated peripheral vasoconstriction and reduced cold-induced metabolic heat production. Finally, we present the age-related changes in sweating and cardiovascular function associated with heat stress. Although epidemiological evidence of increased mortality among older adults from hypo- and hyperthermia exists, this outcome does not reflect an inability to thermoregulate with advanced age. In fact, studies that have attempted to separate the effects of chronological age from concurrent factors, such as fitness level, body composition, and the effects of chronic disease, have shown that thermal tolerance appears to be minimally compromised by age.

heat stress; cold stress; thermoregulation; sweating; skin blood flow

AGE AND BASELINE BODY TEMPERATURE

Is there an inherent difference in baseline body core temperature (Tc) between young and older adults under resting thermoneutral conditions? Several published reports suggest that baseline Tc decreases with advancing age and has greater variability in older populations (17, 44, 48). For example, the British National Survey (13) reported that as many as 10% of individuals age 65 yr and older had early morning temperatures /H11021/35.5°C. Keilson et al. (22) investigated the prevalence of low body temperatures in 97 ambulatory elderly (mean age 74 yr) and 20 younger (mean age 32 yr) subjects in northern Maine. Early morning urine temperatures (Tur) were measured as an estimate of Tc. That study detected no Tur <35.5°C, and average Tur and oral temperatures (Tor) were 0.3 and 0.2°C warmer than those presented in the British survey (13). More importantly, there was no age effect on waking on either Tur or Tor, which averaged 36.41 ± 0.34°C (mean ± SD) and 36.21 ± 0.42°C for older subjects and 36.53 ± 0.36°C and 36.41 ± 0.42°C for young subjects.

The lower Tc of older men and women reported in various studies appear to reflect nutritional, disease, and medication effects. Fox et al. (13) noted that the subgroup of the elderly with the most reports of low Tc was the impoverished. Furthermore, exclusion of the following factors negated any relationship between chronological age and Tc in a sample of 93 volunteers aged 62–96 yr (32): diabetes and neurological disorders, low body weight and consumption of less than two meals per day, smoking, lack of self-sufficiency, alcohol intake >3 oz. per wk, and use of various medications. In conclusion, baseline Tc levels in healthy, older adults are not different from those in younger individuals under resting thermoneutral conditions.

AGE AND CIRCADIAN TEMPERATURE CYCLES

Tc is one of the most powerful and stable indicators of circadian synchrony, reflecting activity of the circadian rhythm’s “strong oscillator.” In agreement with animal data (18), some human studies suggest that aging is associated with flatter and earlier phasing rhythms, even with self-regulated diurnal activity (56). Although neither the mean 24-h Tc nor the mean Tc during sleep was dependent on age, the mean Tc during the time...
COLD STRESS

The physiological response to cold stress involves both decreased heat loss and increased heat production. The former is accomplished by increasing effective tissue insulation (primarily by peripheral vasoconstriction), whereas the latter involves increasing metabolic rate by nonshivering and shivering thermogenesis. Most cross-sectional studies report that aging is associated with a relative inability to maintain $T_c$ when exposed to cold. Whereas some investigations have shown that older men seem to differ more often from their younger counterparts, older women typically show no alterations in circadian $T_c$ rhythm when compared with young men or women (38, 55, 56). Thus subtle changes in the circadian $T_c$ rhythm of older adults may primarily reflect a gender effect. Figure 1 summarizes the age-related changes in thermoregulation at rest during normothermia.

Vasoconstrictor responses. In 1977, Collins et al. (4) stated, “People at risk of developing hypothermia also seem to have . . . a non-constrictor pattern of vasomotor responses to cold.” Aging is associated with an attenuated vasoconstrictor response during cold exposure, even when subjects are matched for fitness and body size and composition (10, 24). The diminished ability of aged skin to vasoconstrict is evident in both acral (palms, soles, lips, ears, and so forth) skin (28) and nonacral (limbs, torso) skin (10, 24). In fit, healthy subjects, these differences in peripheral blood flow are not accompanied by alterations in atrial natriuretic factor, arginine vasopressin, plasma renin activity, or plasma norepinephrine concentrations (54).

Thermogenesis. Because both skin and muscle vasoconstriction contribute in series to insulation from cold, the impact of the diminished vasoconstrictor response on thermal balance is exacerbated by sarcopenia, that is, the age-related loss of muscle mass. Basal and resting heat production decreases 20% from age 30 yr to age 70 yr primarily because of the loss of active muscle mass (43). Cold-induced metabolic heat production tends to be lower in older adults across studies (2, 15, 29, 59), although reports to the contrary exist (34, 41, 58). A study that matched subject groups for surface area-to-mass ratio (58) reported no age difference in the $T_{re}$ response of men who sat for 30 min at $17^\circ C$, although muscle mass was not measured. Budd et al. (3) studied 12 Antarctic male expeditioners (age range of 26–52 yr) who were exposed to $10^\circ C$ while wearing only nylon shorts; thermal, metabolic, and cardiovascular responses were monitored in these subjects. When the relative influences of maximal $O_2$ consumption ($V_{O2\text{max}}$), adiposity, and age were examined by regression analyses, $V_{O2\text{max}}$ had no effect on any measured response. However, increased adiposity was associated with reduced heat loss, whereas age was associated with increased heat loss. When fatness effects were held constant, the older men had poorer vasoconstrictor responses to the cold.

Gender effect. A notable gender difference exists when older and younger men and women are exposed to the cold. Mortality during cold spells is higher in older men than in age-matched women (31). Older women are often able to maintain body temperatures as well as younger women (and better so than older men) during laboratory-based cold exposures (2, 57). Bernstein et al. (2) reported no age difference in the $T_{re}$ response to 3 h of rest in a cool ($17^\circ C$) room. In addition, Wagner and Horvath (58) reported that older women (average age of 61 yr) were able to maintain their baseline $T_c$ during 2 h at $10^\circ C$, whereas a group of young women (21 yr) had a slight decrease in $T_c$. Thus, despite the clear age difference in vasoconstrictor responses to body cooling, it has been suggested that age may be a secondary factor in determining the overall responses to passive cooling (25). In conclusion, the diminished ability of older adults to maintain $T_c$ during cold stress is the result of decreased peripheral resistance and reduced thermogenesis. However, the independent effect of body composition has a major influence on these thermoregulatory responses. Figure 2 summarizes the age-related changes in thermoregulation during cold stress.
HEAT STRESS

Several experimental procedures have been employed to raise Tc under resting conditions, as reviewed by Rowell (47). Rest in hot ambient conditions (natural environments) increases skin temperature but has a limited effect on Tc unless the exposures are extreme and prolonged. “Indirect heating” usually involves subjects immersing their lower limbs in hot-water baths while keeping the upper body warm with blankets. Finally, “direct heating” with water-perfused suits has been used to clamp skin temperature at an elevated temperature, allowing Tc to systematically increase as that heat is convected to the core. Unfortunately, few aging comparisons have used the direct heating approach to examine responses to a sustained and purely thermoregulatory reflex drive. Studies exposing subjects of different ages to hot natural environments have not reported age differences in the Tc response (6, 52), although this may reflect an inadequate thermal stimulus imposed under such conditions.

Sweat gland function. Under heat stress conditions, humans rely to a large extent on the ability to activate eccrine sweat glands (i.e., those under sympathetic cholinergic control) and the ability of those glands to secrete sweat to regulate body temperature. Although there is a large interindividual variability in the response of sweat glands to pharmacological stimuli [e.g., by cholinergic analogs such as methylcholine (MCh) or pilocarpine], some clear effects of aging are evident. Local sweating rates are lower in older subjects for a given pharmacological stimulus. Because the density of pharmacologically activated glands appears to be unaffected by age, this effect is attributable to a smaller output per activated gland (8, 26, 50, 53).

Sato (49) suggests that

[al]aging has very little effect on the pharmacologically induced maximal sweat rate until the 60s, but glandular function gradually declines in the 70s and 80s.

However, our group (26) and others (8) have noted progressive age-related changes in in vivo function. When varying concentrations of MCh were injected intradermally into the thighs of three distinct age groups (22–24, 33–40, and 58–67 yr) of heat-acclimated men, all well matched for \( \dot{V}O_2 \max \) and/or \( \dot{V}CO_2 \max \), there were no age differences in active gland density. However, the oldest and youngest groups differed significantly in the sweat output per active gland at each MCh concentra-

Fig. 2. Summary of age-related changes in thermoregulation during cold stress. Compared with young adults during cold stress, older individuals typically respond with a reduced peripheral vasoconstriction and decreased metabolic heat production. Furthermore, the 33- to 40-yr-old group exhibited sweat outputs that were intermediate in each case, suggesting a continuous decline throughout adulthood.

Additional findings indicate that regional differences in sweat gland function exist between older and younger persons. A greater age effect is noted for sweat gland function on the forehead and limbs than on the trunk in response to MCh injection (12). Sweat glands can undergo “local training” by repeated immersions of the skin in hot water. When such a protocol is performed, older individuals increase local sweat production, although to a lesser degree than young men and women (40). As a final note, in older subjects who exhibit higher sweat outputs, “the texture and appearance of the skin . . . appear more youthful and elastic and less wrinkled to the naked eye than of those [older subjects] whose sweat response [is] poor or absent” (8).

Lifetime ultraviolet exposure and other environmental factors may have an interactive effect with chronological age in determining sweat gland responsiveness.

Sweating rate. Evidence suggests that older men and women sweat less during passive heat exposure (5, 11, 20, 52) than young gender-matched subjects. Age differences have been noted even during brief exposures to extreme dry heat of 84–90°F (52). In addition, an elevated Tc threshold has been reported in older men (5, 11). Often, however, the common link among cross-sectional comparisons of older and young groups is the lack of control for concomitant influences such as acclimation, body size, and/or \( \dot{V}O_2 \max \). On the other hand, Drinkwater and colleagues (6) exposed 10 postmenopausal women (mean age of 58 yr) and 10 younger women (38 yr) to a 40°C (20% relative humidity) environment for 2 h. Subjects were matched for body surface area, but \( \dot{V}O_2 \max \) varied within the cohort of women tested. These investigators found no age differences in sweating; instead, sweating rate was correlated with \( \dot{V}O_2 \max \). Similar results were reported in a study that examined thermal transients (14). Sweating rate was again strongly determined by \( \dot{V}O_2 \max \) of the subjects rather than by chronological age.

The regional pattern of sweating distribution mentioned above is also evident in sweating rate during passive heating; i.e., age differences have been more commonly noted on the limbs but not on the torso (19). A logical hypothesis may be that glandular function declines in a peripheral-to-central direction as skin
ages. An alternate finding by Inoue and Shibasaki (21) suggests that successive decrements in sweat gland function might develop sequentially in a lower-to-upper body direction, although less support for this concept exists.

**Skin blood flow response to local heating.** The cutaneous blood flow response to direct local heating of nonacral skin is attenuated with age (9, 45, 60). Weiss et al. (60) concluded that, because the magnitude but not the pattern of skin blood flow (SkBF) is altered in aged skin, the lower cutaneous perfusion of older individuals is associated with a loss of capillary plexus functional units (i.e., a structural alteration). In contrast to these findings, no age differences in red blood cell volume or blood flow velocity of the skin were reported by a study in which the toe pulp was locally heated to 44°C (9). Because toe pulp contains arteriovenous anastomoses, age-related attenuations in SkBF observed with local heating may be confined to nonacral sites absent of arteriovenous anastomoses.

Prolonged local heating elicits a maximal SkBF response that declines with advanced age in a relatively linear manner, presumably reflecting structural changes in the cutaneous vessels (33, 46). One notable feature of aged skin is a flattened underside of the epidermis and a decrease in rete ridges, which become almost completely smoothed out in very old persons (39). This transformation is associated with collapse, disorganization, and, in some cases a total disappearance of the vessels of the microcirculation in the dermal papillary and superficial vascular plexus (39). These anatomic observations support the role of structural alterations in the diminished maximal SkBF capacities of older individuals. Mechanistic changes underlying this age-related decrement in SkBF (e.g., nitric oxide and axon reflexes) have only recently been revealed (35).

**Whole body cardiovascular responses.** Reflex increases in SkBF in response to increasing $T_c$ are likewise attenuated in aged skin (1, 27, 62). Augmented noradrenergic vasoconstriction plays little or no role in this response; rather, decreased active vasodilator sensitivity coupled with the aforementioned structural changes combine to limit the SkBF at a given $T_c$ (27). Although $V_{O2\text{max}}$, acclimation status, hydration, diseases, and medications all influence SkBF, the relative inability of aged skin to vasodilate appears to be a primary consequence of advanced age.

Minson et al. (36) studied the cardiovascular responses of young and older men during direct passive heating to the individual limits of thermal tolerance. They found that an age-related reduction in SkBF was associated with both a smaller increase in cardiac output as well as less redistribution of blood flow from the splanchnic and renal circulations. The reduced cardiac output was primarily the result of a lower stroke volume, since the older subjects were able to increase their heart rate to a similar extent as the young men. However, to achieve this increase in heart rate, the older men had to attain a greater proportion of their heart rate reserve. Despite these results for men, an investigation that used an identical heating protocol found that older women (52–80 yr) had no decrease in stroke volume with direct passive heating (7). This was true for women receiving no hormone replacement therapy, estrogen replacement therapy, and combined estrogen and progesterone replacement therapy. The mechanisms behind this apparent gender difference have not been elucidated.

When an orthostatic challenge (tilt) is added to passive heating, older (61–73 yr) men respond with a significantly attenuated reduction in peripheral blood flow compared with young men (21–39 yr) (37, 51). Thus aging seems to be associated with a diminished SkBF response to both reflex active vasodilation and nonthermoregulatory reflexes (i.e., baroreflexes) directed toward the cutaneous vasculature during heat stress. Further evidence for this altered peripheral

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**Fig. 3.** Summary of age-related changes in thermoregulation during heat stress. Compared with young adults during heat stress, older individuals typically respond with attenuated individual sweat gland outputs, decreased skin blood flows, reduced cardiac outputs and smaller redistributions of blood flow from the splanchnic and renal circulations.
responsiveness is supported by a study that found that, during head-up tilt in normothermic conditions, older (64–81 yr) men had an attenuated increase in forearm vascular resistance compared with young (19–28 yr) men (37). However, in this study, splanchnic vascular resistance rose to greater extent in the elderly group. These findings suggest that age-related changes in the structure and regulation of the peripheral vasculature necessitate modifications of the cardiovascular system’s homeostatic control mechanisms.

In conclusion, the ability of older adults to maintain Tc during heat stress is usually not compromised with age. Although pharmacologically induced sweat gland output is attenuated in older individuals, sweat rate is more closely related to Vo2 max. However, with both local and whole body heating, reductions in SkBF do occur as a function of chronological age. Associated with decreases in SkBF during whole body heat stress are reduced cardiac outputs and smaller redistributions of blood flow from the splanchnic and renal circulations of older individuals. These central cardiovascular adjustments during heat stress seem to have a gender component that has not been clearly identified. Figure 3 summarizes the age-related changes in thermoregulation during heat stress.

SUMMARY

Epidemiological evidence of increased mortality among older men and women from hyper- and hypothermia should not be interpreted as implying that aging per se confers an intolerance to environmental extremes. Relatively few studies have attempted to delineate the effects of chronological age from concomitant factors (for example, decreases in Vo2 max, lowered habitual activity levels, and alterations in body mass and composition) in determining thermoregulatory responses to rest and exercise in extreme environments. When the effects of chronic diseases and sedentary lifestyle are minimized, thermal tolerance appears to be minimally compromised by age.

FUTURE RESEARCH DIRECTIONS

From the existing literature, several questions with regard to thermoregulation and aging emerge that require further investigation. For example, the mechanisms of reduced cutaneous vasoconstriction during cold stress remain to be identified. Furthermore, regional differences in the age-related thermoregulatory responses to heat stress (i.e., sweating and SkBF) call for inquiry into identification of both the pattern and functional bases of these spatial variations. Work also remains in the effort to comprehensively understand how the cardiovascular system maintains homeostasis during heat stress after adaptation to the thermoregulatory alterations associated with aging. Importantly, the apparent gender and/or hormonal differences involved in many of the aforementioned changes in body temperature regulation should be explored in greater detail. Finally, the need persists for controlled studies capable of separating the effects of chronological age from confounding factors such as Vo2 max, body composition, acclimatization, and training in human temperature regulation.

REFERENCES

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