A Physiological Systems Approach to Human and Mammalian Thermoregulation

Neural control and mechanisms of eccrine sweating during heat stress and exercise

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1Department of Environmental Health, Nara Women’s University, Nara, Japan; 2Departments of Pharmacology and Physiology and of Dermatology, Drexel University College of Medicine, Philadelphia, Pennsylvania; 3Institute for Exercise and Environmental Medicine, Presbyterian Hospital of Dallas, Dallas; and 4Department of Internal Medicine, University of Texas Southwestern Medical Center, Dallas, Texas

Shibasaki, Manabu, Thad E. Wilson, and Craig G. Crandall. Neural control and mechanisms of eccrine sweating during heat stress and exercise. J Appl Physiol 100: 1692–1701, 2006; doi:10.1152/japplphysiol.01124.2005.—In humans, evaporative heat loss from eccrine sweat glands is critical for thermoregulation during exercise and/or exposure to hot environmental conditions, particularly when environmental temperature is greater than skin temperature. Since the time of the ancient Greeks, the significance of sweating has been recognized, whereas our understanding of the mechanisms and controllers of sweating has largely developed during the past century. This review initially focuses on the basic mechanisms of eccrine sweat secretion during heat stress and/or exercise along with a review of the primary controllers of thermoregulatory sweating (i.e., internal and skin temperatures). This is followed by a review of key nonthermal factors associated with prolonged heat stress and exercise that have been proposed to modulate the sweating response. Finally, mechanisms pertaining to the effects of heat acclimation and microgravity exposure are presented.

thermoregulation; hyperthermia; dehydration; cholinergic nerve; perspiration; sweat gland

BRIEF HISTORY OF THE STUDY OF SWEATING

Heat dissipation is vital for mammalian survival during exercise and heat stress. In humans, an important mode of heat dissipation occurs through evaporation of sweat secreted from eccrine glands. The first description of sweating dates back to the ancient Greeks (97). In Aristotle’s writings entitled Parts of Animals, as translated by Peck (6), he summarized their understanding of sweating as follows:

The blood vessels get progressively smaller as they go on until their channel is too small for the blood to pass through. But although the blood cannot get through them, the residue of the fluid moisture, which we call sweat can do so, and this happens when the body is thoroughly heated and the blood vessels are open widely at their mouth.

Although in the 1600s the basic sweat gland duct was described, the existence of a sweat gland was not accepted until the 1800s (96). Furthermore, the importance of sweating for thermoregulation was not fully recognized until the 20th century. Especially noteworthy is Kuno’s monograph published in 1934 as The Physiology of Human Perspiration, and later updated as “Human Perspiration” (65), which at that time provided the most comprehensive review of sweating. Subsequently, many researchers have studied the physiology of sweating toward a greater understanding of the mechanisms and controllers of sweating. The objective of this review is to outline these mechanisms and controllers of sweating, specifically during exercise and heat stress.

CONTROL OF THE ECCRINE SWEAT GLAND

Human sweat glands are generally divided into two types, the apocrine and the eccrine gland. The eccrine gland is the primary gland responsible for thermoregulatory sweating in humans (110) and thus will be the focus of this review. For a review of the apocrine gland the reader is referred to other articles (28, 103). Eccrine sweat glands are distributed over nearly the entire body surface. Sweat glands become identifiable in the palm and sole of the feet in the 16th fetal wk, and in the 22nd wk or later sweat glands are identifiable on the rest of the body (65). The number of sweat glands in humans varies greatly, ranging from 1.6 to 4.0 million, with the density of eccrine sweat glands associated with thermoregulation (i.e., precluding glands on the palms of the hands and soles of the feet) being the greatest on the forehead, followed by the upper limbs, and finally the trunk and lower limbs (60, 65, 109). The structure of the eccrine sweat gland consists of a bulbous secretory coil leading to a duct. The secretory coil is located in
the lower dermis, and the duct extends through the dermal layer and opens directly onto the skin surface. The uncoiled dimension of the secretory portion of the gland approximates 30–50 μm in diameter and 2–5 mm in length. The size of the adult secretory coil ranges from 1 to 8 × 10⁻³ mm² (111). There is a positive correlation between the size of an individual sweat gland and the maximal sweat rate of that gland (111).

Given the challenges of identifying neural tracks in humans, the exact neurological pathways responsible for sweating are not entirely understood. Evidence from animal studies suggests that effluent signals from the preoptic hypothalamus travel via the tegument of the pons and the medullary raphe regions to the intermediolateral cell column of the spinal cord. In the spinal cord, neurons emerge from the ventral horn, pass through the white ramus communicans, and then synapse in the sympathetic ganglia. Postganglionic nonmyelinated C fibers pass through the gray ramus communicans, combine with peripheral nerves and travel to sweat glands (65, 72, 84, 110). Sympathetic nerve terminals cluster mainly around the secretory coil of the sweat gland, but a few projections extend to the sweat duct (22, 23, 56, 143).

Direct recordings of postganglionic skin sympathetic nerve activity (SSNA) is possible in humans and much of the early work in this area was performed by Wallin and colleagues (25, 43, 149). This technique permits the assessment of the neural signal responsible for sweating, as well as cutaneous vascular and perhaps pilomotor responses (11, 12, 25). Because of the potential for the integrated skin sympathetic recording to contain neural signals innervating these differing efferent structures, caution must be taken when trying to link the skin neural signal to a particular efferent event (e.g., sweating, cutaneous vasoconstriction, etc.). Nevertheless, during heat stress, SSNA is partially synchronized with galvanic skin response (an index of sweating) and pulsatile sweat expulsion (11, 133), and ∼80% of SSNA bursts have been reported to be synchronized with pulsatile sweat expulsion (134). These observations suggest that a large fraction of the recorded skin sympathetic neural signal in heat stressed subjects is sudomotor in nature.

Acetylcholine is the primary neurotransmitter released from cholinergic sudomotor nerves and binds to muscarinic receptors on the eccrine sweat gland (94, 142), although sweating can also occur via exogenous administration of α- or β-adrenergic agonists (90, 94, 99, 107). Nevertheless, the observation that local and systemic administration of atropine (a muscarinic-receptor antagonist) greatly attenuates or abolishes sweating during a thermal challenge or during exogenous administration of acetylcholine or its analogs (32, 55, 58, 71, 73) strongly suggests that thermoregulatory sweating primarily occurs through stimulation of muscarinic receptors. Released acetylcholine is rapidly hydrolyzed by acetylcholinesterase, and this response may be one of a number of mechanisms by which sweat rate is regulated (71, 120). Immunochemistry studies have identified a number of possible peptide neuromodulators (e.g., vasoactive intestinal polypeptide, calcitonin gene-related peptide) in and around cholinergic sudomotor nerve terminals and eccrine sweat glands (56, 116, 131, 135). Although some evidence is present (64), the precise role of these peptides in modulating sweating remain unclear.

When acetylcholine binds to muscarinic receptors on the sweat gland, intracellular Ca²⁺ concentrations increase. This results in an increase in the permeability of K⁺ and Cl⁻ channels, which initiates the release of an isotonic precursor fluid from the secretory cells (110). This precursor fluid is much like plasma but is devoid of proteins. In a noteworthy series of in vitro studies, Sato (108) collected sweat samples from an isolated secretory coil and from the sweat duct and found that the solution from the duct was hypotonic relative to the secretory coil. These and a number of earlier observations led to the conclusion that, as the fluid travels up the duct toward the surface of the skin, sodium and chloride are reabsorbed, resulting in sweat on the skin’s surface being hypotonic relative to plasma. However, when the rate of sweat production is elevated, as occurs during exercise or heat stress, ion reabsorption mechanisms can be overwhelmed due to the large quantity of sweat secreted into the duct, resulting in higher ion losses. Thus the sodium content in sweat on the skin’s surface is greatly influenced by sweat rate (14, 90, 109, 117, 118).

**THERMAL CONTROL OF SWEATING**

In the late 19th and early 20th centuries, the existence of a thermoregulatory center within the hypothalamic region of the brain was identified. Studies demonstrated that elevated brain temperature engaged heat loss mechanisms in animals (8, 53, 80, 89). Reports from early investigators were somewhat mixed with respect to the location of the primary controller of sweating. Before the middle of the 20th century, it was thought that skin temperature was more important in the control of sweating relative to internal temperature (44, 154). For example, in 1923, Adolph (1) reported that, in nonexercising subjects, sweat rate was proportional to the effective environmental temperature above 90°F (~32°C) and suggested a close correlation between sweating and superficial body temperature. Kuno (65) later suggested that central thermoregulatory centers were more important for temperature control, because sweating responses were delayed despite increasing skin temperature when exposed to elevated environmental temperatures. Kuno proposed that, if skin temperature was the primary controller of sweating, then sweating should have occurred immediately on exposure to the elevated environmental conditions. Nevertheless, Kuno did not evaluate sweating as a function of internal temperature in those studies.

In 1959, Benzinger (9, 10) proposed that, under steady-state conditions the increased sweat rate caused by exercise and/or variations in the environmental temperature were very closely correlated to rises in tympanic temperature and that this relationship was stronger than the relationship between skin temperature and sweating. His proposition was later supported by Nielsen and Nielsen (85), although they observed that rapid decreases in mean skin temperature reduced sweat rate when internal temperature remained stable. Given findings that internal and mean skin temperatures can control sweating, researchers began to assess the relationship between sweating and various combinations of internal and skin temperatures (45, 75, 81, 104, 105, 132, 153). This resulted in the concept of mean body temperature, which represents the sum of a fraction of internal and skin temperatures (e.g., 0.9-internal temperature + 0.1-mean skin temperature) (34, 38), and it is now frequently used when expressing sweating responses during exercise and during exposure to elevated ambient air temperatures (87, 156, 157).
Although alluded to by others, Nadel and colleagues (82, 83) were among the first to directly access the relationship between the increase in sweat rate relative to dynamic increases in internal temperature in humans. Later, this concept was confirmed in monkeys in which direct measures of brain temperature were obtained while sweating was assessed by Smiles et al. (128). They concluded that sweating is primarily controlled by central brain temperature and secondarily affected by mean skin temperature. Given these findings, sweating responses are now commonly characterized by the internal or mean body temperature threshold for the onset of sweating, as well as the slope of the relationship between the elevation in sweating and the elevation in internal or mean body temperature (see Fig. 1), as eloquently outlined in the reviews by Gisolfi and Wenger (38). An increase in the internal or mean body temperature threshold for the onset of sweating and/or an attenuation of the elevation in sweating relative to the elevation in internal or mean body temperature is recognized as impaired sweating responsiveness.

Whereas mean skin temperature alters sweating via central mechanisms, sweat rate is also influenced by local temperature of the sweat gland via peripheral mechanisms (145). For example, local heating accentuates sweat rate while local cooling attenuates sweat rate (13, 69, 73, 86). Possible mechanisms by which local temperature alters sweating may be an effect of temperature on neurotransmitter release [i.e., local heating augments the release of acetylcholine for a given neural stimulus, whereas local cooling attenuates neurotransmitter release (73, 81, 82)] or sensitization or desensitization of the receptors on sweat glands by temperature (26, 86). It remains unclear which of these mechanisms, or whether both, are responsible for these observations.

Increases in sweating occur through the combination of increasing the number of sweat glands that are activated and increasing the amount of sweat released per gland. Randall et al. (92, 93) and Kondo et al. (59) reported that the initial increase in sweat rate during a heat stress is due to an increase in the number of activated sweat glands, whereas further elevations in sweating occur through increases in the production of sweat per gland. Kondo et al. extended those observations by reporting that recruitment of sweat glands was very fast, with near maximal recruitment being achieved in as little as 8 min of exercise or passive heat stress. In contrast, increases in sweat output per gland were more gradual and continued to rise until the heating perturbation ceased.

Humans have the capability of producing a tremendous amount of sweat during prolonged exercise in the heat. For example, the highest reported sweat rate was >3 l/h (7), although average maximum sweat rates for humans are ~1.4 l/h (36). These high rates of sweating cannot be maintained for prolonged periods of time, given findings that 4–6 h of heat exposure decreases the rate of sweating (36, 141, 152, 155). When sweating is reduced during prolonged heat stress or exercise, the mechanism for this event, despite sustained elevations in internal temperature, is not entirely clear, although both central and peripheral factors have been implicated. For example, dehydration (i.e., hypohydration and elevated plasma osmolality) inhibits sweating primarily through central mechanisms (see section below for an in-depth discussion of this topic). However, dehydration does not explain decreases in sweating during prolonged exposure to hyperthermic conditions when individuals are adequately hydrated. Under these conditions, decreases in sweat rate may be due to the skin being wet for prolonged periods of time, which can swell the keratinized layer around the sweat duct, thereby mechanically occluding the ducts and reducing sweat secretion (95).

**EFFECT OF BODY FLUID REGULATION ON SWEATING**

Prolonged exposure to hyperthermic conditions and/or prolonged exercise in the heat can induce water deficits due to profuse sweating, resulting in dehydration. This water deficit lowers both intracellular and extracellular volumes and results in plasma hyperosmolality and hypovolemia, both of which impair sweating. For example, Greenleaf and Castle (41) proposed that the excessive rise in internal temperature in dehydrated subjects was due to inadequate sweating. Expanding this concept, Sawka et al. (115) observed that in progressively dehydrated subjects sweat rate was dramatically reduced despite greater elevations in rectal temperature. Later, Montain et al. (79) demonstrated that the threshold for the onset of sweating was elevated, whereas the slope of the relationship between the elevation in sweat rate relative to the elevation in internal temperature was attenuated, as a function of the level of dehydration, both of which are strongly suggestive of impaired sweating responsiveness.

Fortney et al. (31) conducted a study to identify the importance and independence of decreases in fluid volume (hypovolemia) from increases in plasma osmolality (hyperosmotic) on sweat rate. Normovolemic subjects were exposed to heat stresses under hyperosmotic and isoosmotic conditions while sweat rate was assessed. During the ensuing exercise bout, the internal temperature threshold for the onset of sweating was significantly elevated relative to the response during exercise under isoosmotic conditions. The slope of the relationship between the elevation in sweating and the elevation in internal temperature was not affected by increased plasma osmolality. Takamata et al. (136, 138) extended these findings on assessing sweat rate in heat-stressed subjects who received an infusion of 0.9 or 3% saline. They found that the threshold for sweating in the hyperosmotic condition (i.e., 3% saline infusion) was greatly shifted to a higher internal temperature relative to the isoosmotic condition. This hyperosmolality-induced suppres-
sion of the sweating occurred regardless of heat acclimation status (47). In a follow-up study, Takamata et al. (136) found that when hyperosmotic subjects drink deionized water (38°C), sweat rate immediately increases without changes in plasma osmolality, although drinking deionized water in isoosmotic subjects did not alter sweat rate. These findings demonstrate that increased plasma osmolality, independent of plasma volume, impairs sweating responses and that an oral-pharyngeal reflex can modulate the sweating response in hyperosmotic individuals (136).

Fortney et al. (30) addressed the opposite question relative to that presented above, in that they investigated whether changes in blood volume, while keeping plasma osmolality constant, modulates the sweating response. They found that isoosmotic hypovolemia reduced the slope of the relationship between the change in sweating relative to the change in internal temperature, without altering the internal temperature threshold for the onset of sweating (30). Such a finding suggests that, once sweating has begun for the same elevation in internal temperature, there was less of an elevation in sweating. Conversely, isoosmotic hypervolemia does not change the internal temperature threshold for sweating or the aforementioned slope (30, 66), unless plasma and blood volume expansion occurs via erythrocyte infusion (113). These observations suggest that sweating can be inhibited by isoosmotic hypovolemia, whereas hypervolemia in the absence of erythrocyte infusion does not alter sweating responses.

MODIFICATION OF SWEATING DUE TO BARORECEPTOR UNLOADING

Given that prolonged exposure to hyperthermic conditions and/or exercise reduces blood volume if fluid intake is not adequate, coupled with baroreceptors being sensitive to changes in blood volume, it seems reasonable to hypothesize that sweating associated with these conditions could be modulated by baroreceptor unloading. However, the effects of baroreceptor unloading on attenuating the elevation in sweat rate are controversial. Johnson and Park (51) assessed the internal temperature threshold for the onset of sweating during exercise and found that this threshold was unaltered regardless of whether the individual exercised in the upright position (i.e., baroreceptor unloading) or supine position. In contrast, Mack et al. (74) observed an increase in the internal temperature threshold for the onset of sweating (i.e., a delayed sweating response) during exercise in combination with lower body negative pressure (LBNP), which simulates the upright position and unloads baroreceptors.

The effect of baroreceptor unloading on sweat rate was further addressed by applying LBNP in passively (i.e., nonexercise) heat-stressed subjects (21, 130, 148). These studies suggested that sweat rate was not affected by baroreceptor unloading. A possible explanation for differences in findings between LBNP studies (21, 74, 130, 148) was proposed by Vissing et al. (148). They suggested that reduced electrodermal response (index of sweating) and SSNA during LBNP results from skin cooling that frequently occurs with application of the negative pressure, not via baroreceptor unloading. To address this question, Wilson et al. (150) assessed sweat rate and peroneal SSNA in heat-stressed subjects during bolus and steady-state infusions of pharmacological agents (nitroprusside and phenylephrine) to perturb baroreceptors without causing cooling that accompanies LBNP. Despite pronounced changes in blood pressure, neither SSNA nor sweat rate was significantly affected. However, it should be stressed that pharmacologically induced decreases in blood pressure will likely perturb baroreceptors differently relative to LBNP or head-up tilt.

Dodt et al. (27) addressed this question differently by exposing subjects to a mild heat stress, followed by 30° head-up tilt. They observed significant reductions in forearm SSNA and an index of sweat rate during tilt, and they concluded that baroreceptor unloading could modulate SSNA and sweating. Given what appeared to be a relatively minor heat stress in the Dodt et al. study, differences in conclusions between their study and others (21, 130, 148, 150) may be related to the level of heat stress. For example, baroreceptors may be capable of modulating sweating under mild to moderate heating conditions but not during more pronounced heat stress. To address this question, Wilson et al. (151) measured peroneal SSNA and sweat rate during multiple 30° head-up tilts, with tilting occurring every 10 min throughout the heat stress (Fig. 2). Regardless of the level of heating, they did not see a reduction in sweat rate or SSNA during the same magnitude of tilt used by Dodt et al. (27). Taken together, although findings remain controversial, acute unloading of baroreceptors is unlikely to modulate sweat rate.

MODIFICATION OF SWEATING RESPONSES DUE TO EXERCISE-RELATED FACTORS

Thermoregulation during exercise is very complicated, resulting in a number of proposed theories and concepts (38). Compared with passive heat stress, generation of heat associated with muscular contraction during dynamic exercise rapidly elevates internal temperature, followed by appropriate increases in sweat rate. It is interesting to note that factors unrelated to the elevation in internal temperature that are engaged during exercise may modulate the sweating response. van Beaumont and Bullard (144, 146) were the first to report this phenomenon on observing that sweating occurred immediately (within 1.5–2 s) with the onset of dynamic exercise and
Increased sweat rate during isometric exercise in warm environmental conditions. Importantly, this increase in sweating occurred before a measurable change in internal temperature. Later, Gisolfi and Robinson (37) observed rapid changes in sweating during intermittent exercise independent of changes in internal, muscle, or skin temperatures.

To address possible mechanisms by which exercise increases sweating independent of temperature, one needs to understand the work of Johansson (50), which postulated that two separate and distinct neural mechanisms control cardiovascular responses during exercise. One mechanism arises from the central nervous system that irritates impulses from the motor cortex. Krogh and Lindhard (63) termed this central mechanism as “cortical irradiation,” and later it was called “central command” (39). The other mechanism, termed the exercise pressor reflex, originates from the stimulation of afferent nerve endings within the skeletal muscle and is engaged during muscle contraction (4). Later it was shown that mechanosensitive afferent nerves and metabosensitive afferent nerves were responsible for evoking the exercise pressor reflex (77, 78). Because sweating during exercise can occur before a change in thermal status, coupled with the aforementioned responses associated with modulating cardiovascular responses during exercise, researchers sought to identify whether similar mechanisms could be responsible for modulating sweat rate during exercise.

Partial neuromuscular blockade (e.g., using curare derivatives) has been used to augment central command during exercise, resulting in greater increases in heart rate and blood pressure at a given workload (49, 68, 77). Shibasaki et al. (124) used this technique to test the hypothesis that central command is capable of modulating the sweating response in heat-stressed subjects. Heat-stressed subjects performed isometric exercise under control conditions (without neuromuscular blockade) and when central command was augmented via partial neuromuscular blockade. Under both conditions, isometric exercise increased sweat rate; however, the increase in sweat rate was significantly greater when central command was augmented after partial neuromuscular blockade (Fig. 3B). This, and a related study assessing SSNA to isometric exercise during partial neuromuscular blockade (147), provide strong evidence that central command is capable of modulating sweating during exercise.

Alam and Smirk (3, 4) showed that blood pressure increases during dynamic and static exercise and remains elevated if blood flow to that limb was occluded just before the cessation of exercise. On release of the occlusion, blood pressure returned to preexercise levels. Their observations led to numerous and ongoing studies investigating the role of muscle metaboreceptors in modulating blood pressure during exercise. A number of studies have been performed to investigate the possible role of metaboreceptors in modulating sweating responses during exercise (20, 61, 121). In general, the cited studies were performed by monitoring sweat rate during isometric exercise and subsequent postexercise ischemia, the latter of which isolates muscle metaboreceptor stimulation. In those studies, sweat rate increased during isometric exercise, remained elevated during postexercise ischemia, and then returned toward preexercise levels after release of ischemia (Fig. 3A). This pattern of response provides evidence that metaboreceptors are capable of modulating sweat rate during exercise. However, during postexercise ischemia, blood pressure is also elevated and may therefore contribute to the elevation in sweating via loading of baroreceptors. To test this hypothesis, Shibasaki et al. (121) performed an experiment in which blood pressure during the postexercise ischemia period was restored to preexercise levels via intravenous administration of sodium nitroprusside (Fig. 3C). Under these conditions, muscle metaboreceptors remained stimulated but blood pressure returned to preexercise levels. Despite normalized blood pressure, sweat rate remained elevated throughout the ischemic period (121). Thus the elevation in sweat rate during postex-
exercise ischemia occurred through activation of metaboreceptors and was independent of the increase in blood pressure during postexercise ischemia and presumably during isometric exercise. These findings strongly suggest that the muscle metaboreflex is capable of modulating sweat rate.

Another muscle afferent signal that could contribute to sweating responses during exercise is related to mechanical stimulation of the muscle (52, 62, 101, 123), which has previously been suggested to contribute to the pressor response during exercise (77, 78). These studies used protocols involving passive limb movement or passive cycling while assessing sweating responses in heat-stressed subjects. In general, these findings suggest that stimulation of muscle mechanoreceptors is capable of modulating sweat rate, although responses appear to be less than that observed during augmentation of central command or muscle metaboreceptor stimulation.

Despite the aforementioned studies, not all studies support the concept that sweating can be modulated by nonthermal factors associated with exercise. For example, neither the internal temperature threshold for the onset of sweating nor the slope of the relationship between the elevation in sweating relative to the elevation in internal temperature is different when responses are compared between dynamic exercise and passive heating states (51, 54, 59). Such findings are perplexing given that, relative to resting conditions, central command, muscle metaboreceptor, and muscle mechanoreceptors are stimulated during dynamic exercise. Furthermore, the internal temperature threshold for the onset of sweating is not altered by exercise intensity, whereas the slope of the relationship between elevations in sweating and internal temperature is not changed in the majority of studies (15, 60, 104, 105, 140); however, one study found an elevation of this slope with exercise intensity (79). A key difference between those studies showing an effect of central command and metabo- and mechanoreceptors stimulation in modulating sweating with those that do not may be the magnitude of the heat stress before the perturbation. For example, in those studies in which sweating is already engaged, or is very close to the threshold to be engaged, stimu-
through sweating for a given internal temperature (17, 83, 98, 126). In addition, Ogawa et al. (88) observed that the number of sweat expulsions per minute, which may be indicative of sudomotor neural activity, increased after heat acclimation, suggesting that heat acclimation may alter central modulation of the sweating response.

Conversely, a number of studies support a role of local changes in sweat gland function due to heat acclimation. For example, if local temperature is maintained at a cool temperature throughout heat acclimation, sweat responses at that location were not modified by heat acclimation (16, 33). Chen and Elizondo (16) assessed the effects of heat acclimation on sweat rate during heat stress and due to electrical stimulation of the skin (i.e., peripherally stimulating sweating without a thermal stress). For both perturbations, sweat rate was significantly higher during the postacclimation trials relative to the preacclimation trials. Greater elevations in sweating during local electrical stimulation after heat acclimation further support peripheral modification of sweat gland function due to acclimation. Using an in vitro technique, Sato et al. (106) observed an increase in sweat gland size (tubular length and volume) in heat acclimated monkeys, whereas Inoue et al. (48) observed elevated sweating per gland during exogenous administration of methacholine after heat acclimation in humans.

As discussed earlier, an increased tubular length and volume correlates with greater sweat output of that gland. Given these observations, increases in sweating responses after heat acclimation are likely due to a combination of increased capacity and sensitivity of the sweat gland, coupled with changes in central thermoregulatory responses.

In contrast to improvements in sweating with heat acclimation, spaceflight and ground-based analogs of microgravity impair sweating responses as evidenced by an elevation in the internal temperature threshold for the onset of sweating and a reduced slope of the relationship between the elevation in sweat rate relative to the elevation in internal temperature (18, 29, 42, 67, 76) (Fig. 4). Furthermore, simulated microgravity exposure, using the head-down tilt bed rest model, impairs sweat gland function when assessed by exogenous acetylcholine administration (19). It is interesting to note that, in the cited study, sweating responses to exogenous acetylcholine administration were preserved in a subset of subjects who exercised throughout head-down-tilt bed rest. Consistent with this observation, Shibasaki et al. (125) found that sweating responses to an exercise thermal stress, previously reported to be impaired after simulated and actual microgravity exposure (18, 29, 42, 67, 76), were preserved in subjects who exercise trained throughout bed rest. Together, these findings suggest that adaptations associated with microgravity exposure and its analogs impair thermoregulatory responses; however, these responses may be preserved if individuals adequately exercise during the exposure. Thus it may be that deconditioning associated with these exposures is involved in altering sweating responsiveness. The mechanisms by which exercise during bed rest and presumably spaceflight preserves thermoregulatory responses have not been adequately investigated.

CONCLUSION

Sweating from eccrine glands is essential for thermoregulation during heat stress and/or exercise. On the surface, it may appear that control of sweating is simplistic in that people sweat when they are heat stressed. However, like so many physiological systems, this view is not comprehensive, and, as covered in this review, there are a number of factors that alter the magnitude and composition of sweat (Fig. 5). These factors should be viewed as fine tuners of the sweating response to form a balance between temperature regulation and nonthermal stressors imposed by the condition (i.e., exercise, dehydration, etc.). The objective of this review was to provide a brief and comprehensive summary of the mechanisms and controllers of sweating in humans. For a detailed review of the history of sweating research (96, 97), mechanisms of sweat gland function (90, 91, 103, 107, 110), nonthermal modulation of sweating responses (112, 119, 122, 137), or sweating response to various environmental stressors (35, 40, 100, 139), the reader is referred to these informative articles.

ACKNOWLEDGMENTS

The authors acknowledge the many investigators who focus on this field of study and whose work should be cited in this review but because of page limitations are not included.

GRANTS

Support for the authors was provided by Grant-in-Aid for the Encouragement of Young Scientists from the Japanese Society for the Promotion of Science Grants 14704020 and 17790162 (to M. Shibasaki); the American Heart Association (to T. E. Wilson); National Heart, Lung, and Blood Institute Grants HL-61388 and HL-67422 (to C. G. Crandall) and HL-10488 (to T. E. Wilson); and National Institute of General Medical Sciences Grant GM-68865 (to C. G. Crandall).

REFERENCES


MECHANISMS FOR THE CONTROL OF SWEATING IN HUMANS


