

Review article

The Physiology of Thermoregulation in Exercise: A Brief Review

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Abstract

During physical exercise, the production of heat in the working skeletal muscles increases, imposing heat stress on the body. Thermoregulatory mechanisms induce adjustments of cutaneous vascular conductance and thus skin blood flow (SkBF), sweating rate, and increased cardiac output to achieve thermal homeostasis. The response depends on the intensity, type, duration of exercise, and environmental temperature: during extreme exercise in a hot environment SkBF can attain up to 7 L/min compared to 300 mL/min at rest whereas the sweating rate can reach as high as 4 L/h. Due to opposing non-thermal reflexes, the thermoregulatory response of SkBF during exercise differs from that at rest: the threshold to induce vasodilation in the skin is shifted to higher body core temperature and the sensitivity of the "SkBF to-core temperature" slope is altered. Regular training induces better adaptations to physical stress which enable sportsmen to eliminate additional heat more optimally. The review emphasizes physiological mechanisms involved in thermoregulation during exercise and exposes some thoughts regarding the estimation of the core temperature in humans, as well as some new approaches for an up-to-date assessment of parameters important for appropriate heat dissipation thereby maintaining core temperature.

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Introduction

Humans as homeothermic organisms need to maintain their body temperature irrespective of relatively high fluctuations in their external or internal environment. During resting conditions, it is mainly external temperature that is fluctuating, whereas, during exercise, the most profound temperature perturbation occurs in the internal environment (1, 2). Though, when exercising in extreme environmental temperature conditions, this additionally impacts the human thermoregulatory system (3, 4).

Thermoregulation encompasses reflex mechanisms enabling that heat elimination from the body equals heat production thus maintaining a constant body core temperature. Core temperature is regulated by a classical negative feedback loop including sensors (central and peripheral thermoreceptors), thermoregulatory center and effectors (2, 5). The information on temperature perturbation is relayed by thermoreceptors to the thermoregulatory center located in the central nervous system which compares the sensed value with the more or less flexible reference temperature value ("set-point") and accordingly switches on and off effector mechanisms to eliminate the perturbation and return the core temperature to the "set-point" value (2, 5). The main effectors include skin arterioles and sweat glands, brown adipose tissue and skeletal muscles. In addition, behavioral changes contribute to thermoregulation (2, 5).

Heat is eliminated from the body by four distinct physical principles, namely radiation, conduction, convection and evaporation (passive and active). The physiological thermoregulatory mechanisms in response to core temperature perturbation adjust the fractions of the four physical principles according to the body's needs: during rest, the majority of heat is eliminated by radiation (60%) and only 20% by passive perspiration, while during exercise the majority of heat elimination is achieved by active evaporation and convection (2, 6).

Physiological principles of thermoregulation during exercise

While skeletal muscles consume approximately 1.5 mL oxygen/min/kg body weight in resting conditions, their oxygen consumption might reach up to 150 mL/min/kg during intensive exercise (4, 5, 7), implying additional heat burden that during exercise may exceed 1,000 Watt (W) as compared to only 70 W at rest. A thermal load of this magnitude would raise the core temperature by 10C every 10 minutes if there were no thermoregulatory mechanisms (4). Accordingly, thermoregulatory reflexes are activated to eliminate this additional heat from the body to the environment, respectively preserving thermal homeostasis.

Thermoregulatory center

Situated in the preoptic area of the anterior hypothalamus, the thermoregulatory center is believed to comprise a "cold-sensitive" and "hot-sensitive" area activated by a corresponding temperature perturbation (8–11). Yet, the exact anatomic location, the neurotransmitters involved, and the effector pathways are not precisely known in humans as most of the information has been obtained from animal model experiments (8). The center is regarded as an integrator, integrating thermal information from the periphery and core (2): in response to the mismatch between the perturbation and the reference signal, an autonomic involuntary thermoregulation response is mediated by descending projections from the preoptic area, leading to activation of different thermo-effectors, mainly through the sympathetic pathways (9, 12, 13). An important contribution of oxytocin, modulating autonomic and behavioral mechanisms underlying thermoregulation at both central and peripheral levels has been implicated (14).

Thermoreceptors

The thermoregulatory center receives and integrates information on temperature perturbation from the central and peripheral thermoreceptors, respectively (2). Central thermoreceptors are located mainly in the

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central nervous system (brain, the spinal cord), although other parts, such as blood vessels and skeletal muscles have been implicated (2). However, the most important ones are part of the thermoregulatory center in the preoptic area and anterior hypothalamus (2, 8, 9). The peripheral thermoreceptors are scattered in the skin throughout the body. Similarly, as for the central ones, there are two types of anatomically distinct peripheral thermoreceptors: warmth receptors and cold receptors, whose distribution and density differ regarding skin site (2, 5, 9).

Central thermoreceptors

During exercise, the central thermoreceptors receive the information of increased core temperature (in the range of 2°C to 4°C) (2, 5). When a certain temperature threshold, usually denoted as a "set-point" value, has been reached, effector mechanisms are activated for heat elimination which subsequently establishes thermal homeostasis (2, 5, 9). The exact physiological background of the set-point has not been known; the role of various "transient-receptor potential" (TRP) membrane channels, similarly as for the cold sensing, have been implicated in the activation of these "hot-sensitive" neurons (9, 13, 15). It is worth mentioning that the "set-point" has a rather variable value, as for example during fever it is shifted to higher values (2). Similarly, the value of the "set-point" changes during exercise, i. e. the system is operating at a higher temperature steady state during exercise as compared to resting conditions (2, 5, 7). Moreover, additional factors importantly affect the value of the "set-point", such as the circadian rhythm (6, 16), and sex as well as the phase of the menstrual cycle in premenopausal women (17–19), consequently also impacting exercise performance.

Apart from these reflexes of the negative feedback mechanisms, some of the effector mechanisms are activated before an increase in core temperature, at the very beginning of exercise, denoting a "central command" and assumingly reflecting the anticipatory, feed-forward impulses from the prefrontal, supplementary and premotor cortex (5, 11, 20).

Peripheral thermoreceptors

In addition, the hypothalamus also receives information on the temperature changes over the skin surface relayed by peripheral thermoreceptors, specialized free nerve endings embedded in the skin dermis all over the skin surface (1, 2, 5). Changes in surface skin temperature are sensed before the core temperature is altered and, in this respect, peripheral thermoreceptors represent a protection mechanism that diminishes too extensive fluctuations of core temperature during resting conditions, (5), and might be regarded as an additional feed-forward thermoregulatory mechanism (2, 5, 9). During exercise, the response differs: peripheral thermoreceptors are thought to modulate the response of the thermoregulatory center during exercise (2, 6, 15, 21). As explained later, at the beginning of exercise, vasoconstriction in the skin is sufficient to cause temporal storage of excessive heat produced by the working muscles inducing an increase in core temperature which is then sensed by the central thermoreceptors, and reflexes for heat dissipation are activated (2, 4, 6). In fact, during exercise when a new steady-state core temperature is established, mean skin temperature decreases during exercise because of the increased evaporative cooling of the skin caused by sweating (2), increasing the temperature gradient between the body surface and the environment, thus making conductive-convective heat elimination more efficient (2, 5). In a warm environment and when skin temperature is high, the mechanisms of heat elimination are activated at lower core temperature, i.e. the threshold for heat elimination is lowered (3, 4, 11, 22–24), while the threshold is increased in a cool environment when skin temperature is low (25, 26). Peripheral thermoreceptors have been shown to have a great potential for adaptability, especially when exercising in a hot environment; nevertheless, the mechanisms of these adaptations have not been fully understood (15, 24, 27).

Increased core temperature induces fatigue and might lead to hyperthermia

The increased core temperature has been linked to "central fatigue", which is speculated to represent a protection mechanism from potential brain injury (10, 28, 29). Fatigue and exhaustion are warning signs that exercise should be stopped or adjusted to reduce brain temperature increase. Brain temperature is determined by its metabolic activity and its perfusion, reflecting the temperature of blood (2, 15, 30). Many studies are being conducted on how to reduce brain heating during exercise, accordingly, improving thermoregulatory mechanisms, prolonging exercise duration and improving sports performance. The application of central pre-cooling or whole-body cooling has been advocated, being achieved by drinking cold drinks, applying cooled gel sacks, or whole-body cooling using special cool water-recycling suits (31–33); yet the best regime needs to be defined. As evaporative-heat loss is imminently connected with water loss, the role of an appropriate replacement of fluid and electrolyte could not be overemphasized (1, 15, 34). Hyperthermia exaggerates fluid loss, inducing a self-perpetuating, vicious cycle of both hyperthermia and hypovolemia, potentially leading to heat stroke and hypovolemic shock (1, 2, 5, 35).

Cutaneous circulation is the main effector of thermoregulation during physical exercise

In response to increased heat stress during exercise, the thermoregulatory center activates reflexes to transfer additional heat to the body surface from where heat is dissipated into the surroundings, accordingly, establishing a new steady state.

Besides an increase in cardiac output during exercise, skin perfusion is increased due to profound vasodilation of skin arterioles, reducing cutaneous vascular conductance (CVC) and increasing skin blood flow (SkBF).

These mechanisms enable an efficient heat transfer to the skin from where it is eliminated and significantly increase the surface area for heat exchange between the body and the environment. The vasodilation of skin microvessels can induce an immense increase of SkBF compared to resting conditions, i.e. from 300 mL/min in thermoneutral conditions (while in a cold environment as low as 100 mL/min) up to 7 L/min during exercise in a hot climate (4, 7, 24). The regulation of vascular tone in skin microcirculation is very complex, including neural and local mechanisms (21, 36–39).

A decrease in vascular tone is mainly achieved by the withdrawal of the sympathetic tone regulating CVC as the skin arterioles throughout the body are innervated by sympathetic vasoconstrictor nerve fibers (11, 21, 36, 39–41). In addition, non-glabrous non-acral parts of the skin also receive vasodilatory sympathetic fibers which mediate active vasodilation (21, 36, 39). It is speculated that during exercise, these fibers contribute to active vasodilation in non-acral parts of the skin, such as the trunk, skin of the forehead and face, and non-acral parts of extremities (11, 21, 36). While vasoconstrictor fibers mainly mediate their action via noradrenaline acting on α -adrenergic receptors, the exact neurotransmitter of the sympathetic vasodilatory fibers remains questionable: proposed potential (co)transmitters include acetylcholine (ACh), substance P, calcitonin-gene-related polypeptide (CGRP) and nitric oxide (NO) (21, 36, 38). Respectively, the active role of endothelium seems to importantly contribute to active vasodilation in the skin (38, 39, 42). Special anatomical features present in skin microcirculation of glabrous acral parts, such as fingers, toes, palms, feet, ear lobes and nose, are arteriovenous anastomoses, direct connections between arterioles and venules (43, 44) which when open significantly increase the rate of heat elimination (24, 36, 43, 45).

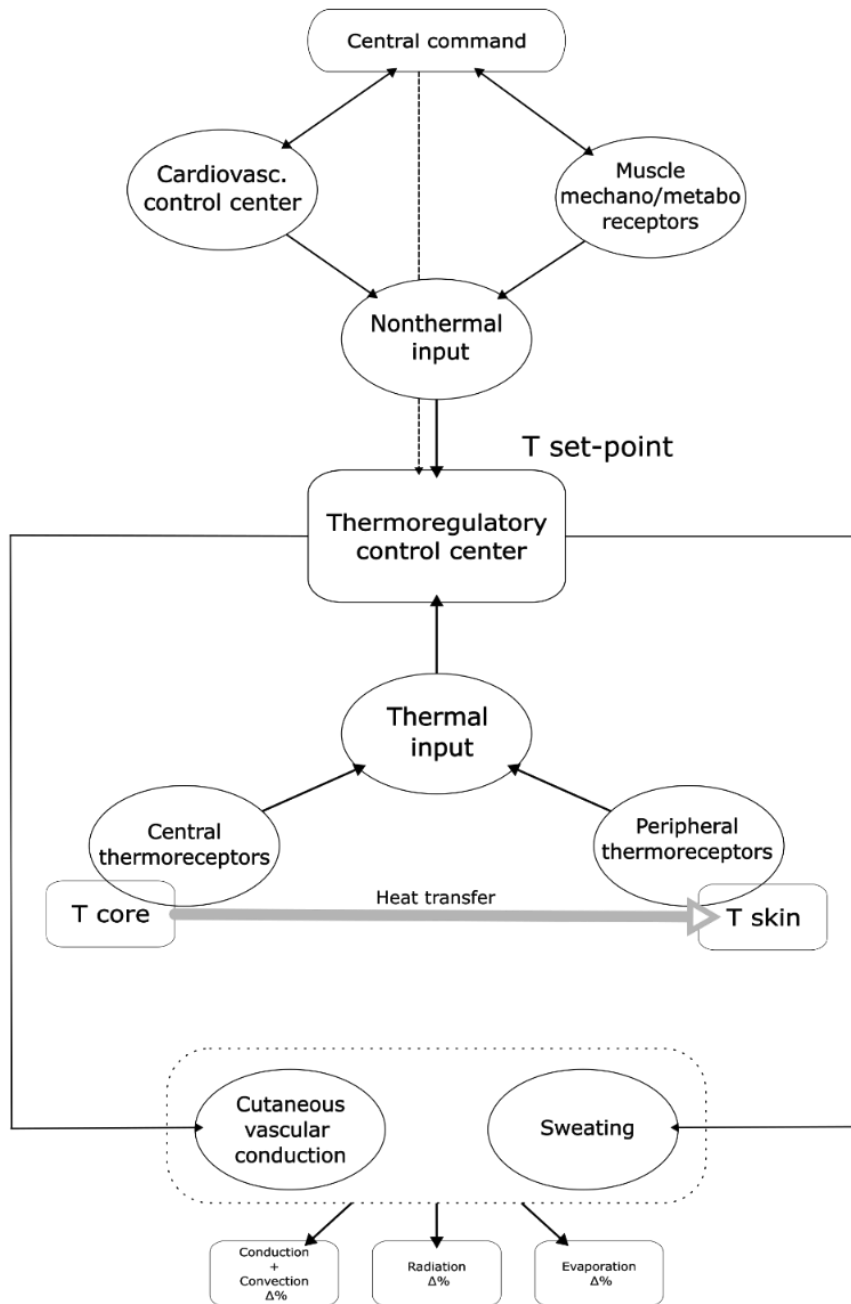


Figure 1. Thermoregulatory mechanisms during exercise.

The thermoregulatory center integrates thermal (from central thermoreceptors sensing changes in core temperature, and peripheral thermoreceptors sensing changes in skin temperature (T)) and non-thermal input, compares the temperature perturbation with the “set-point” value, and activates appropriate reflexes to dissipate excessive heat from the body surface by adjusting the response of cutaneous vascular conductance and sweating, respectively. Temperature gradient determines the quantitative heat transfer from the core to the surface, where heat is dissipated by four physical principles, whose percentages are variable (20%) and modified by physiological response according to the quantity of the produced heat and ambient conditions, respectively.

Evaporation-related heat loss during exercise is increased by sweating

Another very efficient mechanism of heat elimination is active sweating which is tightly linked to changes in CVC. Each gram of water evaporated from the skin surface removes about 2.5 kJ of heat from the body (1, 5). Sweat glands are innervated by the sympathetic nerve fibers with ACh being a putative transmitter acting concomitantly with other cotransmitters (11, 46); an important role of various aquaporins in the skin has recently been reviewed (47). When fully active, sweat glands can increase their sweating rate up to 30 g sweat/min in response to the body's needs which could account for up to 2-4 L/h during high-intensity exercise in a hot environment (1, 11, 15, 24). Indeed, in a hot environment when the ambient temperature exceeds the core temperature, there is no or even a negative temperature gradient for conductive-convective heat transfer, making evaporation the only way to dissipate heat (1, 2, 4, 24). Yet, besides physiologic adjustments in the sweating rate and composition of sweat (46, 48-50), the efficiency of sweating also depends on environmental factors, predominantly on the humidity (3, 15, 50, 51). Increased humidity can make sweating ineffective when there is no water vapor gradient between the environment and the surface of the body, predisposing to the development of hyperthermia which can be fatal (1, 2).

Increased SkBF and sweating rate persist also far in the recovery period after exercise cessation, depending on the duration and intensity of exercise and the production of heat,

until all additional heat is eliminated and the resting temperature steady state is achieved (16, 45, 52-54).

A schematic representation of the mechanisms governing thermoregulation during exercise is depicted in Figure 1.

How could skin blood flow and sweating be assessed

The dynamics of skin microcirculation and skin temperature changes during exercise could be traced by using laser Doppler fluxmetry (LDF) (39, 45) and the corresponding skin temperature measurement (Fig. 2), various laser Doppler imaging techniques (55, 56) or ultrasound Doppler flowmetry (UDF) (57), and have been considered to be a more reliable measure of SkBF than plethysmography (58, 59). To obtain a better insight into the particular physiological mechanism behind it, different approaches and algorithms are being developed for the spectral decomposition of the LDF signal (60). Interestingly, glabrous and non-glabrous parts of the skin behave differently during exercise and its recovery (45, 57, 61) (Fig. 2). A strong cross-coupling between glabrous SkBF and core temperature in thermoregulatory function has recently been established based on experimental and modeling data (62). A promising device for tracing sweat rate during exercise as accurately as possible and providing a low-cost device platform to detect other health-relevant biomarkers in the sweat (vapor) as the next-generation sweat sensor for smart healthcare and personalized medicine has been introduced (63).

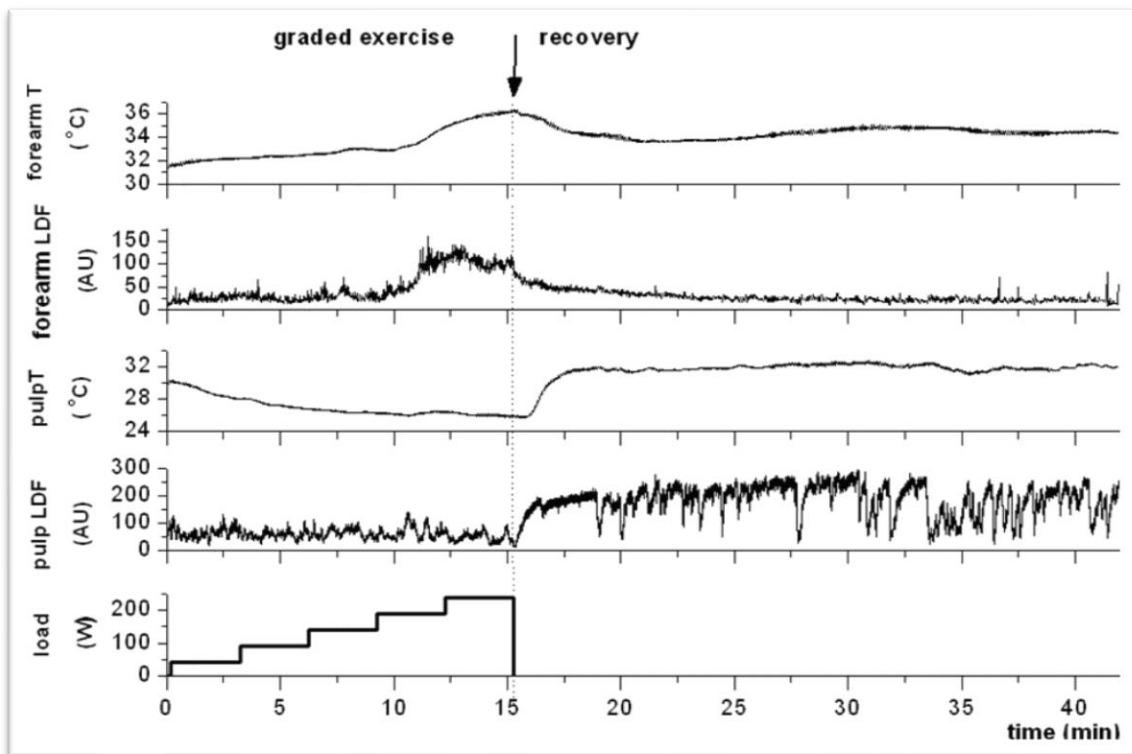


Figure 2. The responses of skin blood flow and the corresponding skin temperature to exercise and its recovery differ between glabrous and non-glabrous areas.

A representative tracing of the laser Doppler flux (LDF), expressed in arbitrary perfusion units (AU) and the corresponding skin temperature (T) in skin microcirculation on the volar forearm (glabrous site) and the finger pulp (non-glabrous site) during graded dynamic exercise and its recovery is shown. Exercise load is expressed in Watts (W). Adapted from (45).

The main differences between thermoregulation during rest and exercise: a summary

Apart from thermoreflexes, many opposing non-thermoregulatory reflexes (mechano-, metabo- and baroreflex to list some) are activated during exercise and its recovery to ensure sufficient perfusion of skeletal muscles and the preservation of blood pressure (7, 15, 20, 54, 64–66). Therefore, thermoregulation during exercise importantly differs from that at rest. The most manifest differences are depicted in Fig. 3, representing the relation between the body core temperature and the SkBF. To assess the characteristics of this relation, i.e. the slope of the curve, the body core temperature and the SkBF, potentially with the corresponding skin temperature, should be traced. Core temperature is usually determined by an esophageal thermo-sensor, although other methodological aspects have been addressed

(5, 20, 22, 62). Nevertheless, the data should be interpreted cautiously, especially when measuring peripheral skin T to estimate core temperature, which is rather questionable (67). On the other hand, there are much more options for assessing skin temperature; besides the above mentioned, infrared thermography has gained increasing importance; yet, similarly to other methods, it has not been standardized (68, 69).

At the beginning of exercise, an increase of the sympathetic tone throughout the body, presumably due to a central command, enables redistribution of blood flow, increasing CVC and reducing SkBF and thus shifting the starting point toward lower SkBF at unchanged core temperature (Fig. 3) (2, 5, 7, 20, 24). Another distinctive difference is a shift in the threshold to induce active vasodilation and sweating in the skin, toward higher core temperatures (Fig. 3); interestingly, the threshold shift depends on

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exercise intensity and is even more pronounced in high-intensity exercise (11, 20, 36). The dependence of the thermoregulatory threshold on the intensity of exercise might partly explain rapid fatigue and exhaustion during intense exercise due to a higher increase in core temperature, which might even lead to hyperthermia (15, 22, 29). The third pronounced difference is the responsiveness of the effectors in the skin: the maximal vasodilation in the skin during exercise comprises only 60% of the maximal vasodilation attained in resting conditions (Fig. 3) (7, 20, 24). Pooling of additional blood in the periphery impedes venous return to the heart, and activates baroreflex, leading to "cardiovascular drift" and heart rate increase that is disproportional to the needs of the skeletal muscles (5, 52, 70).

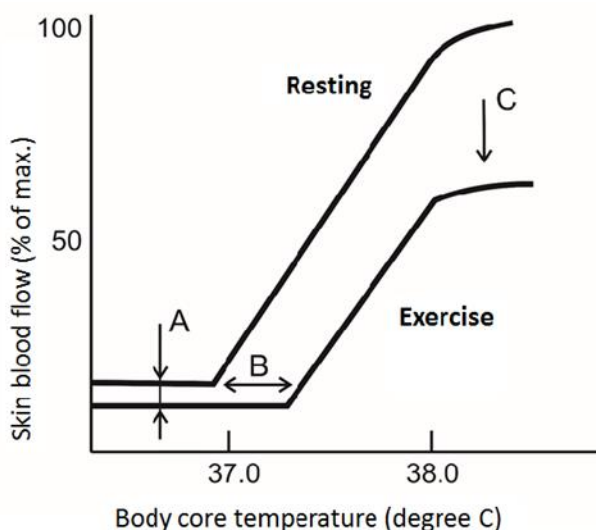


Figure 3. The main differences between thermoregulation during rest and dynamic exercise.

Skin blood flow (SkBF) in relation to body core temperature is shown. The "starting point" is shifted toward lower SkBF at the onset of exercise due to vasoconstriction in the skin (A). The temperature threshold to induce vasodilation is shifted toward a higher core temperature during exercise (B). Maximal vasodilation in the skin is reduced compared to resting conditions (C). Adapted from (4).

In addition, it has been proposed that skin temperature, independently of the core temperature, affects sports performance:

maximal oxygen uptake ($\text{VO}_{2\text{max}}$) at the same core temperature was shown to be lower at higher skin temperatures than at lower ones (23, 70). Increased skin temperature during exercise reduces the temperature gradient for heat elimination, impeding heat exchange. To overcome the decreased temperature gradient, SkBF is increased on account of diminished blood flow through skeletal muscles. From the above observations on opposing thermo- and non-thermoregulatory reflexes during exercise and its recovery, it is obvious that hyperthermia is more often an issue when exercising than when resting. Interestingly, simplified thermoregulation models of the human body exercising in warm conditions have been proposed considering all the above-mentioned players (62, 71).

Exercise and thermoregulation in extreme environmental conditions

Hot environment

Exercising in a hot environment undoubtedly compromises thermoregulation. Pooling of additional blood in the periphery increases cardiovascular drift in a hot climate. It has been shown that a heart rate increase of 20 beats/min could not compensate for the decreased stroke volume due to the pooling of blood in the skin: cardiac output was about 1.5 L/min lower during heavy exercise in the heat than during comparable exercise in a cool environment (1, 5, 15). Due to insufficient muscle perfusion, the amount of anaerobic metabolism increases, decreasing plasma pH and additionally compromising performance (15, 72).

In addition to the pooling of blood, another problem during prolonged exercise is the loss of water and electrolytes, additionally compromising venous return, and consequently jeopardizing the maintenance of blood pressure. To overcome the threatening hypotension, relative cutaneous vasoconstriction issues, rendering the person more susceptible to developing hyperthermia (1, 5, 24). In addition, the reflex of sweating is reset toward higher core temperatures as water preservation due to

reduced osmolarity surpasses the need to eliminate heat by sweating (20, 73–75). Respectively, a vicious cycle could ensue leading to hyperthermia and/or shock (35). In this respect, sufficient fluid and electrolytes substitution is a prerequisite for sustaining exercise (24, 34, 76). It has been shown that even 1% of body mass reduction due to dehydration strongly impacts sports performance and VO_{2max} (77).

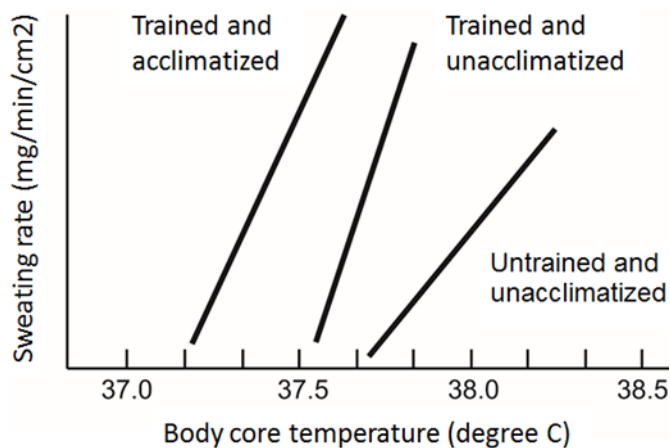


Figure 4. The effect of regular training and acclimatization on thermoregulation

Training and staying in a warm environment for a longer period induce a shift in the temperature threshold for heat elimination (presented as sweating rate) as well as the sensitivity of thermoreflex. Adapted from (81).

When regularly exercising in a warm environment, acclimatization processes take place which improve sports performance: the sensitivity of thermoreflex is reset toward a lower core temperature threshold (Fig. 4), the maximal sweat rate increases and sweat composition changes, becoming more diluted thus helping to preserve body electrolytes (24, 50, 51, 78, 79). In addition, an increase in plasma volume in a longer-term improves circulation and heat exchange (24, 77). All these adaptations improve VO_{2max} and sports performance. Interestingly, similar adaptations have also been shown in endurance elite sportsmen exercising in a thermoneutral environment (Fig. 4) (48, 73, 78–81).

Cold environment

On the other hand, exercising in a cold environment is not problematic from the thermoregulatory point of view provided it is not of too long duration or performed in cold water which has a 25-fold higher heat conductivity compared to air (5, 25–27, 82). As long as the body core temperature is maintained in a physiological range, the low ambient temperature does not impact sports performance and VO_{2max} . Yet, cooling of the muscles impacts their functional abilities in terms of decreasing their strength, maximal force, velocity and reaction time (83, 84). Due to vasoconstriction in the skin, the release of free fatty acids from subcutaneous adipose tissue is reduced, limiting the oxidation of fat as fuel for muscle contraction and accordingly increasing the oxidation of carbohydrates. Potential hypothermia results from a drop in core temperature when exercising for a longer time, or insufficiently dressed or performing water sports (26).

Acclimatization to cold induces adaptive mechanisms which enable better preservation of heat on one side and increased production on the other, including shivering and brown fat adipose tissue thermogenesis (2, 25–27).

Effect of sex and age on thermoregulation during exercise

An interesting issue to be discussed is the effect of sex on thermoregulation. On one side, centrally mediated mechanisms might affect the response regarding sex, and on the other, sex hormones are known to exert direct peripheral effects on the vascular tone (11, 18, 19, 36, 85). Yet, studies reported controversial results. Most often, the main differences are attributed to the sweating response: the slope of the curve representing sweating rate dependency on the body core temperature was reduced in women compared to men (86, 87) even though women exhibited a greater number of sweat glands (51). The differences in the sweat rate were more pronounced when exercising at higher intensities (86). It seems that the temperature threshold to induce vasodilation in the skin is

higher in women (85). However, a recent meta-analysis has shown that despite increased core T in women in the luteal phase of the menstrual cycle this does not significantly impact thermoregulatory response, at least in terms of sweat rate and skin temperature (19, 88). Finally, it is worth emphasizing that aging also affects the thermoregulatory response to exercise (1).

Effect of endurance training on thermoregulation during exercise

Regular training in both men and women induces significant adaptations of the thermoregulatory system, including cutaneous vascular reactivity as well as sweating. The threshold to activate effectors for heat elimination is lower in trained compared to sedentary (64, 77, 81, 89) (Fig. 4). Sweat rate and composition are altered in terms of increased sweat rate at the same exercise intensity (expressed as % VO₂max) and more diluted sweat, respectively enabling more efficient electrolytes preservation in sportsmen (51, 78, 80). In addition, sportsmen have been shown to better acclimatize to the heat, which rather than reflecting structural changes has been attributed to functional vessel alterations (79, 90). A part of altered vascular responsiveness might be attributed to increased endothelium-dependent vasodilation (91, 92) which might additionally contribute to beneficial thermoregulatory adaptations.

References

- McArdle WD, Katch FI, Katch VL. Essentials of Exercise Physiology. 3rd ed. McArdle WD, Katch FI, Katch VL, editors. Baltimore, Philadelphia: Lippincott Williams & Wilkins; 2006.
- Boron WF, Boulpaep EL. Medical Physiology: a cellular and molecular approach. 2nd updated. Boron WF, Boulpaep EL, editors. Philadelphia: Saunders, Elsevier; 2012.
- Jenkins EJ, Campbell HA, Lee JKW, Mündel T, Cotter JD. Delineating the impacts of air temperature and humidity for endurance exercise. *Exp Physiol* 2023 Feb 20; 108(2): 207–20. doi: 10.1113/EP090969.
- González-Alonso J, Crandall CG, Johnson JM. The cardiovascular challenge of exercising in the heat. *J Physiol* 2008 Jan 1; 586(1): 45–53. doi: 10.1113/jphysiol.2007.142158.
- Shephard RJ; APO. Endurance in Sport. London, Edinburg, Boston: Oxford Blackwell Scientific Publications; 1992.
- Namisnak LH, Haghayegh S, Khoshnevis S, Diller KR. Bioheat Transfer Basis of Human Thermoregulation: Principles and Applications. *J Heat Transfer* 2022 Mar 1; 144(3). doi: 10.1115/1.4053195.
- González-Alonso J. Human thermoregulation and the cardiovascular system. *Exp Physiol* 2012 Mar; 97(3): 340–6. doi: 10.1113/expphysiol.2011.058701.
- Hasegawa H, Ishiwata T, Saito T, Yazawa T, Aihara Y, Meeusen R. Inhibition of the preoptic area and anterior hypothalamus by tetrodotoxin alters thermoregulatory functions in exercising rats. *J Appl Southeastern European Medical Journal*, 2023; 7(1)

All these adaptations enable sportsmen better adjustments to physical and thermal stress, reaching higher VO₂max values and performing exercise for longer periods, in thermoneutral, as well as in extreme environmental conditions.

Conclusion

Thermoregulation during exercise differs from that in resting conditions since, during exercise, thermoregulatory reflexes oppose the non-thermoregulatory ones. The opposing reflexes integrate at the level of skin microcirculation which is the main organ for heat elimination. An important issue when exercising is a sufficient substitution of water and electrolytes, especially in a warm and humid environment. Regular physical activity induces several beneficial changes, including better thermoregulatory mechanisms. Yet, exact mechanisms, as well as the most optimal training regime, remain to be determined, and above others, appropriate methods to measure the many players involved in thermoregulation in humans in vivo need to be established.

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Competing interests. None to declare.

Physiol 2005 Apr; 98(4): 1458–62. doi: 10.1152/jappphysiol.00916.2004.

9. Tan CL, Knight ZA. Regulation of Body Temperature by the Nervous System. *Neuron* 2018 Apr; 98(1): 31–48. doi: 10.1016/j.neuron.2018.02.022.

10. Roelands B, Meeusen R. Alterations in Central Fatigue by Pharmacological Manipulations of Neurotransmitters in Normal and High Ambient Temperature. *Sports Medicine* 2010 Mar; 40(3): 229–46. doi: 10.2165/11533670-000000000-00000.

11. Shibasaki M, Crandall CG. Mechanisms and controllers of eccrine sweating in humans. *Frontiers in Bioscience* 2010; S2(2): 94. doi: 10.2741/s94.

12. Morrison SF. Central neural pathways for thermoregulation. *Frontiers in Bioscience* 2011; 16(1): 74. doi: 10.2741/3677.

13. Romanovsky AA, Almeida MC, Garami A, Steiner AA, Norman MH, Morrison SF, et al. The Transient Receptor Potential Vanilloid-1 Channel in Thermoregulation: A Thermosensor It Is Not. *Pharmacol Rev* 2009 Sep; 61(3): 228–61. doi: 10.1124/pr.109.001263.

14. Zayan U, Caccialupi Da Prato L, Muscatelli F, Matarazzo V. Modulation of the thermosensory system by oxytocin. *Front Mol Neurosci* 2023 Jan 9; 15. doi: 10.3389/fnmol.2022.1075305.

15. Périard JD, Eijsvogels TMH, Daanen HAM. Exercise under heat stress: thermoregulation, hydration, performance implications, and mitigation strategies. *Physiol Rev* 2021 Oct 1; 101(4): 1873–979. doi: 10.1152/physrev.00038.2020.

16. Carmo AAL, Goulart KNO, Cabido CET, Martins YAT, Santos GCF, Shang FLT, et al. Active warm-up and time-of-day effects on repeated-sprint performance and post-exercise recovery. *Eur J Appl Physiol* 2023 Jan 24; 123(1): 49–64. doi: 10.1007/s00421-022-05051-w.

17. Costa CMA, Moreira DG, Sillero-Quintana M, Brito CJ, de Azambuja Pussieldi G, de Andrade Fernandes A, et al. Daily rhythm of skin temperature of women evaluated by infrared thermal imaging. *J Therm Biol* 2018 Feb; 72: 1–9. doi: 10.1016/j.jtherbio.2017.12.002.

18. Charkoudian N, Stachenfeld N. Sex hormone effects on autonomic mechanisms of thermoregulation in humans. *Autonomic Neuroscience* 2016 Apr; 196: 75–80. doi: 10.1016/j.autneu.2015.11.004.

19. Greenfield AM, Alba BK, Giersch GEW, Seeley AD. Sex differences in thermal sensitivity and perception: Implications for behavioral and autonomic thermoregulation. *Physiol Behav* 2023 May; 263: 114126. doi: 10.1016/j.physbeh.2023.114126.

20. Kenny GP. Human thermoregulation: separating thermal and nonthermal effects on heat loss. *Frontiers in Bioscience* 2010; 15(1): 259. doi: 10.2741/3620.

21. Johnson JM, Kellogg DL. Local thermal control of the human cutaneous circulation. *J Appl Physiol* 2010 Oct; 109(4): 1229–38. doi: 10.1152/jappphysiol.00407.2010.

22. Demachi K, Yoshida T, Kume M, Tsuji M, Tsuneoka H. The influence of internal and skin temperatures on active cutaneous vasodilation under different levels of exercise and ambient temperatures in humans. *Int J Biometeorol* 2013 Jul 9; 57(4): 589–96. doi: 10.1007/s00484-012-0586-y.

23. Sawka MN, Cheuvront SN, Kenefick RW. High skin temperature and hypohydration impair aerobic performance. *Exp Physiol* 2012 Mar; 97(3): 327–32. doi: 10.1113/expphysiol.2011.061002.

24. Johnson JM. Exercise in a hot environment: the skin circulation. *Scand J Med Sci Sports* 2010 Oct 4; 20: 29–39. doi: 10.1111/j.1600-0838.2010.01206.x.

25. Alba BK, Castellani JW, Charkoudian N. Cold-induced cutaneous vasoconstriction in humans: Function, dysfunction and the distinctly counterproductive. *Exp Physiol* 2019 Aug 16; 104(8): 1202–14. doi: 10.1113/EP087718.

26. Castellani JW, Young AJ, Sawka MN, Pandolf KB. Human thermoregulatory responses during serial cold-water immersions. *J Appl Physiol* 1998 Jul 1; 85(1): 204–9. doi: 10.1152/jappphysiol.1998.85.1.204.

27. Castellani JW, Young AJ. Human physiological responses to cold exposure: Acute responses and acclimatization to prolonged exposure. *Autonomic Neuroscience* 2016 Apr; 196: 63–74. doi: 10.1016/j.autneu.2016.02.009.

28. Gandevia SC. Spinal and Supraspinal Factors in Human Muscle Fatigue. *Physiol Rev* 2001 Jan 10; 81(4): 1725–89. doi: 10.1152/physrev.2001.81.4.1725.

29. Behrens M, Gube M, Chaabene H, Prieske O, Zenon A, Broscheid KC, et al. Fatigue and Human Performance: An Updated Framework. *Sports Medicine* 2023 Jan 18; 53(1): 7–31. doi: 10.1007/s40279-022-01748-2.

30. Nybo L, Secher NH. Cerebral perturbations provoked by prolonged exercise. *Prog Neurobiol* 2004 Mar; 72(4): 223–61. doi: 10.1016/j.pneurobio.2004.03.005.
31. Marino FE. The critical limiting temperature and selective brain cooling: neuroprotection during exercise? *International Journal of Hyperthermia* 2011 Sep 16; 27(6): 582–90. doi: 10.3109/02656736.2011.589096.
32. Ross M, Abbiss C, Laursen P, Martin D, Burke L. Precooling Methods and Their Effects on Athletic Performance. *Sports Medicine* 2013 Mar 5; 43(3): 207–25. doi: 10.1007/s40279-012-0014-9.
33. Wegmann M, Faude O, Poppendieck W, Hecksteden A, Fröhlich M, Meyer T. Pre-Cooling and Sports Performance. *Sports Medicine* 2012 Jul; 42(7): 545–64. doi: 10.2165/11630550-000000000-00000.
34. Tarnowski CA, Rollo I, Carter JM, Lizarraga-Dallo MA, Oliva MP, Clifford T, et al. Fluid Balance and Carbohydrate Intake of Elite Female Soccer Players during Training and Competition. *Nutrients* 2022 Aug 3; 14(15): 3188. doi: 10.3390/nu14153188.
35. Epstein Y, Roberts WO. The pathophysiology of heat stroke: an integrative view of the final common pathway. *Scand J Med Sci Sports* 2011 Dec; 21(6): 742–8. doi: 10.1111/j.1600-0838.2011.01333.x.
36. Charkoudian N. Mechanisms and modifiers of reflex induced cutaneous vasodilation and vasoconstriction in humans. *J Appl Physiol* 2010 Oct; 109(4): 1221–8. doi: 10.1152/jappphysiol.00298.2010.
37. Kellogg DL. Thermoregulatory and thermal control in the human cutaneous circulation. *Frontiers in Bioscience* 2010; S2(3): 105. doi: 10.2741/s105.
38. Kellogg DL, Zhao JL, Wu Y, Johnson JM. Nitric oxide and receptors for VIP and PACAP in cutaneous active vasodilation during heat stress in humans. *J Appl Physiol* 2012 Nov 15; 113(10): 1512–8. doi: 10.1152/jappphysiol.00859.2012.
39. Lenasi H. Assessment of Human Skin Microcirculation and Its Endothelial Function Using Laser Doppler Flowmetry. In: *Medical Imaging InTech*; 2011. doi: 10.5772/27067.
40. Halliwill JR, Taylor JA, Eckberg DL. Impaired sympathetic vascular regulation in humans after acute dynamic exercise. *J Physiol* 1996 Aug 15; 495(1): 279–88. doi: 10.1113/jphysiol.1996.sp021592.
41. Lenasi H. Physical exercise and skin microcirculation. *Period Biol* 2014; 116(1).
42. Lenasi H. The role of nitric oxide- and prostacyclin-independent vasodilatation in the human cutaneous microcirculation: Effect of cytochrome P450 2C9 inhibition. *Clin Physiol Funct Imaging* 2009; 29(4): 263–70.
43. Braverman IM. The Cutaneous Microcirculation: Ultrastructure and Microanatomical Organization. *Microcirculation* 1997 Jan; 4(3): 329–40. doi: 10.3109/10739689709146797.
44. Bergersen TK, Hisdal J, Walløe L. Perfusion of the human finger during cold-induced vasodilatation. *American Journal of Physiology-Regulatory, Integrative and Comparative Physiology* 1999 Mar 1; 276(3): R731–7. doi: 10.1152/ajpregu.1999.276.3.R731.
45. Potočnik N, Lenasi H. The responses of glabrous and nonglabrous skin microcirculation to graded dynamic exercise and its recovery. *Clin Hemorheol Microcirc* 2016 Nov 4; 64(1): 65–75. doi: 10.3233/CH-162045.
46. Derbyshire PJ, Barr H, Davis F, Higson SPJ. Lactate in human sweat: a critical review of research to the present day. *The Journal of Physiological Sciences* 2012 Nov 8; 62(6): 429–40. doi: 10.1007/s12576-012-0213-z.
47. Yin Z, Ren H. Aquaporins in Skin. In 2023. p. 211–23. doi: 10.1007/978-981-19-7415-1_15.
48. Pilardeau PA; LF; VJ; GM; HP; MJN; CMT. Effect of different work-loads on sweat production and composition in man. *J Sports Med Phys Fit* 1998; 28: 247–52.
49. Saat M, Sirisinghe RG, Singh R, Tochiyara Y. Effects of Short-term Exercise in the Heat on Thermoregulation, Blood Parameters, Sweat Secretion and Sweat Composition of Tropic-dwelling Subjects. *J Physiol Anthropol Appl Human Sci* 2005; 24(5): 541–9. doi: 10.2114/jpa.24.541.
50. Buono MJ, Numan TR, Claros RM, Brodine SK, Kolkhorst FW. Is active sweating during heat acclimation required for improvements in peripheral sweat gland function? *American Journal of Physiology-Regulatory, Integrative and Comparative Physiology* 2009 Oct; 297(4): R1082–5. doi: 10.1152/ajpregu.00253.2009.
51. Buono MJ, Martha SL, Heaney JH. Peripheral sweat gland function is improved with humid heat acclimation. *J Therm Biol* 2009 Apr; 34(3): 127–30. doi: 10.1016/j.jtherbio.2008.11.006.
52. Kenney WL, Stanhewicz AE, Bruning RS, Alexander LM. Blood pressure regulation III: what

happens when one system must serve two masters: temperature and pressure regulation? *Eur J Appl Physiol* 2014 Mar 1; 114(3): 467–79. doi: 10.1007/s00421-013-2652-5.

53. Silva AG da, Albuquerque MR, Brito CJ, Stroppa GM, Oliveira SAF, Sillero-Quintana M, et al. Effect of Whole-, Upper-, and Lower-Body High-Intensity Rowing Exercise on Skin Temperature Measured by Thermography. *Res Q Exerc Sport* 2023 Jan 2; 94(1): 226–36. doi: 10.1080/02701367.2021.1964696.

54. Journeay WS, Reardon FD, Martin CR, Kenny GP. Control of cutaneous vascular conductance and sweating during recovery from dynamic exercise in humans. *J Appl Physiol* 2004 Jun; 96(6): 2207–12. doi: 10.1152/jappphysiol.01201.2003.

55. Humeau A, Steenbergen W, Nilsson H, Strömberg T. Laser Doppler perfusion monitoring and imaging: novel approaches. *Med Biol Eng Comput* 2007 May 6; 45(5): 421. doi: 10.1007/s11517-007-0170-5.

56. Schwartz KS, Theis EN, Bunting K, McCaughey RA, Lang JA. Laser speckle contrast imaging and laser Doppler flowmetry reproducibly assess reflex cutaneous vasoconstriction. *Microvasc Res* 2022 Jul; 142: 104363. doi: 10.1016/j.mvr.2022.104363.

57. Lenasi H, Potočnik N, Petrishchev N, Papp M, Egorkina A, Girina M, et al. The measurement of cutaneous blood flow in healthy volunteers subjected to physical exercise with ultrasound Doppler imaging and laser Doppler flowmetry. *Clin Hemorheol Microcirc* 2017 Apr 28; 65(4): 373–81. doi: 10.3233/CH-16204.

58. Mizeva I, Di Maria C, Frick P, Podtaev S, Allen J. Quantifying the correlation between photoplethysmography and laser Doppler flowmetry microvascular low-frequency oscillations. *J Biomed Opt* 2015 Mar 12; 20(3): 037007. doi: 10.1117/1.JBO.20.3.037007.

59. Silva H, Rocha C, Monteiro Rodrigues L. Combining laser-doppler flowmetry and photoplethysmography to explore in vivo vascular physiology. *Journal Biomedical and Biopharmaceutical Research* 2016 Dec; 13(2): 209–17. doi: 10.19277/bbr.13.2.139.

60. Kralj L, Lenasi H. Wavelet analysis of laser Doppler microcirculatory signals: Current applications and limitations. *Front Physiol* 2023 Jan 20; 13. doi: 10.3389/fphys.2022.1076445.

61. YAMAZAKI F. Vasomotor responses in glabrous and nonglabrous skin during sinusoidal exercise. *Med Sci Sports Exerc* 2002 May; 34(5): 767–72. doi: 10.1097/00005768-200205000-00006.

62. Namisnak LH, Khoshnevis S, Diller KR. Interdependency of Core Temperature and Glabrous Skin Blood Flow in Human Thermoregulation Function: A Pilot Study. *J Biomech Eng* 2023 Apr 1; 145(4). doi: 10.1115/1.4056110.

63. Liu Y, Li X, Yang H, Zhang P, Wang P, Sun Y, et al. Skin-Interfaced Superhydrophobic Insensible Sweat Sensors for Evaluating Body Thermoregulation and Skin Barrier Functions. *ACS Nano* 2023 Mar 28; 17(6): 5588–99. doi: 10.1021/acsnano.2c11267.

64. Simmons GH, Wong BJ, Holowatz LA, Kenney WL. Changes in the control of skin blood flow with exercise training: where do cutaneous vascular adaptations fit in? *Exp Physiol* 2011 Sep 1; 96(9): 822–8. doi: 10.1113/expphysiol.2010.056176.

65. Mack GW, Cordero D, Peters J. Baroreceptor modulation of active cutaneous vasodilation during dynamic exercise in humans. *J Appl Physiol* 2001 Apr 1; 90(4): 1464–73. doi: 10.1152/jappphysiol.2001.90.4.1464.

66. Spranger MD, Sala-Mercado JA, Coutsos M, Kaur J, Stayer D, Augustyniak RA, et al. Role of cardiac output versus peripheral vasoconstriction in mediating muscle metaboreflex pressor responses: dynamic exercise versus postexercise muscle ischemia. *American Journal of Physiology-Regulatory, Integrative and Comparative Physiology* 2013 Apr 15; 304(8): R657–63. doi: 10.1152/ajpregu.00601.2012.

67. Fisher JT, Ciuha U, Tipton MJ, Ioannou LG, Mekjavic IB. Predicting Deep Body Temperature (T_b) from Forehead Skin Temperature: T_b or Not T_b? *Sensors* 2022 Jan 22; 22(3): 826. doi: 10.3390/s22030826.

68. Moreira DG, Costello JT, Brito CJ, Adamczyk JG, Ammer K, Bach AJE, et al. Thermographic imaging in sports and exercise medicine: A Delphi study and consensus statement on the measurement of human skin temperature. *J Therm Biol* 2017 Oct; 69: 155–62. doi: 10.1016/j.jtherbio.2017.07.006.

69. Fernandes A de A, Amorim PR dos S, Brito CJ, de Moura AG, Moreira DG, Costa CMA, et al. Measuring skin temperature before, during and after exercise: a comparison of thermocouples and infrared thermography. *Physiol Meas* 2014 Feb 1; 35(2): 189–203. doi: 10.1088/0967-3334/35/2/189.

70. Chou TH, Allen JR, Hahn D, Leary BK, Coyle EF. Cardiovascular responses to exercise when increasing skin temperature with narrowing of the core-to-skin temperature gradient. *J Appl Physiol* 2018 Sep 1; 125(3): 697–705. doi: 10.1152/jappphysiol.00965.2017.
71. Li B, Yang Y, Yao R, Liu H, Li Y. A simplified thermoregulation model of the human body in warm conditions. *Appl Ergon* 2017 Mar; 59: 387–400. doi: 10.1016/j.apergo.2016.09.010.
72. Febbraio MA, Snow RJ, Stathis CG, Hargreaves M, Carey MF. Effect of heat stress on muscle energy metabolism during exercise. *J Appl Physiol* 1994 Dec 1; 77(6): 2827–31. doi: 10.1152/jappphysiol.1994.77.6.2827.
73. Ichinose T, Okazaki K, Masuki S, Mitono H, Chen M, Endoh H, et al. Ten-day endurance training attenuates the hyperosmotic suppression of cutaneous vasodilation during exercise but not sweating. *J Appl Physiol* 2005 Jul; 99(1): 237–43. doi: 10.1152/jappphysiol.00813.2004.
74. Montain SJ, Latzka WA, Sawka MN. Control of thermoregulatory sweating is altered by hydration level and exercise intensity. *J Appl Physiol* 1995 Nov 1; 79(5): 1434–9. doi: 10.1152/jappphysiol.1995.79.5.1434.
75. Takamata A, Nagashima K, Nose H, Morimoto T. Osmoregulatory inhibition of thermally induced cutaneous vasodilation in passively heated humans. *American Journal of Physiology-Regulatory, Integrative and Comparative Physiology* 1997 Jul 1; 273(1): R197–204. doi: 10.1152/ajpregu.1997.273.1.R197.
76. Mora-Rodriguez R, Hamouti N. Salt and Fluid Loading: Effects on Blood Volume and Exercise Performance. In 2012. p. 113–9. doi: 10.1159/000341945.
77. ARMSTRONG LE, COSTILL DL, FINK WJ. Influence of diuretic-induced dehydration on competitive running performance. *Med Sci Sports Exerc* 1985 Aug; 17(4): 456–61. doi: 10.1249/00005768-198508000-00009.
78. Mora-Rodriguez R. Influence of Aerobic Fitness on Thermoregulation During Exercise in the Heat. *Exerc Sport Sci Rev* 2012 Apr; 40(2): 79–87. doi: 10.1097/JES.0b013e318246ee56.
79. Lorenzo S, Minson CT. Heat acclimation improves cutaneous vascular function and sweating in trained cyclists. *J Appl Physiol* 2010 Dec; 109(6): 1736–43. doi: 10.1152/jappphysiol.00725.2010.
80. Pilardeau PA; CMT; HP; VP; VJ; GM. Effect of physical training on exercise induced sweating in men. *J Sports Med Phys Fit* 1988; 28: 176–80.
81. Foss MJ, Keteyian SJ, editors. *Fox's Physiological Basis for Exercise and Sport*. In: 6th ed. Boston, New York, San Francisco: McGraw-Hill; 1998. p. 510–59.
82. Nimmo M. Exercise in the cold. *J Sports Sci* 2004 Oct; 22(10): 898–916. doi: 10.1080/0264041400005883.
83. Cheung SS, Sleivert GG. Lowering of skin temperature decreases isokinetic maximal force production independent of core temperature. *Eur J Appl Physiol* 2004 May 1; 91(5–6): 723–8. doi: 10.1007/s00421-004-1062-0.
84. Comeau MJ, Potteiger JA, Brown LE. Effects of Environmental Cooling on Force Production in the Quadriceps and Hamstrings. *The Journal of Strength and Conditioning Research* 2003; 17(2): 279. doi: 10.1519/1533-4287(2003)017<0279:EOECOF>2.0.CO;2.
85. Kenny GP, Murrin JE, Journeay WS, Reardon FD. Differences in the postexercise threshold for cutaneous active vasodilation between men and women. *American Journal of Physiology-Regulatory, Integrative and Comparative Physiology* 2006 Jan; 290(1): R172–9. doi: 10.1152/ajpregu.00428.2005.
86. Gagnon D, Kenny GP. Sex differences in thermoeffector responses during exercise at fixed requirements for heat loss. *J Appl Physiol* 2012 Sep 1; 113(5): 746–57. doi: 10.1152/jappphysiol.00637.2012.
87. Frye AJ, Kamon E. Responses to dry heat of men and women with similar aerobic capacities. *J Appl Physiol* 1981 Jan 1; 50(1): 65–70. doi: 10.1152/jappphysiol.1981.50.1.65.
88. Giersch GEW, Morrissey MC, Katch RK, Colburn AT, Sims ST, Stachenfeld NS, et al. Menstrual cycle and thermoregulation during exercise in the heat: A systematic review and meta-analysis. *J Sci Med Sport* 2020 Dec; 23(12): 1134–40. doi: 10.1016/j.jsams.2020.05.014.
89. Fritzsche RG, Coyle EF. Cutaneous blood flow during exercise is higher in endurance-trained humans. *J Appl Physiol* 2000 Feb 1; 88(2): 738–44. doi: 10.1152/jappphysiol.2000.88.2.738.
90. Sánchez-Jiménez JL, Tejero-Pastor R, Calzadillas-Valles M del C, Jimenez-Perez I, Cibrián Ortiz de Anda RM, Salvador-Palmer R, et al. Chronic and Acute Effects on Skin Temperature from a Sport Consisting of Repetitive Impacts from Hitting a Ball

with the Hands. *Sensors* 2022 Nov 7; 22(21): 8572. doi: 10.3390/s22218572.

91. Lenasi H, Štrucl M. Regular physical activity alters the postocclusive reactive hyperemia of the cutaneous microcirculation. *Clin Hemorheol*

Microcirc 2010; 45(2-4): 365-74. doi: 10.3233/CH-2010-1320.

92. LENASI H, STRUCL M. Effect of Regular Physical Training on Cutaneous Microvascular Reactivity. *Med Sci Sports Exerc* 2004 Apr; 36(4): 606-12. doi: 10.1249/01.MSS.0000121948.86377.51.

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