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Are Non-Thermal Factors Important in the Cutaneous Vascular Response to Exercise? A Proponent's View

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Direct forearm blood flow measurements showed that the threshold for vasodilation is shifted to a higher core temperature and that the slope describing the relationship between skin blood flow and core temperature is reduced during submaximum exercise in comparison with supine resting conditions. These changes in skin blood flow characteristics have been shown to be proportionately related to work load in at least one study, but not in others. With heavy exercise, indirect evidence was obtained for the elicitation of vasoconstriction after body core temperature had attained a level of 39°C; this caused a dramatic rise of T_{core} to above 40°C. In other studies, such terminal vasoconstriction was not observed; the subjects stopped exercising (75 percent $\dot{V}_{O_2}$ max), independently of its duration, when rectal temperature had reached about 39°C. Such inconsistent results in regard to the importance of extrathermal control of skin blood flow may be traced to variations in the motivational and emotional state; moreover, a phenomenon described as "short-term adaptation" may be responsible for some discrepant results. In conclusion, there is evidence for the concept that blood pressure control by peripheral vasoconstriction may have, under certain circumstances, preference over the demands of temperature regulation.

The particular feature of skin blood flow (SkBF) is its being jointly employed by at least two regulatory systems: namely, those for blood pressure and for temperature control. This brings up the problem of serving two masters with different intentions. From this simplistic point of view, the answer to the main question of this session appears to be very easy: of course, SkBF will obey the commands evolving from various systems; in other words, SkBF will not only be determined by the signals derived from thermal receptors.

According to some calculations by Rowell [1], maximum skin blood flow is 7–8 l/minute in adult males, i.e., about 25–30 percent of maximal cardiac output. This large SkBF is an effective means of keeping the core-surface temperature gradient small in order to avoid a critical increase in core temperature under exercise conditions. This can occur, however, only at the expense of blood flow, and thus of oxygen supply to the muscles, as otherwise blood pressure could not be maintained.

Thus, if we had the task of designing a "bio-machine" named "man" we would certainly try to optimize skin blood flow to the extent that central body temperature remains as low, and muscle blood flow as large, as possible. The microprocessor unit serving this purpose could be taken as the analog model for the skin-muscle-flow partitioning. Certainly, in such a system non-thermal factors should have a role in controlling SkBF. Does such an elaborate system exist, or is there only an unsystematic or perhaps emergency effect of non-thermal factors on skin blood flow? Let me first

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recapitulate some historical and physiological facts and concepts of thermoregulation which I think are pertinent to the problem at hand.

SkBF—CONTROLLED BY THERMAL INPUTS

The original question pertaining to temperature regulation was: which temperature is being controlled, skin temperature or deep-body temperature? If deep-body temperature, then at what site? Research on cutaneous thermal sensation and the electrophysiological properties of cutaneous thermal receptors [2] has resulted in an inclusion of cutaneous thermal signals in thermoregulatory concepts [3,4]. A number of sites in the body have been shown to contain thermosensitive structures. A model which has the properties of a "multiple-input system" has been developed [5,6,7]. As a consequence, in human physiology, thermoregulatory response was described as a function of both skin and core temperature, whereby weighting factors were assigned to skin and core in the order of 5–20 percent and 80–95 percent, respectively.

"WORK FACTORS"

During the period preceding the multiple-input era, the exercise-induced increase in core temperature was difficult to understand. Did this increase mean that thermoregulation was less effective during exercise than at rest, or that it was overtaxed even with light to moderate exercise? "No," was the answer by Marius Nielsen in 1938 [8]. He suggested that the increase in core temperature was due to an increased set-point of the thermoregulatory system. Furthermore, it was surmised that this increase facilitated, in some way (e.g., optimizing enzyme activity), the performance of physical exercise. Primarily, experimental proof for the assumption of a set-point shift during exercise was seen in the fact that, within limits, the exercise-induced increase in core temperature was independent of ambient temperature [8] (Fig. 1A). It has to be considered, however, that in a multiple-input system the effect of an increased core temperature on thermoregulatory responses may be offset by a reduction of skin temperature during exercise in a cool environment and an increased evaporative heat loss due to sweating. As a consequence, a weighted mean body temperature, $\overline{T}_b$, rather than an isolated core temperature, T_c, would be the controlled variable [10]. In contrast to T_c, $\overline{T}_b$ is not independent of ambient temperature during exercise (compare Figs. 1A and 1B). $\overline{T}_b$ increases with both work load and ambient temperature (T_a), indicating a load error in a proportional control system (Fig. 1B). To speak of an increased set-point during exercise would only be justified if there was a concomitant upward shift of all thermoregulatory effector systems as found, e.g., during the luteal phase of the menstrual cycle (Fig. 2). Such changes have never been demonstrated during exercise, and it has been emphasized by several authors [12,13,14] that the thermoregulatory responses during exercise are exclusively governed (except for a short transient period) by the thermal inputs and not by any extrathermal signals or by what has been called a work factor.

In contrast to the no longer accepted concept of an increased set-point during exercise, some investigators claimed that the threshold for heat dissipation reactions was decreased during exercise, when described as a function of skin and core temperatures. Hammel and Sharp [15] found the threshold for the salivation response in dogs at hypothalamic temperatures several degrees lower during exercise than at rest. Furthermore, Mercer and Jessen [16] demonstrated, in the goat, that the threshold hypothalamic temperature for an increase in respiratory evaporative heat

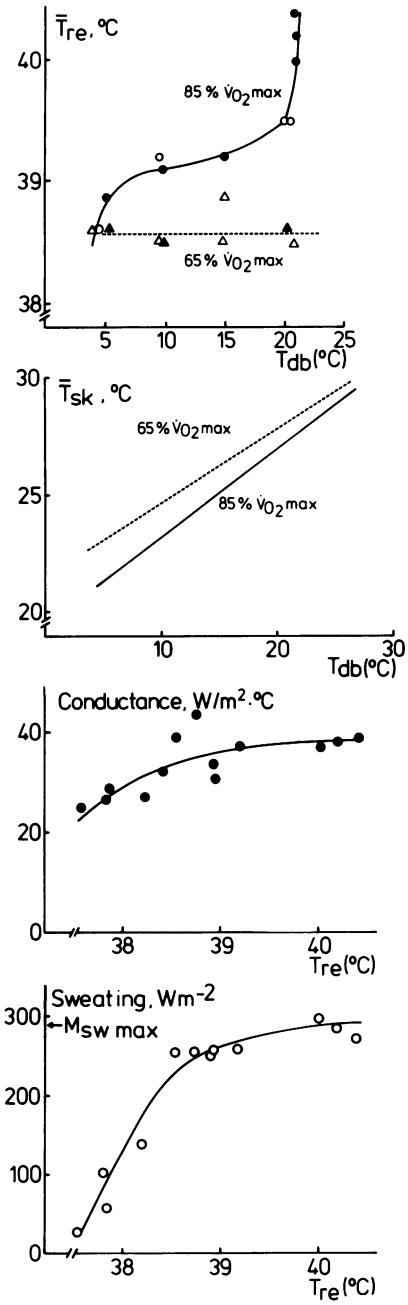
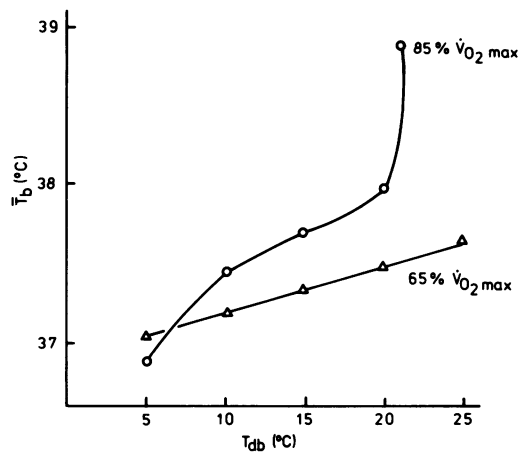


FIG. 1A. Rectal (T_{re}) and mean skin ($\bar{T}_{sk}$) temperatures at the end of one-hour exercise bouts at various ambient temperatures (T_{db}) and at work rates corresponding to 65 percent and 85 percent $\dot{V}_{O_2}$ max. Conductance and sweat rate in relation to T_{re}. After data and graphs from Davies [9].

FIG. 1B. Mean body temperature, $\bar{T}_b$, calculated from the data given in Fig. 1A according to the equation $\bar{T}_b = 0.9 \cdot T_{es} + 0.1 \cdot \bar{T}_{sk}$ in relation to T_{db}. Note that $\bar{T}_b$ is not independent of T_{db}, in contrast to T_{es}; compare with Fig. 1A. Data from Davies [9].



loss (REHL) decreased by 1.2°C during exercise. However, when REHL was related to body core temperature, which was manipulated by an intravascular heat exchanger, there was no longer such threshold difference between rest and exercise. Additional experiments by Jessen et al. [17] showed that muscle temperature plays a role in the control of body temperature. Moreover, Robinson et al. [18] previously showed that muscle temperature in man is very quickly raised in exercising muscles. The previously

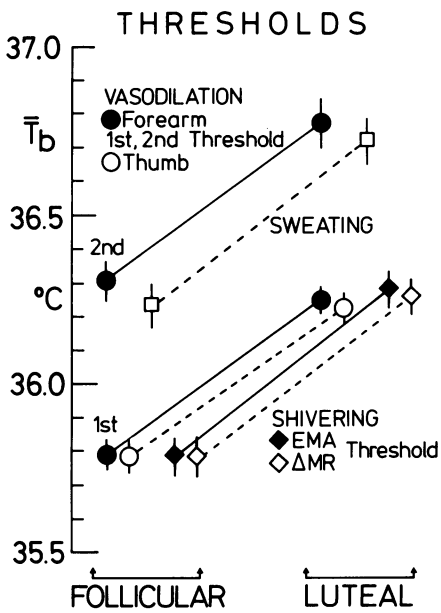


FIG. 2. Shift of threshold temperatures for all autonomous thermoregulatory effectors during the menstrual cycle. Ordinate represents mean body temperature calculated from esophageal and mean skin temperature ($\bar{T}_b = 0.87 \cdot T_{es} + 0.13 \cdot \bar{T}_{sk}$). Shivering determined by electrical muscle activity (**EMA**) and metabolic increment (**ΔMR**). Vasodilation determined by heat conductivity measurements. At the forearm, a two-step increase in skin blood flow was observed. From Hessemer and Brück [11].

described offset of the heat-dissipation control elements to a lower temperature level may thus be explained on the basis of a multiple-input system, including muscle and other temperatures as additional determinants. No non-thermal factor would then have to be postulated in regard to sweating threshold. The exercise-induced inhibition of the shivering response demonstrated during exercise in the cold [19] may be explained by the same reasoning.

NON-THERMAL FACTORS AND CONTROL OF SKIN BLOOD FLOW

In the control of SkBF, non-thermal influences cannot so easily be denied as in the case of sweat rate. The concept of non-thermal factors influencing exercise skin blood flow was first derived by Rowell [1]. From calculated skin blood flow data, he inferred that there was a graded reduction of skin and splanchnic blood flow with increasing work load in a hot environment. Moreover, using venous occlusion plethysmography, Johnson et al. [20] showed a lower forearm blood flow, at any given core temperature, during exercise in an upright position when compared to a supine resting position. It should be mentioned that $\bar{T}_{sk}$ was 38°C in these studies. Recently, Hirata et al., [21], demonstrated a graded shift of the finger blood flow: T_{es} relationship with work loads increasing from 20 to 45 percent of V_{O_2} max (Fig. 3), whereas no such graded effect was seen by Wenger et al. [22]. $\bar{T}_{sk}$ was only 33°C in the study by Hirata et al. [21]; thus a $\bar{T}_{sk}$ of 38°C cannot be a prerequisite for the extrathermal vasoconstrictor reaction as it may appear from some comparative examinations presented by Brengelmann [23].

The examples shown were all from studies with submaximum exercise. But there is indirect evidence for an extrathermal influence on skin blood flow with heavy exercise. A "dramatic fall" in heat conductance was observed in the terminal phase of exercise after rectal temperature had reached a plateau of about 39°C (in two subjects from 60 to 52 and 59 to 49 $W/m^2 \cdot °C$, respectively) [24]. As a consequence, a further increase of core temperature occurred. Thus, some extrathermal factor must have acted on the

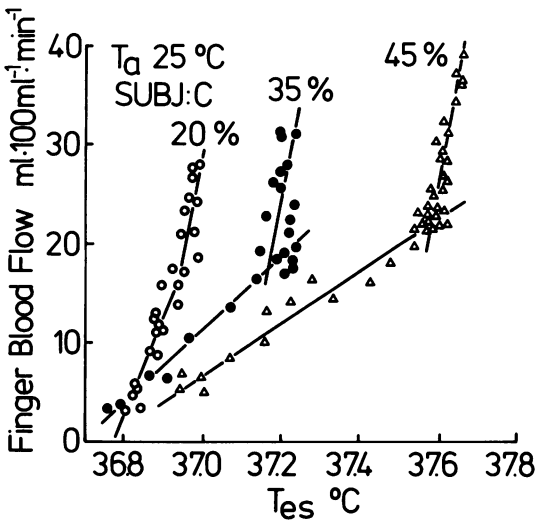


FIG. 3. Effect of exercise intensity from 20 to 45 percent $\dot{V}_{O_2}$ max on the relationship between finger blood flow and esophageal temperature at ambient temperature of 25°C; mean skin temperature 33°C. From Hirata et al. [21].

control of skin blood flow, resulting in a continuation of work at the expense of a further elevation of body temperature. Adams et al. [24] spoke of a "spiraling increase of body temperature" before cessation of exercise.

Similar results were obtained by Davies [9]. With heavy exercise (85 percent of $\dot{V}_{O_2}$ max), core temperature increases steeply at moderate ambient temperatures, reaching values of above 40°C (Fig. 1A). In contrast to Adams et al.'s study [24] there is no clear-cut reduction in conductance (Fig. 1A), but the figures of about 40 $W/m^2 \cdot °C$ may indicate that there was no full vasodilation at this high body temperature. Davies states "that at high metabolic rates the intense sympathetic outflow can override thermal stimuli" [9]. Under these conditions, the organism no longer behaves like a thermostatic system. Any additional heat load, imposed either by external or internal heat sources, can then only be compensated for by a further increase of the core-surface temperature gradient at the expense of an increase of core temperature. This may be an example of blood pressure control having preference over temperature regulation. Maintaining exercise under such conditions is certainly very stressful. Such a situation cannot be tolerated by everyone, but it is a prerequisite for the extreme exercise performance of highly trained subjects. It requires strong motivation and a special emotional state.

In view of those results, it is difficult to reject the conclusion that there is, under certain circumstances at least, an exercise-induced vasoconstrictory impulse affecting the skin blood flow:T_c relationship. This would influence the complex relationship between T_a and body core temperature (Fig. 1A, topmost chart). The quantitative importance of such an exercise-induced offset of vasodilation remains to be studied.

In a study by McDougall et al. [25] exercise was terminated when body temperature had reached a definable level (Fig. 4). The subjects worked at a prescribed work rate of about 70 percent of $\dot{V}_{O_2}$ max at three thermal conditions. In all three situations they gave up exercising as soon as tympanic and rectal temperatures had reached values of 38 and 39°C, respectively. At this time, stroke volume and cardiac output decreased markedly, presumably due to increased peripheral blood pooling [1]. There is no ready answer to the question of why in one situation sharply defined tympanic and rectal

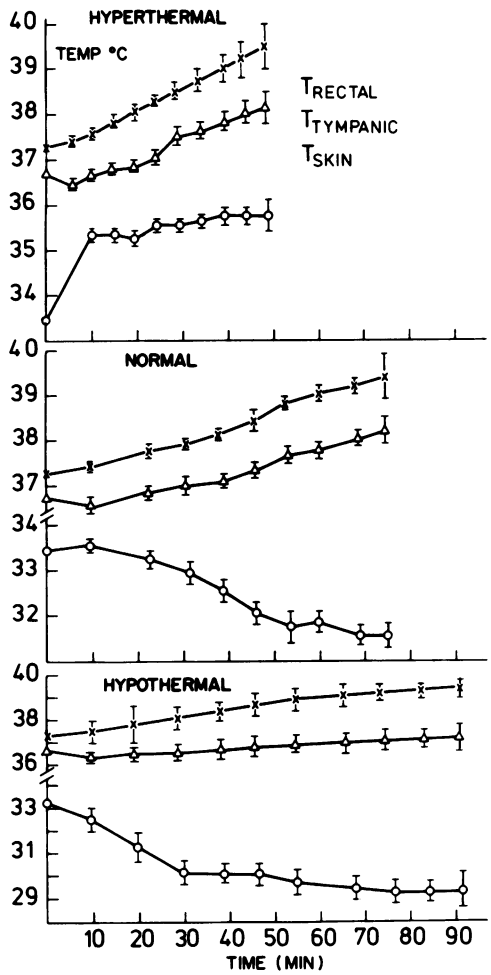


FIG. 4. Course of rectal, tympanic, and mean skin temperature at an ambient temperature of 23°C (NORMAL) and under hyperthermic and hypothermic conditions achieved by use of a water-perfused suit. Treadmill speed was adjusted to demand 70 percent $\dot{V}_{O_2}$ max. For further explanation, see text. From McDougall et al. [25].

temperatures, 38 and 39°C, limit exercise, whereas in another situation almost hyperpyretic body core temperatures caused by skin vasoconstriction may be tolerated. This problem is even more puzzling if one includes some recent studies [26,27,28] in which we demonstrated that a slight decrease of body temperature below the normal level may improve submaximum exercise performance (see below).

WHY ARE THERE CONFLICTING RESULTS IN REGARD TO THE EXERCISE-INDUCED OFFSET OF THE SkBF RESPONSE-TEMPERATURE RELATIONSHIP?

Conflicting results with regard to the exercise-induced offset of the SkBF response-temperature relationship have been traced to the problem of extrapolation of conclusions drawn from results obtained in restricted ranges of skin temperature and work loads [23]. Furthermore, there is a lack of direct blood flow measurements during heavy exercise due to technical difficulties with plethysmography.

Another reason for conflicting results may be the difficulty of quantitatively reproducing a temperature-effector response relationship due to what has been called

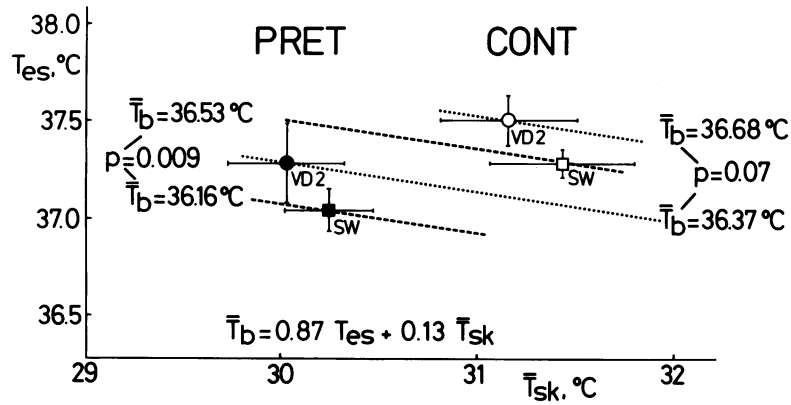


FIG. 5. Threshold temperatures for sweating (**SW**) and vasodilation at the forearm (**VD 2**) measured during exercise of 80 percent $\dot{V}_{O_2}$ max. Average data from seven subjects, each examined after a stay at neutral temperature (**CONT**) and after precooling (**PRET**). Given are means and SE. Mean body temperature ($\bar{T}_{b(es)}$) calculated from esophageal temperature (T_{es}) and mean skin temperature ($\bar{T}_{sk}$) according to $\bar{T}_b = 0.87 \cdot T_{es} + 0.13 \cdot \bar{T}_{sk}$. Data from Olschewski and Brück [28].

"short-term adaptation" [29]. We became aware of this phenomenon when we studied the effects of slightly below-normal body temperatures on exercise performance. The precooling maneuver consisted of two consecutive cold exposures with a short intermittent warming period. In those studies we regularly found the shivering threshold to be shifted to a lower temperature at the second cooling period. Such studies were extended [28] to evaluate sweating and SkBF. In these experiments, the volunteers were subjected twice to an incremental cycle ergometer test at T_a = 18°C. One of the tests was preceded by a precooling maneuver. As shown in Fig. 5, the onset of the increase in heat conductivity of the skin (as a measure of skin blood flow) as well as of chest sweat rate was shifted to lower skin core, and mean body temperatures after precooling. The endurance time for heavy exercise (80 percent $\dot{V}_{O_2}$ max) was increased after precooling from 18.5 to 20.8 minutes [28]. This result documents the "beneficial" effect of a lowered body temperature on exercise performance. It is in contrast to the belief that exercise performance is improved by increased body temperature which was put forward together with Marius Nielsen's set-point concept [8].

Similar short-term threshold deviations were found in the guinea pig [29], and could be related to short-term alterations [30] in the characteristics of neuronal units in the subcoeruleus area (SC) of the lower brain stem (Fig. 6), which is known to control thermoregulatory reactions [29,31,32]. Thus, there is a high degree of neuronal plasticity which accounts for variations in thermoregulatory reactions. In order to avoid such short-term adaptation interference with the investigation of skin blood flow modifications during exercise, we may have to compare only those studies which were separated by sufficiently long intervening time periods, as has been suggested by Brengelmann [23].

Moreover, it has been shown that electrical stimulation of the NRM, even after severing the ascending pathway (Fig. 6), inhibits shivering [33]. The threshold for the skin vasomotor response was shifted to a lower level after destruction of the NRM [34]. This fact suggests that the serotonergic NRM efferents descend to the dorsal

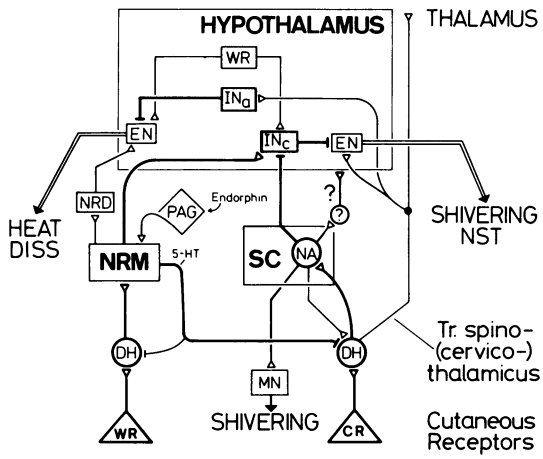


FIG. 6. Schematic representation of the afferent projections and neuronal connectivities between lower brain stem areas and the thermointegrative hypothalamic area. **NRM,** nucleus raphé magnus; **SC,** subcoeruleus area; **NRD,** nucleus raphé dorsalis; **WR,** warm receptors; **CR,** cold receptors; **DH,** dorsal horn; **MN,** motoneurons in lower brain stem and spinal cord. **IN_a** and **IN_c,** interneurons type a and c according to [31]; **PAG,** central grey; **EN,** effector neurons; **NST,** non-shivering thermogenesis. ⟶ , excitatory connection ⊣ , inhibitory connection; **NA,** noradrenalin; **5-HT,** serotonin. For further explanation, see text. Modified after [29] and supplemented by data from [32,33,34].

horn, inhibiting thermal afferents from the trunk skin (Fig. 6), although cold afferents in the caudal trigeminal nucleus could not be inhibited by NRM stimulation [35]. The descending control of thermal input signals may be the neurophysiological correlate for the effects of motivational, emotional, and other behavioral circumstances which appear to influence the interaction of thermal and non-thermal inputs.

In sum, there are a number of results suggesting an extrathermal control of skin blood flow. Inconsistencies may be encountered in the analysis of the responses of SkBF due to technical difficulties in the recording of such parameters during heavy exercise and to ignorance of the fact that, in a multiple-input system, temperatures at various body sites may influence SkBF. Moreover, short-term adaptation and emotional and motivational factors may modify the skin blood flow responses, thus producing a very complex picture which may be difficult to disentangle.

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