Influence of body temperature on the development of fatigue during prolonged exercise in the heat

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González-Alonso, José, Christina Teller, Signe L. Andersen, Frank B. Jensen, Tino Hyldig, and Bodil Nielsen. Influence of body temperature on the development of fatigue during prolonged exercise in the heat. *J. Appl. Physiol.* 86(3): 1032–1039, 1999.—We investigated whether fatigue during prolonged exercise in uncompensable hot environments occurred at the same critical level of hyperthermia when the initial value and the rate of increase in body temperature are altered. To examine the effect of initial body temperature [esophageal temperature (T_{es}) = 35.9 ± 0.2, 37.4 ± 0.1, or 38.2 ± 0.1 (SE) °C induced by 30 min of water immersion], seven cyclists (maximal O_2 uptake = 5.1 ± 0.1 l/min) performed three randomly assigned bouts of cycle ergometer exercise (60% maximal O_2 uptake) in the heat (40°C) until volitional exhaustion. To determine the influence of rate of heat storage (0.10 vs. 0.05°C/min induced by a water-perfused jacket), four cyclists performed two additional exercise bouts, starting with T_{es} of 37.0°C. Despite different initial temperatures, all subjects fatigued at an identical level of hyperthermia (T_{es} = 40.1–40.2°C, muscle temperature = 40.7–40.9°C, skin temperature = 37.0–37.2°C) and cardiovascular strain (heart rate = 196–198 beats/min, cardiac output = 19.9–20.8 l/min). Time to exhaustion was inversely related to the initial body temperature: 63 ± 3, 46 ± 3, and 28 ± 2 min with initial T_{es} of ~36, 37, and 38°C, respectively (all $P <$ 0.05). Similarly, with different rates of heat storage, all subjects reached exhaustion at similar T_{es} and muscle temperature (40.1–40.3 and 40.7–40.9°C, respectively), but with significantly different skin temperature (38.4 ± 0.4 vs. 35.6 ± 0.2°C during high vs. low rate of heat storage, respectively, $P <$ 0.05). Time to exhaustion was significantly shorter at the high than at the lower rate of heat storage (31 ± 4 vs. 56 ± 11 min, respectively, $P <$ 0.05). Increases in heart rate and reductions in stroke volume paralleled the rise in core temperature (36–40°C), with skin blood flow plateauing at T_{es} of ~38°C. These results demonstrate that high internal body temperature per se causes fatigue in trained subjects during prolonged exercise in uncompensable hot environments. Furthermore, time to exhaustion in hot environments is inversely related to the initial temperature and directly related to the rate of heat storage.

hyperthermia; skin blood flow; heart rate; stroke volume

IT IS WELL DOCUMENTED that endurance can be impaired in hot compared with temperate climates (10, 12, 28) and that time to exhaustion is influenced by alterations of the initial body temperature (1, 22, 32, 39). The attainment of a critically high level of body temperature has been proposed as the main factor limiting endurance performance in hot environments (7, 28). The observation that trained subjects working at 60% of peak O_2 uptake ($\dot{V}O_{2\,peak}$) in the heat [40°C, 10% relative humidity (RH)] for 9–12 consecutive days improved exercise performance from 48 to 80 min but fatigued at a core temperature of 39.7°C appears to support this notion (28). This large improvement in exercise time to fatigue, however, was drastically reduced to 7 min when subjects exercised in a humid hot environment, yet fatigue still coincided with a core temperature of ~40°C (30). In the same light, Mac-Dougal et al. (24) previously showed that subjects always became exhausted at a rectal temperature of 39.4°C, even though the rate of rise had been varied markedly with a water-perfused suit. More recently, Fuller et al. (11) found that rats exercising in a hot environment fatigued at the same abdominal and brain temperature (~40°C) after preexercise body temperature was altered.

In opposition to the hypothesis of a critically high body temperature, there are reports indicating that some untrained subjects fatigue during light exercise in uncompensable environments with body temperatures of ~38°C (23, 26, 38). In untrained subjects, core temperature at exhaustion from heat strain has been clearly shown to occur over a range of 38–40°C (23, 26, 38) and to be independent of exercise intensity (26). It has also been shown that, regardless of hydration or acclimation status, subjects with high aerobic fitness perform longer in uncompensable hot environments and tolerate higher levels of hyperthermia than do subjects with lower aerobic fitness levels (7). Therefore, it appears that high body temperature might be the main factor leading to fatigue in the heat in trained and in some, but not all, untrained subjects.

Although previous human studies have emphasized the importance of core temperature, little is known about exercising muscle temperature at exhaustion. High muscle temperature might induce structural and functional alterations in proteins involved in *1*) electrolyte distributions across the sarcolemma, *2*) calcium release and reuptake by the sarcoplasmic reticulum, *3*) actin-myosin interactions, and *4*) mitochondrial respiration, which might potentially contribute to fatigue (19). However, no previous study has systematically manipulated the initial value and the rate of rise of body temperature to determine whether fatigue in hot environments is related to critically high core and/or muscle temperatures.

It is also well established that heat stress reduces stroke volume (SV) and increases heart rate during

moderately intense exercise to the extent to which cardiac output might be compromised (35). In a classic study, Rowell et al. (35) showed a significantly lower cardiac output (~1.0 l/min), central blood volume, and SV during exercise in a 43°C than in a 26°C environment at 63–73% $\dot{V}O_{2peak}$. This reduced cardiac output was due to the larger reductions in SV compared with the parallel increases in heart rate. In a follow-up study, Rowell et al. (36) found that alterations in central blood volume, central venous pressure, SV, and heart rate with heat stress could be restored by perfusing a suit in contact with skin with cold water. In these previous studies, however, skin blood flow was not measured. Thus the contribution of higher skin perfusion to SV reductions in conditions of widely different body temperature remains unknown.

Therefore, the main aim of this study was to investigate whether fatigue in trained athletes occurred at the same critical level of core and muscle temperature, despite differences in starting internal temperature and its rate of rise. A secondary aim was to determine the effect of increased body temperature on heart rate, SV, and skin blood flow under conditions of rather different initial body temperatures. We hypothesized that a similar critical level of internal body temperature would cause fatigue in trained athletes in uncompensable hot environments. Furthermore, we hypothesized that reductions in SV with heat stress are also influenced by factors other than elevations in skin blood flow. This hypothesis is based on previous observations showing that SV declines significantly with core hyperthermia alone and combined hyperthermia and hypovolemia when skin blood flow plateaus or declines during prolonged exercise in the heat (13, 15, 16, 25).

METHODS

General Design

To accomplish these purposes, two different studies were performed. To identify the effect of different initial body temperature, one study was performed in the heat after core temperature had been manipulated to three different levels (~36, 37, and 38°C) by having subjects rest in a water tank for 30 min. Another study examined the influence of the rate of increase in body temperature (0.05 vs. 0.10°C/min) on heat exhaustion during prolonged exercise by having subjects wear a water-perfused jacket.

Subjects

Age, body weight, height, maximal heart rate, and maximal O_2 uptake ($\dot{V}O_{2max}$) of the seven healthy endurance-trained men participating in these studies were 28 ± 3 yr, 77.9 ± 6.4 kg, 187 ± 6 cm, 200 ± 9 beats/min, and 5.13 ± 0.30 l/min, respectively. The subjects were fully informed of any risks and discomforts associated with the experiments before giving their informed consent to participate. The studies were approved by the Ethics Committee of Copenhagen and Frederiksberg communities. Before performing the experimental trials, subjects were familiarized with the experimental setup by cycling in a thermoneutral environment (20°C) for ≥90 min. Most of the subjects had participated in experiments involving endurance performance in hot environments before undergoing these experiments.

Experimental Design

In the study of the initial body temperature, subjects performed three bouts of cycle ergometer exercise (model 829 E, Monark; 228 ± 6 W, 88 ± 1 rpm, 60% $\dot{V}O_{2max}$) in an uncompensable hot environment (40°C, 19% RH; E_{req}/E_{max} ~1.2, where E_{req} is evaporation required for heat balance and E_{max} is maximal evaporation capacity) until volitional exhaustion. The following criteria were used to define volitional fatigue in the present studies: 1) near or maximal values of perceived exertion, 2) near or maximal heart rate, and 3) inability to maintain a cadence of ~50 rpm. Trials were randomly assigned and counterbalanced across subjects. Before exercise, resting body temperatures were manipulated by immersing subjects in water at 17, 36, and 40°C for 30 min. The conditions were as follows: 1) precooling (C) to an esophageal temperature (T_{es}) of 35.9 ± 0.2°C, a muscle temperature (T_m) of 34.3 ± 0.3°C, and an average skin temperature ($\overline{T}_{sk}$) of 29.5 ± 0.3°C, 2) control (Con) with T_{es} of 37.4 ± 0.1°C, T_m of 37.3 ± 0.1°C, and $\overline{T}_{sk}$ of 34.2 ± 0.1°C, and 3) preheating (H) to T_{es} of 38.2 ± 0.1°C, T_m of 38.4 ± 0.1°C, and $\overline{T}_{sk}$ of 35.9 ± 0.1°C (Figs. 1 and 2).

On the day before the experimental testing, the subjects adopted the same diet, exercise bout (i.e., <1 h of low-intensity cycling), and fluid intake to standardize the hydration status. The subjects reported to the laboratory ~1 h before the experiment, after ingestion of a light breakfast and 200–300 ml of fluid. On arrival, nude body weight was recorded. Thereafter, the esophageal probe was inserted through the nasal passage, and the instruments used to measure forearm blood flow, skin blood flow, and skin temperature were attached to the skin. Thereafter, baseline values of skin blood flow were obtained while subjects sat for 5–10 min in a standardized position in the heat. The subjects then rested for 30 min while immersed in a water tank. Thereafter, subjects toweled dry and walked to the climatic chamber. The transition period from the time the subjects emerged from the water tank to the start of exercise was 8–12 min, with the shortest time occurring during the preheating trial. T_m was measured immediately before and after exercise.

During exercise, heart rate, T_{es}, $\overline{T}_{sk}$, and skin blood flow were recorded continuously. O_2 uptake ($\dot{V}O_2$), cardiac output (CO_2 rebreathing), and forearm blood flow were measured during a 10-min period starting at 3 min of exercise and before exhaustion (when T_{es} was ~39.5°C). Forearm blood flow was also measured during the 20- to 25-min period of C and Con. Blood samples by finger prick were also obtained before and immediately after exercise for later analysis of blood glucose and lactate. Nude body weight was recorded immediately after sweat was wiped off. A rating of perceived exertion (RPE) was obtained at 10 min and at exhaustion (2). Subjects received similar encouragement during each of the trials.

The same control of previous exercise, nutrition, and hydration status was applied in the study of the rate of heat storage. On the subjects' arrival at the laboratory, their nude body weight was recorded. Skin and esophageal thermocouples were then attached to the skin or inserted through the nasal passage, respectively. Thereafter, subjects rested for 30 min in the supine position to ensure a similar initial body temperature before exercise.

In this follow-up study, subjects performed two randomly assigned bouts of cycle ergometer exercise (258 ± 20 W, 87 ± 2 rpm, 66 ± 3% $\dot{V}O_{2max}$) in the heat (41°C, 17% RH) until volitional fatigue. During exercise the rate of heat storage
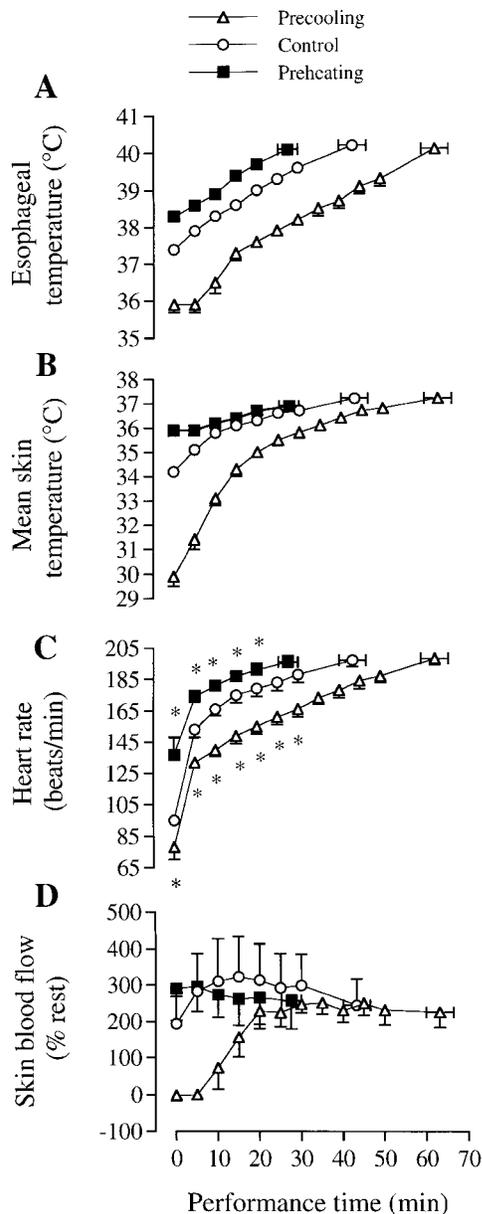
Fig. 1. Esophageal temperature (*A*), mean skin temperature (*B*), heart rate (*C*), and skin blood flow (*D*) during exercise in heat (40°C, 17% relative humidity) during precooling, control, and preheating trials. Skin blood flow is referenced to resting baseline values obtained on arrival at the laboratory (0.2–1.2 V; $n = 4$). Values are means $\pm$ SE for 7 subjects. *Significantly different from control, $P < 0.05$.

was manipulated by changing the water temperature perfusing the jacket in contact with the skin of the trunk and forearms (42 vs. 19°C, i.e., high vs. low rate of heat storage). However, in this study the initial T_{es} and T_m were similar in both trials: 36.9–37.1 $\pm$ 0.1 and 36.3–36.5 $\pm$ 0.2°C, respectively. During exercise, heart rate was recorded continuously. An RPE was obtained at 10 min and at exhaustion.

$\dot{V}o_2$ and Cardiac Output

Pulmonary $\dot{V}o_2$ was measured on-line with a metabolic cart (model CPX/D, Medgraphics, St. Paul, MN). Cardiac output was measured in triplicate using the CPX/D computerized version of the CO_2-rebreathing technique of Collier (8) and corrected for differences between end-tidal and arterial P_{CO_2}

(21). Under similar exercise conditions, we previously observed a tight temporal correlation between end-tidal and arterial P_{CO_2} as well as between the estimated mixed venous P_{CO_2} and femoral venous P_{CO_2} ($r = 0.85$–0.91, $P = 0.0001$) (13). Heart rate was recorded with a PE 3000 Sport Tester (Polar Electro).

Forearm Blood Flow and Skin Blood Flow

Forearm blood flow was measured using venous occlusion plethysmography with a mercury-in-Silastic strain gauge (40), while the wrist of the left forearm rested in a sling. The hand was elevated ~15 cm above the heart level, and the forearm was tilted 40° from the horizontal axis. Forearm blood flow values represent the average of 8–10 single measurements. Skin blood flow was measured using a laser-Doppler flowmeter (model PF2B, Perimed, Stockolm, Swe-

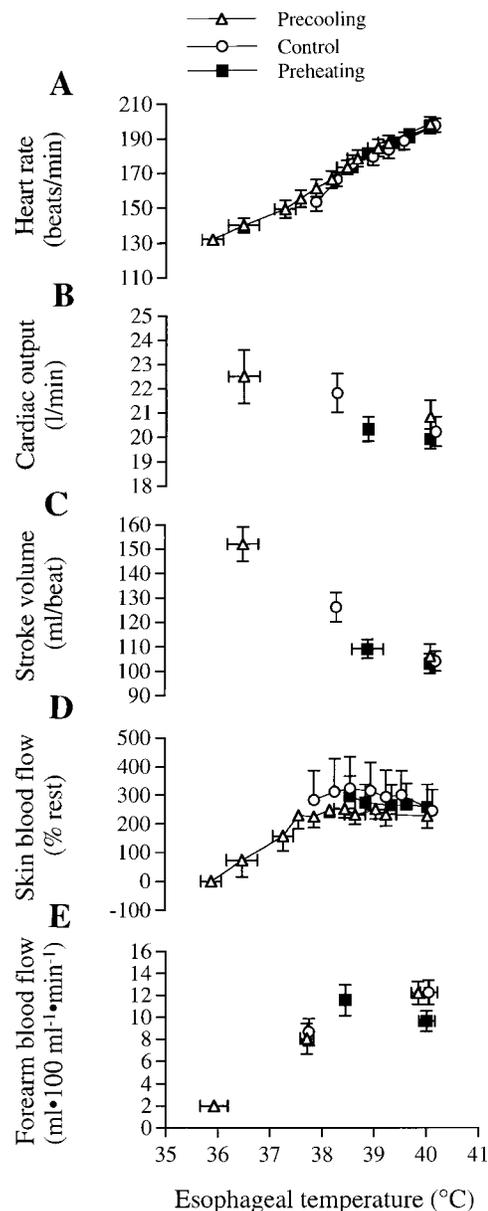
Fig. 2. Heart rate (*A*), cardiac output (*B*), stroke volume (*C*), skin blood flow (*D*), and forearm blood flow (*E*) plotted against core temperature during precooling, control, and preheating trials. Values are means $\pm$ SE for 6 subjects.

den). The laser-Doppler probe was placed on the left forearm on the dorsal side, separated ~2 cm from the plethysmographic strain gauge. Skin blood flow and forearm blood flow were recorded at 100 Hz with use of a MacLab/8s (AD Instruments) data-acquisition system.

Core, Skin, and Muscle Temperature

T_{es} was measured with a thermocouple (model MOV-A, Ellab) inserted through the nasal passage a distance equal to one-fourth of the subject's standing height. $\overline{T}_{sk}$ was calculated from the skin temperatures (model A-H3, Ellab) measured at six sites (i.e., upper arm, forearm, chest, back, thigh, and calf) by using the weighting method of Hardy and DuBois (18). The esophageal and skin thermocouples were connected to a recorder (CTF 90008 precision thermometer, Ellab) interfaced to an IBM-AT computer. T_m was measured in the vastus lateralis with a needle probe (model MKA-A, Ellab) inserted 3 cm into the muscle.

Percent Dehydration

Percent dehydration was estimated from the differences in body weight after exercise compared with the preexercise body weight, with correction for body weight loss due to the exchange of O_2 and CO_2 (33). Nude body weight was determined on a platform scale (model 1-10, Ohaus) with an accuracy of ± 20 g.

Statistical Analysis

A two-way (trial-by-time) repeated-measure ANOVA was performed to test significance between and within treatments. After a significant F test, pairwise differences were identified using Tukey's honestly significant difference post hoc procedure. When appropriate, significant differences were also identified using Student's paired t-tests. The significance level was set at $P < 0.05$. Values are means $\pm$ SE unless otherwise indicated.

RESULTS

Influence of Different Initial Body Temperatures

Body temperatures and performance time. Despite different initial temperatures, all subjects fatigued at an identical level of hyperthermia: T_{es} of 40.1 $\pm$ 0.1, 40.2 $\pm$ 0.1, and 40.1 $\pm$ 0.1°C, T_m of 40.7 $\pm$ 0.1, 40.8 $\pm$ 0.1, and 40.9 $\pm$ 0.1°C, and $\overline{T}_{sk}$ of 37.2 $\pm$ 0.2, 37.2 $\pm$ 0.1, and 37.0 $\pm$ 0.1°C during C, Con, and H, respectively (Fig. 1, Table 1). In three trials the between-subjects

difference in T_{es} at exhaustion was 0.1–0.5°C (Table 1). The rate of heat storage during exercise was the same in the three conditions. Therefore, time to exhaustion was inversely related to starting body temperatures: 63 $\pm$ 3, 46 $\pm$ 3, and 28 $\pm$ 2 min in C, Con, and H, respectively (all $P < 0.05$).

Hydration status. Hydration was similar before exercise, as indicated by similar body weights: 76.6 $\pm$ 6.6, 77.1 $\pm$ 5.8, and 76.4 $\pm$ 6.1 (SD) kg before C, Con, and H, respectively [not significant (NS)]. Furthermore, similar body weight losses occurred from the start of water immersion to the end of exercise: 2.0 $\pm$ 0.3, 1.9 $\pm$ 0.3, and 2.1 $\pm$ 0.2 kg during C, Con, and H, respectively (P = NS). Therefore, the level of dehydration at exhaustion was also similar in each trial: 2.6 $\pm$ 0.4, 2.4 $\pm$ 0.3, and 2.8 $\pm$ 0.3% body wt loss during C, Con, and H, respectively (P = NS).

Cardiovascular responses. After 10 min of exercise, $\dot{V}o_2$ was similar during all conditions (range 3.05 $\pm$ 0.05 to 3.11 $\pm$ 0.13 l/min), despite the 2.4°C difference in T_{es} between C and H. Thereafter, $\dot{V}o_2$ tended to increase over time. In contrast, cardiac output, SV, and heart rate were graded in proportion to the magnitude of hyperthermia. Cardiac output was 22.5 $\pm$ 1.1, 21.8 $\pm$ 0.8, and 20.3 $\pm$ 0.5 l/min, SV was 152 $\pm$ 7, 126 $\pm$ 6, and 109 $\pm$ 4 ml/beat (all $P < 0.05$), and heart rate was 140 $\pm$ 5, 166 $\pm$ 5, and 182 $\pm$ 4 beats/min (all $P < 0.05$) with T_{es} of 36.5, 38.3, and 38.9°C for C, Con, and H, respectively (Fig. 2). Cardiac output was significantly ($P < 0.05$) lower during H than during C (2.2 $\pm$ 0.9 l/min), yet the differences between these two trials and Con (0.7 $\pm$ 0.5 and 1.2 $\pm$ 0.8 l/min) did not reach statistical significance. Concurrently, arterial mixed-venous O_2 difference was 13.9 $\pm$ 0.05, 14.0 $\pm$ 0.04, and 15.2 $\pm$ 0.07 ml/100 ml during C, Con, and H, respectively. However, these large differences in cardiovascular response at 10 min of exercise were markedly reduced at exhaustion (Fig. 2). At exhaustion in C, Con, and H, cardiac output was 20.8 $\pm$ 0.7, 20.2 $\pm$ 0.6, and 19.9 $\pm$ 0.4 l/min; SV was 106 $\pm$ 5, 104 $\pm$ 4, and 103 $\pm$ 4 ml/beat; heart rate was 198 $\pm$ 4, 197 $\pm$ 4, and 196 $\pm$ 4 beats/min; and arterial mixed-venous O_2 difference was 15.1 $\pm$ 0.3, 15.3 $\pm$ 0.6, and 15.8 $\pm$ 0.6 ml/100 ml, respectively (all P = NS). Heart rate at point of fatigue was 98–99% of maximal heart rate.

Table 1. *Individual variability and reproducibility of T_{es}, T_m, and $\overline{T}_{sk}$ at exhaustion in the study of different initial body temperatures*

| Subject | T_{es} | | | T_m | | | $\overline{T}_{sk}$ | | |
	Precooling	Control	Preheating	Precooling	Control	Preheating	Precooling	Control	Preheating
LH	40.3	40.2	39.9	40.4	40.6	40.4	37.3	37.0	36.9
HH	40.0	40.2	40.2	40.2	40.9	41.2	37.3	37.5	37.0
TJ	39.7	40.2	40.3	40.9	41.2	41.2	37.5	37.0	37.1
PM	39.9	40.1	39.9	40.6	40.7	40.5	37.0	37.5	36.9
CJ	40.3	40.3	40.2	41.2	40.7	40.8	37.2	36.6	36.7
JT	40.0	40.4	40.3	40.8	41.0	41.0	36.4	37.4	37.2
HF	40.3	40.2	40.2	40.7	40.8	41.0	37.6	37.3	37.0
Mean $\pm$ SE	40.1 $\pm$ 0.1	40.2 $\pm$ 0.1	40.1 $\pm$ 0.1	40.7 $\pm$ 0.1	40.8 $\pm$ 0.1	40.9 $\pm$ 0.1	37.2 $\pm$ 0.2	37.2 $\pm$ 0.1	37.0 $\pm$ 0.1

T_{es}, esophageal temperature; T_m, vastus lateralis muscle temperature; $\overline{T}_{sk}$, mean skin temperature.

Forearm and skin blood flow. During the first 3–8 min of exercise, forearm blood flow was significantly lower during C than during Con and H: 2.0 ± 0.2 vs. 8.6 ± 1.0 and 11.5 ± 1.4 ml·100 ml^{-1}·min^{-1}, respectively ($P < 0.05$; Fig. 2). At exhaustion, forearm blood flow was lower during H than during Con and C: 9.6 ± 1.0 vs. 12.1–12.2 ± 1.2 ml·100 ml^{-1}·min^{-1}, respectively ($P < 0.05$).

Baseline resting skin blood flow values (before water immersion) were 0.2–1.2 V. During exercise, skin blood flow in Con increased somewhat during the first 10 min and reached a plateau thereafter (Fig. 1). During H, skin blood flow was at plateau levels from the initial minute of exercise. In contrast, skin blood flow during C increased gradually after the first 4 min of exercise and reached a plateau level after 20 min of exercise (Fig. 1). In all trials, skin blood flow reached a plateau level after T_{es} had increased above ~38°C (Fig. 2).

Blood lactate and blood glucose. At exhaustion, neither blood lactate nor blood glucose was different between trials. Blood lactate ranged from 1.6 ± 0.1 to 2.2 ± 0.2 mM, whereas blood glucose was maintained at euglycemic levels in all conditions: 6.3 ± 0.1 to 6.7 ± 0.4 mM.

RPE. At 10 min, RPE was significantly lower during C than during H: 10.6 ± 0.9 vs. 13.7 ± 0.7 units, respectively ($P < 0.05$). RPE increased significantly over time in all trials. However, RPE at exhaustion was equally high in all trials: 18.5 ± 0.2 to 18.6 ± 0.3 units ($P = $ NS).

Influence of Different Rates of Heat Storage

Body temperatures and performance time. With different rate of heat storage, all subjects reached exhaustion at similar T_{es} and T_m (40.3 ± 0.3 vs. 40.1 ± 0.3°C for T_{es} and 40.9 ± 0.3 vs. 40.7 ± 0.3°C for T_m during high vs. lower rate of heat storage, respectively), but with significantly ($P < 0.05$) different $\overline{T}_{sk}$ (38.4 ± 0.4 vs. 35.6 ± 0.2°C for T_{sk} during high vs. lower rate of heat storage, respectively; Fig. 3, Table 2). Reflecting the experimental manipulation, this ~3°C difference in $\overline{T}_{sk}$ was attributable only to the effect of the water-perfused jacket on skin from the trunk and forearms. In both trials the difference in T_{es} at exhaustion in each of the subjects ranged from 0.0 to 0.3°C (Table 2). Time to exhaustion was significantly shorter during the high than during the lower rate of heat storage: 31 ± 4 vs. 56 ± 11 min, respectively ($P < 0.05$). The large SE during the lower rate of heat storage trial was due to differences in relative intensity between subjects. The two subjects who exercised at 71% $\dot{V}_{O_{2\,max}}$ improved time to exhaustion by 8 and 9 min, whereas the two subjects who worked at 61% $\dot{V}_{O_{2\,max}}$ improved much more (34 and 48 min). Heart rate response paralleled the rise in core temperature, being significantly higher during the high heat storage trial, except at exhaustion, when between-trial differences were not significant: 187 ± 7 to 189 ± 7 beats/min or 95–96% of maximal heart rate (Fig. 3C).

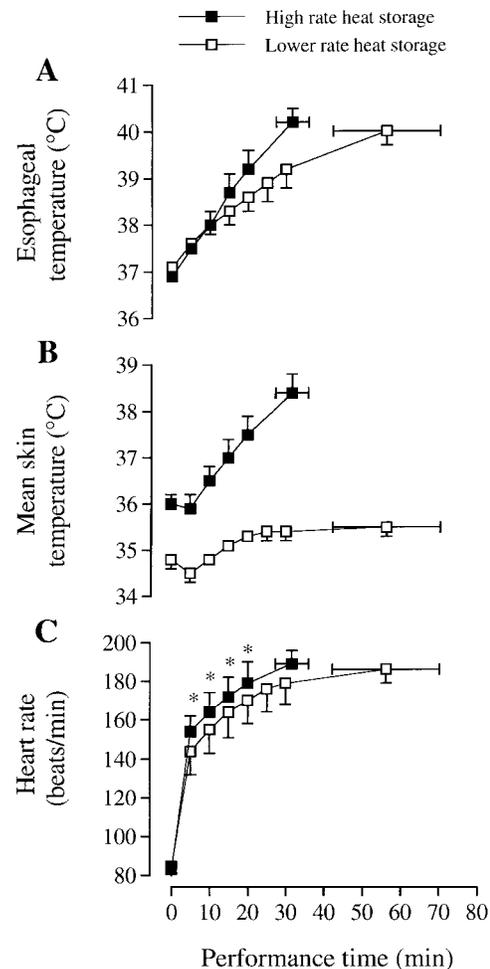*Hydration status.* Hydration was similar before exercise, as indicated by similar body weights: 78.3 ± 4.8

Fig. 3. Esophageal temperature (*A*), mean skin temperature (*B*), and heart rate (*C*) during exercise in heat (40°C, 17% relative humidity) while subjects wore a water-perfused jacket to alter rate of heat storage. Values are means $\pm$ SE for 4 subjects. *Significantly different from lower rate of heat storage trial, $P < 0.05$.

and 78.4 ± 4.6 (SD) kg during the high and lower rate trials, respectively ($P = $ NS). Body weight losses during exercise were higher during the lower rate than during the high rate of heat storage: 1.7 ± 0.3 vs. 1.1 ± 0.1 kg ($P < 0.05$). Therefore, the levels of dehydration were higher during the lower rate than during the high rate of heat storage: 2.1 ± 0.4 vs. 1.5 ± 0.1% body wt loss, respectively ($P < 0.05$).

RPE. At 10 min of exercise, RPE was lower during the lower rate than during the high rate of heat storage: 10.8 ± 0.6 vs. 13.0 ± 0.7 units ($P < 0.05$). At exhaustion, RPE was equally high in both trials: 19.5 ± 0.5 and 19.8 ± 0.3 units ($P = $ NS).

DISCUSSION

The main aim of this study was to determine whether trained subjects fatigued in an uncompensable hot environment at the same core and muscle temperatures, regardless of the initial value and the rate of rise of body temperature. We found that exhaustion during moderate exercise occurred at the same high level of

Table 2. *Individual variability and reproducibility of T_{es}, T_m, and $\overline{T}_{sk}$ at exhaustion in the study of different rate of increase in body temperature*

Subject	T_{es}		T_m		$\overline{T}_{sk}$	
	High rate	Lower rate	High rate	Lower rate	High rate	Lower rate
JR	39.6	39.4	40.6	40.1	37.7	35.6
CJ	41.1	40.8	41.6	41.4	39.6	35.8
HF	40.3	40.1	40.7	40.8	38.3	35.9
PM	40.1	40.1	40.5	40.7	38.1	35.2
Mean ± SE	40.3 ± 0.3	40.1 ± 0.3	40.9 ± 0.3	40.7 ± 0.3	38.4 ± 0.4	35.6 ± 0.2

internal body temperature and RPE when the initial value or the rate of increase in body temperature was altered. We also observed that increases in heart rate and reductions in SV paralleled the rise in core temperature from 36 to 40°C, with skin blood flow plateauing when core temperature reached ~38°C. This suggests that increases in heart rate might contribute to reductions in SV with heat stress.

High Temperature and Fatigue

The main finding of these studies was that fatigue during exercise in the heat was related to high internal body temperature. This is based on the observation that, in both studies, trained subjects fatigued at similar T_{es} and T_m (40.1–40.3 and 40.7–40.9°C, respectively), even though $\overline{T}_{sk}$ was 2–3°C lower during the lower rate of heat storage trial. The between-trial variability in core temperature and T_m at exhaustion was very small in both studies: 0.3 ± 0.1°C (Tables 1 and 2). Time to exhaustion ranged from 28 to 63 min, being shortest with highest initial body temperature and higher rate of heat storage. Fatigue in the present heat stress condition is clearly related to high body temperature, because these trained cyclists could cycle to exhaustion at the same intensity in the heat for >2 h when core temperature rose at a slower rate to 39.7 ± 0.2°C (13).

The present findings confirm previous observations from this laboratory indicating that trained subjects fatigued with core temperatures of ~40°C when working at 50–60% $\dot{V}O_{2\,peak}$ in the heat (40°C, 10% RH) for 9–12 consecutive days (28, 30). Exercise time to fatigue increased from 48 ± 2 to 80 ± 3 min from the first to the last acclimation day, owing in part to a lower initial core temperature with heat acclimation (28). This large improvement in exercise time to fatigue was drastically reduced to 5–10 min when the subjects exercised in a humid environment but still coincided with a core temperature of 39.9 ± 0.1°C (30). Interestingly, fatigue in all these previous studies was not associated with any reductions in cardiac output, exercising leg blood flow, leg substrate availability and utilization, or accumulation of lactate, K^+, or other proposed "fatigue" substances (28–30). Furthermore, muscle glycogen levels at the point of fatigue have been shown to be quite high in these conditions (>300 mmol/kg dry wt) (10, 13, 29). Presently, we also observed low concentrations of blood lactate and euglycemic levels of blood glucose as well as similar heart rate and cardiac output at exhaus-

tion. Taken together, it appears that hyperthermia, rather than altered circulation and metabolism, is the main factor causing fatigue in the present conditions. It is recognized, however, that these and other factors such as dehydration, training status, heat acclimation, and environmental conditions, as well as duration and intensity of exercise, might interact and alter the tolerance to hyperthermia (8, 13, 23, 26, 29, 38).

Evidence in humans and animals also supports the notion that fatigue in hot environments appears to coincide with a critically high internal body temperature (6, 11, 12, 14, 17, 24). There are reports indicating that some untrained subjects fatigued during exercise in uncompensable hot environments with body temperatures of ~38°C (23, 26, 38). In untrained and moderately fit subjects, core temperature at exhaustion from heat strain during low-intensity exercise has been shown to occur over a range of 38–40°C (23, 26, 38). Differences in subjects' training status appear to be the main reason for the discrepancy in the tolerance to heat strain between the present and previous studies (23, 26, 38). In this light, it has been elegantly shown that subjects with higher aerobic fitness perform longer and tolerate higher levels of hyperthermia (39.2 vs. 38.8°C) in uncompensable hot environments than their less fit counterparts (7). Our present results extend previous findings by examining high metabolic rates in highly conditioned athletes. Furthermore, we presently determined the influence of active muscle temperature on fatigue in hot environments.

The mechanism by which hyperthermia causes fatigue is not well understood. We have presently observed a similar muscle and core temperature at the point of fatigue, despite a different upper body skin temperature in the rate study. Under these conditions, it is expected that hypothalamic and other internal organ temperatures would also reach a similarly high level at the point of fatigue (11). In this context, we could speculate that fatigue mainly responded to signals originating in the active muscle, internal organs, and/or central nervous system, secondary to the rise in temperature. The detrimental effects of hyperthermia on muscle function and metabolism are well documented (4, 9, 10). Furthermore, hyperthermia is known to stimulate the release of endotoxins and heat shock proteins from the internal organs, which might contribute to fatigue (see Ref. 17 for review). Alternatively, hyperthermia might reduce the central drive for exercise by influencing the motor control center in the brain

(5, 28). Whether these factors interact or act independently awaits further investigations. Irrespective of its origin, however, it is clear that this mechanism acts to protect humans and animals from reaching tissue temperatures that jeopardize cell function.

Cardiovascular Responses to Exercise

Another interesting observation of the study of different initial temperatures was that cardiac output was 2.2 ± 0.9 l/min lower during preheating than during the precooling trial at 10 min of exercise, yet whole body $\dot{V}o_2$ was unaltered. Previous studies comparing exercise in hot (36–44°C) vs. neutral environments and exercise with hot vs. cold water perfusing a suit in contact with the skin have shown cardiac output to be increased (27, 29, 35), unchanged (27, 35), or reduced (35). The present finding that the combined elevations in $\bar{T}_{sk}$, T_{es} (2.4–3.1°C), and skin blood flow (~8 ml·100 ml^{-1}·min^{-1} or 4-fold elevation) reduced cardiac output during moderately intense exercise confirms previous results of Rowell et al. (35) in untrained subjects. They observed a significantly lower cardiac output (1.0–1.2 l/min), central blood volume (0.1–0.2 liter), and SV (~20 ml) when subjects exercised in a 43°C than in a 26°C environment at 63–73% $\dot{V}o_{2\,peak}$ (34).

In the present study and the study of Rowell et al. (35), the decrease in cardiac output with hyperthemia is attributed to the larger decline in SV (Fig. 2). The mechanism mediating this reduced SV with hyperthermia has not been directly elucidated. The prevailing hypothesis is that reductions in SV with heat stress are due to increased skin blood flow and volume (20, 34). Rowell (34) speculated that increased skin blood flow reduces SV by reducing ventricular filling as a result of displacement of blood from the central circulation to peripheral skin veins as core temperature increases. Evidence showing that the lower SV, central venous pressure, and central blood volume with whole body heating are reversed by whole body cooling (36) appears to support this notion. However, this manipulation alters not only skin blood flow and $\bar{T}_{sk}$, but also core temperature, which have been shown to alter heart rate and SV independently (16). An increase in T_{es} of 1°C has been shown to increase heart rate by 9 ± 1 beats/min and reduce SV by 11 ± 3 ml when skin blood flow was the same (16). It seems, therefore, that the mechanism mediating SV reductions with heat stress is complex and might be influenced by several factors.

In the present study with markedly different heat strain conditions at 10 min of exercise (Fig. 1), it seems likely that central blood volume and right atrial pressure were also significantly reduced in H compared with C. An interesting observation was that skin blood flow reached a plateau at T_{es} of ~38°C in all trials, in agreement with early and recent reports (3, 13, 15, 25, 30). This indicates that the observed further reductions in SV with core temperature above ~38°C (i.e., ~20 ml) were clearly not associated with increased skin blood flow (Fig. 2, C–E). This agrees with the observations that most of the reductions in central blood volume and right atrial pressure with heat stress occur early in exercise (31, 35) and that right atrial pressure declines only slightly after skin blood flow has reached a plateau level (31). As shown in Fig. 2A, increases in heart rate from 130 beats/min to almost maximal levels (196–198 beats/min) were strongly correlated with increases in core temperature ($r^2 = 0.98$, $P = 0.001$). Heart rate at a given temperature was remarkably similar among trials. Because heart rate is influenced by multiple factors, it is not clear from our experiment to what extent this increase in heart rate responds to decreased SV and reduced stretching of the heart (Frank-Starling mechanism) and/or direct effect of warm blood on the sinus node and neurohumoral stimuli (37). It seems reasonable, however, to speculate that the increase in heart rate at $T_{es} > 38°C$ was largely related to increases in body temperature. This theory suggests that reduced cardiac filling time (i.e., higher heart rate) might also contribute to reductions in SV with hyperthermia, particularly in conditions of reduced central venous pressure and central blood volume. Another possibility is that high cardiac temperature reduces SV by altering cardiac contractility.

In conclusion, these results demonstrate that high body temperature per se causes fatigue in trained subjects during prolonged exercise in uncompensable hot environments. Furthermore, time to exhaustion in hot environments in trained subjects is inversely related to the initial level of body temperature and directly related to the rate of heat storage. In addition, marked elevations in body temperature (2–3°C) and skin blood flow (4-fold) resulted in significant reductions in cardiac output due to the larger decline in SV, yet whole body $\dot{V}o_2$ was unaltered. The observation that increases in heart rate and reductions in SV paralleled the rise in core temperature from 36 to 40°C, while skin blood flow plateaus at T_{es} of ~38°C, supports the contention that increases in heart rate contribute to reductions in SV with heat stress.

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