Dehydration markedly impairs cardiovascular function in hyperthermic endurance athletes during exercise

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González-Alonso, José, Ricardo Mora-Rodríguez, Paul R. Below, and Edward F. Coyle. Dehydration markedly impairs cardiovascular function in hyperthermic endurance athletes during exercise. *J. Appl. Physiol.* 82(4): 1229–1236, 1997.—We identified the cardiovascular stress encountered by superimposing dehydration on hyperthermia during exercise in the heat and the mechanisms contributing to the dehydration-mediated stroke volume (SV) reduction. Fifteen endurance-trained cyclists [maximal O_2 consumption ($\dot{V}O_{2\,max}$) = 4.5 l/min] exercised in the heat for 100–120 min and either became dehydrated by 4% body weight or remained euhydrated by drinking fluids. Measurements were made after they continued exercise at 71% $\dot{V}O_{2\,max}$ for 30 min while *1*) euhydrated with an esophageal temperature (T_{es}) of 38.1–38.3°C (control); *2*) euhydrated and hyperthermic (39.3°C); *3*) dehydrated and hyperthermic with skin temperature (T_{sk}) of 34°C; *4*) dehydrated with T_{es} of 38.1°C and T_{sk} of 21°C; and *5*) *condition 4* followed by restored blood volume. Compared with control, hyperthermia (1°C T_{es} increase) and dehydration (4% body weight loss) each separately lowered SV 7–8% (11 ± 3 ml/beat; $P < 0.05$) and increased heart rate sufficiently to prevent significant declines in cardiac output. However, when dehydration was superimposed on hyperthermia, the reductions in SV were significantly ($P < 0.05$) greater (26 ± 3 ml/beat), and cardiac output declined 13% (2.8 ± 0.3 l/min). Furthermore, mean arterial pressure declined 5 ± 2%, and systemic vascular resistance increased 10 ± 3% (both $P < 0.05$). When hyperthermia was prevented, all of the decline in SV with dehydration was due to reduced blood volume (~200 ml). These results demonstrate that the superimposition of dehydration on hyperthermia during exercise in the heat causes an inability to maintain cardiac output and blood pressure that makes the dehydrated athlete less able to cope with hyperthermia.

cardiovascular strain; stroke volume; cardiac output; blood pressure

DURING COMPETITION in hot environments, endurance athletes exercise at intensities that stress their cardiovascular system to its absolute limit (e.g., 90–100% of maximal heart rate). Therefore, athletic success and avoidance of heat-related injury mostly depend on the maintenance of adequate cardiac output, blood pressure, and organ perfusion. We have recently reported that dehydration, in competitive cyclists during 2 h of exercise, induces hyperthermia [esophageal temperature (T_{es}) 39.3°C], producing a phenomenon whereby cardiac output and blood pressure decline significantly (18 and 5%, respectively), systemic vascular resistance increases, and skin blood vessels vasoconstrict (10).

It is unclear whether this inability to maintain cardiac output is due specifically to either hyperthermia per se, dehydration per se, or the combination of dehydration and hyperthermia. Previous studies that have made people hyperthermic through exercise in hot (36–44°C) compared with neutral (18–26°C) environments or exercise with hot compared with cold water perfusing a suit in contact with skin have found cardiac output to be either increased when subjects are hyperthermic, particularly when exercise intensity is low (20, 21, 25), or similar to that in normothermic conditions during moderately intense exercise (20, 24). However, Rowell et al. (23, 24) found some indications that heat stress (in euhydrated untrained subjects) results in lower cardiac output and blood pressure during 14 min of exercise when the relative exercise intensity is high [2.4–2.7 l/min; 63–73% maximal oxygen consumption ($\dot{V}O_{2\,max}$)]. Unfortunately, there are few data regarding the cardiovascular responses to hyperthermia of heat-acclimated, competitive, endurance athletes who exercise for prolonged periods at higher rates of heat production and oxygen consumption ($\dot{V}O_2$; 3–4 l/min or more; ≥70% $\dot{V}O_{2\,max}$). Therefore, our purpose was to quantify the amount of cardiovascular stress produced by *1*) hyperthermia alone (T_{es} 39.3°C in euhydrated subjects), *2*) dehydration alone (4% body weight loss when hyperthermia was prevented by exercising in the cold), and *3*) the combination of dehydration and hyperthermia, typical of moderately intense exercise in the heat. We also determined whether all of the decline in stroke volume with dehydration was due to reduced blood volume when hyperthermia is prevented.

We hypothesized that both hyperthermia and dehydration would independently cause a decline in stroke volume and an increase in heart rate without compromising the maintenance of cardiac output and blood pressure. However, when dehydration is imposed on hyperthermia during exercise in the heat, we hypothesize that the circulatory strain will be significantly greater, resulting in an inability to maintain cardiac output and blood pressure.

METHODS

General Design

To accomplish these purposes, two different studies were performed. To identify the circulatory effects of hyperthermia alone [elevation of T_{es} by 1°C (from 38 to 39°C)], one study was performed in the heat (35°C) in subjects who were euhydrated by having them begin exercise with elevated core temperatures while also limiting heat dissipation (a condition common for athletes exercising in heat) (Figs. 1 and 2). These responses were compared with those when subjects were equally hyperthermic and also dehydrated to identify the combined effects of dehydration and hyperthermia. Another study isolated the cardiovascular effects of dehydration alone
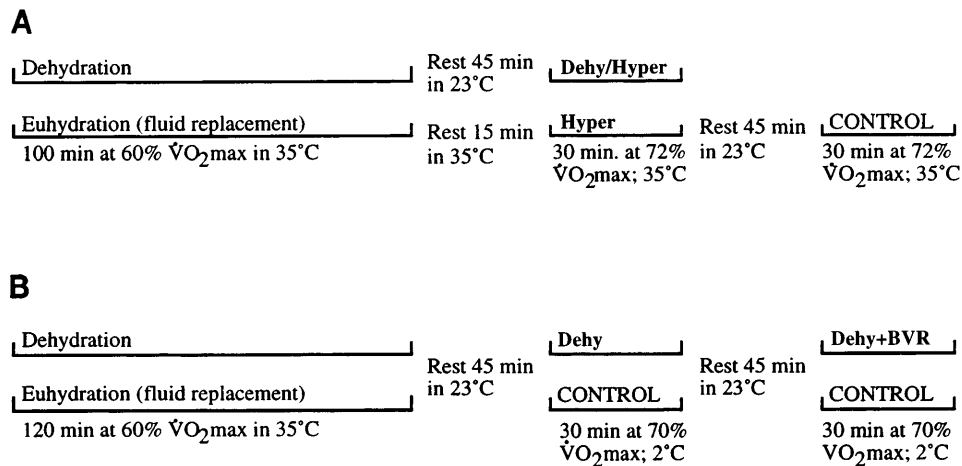
Fig. 1. Designs of hyperthermia and dehydration studies. *A*: in hyperthermia study, subjects (*n* = 7) first exercised for 100 min to become dehydrated or remain euhydrated (by fluid replacement) and then were evaluated (during additional 30-min exercise bouts in a 35°C environment) when both dehydrated and hyperthermic (Dehy/Hyper), when just hyperthermic (Hyper), or when neither dehydrated nor hyperthermic (control). *B*: in dehydration study, subjects (*n* = 8) first exercised for 120 min to become dehydrated or remain euhydrated (by fluid replacement) and then were evaluated during additional 30-min exercise bouts in a 2°C environment to prevent hyperthermia. They were dehydrated (without hyperthermia; Dehy) in 1 trial and then intravenously infused with 349 ml of a dextran solution to have blood volume restored during subsequent bout of exercise (Dehy+BVR). These responses were compared with those when subjects were euhydrated (control). $\dot{V}_{O_{2max}}$, maximal O_2 consumption.
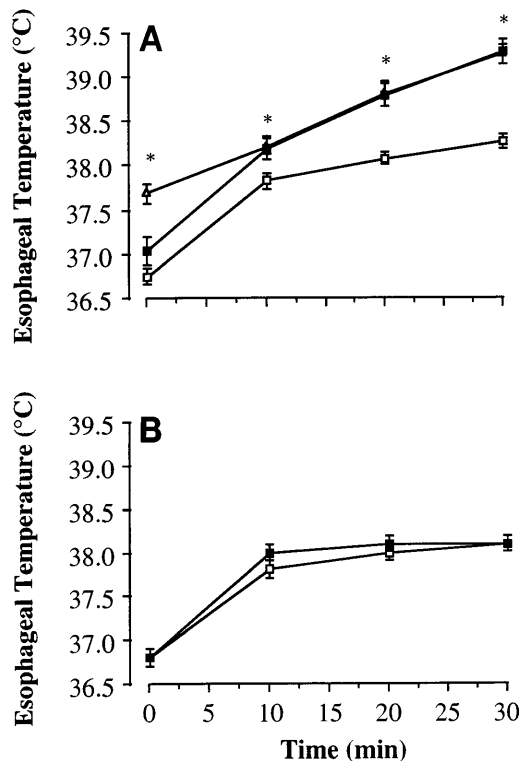

Fig. 2. *A*: esophageal temperature response during 30 min of exercise (70 ± 2% $\dot{V}_{O_{2max}}$ in a 35°C environment) to compare effects of Hyper (△; when euhydrated) vs. Dehy/Hyper (■) vs. when euhydrated with an esophageal temperature of 38°C (□; control). Values are means ± SE; *n* = 7 subjects. *Hyper and Dehy+Hyper values higher than control, *P* < 0.05. *B*: esophageal temperature response during 30 min of exercise [72 ± 2% $\dot{V}_{O_{2max}}$ in a cold environment (2°C)] to compare effects of Dehy (■) vs. euhydration when Hyper is prevented (□; control). Identical response was observed during Dehy+BVR trial compared with control. Values are means ± SE; *n* = 8 subjects.

(4% body weight loss), without the typical hyperthermia experienced in cool and hot environments, by having subjects exercise in the cold (windchill −5°C) (Fig. 2). The reductions in blood volume accompanying whole body dehydration were also prevented in another trial by intravenous infusion of a dextran solution to distinguish the effects of vascular compared with intracellular and interstitial dehydration (Figs. 1 and 3).

Subjects

The seven endurance-trained competitive cyclists participating in the study of hyperthermia possessed a mean (±SD) age, body weight, height, maximal heart rate, and $\dot{V}_{O_{2max}}$ of 25 ± 4 yr, 71 ± 3 kg, 179 ± 7 cm, 185 ± 6 beats/min, and 4.4 ± 0.4 l/min, respectively. The eight cyclists participating in the study of dehydration alone possessed a mean (±SD) age, body weight, height, maximal heart rate and $\dot{V}_{O_{2max}}$ of 24 ± 3 yr, 72 ± 7 kg, 181 ± 7 cm, 183 ± 6 beats/min, and 4.6 ± 0.5 l/min, respectively. The studies were approved by the Internal Review Board at The University of Texas at Austin, and written informed consent was obtained. During preliminary testing, $\dot{V}_{O_{2max}}$ was first determined. The subjects then acclimated to the heat during four practice trials (2-h cycling exercise at 60% $\dot{V}_{O_{2max}}$ in a 35°C environment), during which sweating rate was determined for estimation of the rate of fluid replacement during the experimental trials.

Experimental Design

In the study of hyperthermia, on two separate occasions at the same time of the day, the subjects first cycled for 100 min in the heat (35°C, 50% relative humidity, 1.5 m/s wind speed) and, by ingesting different volumes of fluid (0.2 ± 0.1 vs. 3.1 ± 0.3 liters), either became dehydrated (4.4 ± 0.2% body weight loss) or remained euhydrated. Trials were randomly assigned and counterbalanced across subjects. After the initial 100-min bout of the dehydration trial, subjects rested for 45 min in a 23°C environment while drinking 0.3 ± 0.1 liter of fluid and then performed an additional 30-min bout of exercise
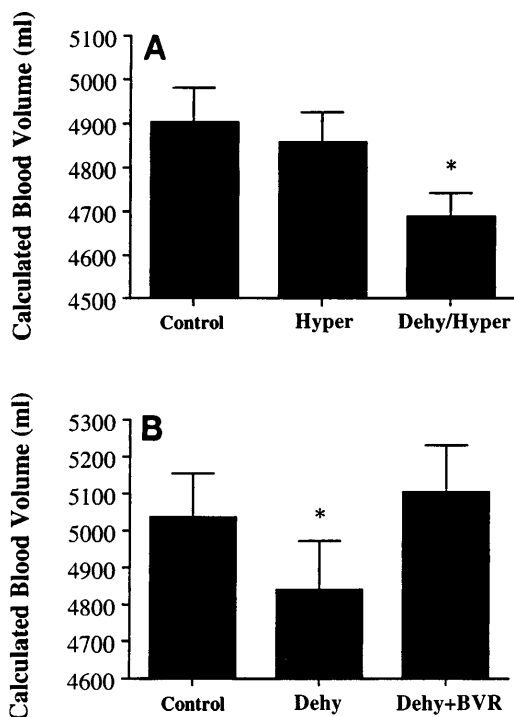
Fig. 3. *A*: calculated blood volume responses during 30 min of exercise ($70 \pm 2\%$ $\dot{V}o_{2\,max}$ in a 35°C environment) to compare effects of Hyper alone (when euhydrated) vs. Dehy+Hyper vs. when euhydrated (control). Blood volume was calculated by predicting absolute baseline resting euhydrated values (29) and then calculating changes in blood volume from changes in hemoglobin (7). Values are means $\pm$ SE; n = 7 subjects. *Blood volume significantly lower than control, $P < 0.05$. *B*: calculated blood volume response during 30 min of exercise [$72 \pm 2\%$ $\dot{V}o_{2\,max}$ in a cold environment (2°C)] to compare effects of Dehy vs. euhydration (control) and Dehy+BVR vs. control. Values are means $\pm$ SE; n = 8 subjects. *Blood volume significantly lower than control, $P < 0.05$.

that produced hyperthermia (Dehy/Hyper; T_{es} = 39.3 $\pm$ 0.1°C) while cardiovascular responses were evaluated (Fig. 1). After the initial 100-min bout of the euhydration trial, subjects first rested for 15 min in the heat and drank 1.0 $\pm$ 0.1 liter of warm fluid (38°C). During this period they were partially covered to also prevent core temperature from fully declining, while care was taken to prevent elevations in skin temperature that averaged 35.2°C. They subsequently exercised for 30 min in the heat while euhydrated but hyperthermic with a T_{es} of 39.3 $\pm$ 0.1°C (i.e., Hyper). Thereafter, they rested for 45 min in a 23°C environment to fully lower core temperature while drinking 0.9 $\pm$ 0.1 liter of fluid (22°C). They then performed a second 30-min bout of exercise in the heat while maintaining a low core temperature (T_{es} = 38.3 $\pm$ 0.1°C) when euhydrated (control trial) (Fig. 1). In support of the validity of this control measure, we observed identical cardiovascular responses to exercise in subjects who performed this control trial after Hyper compared with a control trial performed on a different day. All 30-min bouts of exercise were performed in a 35.5°C environment (53% relative humidity) at an intensity eliciting 72 $\pm$ 2% $\dot{V}o_{2\,max}$ (239 $\pm$ 23 W). Trials were separated by 2–4 days.

In the study of dehydration without the concomitant hyperthermia, cardiovascular function was evaluated while the subjects exercised in a cold environment. On two separate occasions, the subjects first cycled for 120 min in the heat (35°C, 50% relative humidity, 1.5 m/s wind speed) and, by ingesting different volumes of fluid (3.2 $\pm$ 0.2 vs. 0.2 $\pm$ 0.0

liter), either remained euhydrated (control trial) or became dehydrated (i.e., 4.1 $\pm$ 0.1% body weight loss) (Fig. 1). Trials were randomly assigned and counterbalanced across subjects. In each trial, they then rested for 45 min in a 23°C environment while drinking 0.6 $\pm$ 0.1 and 0.3 $\pm$ 0.1 liter of fluid during control and Dehy trials, respectively. Thereafter, cardiovascular function was evaluated as they performed two additional 30-min bouts of exercise (70 $\pm$ 2% $\dot{V}o_{2\,max}$; 242 $\pm$ 24 W) in a cold environment (2°C with fans blowing to produce a windchill index = about -5°C), interspersed by another 45-min rest period (Fig. 1). Similar cardiovascular responses were observed during both control trials. Responses were determined during the first 30-min bout when subjects were dehydrated (Dehy) (Fig. 1). During the subsequent rest period, the subjects were intravenously infused with 349 $\pm$ 60 ml of a blood volume expander (Macrodex; 6% wt/vol Dextran 70 in normal saline, Pharmacia Laboratories) preceded by 20 ml of Dextran 1 (Promit) to reduce the risk of anaphylactic reactions. In this trial, blood volume was restored (Dehy+BVR) to control levels experienced during exercise while euhydrated. The remaining bodily fluid compartments remained dehydrated during Dehy+BVR (Fig. 1). Trials were separated by 3–4 days.

The fluid-replacement solution in both studies was made from a commercially available sports drink (Gatorade, Quaker Oats). Different carbohydrate and electrolyte concentrations were mixed to achieve different hydration statuses with the same amount of carbohydrate and electrolyte ingestion. On the day before the experimental testing, the subjects' hydration statuses were standardized by having them adopt the same diet, exercise bout (i.e., ≥ 1 h of low-intensity cycling), and fluid intake. They also ingested 200–300 ml of fluid 2 h before arriving at the laboratory. On their arrival, nude body weight was recorded and subjects were clothed in shorts, socks, and cycling shoes. They then sat in the heat (35°C) for ≥ 20 min while an esophageal thermistor was inserted, a Teflon catheter was inserted into an antecubital vein, and a baseline blood sample was obtained while the forearm was relaxed and extended at the heart level. Subjects then cycled for 100–120 min at ~60% $\dot{V}o_{2\,max}$.

On completion of the first 100–120 min of exercise during all trials except Hyper, the subjects removed their clothing, toweled dry, and their postexercise body weight was recorded. Skin thermistors were attached before each 30-min bout. During Hyper, subjects exercised without fan cooling for the first 10 min to increase heat storage and ensure the target core temperature (T_{es} = 39.3°C) at 30 min of exercise. From the 10- to 30-min period of Hyper, the fan speed was the same as in the Dehy/Hyper trial (2 m/s), resulting in identical skin and core temperatures during this time period in both trials (Fig. 2). The fan speed was increased to 3 m/s during the control trial to ensure a 1°C lower T_{es}.

During each 30-min exercise bout, $\dot{V}o_2$, heart rate, T_{es}, and mean skin temperature were measured continuously. Cardiac output and blood pressure were measured in quadruplicate from 20 to 28 min. A 10-ml blood sample was also withdrawn at 30 min of exercise under the same conditions as the resting baseline sample while the subject was still pedaling the ergometer. A rating of perceived exertion was also recorded at this time (1).

Analytical Methods

$\dot{V}o_2$ was measured while the subject breathed through a Daniel's valve connected to a mixing chamber on the expiration side and to a dry gas meter (CD4, Parkinson-Cowan) on the inspiration side. Expired air was analyzed for O_2 (S-3A/I, Ametek) and CO_2 (CD-3A, Ametek) concentrations. Both

analyzers and the gas meter were interfaced with a laboratory computer (Apple IIe) through an analog-to-digital conversion board (REP-200B, Rayfield, Chicago, IL).

Cardiac output was determined by using a computerized version of the CO_2-rebreathing technique of Collier (6) and adjusted for hemoglobin concentration (14). Cardiac output was calculated by using the indirect Fick equation [cardiac output = CO_2 output ($\dot{V}CO_2$)/mixed venous CO_2 content ($C\bar{v}_{CO_2}$) − arterial CO_2 content (Ca_{CO_2})]. Expired air was sampled from a mixing chamber and analyzed for O_2 and CO_2 concentration as described above. End-tidal PCO_2 was determined on a breath-by-breath basis by continuous sampling at the mouthpiece by using a CO_2 analyzer (CD-3A, Ametek) interfaced with a laboratory computer. Mixed venous PCO_2 was estimated from the PCO_2 equilibrium attained during the rebreathing procedure. The criteria for CO_2-rebreathing equilibrium were that *1*) equilibrium was obtained within the 15 s of rebreathing procedure and *2*) maximal PCO_2 varied <1 Torr for a 5-s period. Heart rate was measured by using a monitor (Uniq CIC Heartwatch). The average heart rate over the last 10 min of exercise was considered as the steady-state heart rate in each 30-min experimental bout.

Systolic blood pressure and diastolic blood pressure were measured by using an automatic blood pressure monitor (STBP-680, Colin Medical Instruments). Mean arterial pressure was calculated as [(2 × diastolic blood pressure) + systolic blood pressure]/3. Cardiac output and blood pressure values represent the average of four measurements. Systemic vascular resistance was calculated as mean arterial pressure divided by cardiac output and expressed in peripheral resistance units (mmHg·l^{-1}·min).

Percent dehydration was estimated from the difference in body weight after each 30-min bout compared with the preexercise body weight, while correcting for body weight loss because of the exchange of O_2 and CO_2 (20). Nude body weight was determined on a platform scale (FW 150 KAI, Acme Scale) with an accuracy of ±20 g.

T_{es} was measured with a thermistor (YSI 491) inserted through the nasal passage a distance equal to one-quarter of the subject's standing height. Mean skin temperature was calculated from six sites (i.e., upper arm, forearm, chest, back, thigh, and calf) by using the weighting method of Hardy and DuBois (12). Skin thermistors (YSI 409A) were interfaced with a telethermometer (YSI 2100). In the hyperthermia study, cutaneous blood flow was measured on five sub-jects during Hyper and control by using a laser-Doppler flowmeter (model ALF 21, Transonic Systems, Ithaca, NY). The probe was placed on the dorsal side of the left forearm and remained in place during both of these trials. The T_{es} and cutaneous blood flow were averaged during the last 5 min.

Blood volume and plasma volume values were calculated by predicting the absolute baseline resting euhydrated values (29) and then calculating changes in blood volume and plasma volume from changes in hematocrit and hemoglobin (7). Hematocrit was measured in triplicate after microcentrifugation and corrected for trapped plasma (4) and venous sampling (5). Hemoglobin concentration was determined by using the cyanmethemoglobin technique. Serum was analyzed for osmolality (3MO, Advanced Instruments) and sodium (Nova 5), glucose (YSI23), and lactate concentrations (11).

Statistical Methods

Data from a given experiment were analyzed by using a one-way analysis of variance with repeated measures. After a significant *F*-test, pairwise differences were identified by using Tukey's highly significant difference post hoc procedure. The effects of combined dehydration and hyperthermia were compared with the effects of dehydration alone by using Student's unpaired *t*-tests. The significance level was set at $P < 0.05$. Data are presented as means ± SE.

RESULTS

Establishment of Experimental Conditions of Dehydration and Hyperthermia

$\dot{V}O_2$ during exercise was identical during the experimental and control trials of both studies (70–72 ± 2% $\dot{V}O_{2\,max}$) (Table 1). After subjects finished the 30-min bouts of exercise, body weight was similar (i.e., ±0.1 kg) to preexercise values during the control and Hyper trials, indicating euhydration. In contrast, body weight declined ~4% during Dehy, Dehy+BVR, and Dehy/Hyper (Table 1).

T_{es} was maintained at 38.1 ± 0.1 to 38.3 ± 0.1°C during the control trials of both studies and during Dehy and Dehy+BVR (Table 1, Fig. 2). This indicates the success of the cold environment in preventing an increase in core temperature when subjects are dehy-

Table 1. *Cardiovascular responses to moderately intense exercise with hyperthermia alone, with both dehydration combined with hyperthermia, dehydration alone, and dehydration with blood volume restoration compared with euhydration control values*

Variables	Control	Hyperthermia	Dehydration/ Hyperthermia	Control	Dehydration	Dehydration+Blood Volume Restoration
Esophageal temperature, °C	38.3 ± 0.1	39.3 ± 0.1*	39.3 ± 0.1*	38.1 ± 0.1	38.2 ± 0.1	38.1 ± 0.1
Mean skin temperature, °C	34.0 ± 0.2	34.6 ± 0.3	34.6 ± 0.4	20.9 ± 0.5	20.4 ± 0.4	20.9 ± 0.3
%Body weight loss	0.0 ± 0.1	0.1 ± 0.2	4.4 ± 0.2*	0.0 ± 0.1	4.1 ± 0.1*	4.1 ± 0.1*
$\dot{V}O_2$, l/min	3.15 ± 0.11	3.16 ± 0.10	3.14 ± 0.11	3.22 ± 0.12	3.20 ± 0.12	3.22 ± 0.12
Cardiac output, l/min	21.1 ± 0.8	20.4 ± 0.7	18.4 ± 0.7*†	21.4 ± 0.9	20.7 ± 0.9	22.1 ± 0.9
Heart rate, beats/min	164 ± 4	172 ± 4*	178 ± 4*†	147 ± 4	154 ± 4*	153 ± 4
Stroke volume, ml/beat	130 ± 8	119 ± 7*	104 ± 6*†	146 ± 8	136 ± 7*	145 ± 7
Mean arterial pressure, mmHg	101 ± 1	99 ± 1	96 ± 2*†	112 ± 3	110 ± 3	112 ± 3
Systolic BP, mmHg	184 ± 2	185 ± 3	180 ± 5*†	186 ± 5	186 ± 6	188 ± 5
Diastolic BP, mmHg	59 ± 1	56 ± 3	55 ± 3*	75 ± 3	72 ± 2	75 ± 3
Systemic vascular resistance, PRU	4.8 ± 0.1	4.9 ± 0.2	5.3 ± 0.2*†	5.3 ± 0.2	5.4 ± 0.2	5.1 ± 0.1
Perceived exertion, U	14.7 ± 0.3	17.0 ± 0.6*	17.6 ± 0.4*	13.1 ± 0.8	14.1 ± 0.5*	14.6 ± 1.0*

Values are means ± SE; *n* = 7 and 8 subjects in the hyperthermia and dehydration studies, respectively. $\dot{V}O_2$, O_2 consumption; BP, blood pressure; PRU, peripheral resistance units. *Significantly different from corresponding control, $P < 0.05$. †Significantly different from hyperthermia alone, $P < 0.05$.

drated. In contrast, T_{es} was $39.3 \pm 0.1°C$ during both Hyper and Dehy/Hyper (Fig. 2). Therefore, T_{es} was successfully manipulated to create the proper experimental conditions. Resting mean skin temperatures were 33.8 ± 0.3, 34.2 ± 0.2, and $35.2 \pm 0.3°C$ during control, Dehy/Hyper, and Hyper, respectively. During the 10- to 30-min period of exercise, mean skin temperature was maintained at $34.6 \pm 0.4°C$ during both Hyper and Dehy/Hyper and at $34.0 \pm 0.2°C$ during control (Table 1). Additionally, cutaneous blood flow during exercise was not significantly elevated during Hyper compared with control (i.e., 0.88 ± 0.17 vs. 0.78 ± 0.15 V). Mean skin temperature was similar during the four trials of the dehydration study performed in the cold environment (i.e., $20.4-20.9°C$).

As expected, blood volume and plasma volume were significantly lower during Dehy and Dehy/Hyper compared with their corresponding control values ($\sim$200 ml; $P < 0.05$; Table 2, Fig. 3). Infusion of the dextran solution (Dehy+BVR) successfully reversed the declines in blood volume and plasma volume that occurred during Dehy, as evidenced by values that were similar to control (Table 2, Fig. 3). Finally, blood volume and plasma volume were similar during Hyper and control (Table 2, Fig. 3). Therefore, alterations in blood volume paralleled dehydration (except, of course, during BVR) and were not confounded by hyperthermia.

Serum osmolality and serum sodium concentration reflected the hydration status, being significantly ($P < 0.05$) increased during Dehy as well as during Dehy/Hyper compared with control trials (Table 2). These values remained elevated during Dehy+BVR. Finally, these variables were all similar during Hyper and control, reflecting the similar euhydration status (Table 2).

Serum glucose and lactate concentrations were similar between the experimental and control trials, indicating that the observed alterations in cardiovascular responses were independent of these metabolic factors.

Cardiovascular Responses to Exercise

Individual effect of hyperthermia (i.e., Hyper vs. control). Hyperthermia alone reduced stroke volume by $8 \pm 2\%$ (11 ± 3 ml/beat; $P < 0.05$) and increased heart rate by $5 \pm 1\%$ (9 ± 1 beats/min; $P < 0.05$) without significantly affecting the other cardiovascular responses compared with control values (Table 1, Fig. 4).

Combined effect of dehydration with hyperthermia (i.e., Dehy/Hyper vs. control). The greatest effect of Dehy/Hyper was that it reduced stroke volume by $20 \pm 1\%$ below control (26 ± 3 ml/beat; $P < 0.05$; Table 1). This was accompanied by a $9 \pm 1\%$ increase (14 ± 1 beats/min; $P < 0.05$) in heart rate. As a result, cardiac output was reduced $13 \pm 2\%$ (2.8 ± 0.3 l/min; $P < 0.05$; Table 1). Mean arterial pressure declined $5 \pm 2\%$ (5 ± 2 mmHg; $P < 0.05$), indicating that systematic vascular resistance had increased $10 \pm 3\%$ (0.5 ± 0.1 mmHg·l^{-1}·min; $P < 0.05$) (Fig. 4).

Individual effect of dehydration (i.e., Dehy vs. control). Dehydration alone reduced stroke volume by $7 \pm 2\%$ (11 ± 3 ml/beat; $P < 0.05$) and increased heart rate by $5 \pm 1\%$ (7 ± 2 beats/min; $P < 0.05$) without significantly affecting the other cardiovascular responses compared with control values (Table, Fig. 4). Therefore, the relative individual effects of Dehy and Hyper were identical.

Effect of reductions in blood volume (i.e., Dehy+BVR vs. control). Dehy+BVR elicited cardiovascular responses that were no different from control (Table 1, Fig. 4). The reduction in stroke volume during Dehy was reversed during Dehy+BVR, and the increase in heart rate was no longer significant. This indicates that when dehydration does not result in hyperthermia, the reduced stroke volume is due solely to dehydration of the blood.

DISCUSSION

When dehydrated subjects exercise in the heat at moderate intensities, they experience hyperthermia because of reduced heat dissipation, resulting largely from an impaired skin blood flow and sweating response (8–10, 13, 15–19, 22, 26–28, 30–32). This stress produced by dehydration and hyperthermia (Dehy/Hyper trial) elicits cardiovascular strain during exercise, as characterized presently by a markedly reduced cardiac output ($13 \pm 2\%$ or 2.8 ± 0.3 l/min) and increased systemic vascular resistance ($10 \pm 3\%$ or 0.5 ± 0.1 mmHg·l^{-1}·min) with smaller but significant reductions in mean arterial blood pressure ($5 \pm 2\%$ or 5 ± 2 mmHg). The most important finding of this study is that this cardiovascular instability results from the synergistic effect of dehydration combined with hyperthermia on reducing cardiac output during exercise.

Table 2. *Hematological responses to moderately intense exercise with hyperthermia alone, both dehydration and hyperthermia, dehydration alone, and dehydration with blood volume restoration compared with euhydration control values*

Variables	Control	Hyperthermia	Dehydration/ Hyperthermia	Control	Dehydration	Dehydration+Blood Volume Restoration
Calculated BV, ml	$4,902 \pm 78$	$4,858 \pm 70$	$4,689 \pm 55^*$	$5,035 \pm 118$	$4,840 \pm 131^*$	$5,106 \pm 128$
Calculated PV, ml	$2,946 \pm 58$	$2,913 \pm 53$	$2,756 \pm 49^*$	$3,035 \pm 62$	$2,884 \pm 73^*$	$3,124 \pm 74$
Osmolality, mosmol/kg	279 ± 1	281 ± 1	$299 \pm 2^*$	280 ± 1	$296 \pm 2^*$	$295 \pm 2^*$
[Na$^+$], mmol/l	142 ± 1	143 ± 1	$152 \pm 1^*$	143 ± 1	$150 \pm 1^*$	$149 \pm 1^*$
Glucose concentration, mmol/l	4.1 ± 0.3	3.9 ± 0.5	4.3 ± 0.3	3.8 ± 0.2	3.6 ± 0.2	4.1 ± 0.1
Lactate concentration, mmol/l	2.9 ± 0.4	2.9 ± 0.2	3.0 ± 0.2	2.3 ± 0.3	2.5 ± 0.3	2.6 ± 0.4

Values are means $\pm$ SE; $n = 8$ and 7 subjects in the hyperthermia and dehydration studies, respectively. BV, blood volume; PV, plasma volume; [Na$^+$], serum sodium concentration. BV and PV were calculated by predicting absolute baseline resting euhydrated values (29) and then calculating changes in BV and PV from changes in hematocrit and hemoglobin (7). *Significantly different from corresponding control condition, $P < 0.05$.
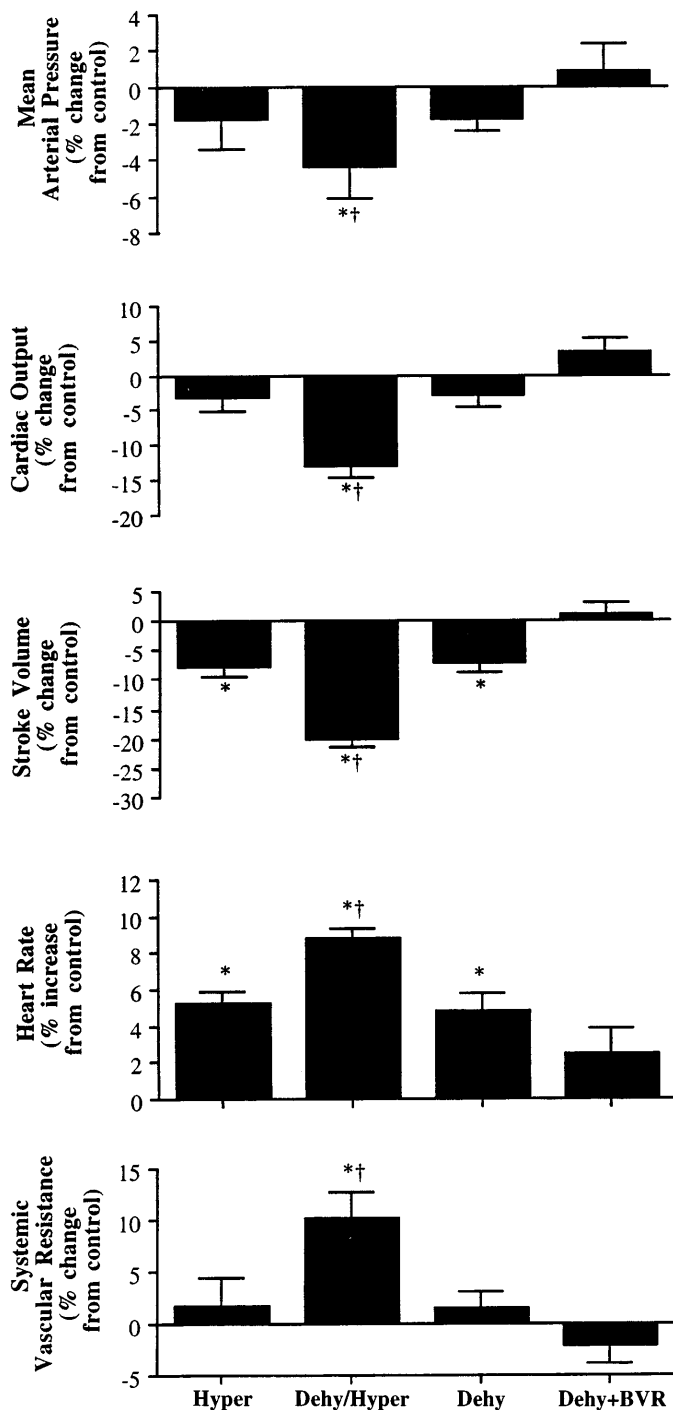
Fig. 4. Percent change in cardiovascular responses from control (i.e., euhydrated and normothermic within a given environment) with Hyper alone (i.e., without Dehy), with Dehy/Hyper, with Dehy (i.e., without Hyper), and with Dehy+BVR. Values are means ± SE; $n = 7$ and 8 subjects. *Significantly different from control, $P < 0.05$. †Significantly different from Hyper and Dehy alone, $P < 0.05$.

Hyperthermia or dehydration alone did not significantly reduce cardiac output or mean arterial pressure. Under the present conditions, the individual effects of hyperthermia and dehydration were similar, in that each separately reduced stroke volume 7–8 ± 2% and increased heart rate 5 ± 1%. However, compared with

the individual effect of hyperthermia, the superimposition of dehydration on hyperthermia caused a significantly greater decline in stroke volume (20 ± 1%), which was not fully compensated for by the 9 ± 1% rise in heart rate, and thus cardiac output declined 13 ± 2%. Because stroke volume was markedly reduced with a heart rate close to maximal (~96%), it appears that the cardiac output generated was the highest possible. However, this highest possible cardiac output when subjects are exposed to the combination of dehydration and hyperthermia was inadequate for maintaining cardiovascular function (i.e., blood pressure fell and systemic vascular resistance increased) despite the fact that the exercise intensity still elicited only 72% of $\dot{V}O_{2\,max}$.

Previous studies evaluating the influence of heat stress on cardiovascular function during exercise in humans have compared average responses during exercise in hot (36–44°C) vs. thermoneutral (18–26°C) environments (20, 21, 24) or during exercise with hot vs. cold (45 vs. 10°C) water perfusing a suit in contact with skin (23, 25). These approaches cause hyperthermic stress by elevating both skin temperature (≥5°C) and core temperature (0.5–1.2°C) (20, 21, 23–25). It is well known that a marked increase in skin temperature, by itself, will increase skin blood flow and potentially reduce stroke volume during exercise through mechanisms other than simple elevation in core temperature (23). This hyperthermic stress, however, is different from that normally observed during prolonged exercise in the heat with fan cooling, in which skin temperature declines or is maintained but core temperature increases with dehydration (2, 3, 10, 15, 16, 18). The present study was carefully designed to produce significant hyperthermia (i.e., increase T_{es} 1°C to 39.3°C) with only minimal differences in skin temperature and cutaneous blood flow during exercise in a 35°C environment for both the control and Hyper trials. This was accomplished by having euhydrated subjects begin exercise with core temperature slightly elevated from previous exercise and by slightly reducing heat dissipation during exercise by lowering wind speed. These slight manipulations simulate the actual thermal variations that endurance athletes may experience, keeping in mind that, with their very high rates of heat production (~51.6 kJ/min in the present study), even small reductions in heat dissipation can produce rapid hyperthermia.

Clearly, declining stroke volume is the primary problem encountered with both hyperthermia and dehydration because general cardiovascular strain develops when declines are large enough to elicit near-maximal heart rate and cardiac output. The extent to which hyperthermia alone can cause reductions in cardiac output and blood pressure during high-intensity exercise is unclear, yet it seemingly depends on how hyperthermic subjects are allowed to become in experiments. Our present observation that cardiac output was not altered by hyperthermia up to 39.3°C (i.e., 1°C higher T_{es} than control) is in agreement with previous results from studies using untrained men during 15–60 min

(20, 21, 24, 25). As mentioned above, hyperthermic stress in previous studies resulted from the combined elevation of skin and core temperature (20, 21, 24, 25). Interestingly, most previous studies show a higher average cardiac output (1.5–3.2 l/min) with heat stress during low- and moderate-intensity exercise (20, 21, 25). With similar or slightly reduced stroke volume, this increased cardiac output was due to increases in heart rate (20, 21, 25). During more intense exercise, however, heat stress results in a similar cardiac output compared with that in thermoneutral conditions (20). Hence, the cardiovascular system responds to heat stress adequately at levels below maximal heart rate and maximal cardiac output, as in the present study with hyperthermia alone. Of note is that Rowell et al. (24) observed that when environmental heat stress was superimposed on moderately intense exercise (63–73% $\dot{V}_{O_2 max}$) in untrained men, cardiac output was reduced but blood pressure and systemic vascular resistance were not impaired. It remains to be determined whether higher levels of hyperthermia in euhydrated heat-acclimated endurance athletes would reduce cardiac output and blood pressure and cause systemic vasoconstriction during exercise at higher intensities typical of competitive events lasting 13–60 min. It is clear, however, that the present superimposition of dehydration on hyperthermia (up to 39.3°C for T_{es}) during exercise in the heat not only caused larger declines in stroke volume and cardiac output, but it also compromised blood pressure and caused systemic vasoconstriction. We have recently reported that it also causes a 50% increase in plasma norepinephrine and cutaneous vasoconstriction that is largely responsible for the hyperthermia associated with dehydration (10, 18).

Sawka et al. (28) have recently found that when subjects are hypohydrated, they become exhausted sooner (55 vs. 121 min) during treadmill walking in a 49°C environment despite the fact that they have a significantly lower core temperature (38.7 vs. 39.1°C) at exhaustion compared with when euhydrated. A lower core temperature at exhaustion when subjects are hypohydrated may seem paradoxical but, actually, is not. It agrees with our present findings that, at a given core temperature (39.3°C), dehydrated subjects experience lower cardiac output and blood pressure and greater vascular resistance, making them potentially more prone to ischemic injury. With the idea that heat exhaustion might result from cardiovascular instability (i.e., fall in stroke volume, cardiac output, and, eventually, blood pressure) in response to dehydration and/or hyperthermia, hypohydrated subjects would be expected to tolerate less hyperthermia before becoming exhausted. Therefore, clinicians should consider hyperthermia to be more serious in dehydrated compared with euhydrated subjects and not assume that hyperthermia is an acceptable occurrence when sujects are dehydrated.

This study also examined the effects of dehydration when hyperthermia was prevented. To maintain T_{es} at 38.1°C when subjects are dehydrated, we had subjects exercise in a very cold environment (−5°C windchill).

The necessity of these extraordinary measures provides a remarkable example of the extent to which dehydration reduces evaporative heat loss and causes hyperthermia. Another important finding was that when hyperthermia was prevented, all of the decline in stroke volume was due specifically to reduced blood volume (~200 ml), which probably reduced ventricular filling. This is based on our simple observation that blood volume restoration (from intravenous infusion of 349 ml of 6% dextran) in subjects who maintained a similar level of intracellular and interstitial dehydration totally reversed the decline in stroke volume. Given the observations that the alterations in cardiovascular response with dehydration during exercise in the cold are small and that the circulatory strain is always lower in cold than in hot environments (e.g., >17 beats/min lower heart rate at similar $\dot{V}_{O_2}$ in the present studies), it would be expected that the superimposition of hyperthermia on dehydration in subjects exercising with a low skin temperature would not lead to reductions in cardiac output and blood pressure, as presently observed in subjects exercising with high skin temperature.

It has previously been found that blood volume restoration in dehydrated subjects who are hyperthermic only partially restored stroke volume toward euhydrated levels (15). Additionally, this reduced stroke volume in hyperthermic and blood volume-restored subjects occurred despite a reduced skin blood flow and a declining skin temperature (15). Our present finding that hyperthermia alone (when subjects are euhydrated) also reduces stroke volume, without reducing total blood volume or increasing cutaneous blood flow compared with control, complements the previous findings of Montain and Coyle (15). From a past (15) study and our present study, it appears that hyperthermia causes reductions in stroke volume during exercise (with fan cooling) in both euhydrated and dehydrated subjects by a mechanism that is independent of increases in skin temperature and skin blood flow and lowered blood volume.

In summary, when endurance-trained athletes exercised at 70–72% $\dot{V}_{O_2 max}$, we found that hyperthermia (when subjects are euhydrated during exercise in the heat) and dehydration (when hyperthermia was prevented during exercise in the cold) each lowered stroke volume 7–8% and increased heart rate sufficiently to prevent a significant decline in cardiac output. However, when dehydration was allowed to cause hyperthermia during exercise in the heat, the decline in stroke volume was greater (20%) and cardiac output declined synergistically (13%). The resulting cardiac output appears to be the highest possible by the stressed cardiovascular system, yet it was insufficient for maintaining arterial blood pressure and a low vascular resistance during exercise. Clearly, the superimposition of dehydration on hyperthermia during exercise in the heat causes greater reductions in stroke volume and cardiovascular function that make the dehydrated athlete much less able to cope with hyperthermia.

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