Fluid replacement and glucose infusion during exercise prevent cardiovascular drift

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HAMILTON, MARC T., JOSE GONZALEZ-ALONSO, SCOTT J. MONTAIN, AND EDWARD F. COYLE. *Fluid replacement and glucose infusion during exercise prevent cardiovascular drift.* J. Appl. Physiol. 71(3): 871–877, 1991.—This study examined the influence of both hydration and blood glucose concentration on cardiovascular drift during exercise. We first determined if the prevention of dehydration during exercise by full fluid replacement prevents the decline in stroke volume (SV) and cardiac output (CO) during prolonged exercise. On two occasions, 10 endurance-trained subjects cycled an ergometer in a 22°C room for 2 h, beginning at 70 ± 1% maximal O_2 uptake ($\dot{V}O_{2\,max}$) and in a euhydrated state. During one trial, no fluid (NF) replacement was provided and the subject's body weight declined 2.09 ± 0.19 kg or 2.9%. During the fluid replacement trial (FR), water was ingested at a rate that prevented body weight from declining after 2 h of exercise (i.e., 2.34 ± 0.17 l/2 h). SV declined 15% and CO declined 7% during the 20- to 120-min period of the NF trial while heart rate (HR) increased 10% and O_2 uptake ($\dot{V}O_2$) increased 6% (all $P < 0.05$). In contrast, SV was maintained during the 20- to 120-min period of FR while HR increased 5% and thus CO actually increased 7% (all $P < 0.05$). Rectal temperature, SV, and HR were similar during the 1st h of exercise during NF and FR. However, after 2 h of exercise, rectal temperature was 0.6°C higher ($P < 0.05$) and SV and CO were 11–16% lower ($P < 0.05$) during NF compared with FR. In another experiment, using similar subjects ($n = 8$) and exercise conditions, we observed that continuous intravenous infusion of glucose in water (1,224 ± 55 ml of 18% glucose, wt/vol) totally prevented the 5–7% increase ($P < 0.05$) in $\dot{V}O_2$, CO, and HR observed during 2 h of exercise when hydration was maintained by simply ingesting water. In conclusion, the maintenance of euhydration by fluid replacement throughout exercise attenuates hyperthermia and prevents the decline in SV and CO observed during the 2nd h exercise when no fluid is replaced. Additionally, when dehydration is offset during 2 h of cycle exercise performed at 70% $\dot{V}O_{2\,max}$, it appears that factors that are influenced by hyperglycemia are responsible for the 5–7% increase in $\dot{V}O_2$, HR, and CO and that these increases are prevented when both glucose and water are infused intravenously.

cardiac output; stroke volume; drinking; hydration; hyperthermia; glucose; thermoregulation

FOLLOWING THE INITIAL RESPONSES after the first few minutes of exercise at a constant work rate [i.e., 70–80% maximal O_2 uptake ($\dot{V}O_{2\,max}$)], there is a gradual decrease in stroke volume (SV) and increase in heart rate (HR) (11, 22). These two responses, as well as a progressive reduction of arterial, pulmonary arterial, and right ventricular end-diastolic pressures, are the salient components of the general phenomenon of cardiovascular instability during prolonged exercise, termed "cardiovascular drift" (22). Cardiac output (CO) has also been observed to decline during prolonged exercise when the decline in SV is relatively greater than the concomitant increase in HR (28). Two factors that likely contribute to the progressive cardiovascular drift during prolonged exercise are the concomitant body water loss that occurs throughout prolonged exercise and a peripheral vasodilation and shift in the distribution of blood volume from the central circulation to the periphery (22). To our knowledge, however, no study has simply determined if the decline in SV during prolonged exercise without fluid replacement can be prevented by fluid ingestion at a rate that maintains euhydration throughout exercise.

Many of our theories regarding of the effects of body water loss on cardiovascular function and thermoregulation have developed from studies that induced large amounts of hypohydration (i.e., 3–7% loss of body weight) before exercise and then monitored responses to subsequent exercise (20, 26, 27, 29). From these studies, it seems that hypohydration before exercise results in a relatively large reduction in plasma volume and increased plasma osmolality, a reduced skin blood flow and sweating rate, and elevated body temperature. Additionally, SV is lower and HR higher during the early minutes of exercise in the hypohydrated compared with the euhydrated state (12, 20, 29). Dehydration induced during exercise may not result in these same sequence of events or magnitude of change in these factors. For example, reductions in plasma volume during exercise are much less when hypohydration is induced during exercise than when subjects are hypohydrated before exercise (8, 27, 28).

The primary purpose of this investigation was to determine if fluid replacement during prolonged exercise prevents the decline in SV. In the process, we observed that some of the increase in HR is independent of hydration and related to increased oxidative metabolism. In a second experiment, we demonstrated that increases in O_2 uptake ($\dot{V}O_2$) and HR and decreases in SV during 2 h of cycle exercise (i.e., 70% $\dot{V}O_{2\,max}$) can be totally prevented by intravenous infusion of water and sufficient glucose to produce hyperglycemia.

METHODS

Comparison of No Fluid With Fluid Replacement

Subjects. Ten endurance-trained cyclists participated in this study. They were all heat acclimated and accustomed to prolonged intense exercise. Their mean age, weight, and $\dot{V}O_{2\,max}$ were 27.8 ± 5.0 (SD) yr, 72.5 ± 5.0 kg, and 4.52 ± 0.35 l/min, respectively. The study was approved by the Internal Review Board of The University of Texas, and subjects gave written informed consent.

General testing protocol. The subjects cycled on a stationary ergometer (Monark 816) for 2 h at a constant work rate that initially elicited 70% $\dot{V}O_{2\,max}$. This was performed on two occasions, in a balanced order, at 1-wk intervals. During one trial, no fluid was ingested during exercise (NF). During the fluid replacement (FR) trial, water was ingested at a rate that, according to pilot studies, prevented a loss of body weight. Drinking began within 5 min before exercise and continued at 20-min intervals until 100 min. Subjectively, the subjects did not feel much fluid in their stomach after exercise. The laboratory was maintained at 22°C, and two fans provided a wind speed of ~3 m/s.

Subjects began each trial euhydrated. To accomplish this, the subjects were instructed to drink liberally the night before testing and to drink freely the morning of testing but no later than 1 h before testing, which was performed after an overnight fast. On reporting to the laboratory, an indwelling catheter was placed in an antecubital vein for blood sampling. The subjects voided, and their nude weight was recorded with an accuracy of ±20 g before and after exercise. They sat on the cycle ergometer for 20 min before a venous blood sample was obtained immediately before exercise.

During the 2-h period of exercise, continuous measurements were made of HR (Uniqu CIC Heart Watch) and rectal temperature (YSI thermistor probe). $\dot{V}O_2$ was measured for 4-min intervals beginning at 8, 38, 68, 98, and 116 min. CO was measured in triplicate during 8-min periods beginning at 16, 56, 76, and 112 min. Six milliliters of venous blood were obtained before and after 20, 40, 60, 80, and 120 min of exercise for determination of hematocrit and hemoglobin (cyanomethemoglobin method). Percent changes from rest in BV were calculated from hemoglobin (10), whereas changes in plasma volume were calculated from hematocrit and hemoglobin as reported by Dill and Costill (10).

Determination of $\dot{V}O_2$. The subjects breathed through a Daniel's valve while inspired volume was measured using a dry gas meter (Parkinson-Cowan CD4). Expired gases were sampled from a mixing chamber and analyzed for O_2 (Applied Electro-chemistry S3A) and CO_2 (Ametek CD-3A). Analog outputs from the instruments were directed to a laboratory computer for calculation of $\dot{V}O_2$ and respiratory exchange ratio (RER). The gas analyzers were calibrated with gases of known concentration. The dry-gas meter was calibrated against a Tissot spirometer.

Determination of CO. CO was measured three times during the course of each 8-min collection period by using the CO_2 rebreathing method of Collier (4). During each determination of CO, inspired gas volume was measured using a dry-gas meter, expired air was sampled from a mixing chamber and analyzed for O_2 and CO_2 concentrations, and $\dot{V}O_2$ and CO_2 production were calculated, as described above, for the 60-s period before the rebreathing. End-tidal P_{CO_2} was also measured continuously on a breath-by-breath basis during this 60-s period by sampling at the mouthpiece using another CO_2 analyzer (Ametek CD-3A) interfaced with a laboratory computer. Mixed venous P_{CO_2} was estimated from the P_{CO_2} equilibrium attained after the subjects rebreathed a gas containing ~14% CO_2-86% O_2. The criteria for equilibrium were that *1*) it occurred within 12 s and *2*) the P_{CO_2} variation did not exceed 1 Torr for a 5-s period. A venous blood sample was obtained during each 8-min period, and hemoglobin concentration was determined so that arterial and venous CO_2 content could be calculated from the CO_2-dissociation curve presented by McHardy (19).

Comparison of Fluid Replacement With Intravenous Infusion of Glucose and Water

Subjects and general testing protocol. The purpose of these trials was to determine if hyperglycemia prevents a decline in SV and an increase in HR when hydration is partially maintained. These trials were performed using a balanced design in eight subjects, six of whom participated in the NF and FR comparisons. Their mean age, weight, and $\dot{V}O_{2\,max}$ were 26.8 ± 5.1 (SD) yr, 69.5 ± 2.3 kg, and 4.54 ± 0.37 l/min, respectively. The experimental conditions and procedures of this FR trial and the previously described FR trial were identical.

During the glucose infusion (GI) trial, a sterile 18% (wt/vol) glucose solution in water was infused into a forearm vein beginning at 8 min and ending at 118 min of exercise. The infusion rate was adjusted every few minutes to maintain blood glucose concentration at 10.1 ± 0.4 mM (i.e., 182 ± 7 mg/100 ml) as previously described (9), whereas blood glucose concentration remained in the euglycemic range (i.e., 3.7–4.6 mM) during FR as previously reported (9). GI resulted in a total infusion volume of 1,224 ± 55 ml. Water ingestion was limited to an average of 119 ml, and thus a total of 1,343 ± 60 ml of fluid were replaced during the GI trial.

Statistical analysis. Data are presented as means ± SE. Comparisons were made using a two-way (trial-by-time) repeated measures analysis of variance. Significant differences were identified using Tukey's post hoc test. The level of statistical significance is $P < 0.05$.

RESULTS

Comparison of No Fluid With Fluid Replacement

$\dot{V}O_2$. The exercise bout elicited 70 ± 1% of $\dot{V}O_{2\,max}$ after 10 min during both the NF and FR trials. $\dot{V}O_2$ increased 6% ($P < 0.05$) during the 10- to 120-min period of both the NF and FR trials (i.e., 3.11 ± 0.11 to 3.31 ± 0.10 l/min during NF, $P < 0.05$; and 3.15 ± 0.10 to 3.34 ± 0.11 l/min during FR; $P < 0.05$). Thus FR did not attenuate the increase in $\dot{V}O_2$ during the 2-h period of exercise.

Hydration status. Table 1 shows the body weight changes, which reflect changes in total body water, during 2 h of exercise with NF compared with FR. Body weight declined 2.09 ± 0.19 kg during NF ($P < 0.05$), which corresponded to a 2.9% loss of body weight. During

TABLE 1. *Body weight changes and fluid ingestion during no-fluid and fluid replacement trials*

	Preexercise Body Wt, kg	Postexercise Body Wt, kg	Body Wt Change, kg	Volume of Water Ingested, liters
No fluid	72.59±1.65	70.50±1.54	−2.09±0.19	0
Fluid replacement	72.41±1.65	72.45±1.68*	+0.04±0.01*	2.34±0.17*

Values are means ± SE for 10 subjects. Postexercise body wt values are calculated after subtracting volume of urine produced after exercise, which averaged 0.27±0.09 liter after the fluid replacement trial. * Significance difference between trials ($P < 0.05$).

FR, an average of 2.34 ± 0.17 liters of water was ingested throughout the trial. As a result, there was almost no change in body weight, and thus total body water during FR was maintained, after accounting for the volume of urine (0.27 ± 0.09 liter) produced during FR (Table 1). Six subjects were able to urinate after FR, and none were able to urinate after NF. Calculated sweating rate was not significantly different during NF and FR.

BV and plasma volume. Table 2 shows the hematologic responses during exercise under the two conditions. The transition from rest to exercise during both NF and FR produced significant increases in hemoglobin concentration (Table 2; $P < 0.05$), and thus BV declined as shown in Fig. 1. BV during NF was 4.4 ± 0.5%, 5.7 ± 0.4%, and 6.7 ± 0.6% below resting levels ($P < 0.05$) after 20, 60, and 120 min of exercise, respectively. The 2.3% decline in BV during the 20- to 120-min period of NF was statistically significant ($P < 0.05$). However, BV did not significantly decline during the 60- to 120-min period (i.e., 2nd h) of NF. BV was maintained at levels only 2% below resting levels during the 60- to 120-min period of FR (NS), indicating that FR effectively prevented a reduction of BV. BV was therefore maintained at significantly ($P < 0.05$) higher levels during the 2nd h of exercise with FR compared with NF (Fig. 1, Table 2). Changes in plasma volume followed a similar pattern (Table 2).

CO, SV, and HR. Figure 1 shows the cardiovascular effects of FR compared with NF throughout 2 h of exercise. During the 20- to 120-min period of NF, CO declined 7% ($P < 0.05$) due to a 15% decline ($P < 0.05$) in SV during a time when HR increased 10% ($P < 0.05$). In contrast, SV remained fairly constant throughout exercise during FR and heart rate increased 5% ($P < 0.05$). As a result, CO increased 7% ($P < 0.05$) during the 20- to 120-min period of FR.

HR, SV, and CO were not significantly different during the 1st h of exercise with NF compared with FR (Fig. 1). However, during the 2nd h of exercise, SV and CO were significantly lower during NF compared with FR ($P < 0.05$), whereas HR was significantly elevated ($P < 0.05$).

Rectal temperature. During NF, the rectal temperature increased progressively to 38.5 ± 0.11°C after 60 min, and it continued to increase significantly ($P < 0.05$) to 38.9 ± 0.15°C after 120 min of exercise (Fig. 2). Compared with NF, FR did not significantly attenuate the increase in rectal temperature during the first 60 min of exercise. However, rectal temperature stabilized at 38.3 ± 0.12°C during the 60- to 120-min period of FR. Therefore, rectal temperature was significantly ($P < 0.05$) lower during the 2nd h of exercise with FR compared with NF (Fig. 2).

Comparison of Water Ingestion and Intravenous Glucose Infusion

$\dot{V}O_2$. During 2 h of exercise beginning at 70% $\dot{V}O_{2\,max}$ with FR, a second group of subjects ($n = 8$) displayed a 5% increase in $\dot{V}O_2$ during the 10- to 120-min period (i.e., 3.23 ± 0.11 at 10 min vs. 3.38 ± 0.12 l/min at 120 min; $P < 0.05$; Fig. 3). Almost all of this 5% increase in $\dot{V}O_2$ reflected increased caloric expenditure because the decline in RER observed during this time (cf. Ref. 9), and thus the increase in fat oxidation, was responsible for only 1% of the 5% increase in $\dot{V}O_2$. Interestingly, intravenous GI prevented $\dot{V}O_2$ from increasing and RER from declining during the 10- to 120-min period of exercise (i.e., 3.21 ± 0.12 to 3.24 ± 0.12 l/min; cf. Ref. 9; Fig. 3). Therefore, GI prevented the significant increase in whole body caloric expenditure.

BV. As shown in Fig. 3, BV was maintained at levels that were not significantly different from resting levels during the entire GI trial and during the 2nd h of the FR trial. BV during the GI trial was not significantly different from the FR trial at any time.

CO, SV, and HR. CO increased 6% ($P < 0.05$) during the 20- to 120-min period of FR due to a 5% increase in HR, whereas SV remained stable ($P < 0.05$). Therefore, 2

TABLE 2. *Hematologic changes during exercise with no fluid and fluid replacement*

	Time, min				
	0	20	60	80	120
Hemoglobin, g/100 ml					
No fluid	14.5±0.1	15.2±0.2*	15.4±0.1*	15.4±0.2*	15.5±0.1*
Fluid replacement	14.5±0.2	14.9±0.3*	14.8±0.3†	14.9±0.2†	14.8±0.1†
Hematocrit, %					
No fluid	40.1±0.5	41.5±0.5*	41.4±0.4*	41.6±0.3*	41.7±0.4*
Fluid replacement	40.8±0.6	41.5±0.6	41.1±0.6	41.3±0.5	41.2±0.6
Change in plasma volume					
No fluid	0	−6.7±0.9*	−7.6±0.8*	−7.9±1.0*	−9.1±0.8*
Fluid replacement	0	−3.5±0.7*†	−2.8±1.0*†	−3.3±1.1*†	−2.3±1.1†

Values are means ± SE for 10 subjects. Hematocrit has been corrected for difference between large-vessel hematocrit and whole body hematocrit (0.96) and trapped plasma (0.91). * Significantly different from resting value (0 min) for that trial ($P < 0.05$). † Fluid replacement is significantly different from no fluid at this corresponding time ($P < 0.05$).

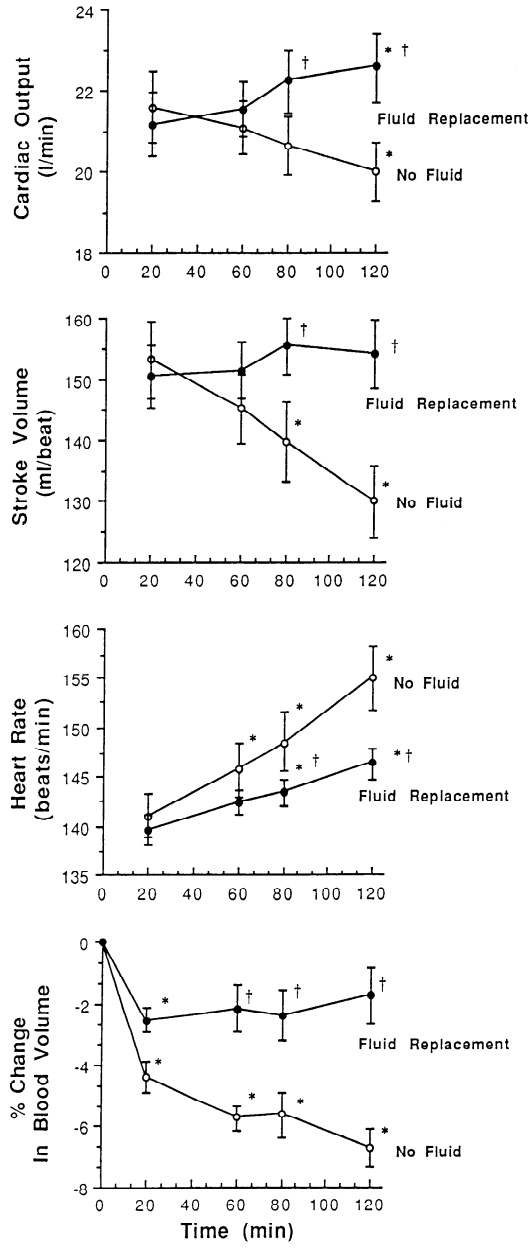

FIG. 1. Cardiovascular responses to 120 min of exercise at 70% maximal O_2 uptake ($\dot{V}O_{2\,max}$) with subjects ingesting no fluid or with fluid replacement at a rate that maintained hydration. Values are means ± SE for 10 subjects. *Significantly different from initial value (i.e., 0 min for blood volume and 20 min for other measures) for that trial ($P < 0.05$). †Fluid replacement is significantly different from no fluid at this corresponding time ($P < 0.05$).

h of exercise during FR was characterized by a 5–6% increase in $\dot{V}O_2$, CO, and HR.

Infusion of 1,224 ± 55 ml of an 18% glucose solution in water during the 2 h of exercise prevented cardiovascular drift. HR did not increase by more than 2 beats/min during the 20- to 120-min period while SV and thus CO also remained remarkably stable during this period. After 120 min of exercise, $\dot{V}O_2$ and HR were significantly higher ($P < 0.05$) during FR compared with GI (Fig. 3).

DISCUSSION

The primary purpose of this investigation was to determine if the prevention of dehydration, by ingestion of a sufficient volume of water to prevent body weight from declining after 2 h of cycling (70% $\dot{V}O_{2\,max}$), is effective in preventing the decline in SV and CO that often occur during prolonged exercise (11, 27). To our knowledge there are no direct data available regarding this question.

It appears that FR was completely effective in maintaining euhydration during exercise as evidenced by the fact that body weight (Table 1) and even BV after 2 h of exercise were not different from preexercise values (Fig. 1). The major finding of this study was that FR prevented SV and CO from declining during exercise (Fig. 1). However, HR did increase by 5% during the 20- to 120-min period of FR, yet this increase was only one-half as large as that observed during NF (i.e., 5% compared with 10%). As a result, FR promoted a 7% increase in CO during the 20- to 120-min period of exercise, which is in contrast to a 7% decline during exercise with NF (Fig. 1). The 7% increase in CO during FR occurred over a time when $\dot{V}O_2$ increased 6%. Additionally, Fig. 1 shows that the maintenance of hydration during FR compared with NF had little cardiovascular influence during the 1st h of exercise. It was during the 2nd h of exercise that differences emerged as rectal temperature and HR increased while SV and CO declined during NF compared with FR.

Having directly made these observations, the next logical questions are "what causes stroke volume to fall during the 2nd h of exercise without fluid replacement and by what mechanism does fluid replacement during exercise prevent stroke volume from declining"? Ekelund (11) has observed that the progressive decline in SV during prolonged exercise without FR is associated with a progressive decline in venous return to the heart as reflected by reductions in right ventricular and pulmonary arterial pressures. The reductions in SV during exercise occurred even when BV was maintained (11). Rowell (22, 23) has hypothesized that venous return and SV decline primarily due to a translocation of blood away from the central circulation due to reductions in venous tone caused by hyperthermia. In support of these ideas, Rowell and co-workers (24, 25) have observed that reductions in skin temperature and core temperature during exercise prevented SV from declining during exer-

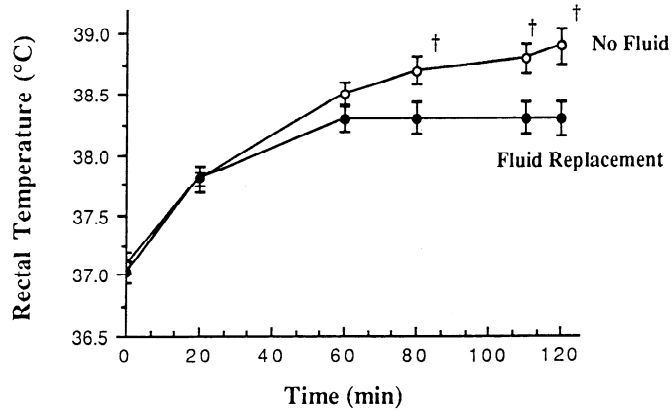

FIG. 2. Rectal temperature during 120 min of exercise at 70% $\dot{V}O_{2\,max}$ with subjects ingesting no fluid or with fluid replacement at a rate that maintained hydration. Values are means ± SE for 7 subjects. †At this time, no fluid is significantly higher than 60-min no fluid value as well as being different from fluid replacement at that corresponding time ($P < 0.05$).

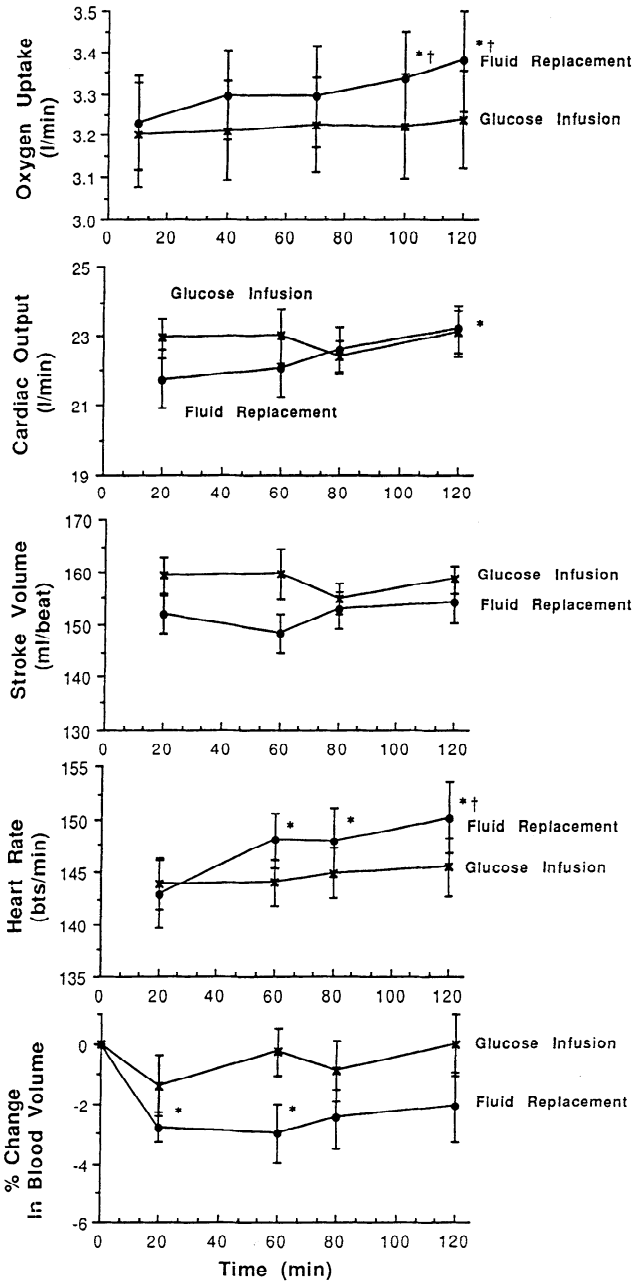

FIG. 3. Cardiovascular responses to 120 min of exercise at 70% $\dot{V}O_{2\,max}$ with fluid replacement at a rate that maintained hydration compared with intravenous glucose infusion of 1,224 ± 55 ml of an 18% glucose in water solution. Values are means ± SE for 8 subjects. *Significantly different from initial value (i.e., 0 min for blood volume, 10 min for $\dot{V}O_2$, and 20 min for other measures) for that trial ($P < 0.05$). †Fluid replacement is significantly different from glucose infusion at this corresponding time ($P < 0.05$).

cise. Therefore, it is likely that FR prevents the decline in SV because it somehow attenuates the increase in body temperature.

We have presently observed that FR stabilizes rectal temperature at 38.3 ± 0.1°C during the 2nd h of exercise, whereas rectal temperature continued to increase during exercise with NF ingestion and was 0.6°C higher after 120 min (Fig. 2). These observations agree with previous reports by others (5, 15). Because $\dot{V}O_2$ and therefore the rate of heat production were identical during the NF and FR trials, the lower rectal temperature during the 2nd h of FR resulted from greater heat dissipation. Sweating rate did not appear to be very different during FR than during NF (Table 1) and therefore we speculate that skin blood flow might have been higher during FR, which allowed a more effective core to skin heat transfer and, in turn, a smaller rise in rectal temperature. It should be realized, however, that to our knowledge, presently there are no direct data regarding the effects of FR during exercise on skin blood flow.

Despite the widespread interest in the influence of hydration on the physiological responses to exercise, it is surprising that the present study is the first to compare the SV and CO responses with exercise with and without FR. A few studies have examined the effects of dehydration vs. FR during exercise on the HR and BV responses to prolonged exercise (3, 5, 13, 18). Costill et al. (5) and Maughan et al. (18) have reported that fluid ingestion during 2 h of intense exercise (i.e., 70% $\dot{V}O_{2\,max}$) does not significantly alter the HR or BV responses to exercise compared with when no fluid was consumed. Candas et al. (3) and Francis (13) have shown that FR attenuates the increase in HR during mild exercise (<60% $\dot{V}O_{2\,max}$) and possibly minimizes the reductions in BV. However, these studies (3, 13) are difficult to interpret because BV appears to have been measured during rest intervals between exercise bouts. As shown in Fig. 1 and Table 2, we have observed that BV and plasma volume declined 4–7% below resting levels during the transition from rest to exercise and then displayed a further 2–3% reduction during the 20- to 120-min period of exercise with NF. In contrast, BV and plasma volume were maintained only 2% below resting levels throughout the duration of FR. These patterns are similar to those theorized by Costill and Miller (6). Therefore, BV was 5% ($P < 0.05$) or ~300 ml lower after 120 min of exercise during NF compared with FR, assuming that total BV was ~80 ml/kg in these subjects (16). Presently, we have no information regarding the extent to which these differences in BV (i.e., 300 ml at 120 min) contributed to differences in rectal temperature and SV during the 2nd hour of NF compared with FR. We previously reported that BV expansion by 300 ml increases SV during exercise in untrained men but not in endurance-trained subjects similar to those of the present study (16). It is unlikely that the presently observed differences in BV were the primary reason for SV differences during NF and FR because as previously discussed, SV has been observed to decline even when BV is maintained (11, 28). Furthermore, several of the subjects in the present study displayed little difference in BV during the 20- to 120-min period of NF and FR, yet rectal temperature was always higher, and SV lower, during the 2nd h of NF compared with FR.

Although the maintenance of hydration with water ingestion prevented SV from declining, it did not prevent HR and CO from increasing, probably in response to increased whole body $\dot{V}O_2$, all of which increased 5–7% during the 20- to 120-min period of exercise during FR (Figs. 1 and 3). Recently, Nielsen et al. (21) have observed that the whole body $\dot{V}O_2$ drift during exercise in the heat is not due to increased $\dot{V}O_2$ across the working legs, which suggests it is due to increased metabolism in organs and/or tissues other than the exercising skeletal

muscles. We observed that intravenous infusion of glucose and water, which maintained blood glucose concentration at 10 mM and partially offset dehydration, totally prevented $\dot{V}O_2$ and HR from increasing >1% during the 10- to 120-min period of exercise (i.e., 0.03 l/min and 1.5 beats/min, respectively; Fig. 3). It has been reported that β-receptor blockade with propranolol also prevents the drift upward in $\dot{V}O_2$ and HR during prolonged exercise, whereas cardioselective β_1-receptor blockade does not attenuate drift, which suggests that the $\dot{V}O_2$ drift may be due to catecholamine stimulation of β_2-receptors in peripheral tissues (17). Because intravenous GI during exercise reduces plasma epinephrine (14), it is possible that reductions in β_2-receptor stimulation of metabolism in peripheral tissue was also responsible for the absence of cardiovascular drift in the present study. We suspect that the liver may be a key organ responsible for some $\dot{V}O_2$ drift because during prolonged exercise in the fasted state, liver metabolism increases dramatically with the purpose of increasing glucose production (1, 2). Additionally, intravenous GI markedly suppresses liver metabolism and glucose production (30). It should be noted, however, that carbohydrate feedings during exercise that maintain blood glucose concentration at 5 mM do not appear to reduced the upward drift in $\dot{V}O_2$ during exercise (7).

We interpret these observations to suggest that the 5–7% increase in HR and CO during FR is in response to increased whole body oxidative metabolism in tissues that respond directly or indirectly (i.e., via catecholamines) to blood glucose concentration because the increase in oxidative metabolism was suppressed by hyperglycemia. When hydration was not maintained during exercise and SV declines, there is a further increase in HR (i.e., 10% during the 20- to 120-min period).

In summary, FR during exercise prevented the decline in SV observed during exercise without fluid replacement and resulted in a 7% increase in CO instead of a 7% decline in CO during 2 h of exercise. The cardiovascular benefits of fluid replacement became evident during the 2nd h of exercise and it was during this time that FR also prevented progressive hyperthermia. $\dot{V}O_2$ increased 6% during exercise both with and without FR. However, intravenous infusion of both glucose and water totally prevented an increase in $\dot{V}O_2$ or cardiovascular drift of HR or SV. Therefore, when euhydration is maintained during prolonged exercise, it appears that HR and CO increase in response to increased whole body oxidative metabolism, whereas dehydration and hyperthermia cause SV to decline and HR to increase disproportionate to $\dot{V}O_2$.

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