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Effect of carbohydrate ingestion on glucose kinetics during exercise in the heat

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Angus, Damien J., Mark A. Febbraio, David Lasini, and Mark Hargreaves. Effect of carbohydrate ingestion on glucose kinetics during exercise in the heat. *J Appl Physiol* 90: 601–605, 2001.—Six endurance-trained men [peak oxygen uptake ($\dot{V}O_2$) = 4.58 ± 0.50 (SE) l/min] completed 60 min of exercise at a workload requiring $68 \pm 2\%$ peak $\dot{V}O_2$ in an environmental chamber maintained at 35°C (<50% relative humidity) on two occasions, separated by at least 1 wk. Subjects ingested either a 6% glucose solution containing $1 \mu\text{Ci}$ [$3\text{-}^3\text{H}$]glucose/g glucose (CHO trial) or a sweet placebo (Con trial) during the trials. Rates of hepatic glucose production [HGP = glucose rate of appearance (R_a) in Con trial] and glucose disappearance (R_d), were measured using a primed, continuous infusion of [$6,6\text{-}^2\text{H}$]glucose, corrected for gut-derived glucose (gut R_a) in the CHO trial. No differences in heart rate, $\dot{V}O_2$, respiratory exchange ratio, or rectal temperature were observed between trials. Plasma glucose concentrations were similar at rest but increased ($P < 0.05$) to a greater extent in the CHO trial compared with the Con trial. This was due to the absorption of ingested glucose in the CHO trial, because gut R_a after 30 and 50 min ($16 \pm 5 \mu\text{mol}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$) was higher ($P < 0.05$) compared with rest, whereas HGP during exercise was not different between trials. Glucose R_d was higher ($P < 0.05$) in the CHO trial after 30 and 50 min (48.0 ± 6.3 vs $34.6 \pm 3.8 \mu\text{mol}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$, CHO vs. Con, respectively). These results indicate that ingestion of carbohydrate, at a rate of ~ 1.0 g/min, increases glucose R_d but does not blunt the rise in HGP during exercise in the heat.

heat stress; liver glucose output; muscle glucose uptake

THE REGULATION OF HEPATIC glucose production (HGP) during exercise involves a complex interplay of neural and hormonal factors and both “feedback” and “feed-forward” mechanisms (for review, see Ref. 9). Our laboratory has previously demonstrated that increasing circulating glucose concentration by exogenous feeding (10) or glucose infusion (6) blunts the increase in HGP during exercise. However, in the absence of exogenous carbohydrate supply, exercise in the heat results in hyperglycemia, which is due to an exaggerated increase in HGP (4). This is likely to be mediated by the augmented epinephrine response observed during exercise and heat stress (3, 4) because, in the

absence of differences in pancreatic hormones, elevated epinephrine results in greater HGP during exercise (7). Interestingly, when carbohydrate is ingested during exercise in the heat, the rise in plasma glucose is greater than that observed with carbohydrate ingestion during exercise at lower ambient temperatures (2). This suggests that, unlike carbohydrate feeding in comfortable ambient conditions, glucose ingestion in the heat may not have such marked suppression of HGP; however, this has never been experimentally investigated. Thus the aim of the present study was to investigate the effect of glucose ingestion on glucose kinetics during exercise in the heat to contrast the relative importance of the so-called feed-forward and feedback mechanisms. We hypothesized that glucose ingestion would elevate blood glucose concentration and would partially, but not completely, attenuate the increase in HGP during exercise in the heat.

METHODS

Subjects. Six male endurance-trained cyclists and/or triathletes [age 31 ± 1 (SE) yr, weight 79.9 ± 3.2 kg, height 181 ± 3 cm, peak pulmonary oxygen uptake ($\dot{V}O_{2\text{ peak}}$) 4.58 ± 0.20 l/min] volunteered to serve as subjects for the investigation, which was approved by the Deakin University Human Research Ethics Committee. The subjects had been involved in training for endurance sports for at least 5 yr and routinely trained in excess of 300–400 km/wk. Subjects were made fully aware of the procedures and risks associated with the study, both verbally and in writing. All subjects completed a medical questionnaire and provided written, informed consent. To determine $\dot{V}O_{2\text{ peak}}$, each subject performed incremental cycling (Lode, Groningen, The Netherlands) to volitional fatigue in mild environmental conditions ($20\text{--}22^\circ\text{C}$), with an electric fan circulating air to minimize thermal stress. $\dot{V}O_{2\text{ peak}}$ was determined at least 7 days before the first experimental trial.

Preexperimental protocol. Subjects were provided with a food parcel (~ 15.6 MJ, 71% carbohydrate, 15% protein, 14% fat) for the 24 h before an experimental trial. They were instructed to adhere to the diet, consume water ad libitum, and abstain from exercise, alcohol, tobacco, and caffeine in this period. On the morning of an experimental trial, subjects consumed 5 ml/kg of tap water on waking and arrived at the

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laboratory in a 10- to 12-h postabsorptive state. Our laboratory has previously found that these pretrial exercise and lifestyle controls result in reproducible metabolite and hormonal levels in subjects before each experimental trial (4).

Experimental trials. Each subject was studied on two separate occasions, separated by at least 7 days. All trials were performed in an environmental chamber maintained at 35°C, with a relative humidity of ~50%. In addition, an electric fan circulated air to facilitate evaporative cooling and to ensure a uniform temperature within the chamber. On arrival at the laboratory, subjects voided and were weighed nude, and a rectal thermistor probe (Monotherm, Mallenckrodt Medical, St. Louis, MO) was positioned 10–15 cm beyond the anal sphincter. Subjects rested supine, and catheters were inserted into an antecubital vein of one forearm for the collection of blood samples and in the contralateral arm for tracer infusion. The catheter for blood sampling was kept patent by flushing with 0.9% saline every 30 min during rest and after each blood sample. An initial blood sample was obtained, after which a primed (3.3 mmol), continuous (54.3 ± 2.3 $\mu\text{mol}/\text{min}$) infusion of [6,6-²H]glucose (Cambridge Isotope Laboratories, Cambridge, MA) was commenced and maintained during 2 h of rest and 60 min of exercise. Subjects sat in a chair at 20–25°C for the 2-h rest period before entering the chamber and commencing cycle ergometer exercise at $68 \pm 2\%$ $\dot{V}O_{2\text{ peak}}$. Subjects ingested either a 6% (wt/vol) glucose solution containing 1 μCi [3-³H]glucose/g glucose (CHO) or a sweet placebo (Con) during the exercise trials. At the onset of exercise, subjects consumed a 400-ml bolus of the test beverage, with an additional 150 ml ingested after 10, 20, 30, and 40 min of exercise for a total ingested volume of 1,000 ml during each trial. The beverages were administered in opaque containers in a randomized order, and the subject was unaware of the beverage type. Every 15 min during exercise, expired gas was collected into Douglas bags for measurement of ventilation rate, oxygen uptake ($\dot{V}O_2$), and respiratory exchange ratio (RER). Heart rate (Electro, Polar, Finland) and rectal temperature were monitored continuously and recorded every 10 min throughout exercise. Venous blood samples were obtained 10 and 5 min before exercise, immediately before exercise, and at 10-min intervals during exercise for analysis of plasma glucose and [6,6-²H]glucose enrichment and for [³H]glucose specific activity in the CHO trial. Additional blood samples were obtained before exercise and after 30 and 60 min of exercise for analysis of plasma lactate, insulin, glucagon, cortisol, epinephrine, and norepinephrine.

Analytic techniques. Dried expirate was analyzed for oxygen and carbon dioxide (Applied Electrochemistry S-3A/II and CD-3A, Ametek, Pittsburgh, PA) concentration. These analyzers were calibrated using commercial gases of known composition. The volume of expired air was measured on a gas meter (Parkinson-Cowan, Manchester, UK). Ten milliliters of blood were collected at each sampling time, an aliquot of which was placed into a tube containing fluoride heparin and spun in a centrifuge. The plasma was extracted and stored at –80°C for later analysis of plasma glucose and lactate using an automated method (EML-105, Electrolyte Metabolite Laboratory, Radiometer, Copenhagen, Denmark). From the same aliquot, plasma insulin (Inctar, Stillwater, MN), cortisol (Orion, Espoo, Finland), and glucagon (1) were measured by radioimmunoassay. A further aliquot (~1.5 ml) of the whole blood sample was placed into a tube containing a preservative (EGTA and reduced glutathione). The plasma was separated by centrifugation and was frozen at –80°C for later analysis of catecholamine concentrations using a single-isotope radioenzymatic method (TRK995, Amersham).

Plasma [6,6-²H]glucose enrichment was measured as described previously (10). Briefly, 500 μl of each plasma sample were deproteinized by addition of 500 μl of 0.3 M ZnSO_4 and 500 μl of 0.3 M $\text{Ba}(\text{OH})_2$ and subsequent mixing, preceding centrifugation. To remove charged metabolites, the supernatant was passed down an ion-exchange column (Dowex 2 \times 8, 200–400 mesh, Bio-Rad, Richmond, CA). The columns were washed with distilled water, and the resultant eluant was oven dried overnight to remove any deuterated water. The samples were then redissolved in 1.0 ml of distilled water. To determine the [³H]glucose specific activity in the plasma samples in the CHO trials, 100- μl aliquots of the reconstituted eluant were placed in scintillation vials and dried overnight, with the remaining 900 μl retained for evaluation of [6,6-²H]glucose enrichment. In addition, samples of the ingested [³H]glucose beverage were dehydrated. The resulting dry residues from both plasma and beverage samples were dissolved in 0.5 ml of distilled water and 10 ml of scintillation cocktail (Ready Value, Beckman, Fullerton, CA) before refrigeration for 60 min. The samples were counted in a liquid scintillation counter (model LS 3801, Beckman), and the specific activity of each sample calculated. The remaining 900 μl of the reconstituted eluant were placed in glass vials, dehydrated, and derivatized to the pentaacetate derivative by the addition of a pyridine and acetic anhydride cocktail. The derivatized-glucose level was measured with a gas chromatograph-mass spectrometer (5890 series 2 gas chromatograph, 5971 mass spectrometer detector, Hewlett-Packard, Avondale, PA). Glucose kinetics at rest and during exercise were calculated with a modified one-pool, non-steady-state model (15), assuming a pool fraction of 0.65 and estimating the apparent glucose space as 25% of body weight. Glucose rate of appearance (R_a) and glucose rate of disappearance (R_d) were determined from changes in the percent enrichment in the plasma of [6,6-²H]glucose. In the Con trial, glucose R_a measures total endogenous glucose R_a . Although the kidney is capable of gluconeogenesis, during exercise the liver is likely to be the predominant, if not sole, source of the increase in glucose production (16). Thus, in the Con trial, HGP was equal to total R_a , whereas, in the CHO trial, HGP was calculated as the difference between the measured total R_a and the glucose R_a from the ingested beverage (gut R_a ; Ref. 14). The metabolic clearance rate (MCR) of glucose was calculated by dividing glucose R_d by the prevailing plasma glucose concentration.

Statistical analysis. The data from the Con and CHO trials were compared using a two-factor (time and treatment) ANOVA with repeated measures with significance at the $P < 0.05$ level. Specific differences were located using the Student-Newman-Keul's post hoc test when ANOVA revealed a significant interaction. All data are reported as means \pm SE.

RESULTS

During 60 min of exercise at $68 \pm 2\%$ of $\dot{V}O_{2\text{ peak}}$, there were no differences between trials in average $\dot{V}O_2$, RER, and heart rate (Table 1). The increase ($P < 0.05$) in rectal temperature during exercise was similar in the two trials (Table 1).

Plasma glucose concentrations were similar at rest and increased during exercise in both trials (Fig. 1). After 40 min of exercise, plasma glucose was higher ($P < 0.05$) in the CHO trial, compared with the Con trial, whereas, at 60 min, it tended ($P = 0.06$) to be higher in the CHO trial. HGP was similar at rest and increased during exercise in both trials (Fig. 1). There

Table 1. Average $\dot{V}O_2$, RER, and heart rate during, and rectal temperature before and after, 60 min of exercise at $68 \pm 2\%$ $\dot{V}O_{2peak}$ in CHO and Con trials

	Con Trial	CHO Trial
$\dot{V}O_2$, l/min	3.01 ± 0.20	3.21 ± 0.11
RER	0.94 ± 0.02	0.95 ± 0.02
Heart rate, beats/min	163 ± 6	162 ± 5
T_{re} , °C		
Preexercise	36.9 ± 0.1	37.0 ± 0.0
Postexercise	38.7 ± 0.1	38.7 ± 0.1

Values are means \pm SE for 6 subjects. Con trial, without carbohydrate ingestion; CHO trial, with carbohydrate ingestion; $\dot{V}O_2$, oxygen uptake; $\dot{V}O_{2peak}$, peak $\dot{V}O_2$; RER, respiratory exchange ratio; T_{re} , rectal temperature.

were no differences, however, in HGP between trials. Total glucose R_a increased during exercise and was higher ($P < 0.05$) during the last 30 min in the CHO trial compared with the Con trial. The elevated glucose

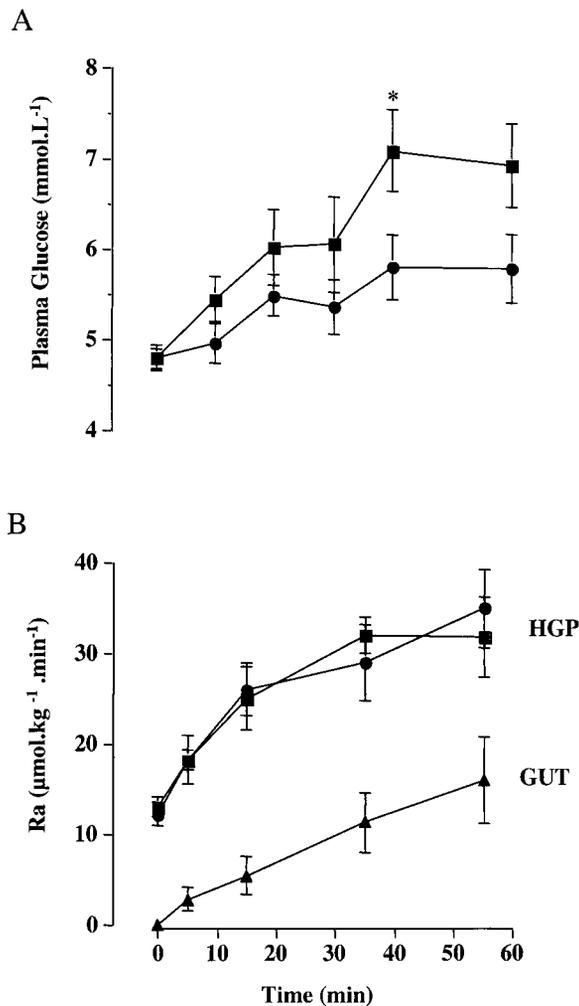


Fig. 1. Plasma glucose concentrations (A) and rates of glucose appearance (R_a ; B) from the liver [hepatic glucose production (HGP)] and ingested glucose (GUT) during 60 min of exercise at $68 \pm 2\%$ peak oxygen uptake in the heat during trials with (■) and without (●) carbohydrate ingestion. Values are means \pm SE for 6 subjects. *Different from the Con trial, $P < 0.05$. All exercise values beyond 10 min are different from preexercise, $P < 0.05$.

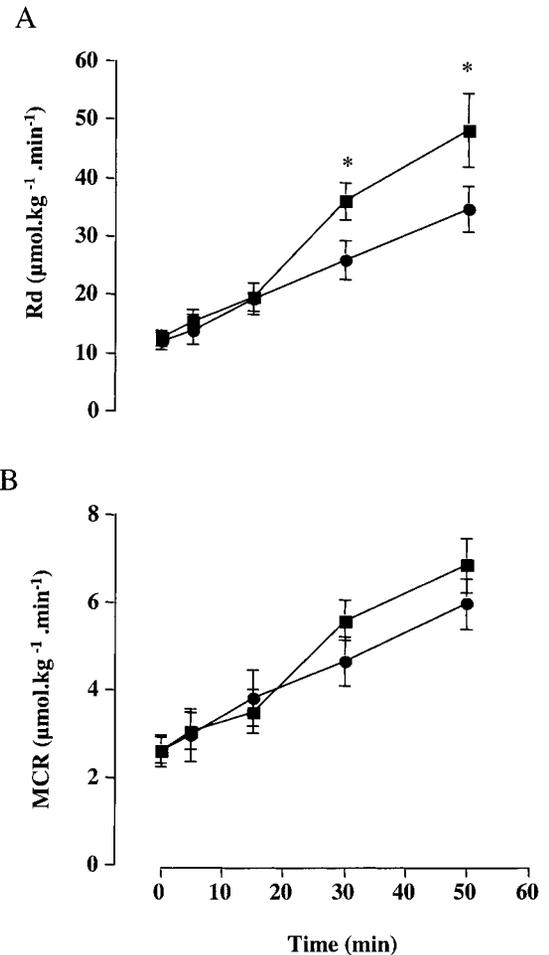


Fig. 2. Whole body glucose uptake (glucose R_d ; A) and metabolic clearance rate (MCR; B) during 60 min of exercise at $68 \pm 2\%$ peak oxygen uptake in the heat during trials with (■) and without (●) carbohydrate ingestion. Values are means \pm SE for 6 subjects. *Different from the Con trial, $P < 0.05$. All exercise values beyond 20 min are different from preexercise, $P < 0.05$.

R_a in the CHO trial was not due to changes in HGP but rather the appearance of glucose from the ingested beverage. Gut R_a increased throughout exercise in the CHO trial, reaching a peak value of $16 \pm 5 \mu\text{mol}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$ in the final 10 min of exercise (Fig. 1). Glucose R_d increased in both trials; however, during the last 30 min of exercise, it was higher ($P < 0.05$) in the CHO than in Con trial (Fig. 2).

MCR during exercise was similar in the two trials (Fig. 2). There were no differences between trials in plasma lactate, insulin, glucagon, cortisol, epinephrine, or norepinephrine during exercise (Table 2), although all except plasma insulin increased during exercise (Table 2).

DISCUSSION

The major finding of the present study was that, during exercise in a hot environment, glucose ingestion at the rate of ~ 1 g/min did not attenuate HGP even though it significantly elevated plasma glucose. This finding is in contrast with previous observations (8, 10)

Table 2. Plasma concentrations of lactate, insulin, glucagon, epinephrine, norepinephrine, and cortisol before and during 60 min of exercise at $68 \pm 2\%$ $\dot{V}O_{2peak}$ in CHO or Con trials

	Preexercise	30 min	60 min
Lactate, mmol/l			
Con	0.9 ± 0.1	3.8 ± 0.7*	4.4 ± 1.1*
CHO	0.9 ± 0.1	4.2 ± 1.3*	4.2 ± 1.2*
Insulin, pmol/l			
Con	74 ± 10	58 ± 8	65 ± 16
CHO	64 ± 3	88 ± 15	94 ± 15
Glucagon, ng/ml			
Con	47 ± 5	50 ± 7	71 ± 10*
CHO	45 ± 13	53 ± 10	71 ± 20*
Epinephrine, nmol/l			
Con	0.46 ± 0.28	1.37 ± 0.36*	1.96 ± 0.79*
CHO	0.63 ± 0.17	1.53 ± 0.56*	1.69 ± 0.45*
Norepinephrine, nmol/l			
Con	2.0 ± 0.5	12.5 ± 4.5*	16.0 ± 6.3*
CHO	2.0 ± 0.9	12.1 ± 5.7*	15.0 ± 7.4*
Cortisol, nmol/l			
Con	422 ± 47	497 ± 82	655 ± 231*
CHO	390 ± 80	524 ± 74	703 ± 231*

Values are means ± SE for 6 subjects. *Different from preexercise, main effect, $P < 0.05$.

during exercise in comfortable ambient conditions, where even modest amounts of ingested carbohydrate blunted the exercise-induced rise in liver glucose output. Our data suggest a marked feed-forward stimulation of liver glucose output during exercise and heat stress that is less sensitive to inhibition by increased blood glucose availability.

It has been previously demonstrated that increasing circulating glucose by glucose ingestion (5, 8, 10) or infusion (6) attenuated the rise in HGP during exercise in comfortable ambient conditions. It is interesting to note that, in these previous studies that have measured HGP with glucose ingestion, the amount ingested was 0.6 (8), 1.7 (10), and 3.0 g/min (8). Despite the wide range in the amount of exogenous carbohydrate supplied in these studies, HGP did not rise during exercise. In contrast, although we fed the subjects carbohydrate at a rate of ~1 g/min, HGP was increased to a similar extent in the two trials (Fig. 1). Thus our data suggest that exogenous heat stress renders glucose availability less important in mediating HGP during exercise. During exercise in the heat, blood flow to the splanchnic bed is reduced (13), which may be a consequence of increased plasma catecholamines during exercise in the heat (Table 2; Ref. 4). This reduction in splanchnic blood flow, and a decreased rate of gastric emptying (11), could delay the absorption and appearance of ingested glucose. Indeed, the measured gut R_a in the present study was lower than values our laboratory have observed after carbohydrate ingestion during exercise at 20–22°C, albeit with a higher beverage glucose concentration (10). Despite this, the peak plasma glucose levels observed in CHO (Fig. 1) were still 1–2 mmol/l higher than in previous studies in which an attenuated HGP has been observed (5, 8, 10).

The inhibitory effects of increased blood glucose availability on liver glucose output during exercise may be due to a direct effect on the liver (12) and/or alterations in the plasma levels of various glucoregulatory hormones thought to regulate liver glucose output. Our laboratory has previously observed that glucose ingestion or infusion increases plasma insulin levels (10) and attenuates the increases in plasma glucagon (10) and catecholamines (6, 10) during strenuous exercise. Furthermore, our laboratory has suggested that higher plasma levels of catecholamines, cortisol, and growth hormone could contribute to the greater liver glucose output during exercise in the heat (4). In the present study, there were no differences in plasma hormone levels between trials (Table 2), despite the higher plasma glucose levels when carbohydrate was ingested (Fig. 1). Thus the combination of exercise and heat stress results in greater activation of the neuroendocrine pathways responsible for liver glucose output and renders blood glucose less effective in modifying these responses. Our laboratory has previously suggested that the balance between neuroendocrine feed-forward activation and humoral feedback inhibition of liver glucose output depends on the interaction between motor center activity, as determined by exercise intensity, and the prevailing glucose and insulin levels (6). Our present results suggest that the addition of heat stress at a given exercise intensity shifts this balance in favor of activation. We are not able to ascertain the exact signal responsible for this exaggerated feed-forward activation with heat stress. Core temperature is higher during exercise in the heat (3, 4), although our laboratory has observed differences in perceived exertion after only 5–10 min of exercise in the heat at a time when rectal temperatures are not yet significantly different (4). One possibility is that the increased skin temperature contributes to the greater “stress” experienced during exercise in the heat.

Glucose R_d , a measure of skeletal muscle glucose uptake during exercise, was increased during the latter stages of exercise when the subjects were fed carbohydrate (Fig. 2), consistent with previous observations (8, 10). This is most likely a consequence of increased plasma glucose because MCR was similar in the two trials (Fig. 2). The functional significance of this small increase in glucose R_d is small. The slight increase in total carbohydrate oxidation we observed in the CHO trial was not statistically significant. If we assume that all of the glucose R_d was taken up and oxidized by contracting skeletal muscle, we can derive a minimal estimate of total glycogen oxidation, which was not different between trials (data not shown).

In summary, in contrast to studies conducted in comfortable ambient conditions, carbohydrate feeding at a rate of ~1 g/min does not attenuate liver glucose output during exercise in the heat, despite relative hyperglycemia. Thus the stress associated with exercise in the heat results in marked feed-forward stimulation of liver glucose output, which renders feed-back mechanisms less effective.

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REFERENCES

1. Alford FP, Bloom SR, and Nabarro JDN. Glucagon levels in normal and diabetic subjects: use of a specific immunoabsorbent for glucagon radioimmunoassay. *Diabetologia* 13: 1–6, 1977.
2. Febbraio MA, Murton P, Selig SE, Clark SA, Lambert DL, Angus DJ, and Carey MF. Effect of CHO ingestion on exercise metabolism and performance in different ambient temperatures. *Med Sci Sports Exerc* 28: 1380–1387, 1996.
3. Febbraio MA, Snow RJ, Hargreaves M, Stathis CG, Martin IK, and Carey MF. Muscle metabolism during exercise and heat stress in trained men: effect of acclimation. *J Appl Physiol* 76: 589–597, 1994.
4. Hargreaves M, Angus D, Howlett K, Marmy Conus N, and Febbraio M. Effect of heat stress on glucose kinetics during exercise. *J Appl Physiol* 81: 1594–1597, 1996.
5. Horowitz JF, Mora-Rodriguez R, Byerley LO, and Coyle EF. Substrate metabolism when subjects are fed carbohydrate during exercise. *Am J Physiol Endocrinol Metab* 276: E828–E835, 1999.
6. Howlett K, Angus DJ, Proietto J, and Hargreaves M. Effect of increased blood glucose availability on glucose kinetics during exercise. *J Appl Physiol* 84: 1413–1417, 1998.
7. Howlett K, Febbraio M, and Hargreaves M. Glucose production during strenuous exercise in humans: role of epinephrine. *Am J Physiol Endocrinol Metab* 276: E1130–E1135, 1999.
8. Jeukendrup AE, Wagenmakers AJ, Stegen JH, Gijzen AP, Brouns F, and Saris WH. Carbohydrate ingestion can completely suppress endogenous glucose production during exercise. *Am J Physiol Endocrinol Metab* 276: E672–E683, 1999.
9. Kjaer M. Hepatic fuel metabolism during exercise. In: *Exercise Metabolism*, edited by Hargreaves M. Champaign, IL: Human Kinetics, 1995, p. 73–97.
10. McConell G, Fabris S, Proietto J, and Hargreaves M. Effects of carbohydrate ingestion on glucose kinetics during exercise. *J Appl Physiol* 77: 1537–1541, 1994.
11. Neuffer PD, Young AJ, and Sawka MN. Gastric emptying during exercise: effect of heat stress and hypohydration. *Eur J Appl Physiol* 58: 433–439, 1989.
12. Rossetti L, Giaccari A, Barzalai N, Howard K, Sebel G, and Hu M. Mechanisms by which hyperglycemia inhibits hepatic glucose production in conscious rats. Implications for pathophysiology of fasting hyperglycemia in diabetes. *J Clin Invest* 92: 1126–1134, 1993.
13. Rowell LB, Brengelmann GL, Blackmon JR, Twiss RD, and Kasumi F. Splanchnic blood flow and metabolism in heat-stressed man. *J Appl Physiol* 24: 475–484, 1968.
14. Steele R, Bjerknes C, Rathgeb I, and Altszuler N. Glucose uptake and production during the oral glucose tolerance test. *Diabetes* 17: 415–421, 1968.
15. Steele R, Wall JS, DeBodo RC, and Altszuler N. Measurement of the size and turnover rate of body glucose pool by isotopic dilution method. *Am J Physiol* 187: 15–24, 1956.
16. Wahren J, Felig P, Ahlborg G, and Jorfeldt L. Glucose metabolism during leg exercise in man. *J Clin Invest* 50: 2715–2725, 1971.

