Preexercise medium-chain triglyceride ingestion does not alter muscle glycogen use during exercise

Jeffrey F. Horowitz, Ricardo Mora-Rodriguez, Lauri O. Byerley, and Edward F. Coyle

Department of Kinesiology and Health Education, The Human Performance Laboratory, The University of Texas at Austin, Austin, Texas 78712

Preexercise medium-chain triglyceride ingestion does not alter muscle glycogen use during exercise. J. Appl. Physiol. 88: 219–225, 2000.—This investigation determined whether ingestion of a tolerable amount of medium-chain triglycerides (MCT; 25 g) reduces the rate of muscle glycogen use during high-intensity exercise. On two occasions, seven well-trained men cycled for 30 min at 84% maximal O2 uptake. Exactly 1 h before exercise, they ingested either 1) carbohydrate (CHO; 0.72 g sucrose/kg) or 2) MCT (0.36 g tricaprin C10:0/kg plus 0.72 g sucrose/kg). The change in glycogen concentration was measured in biopsies taken from the vastus lateralis before and after exercise. Additionally, glycogen oxidation was calculated as the difference between total carbohydrate oxidation and the rate of glucose disappearance from plasma (Rd glucose), as measured by stable isotope dilution techniques. The change in muscle glycogen concentration was not different during MCT and CHO (42.0 ± 4.6 vs. 38.8 ± 4.0 µmol glucosyl units/g wet wt). Furthermore, calculated glycogen oxidation was similar (331 ± 18 vs. 329 ± 15 µmol·kg−1·min−1). The coingestion of MCT plus CHO did increase (P < 0.05) Rd glucose at rest compared with CHO (26.9 ± 1.5 vs. 20.7 ± 0.7 µmol·kg−1·min−1), yet during exercise Rd glucose was not different during the two trials. Therefore, the addition of a small amount of MCT to preexercise CHO meal did not reduce muscle glycogen oxidation during high-intensity exercise, but it did increase glucose uptake at rest.

medium-chain triglycerides; glucose uptake; glycogenolysis; ketone bodies; stable isotopes

The costs of publication of this article were defrayed in part by the payment of page charges. The article must therefore be hereby marked “advertisement” in accordance with 18 U.S.C. Section 1734 solely to indicate this fact.
for MCT to reduce muscle glycogen utilization during exercise. Muscle glycogen use was assessed by using two independent methods. The change in glycogen concentration during exercise in the vastus lateralis was determined from biopsies. Additionally, glycogen oxidation during exercise was calculated as total carbohydate oxidation minus the rate of glucose disappearance from plasma (Ra) (determined from dilution of a constant-rate intravenous infusion of \([6,6\text{-d}_2]\text{glucose}\)).

**METHODS**

Subjects and general experimental design. Seven, well-trained cyclists participated in this experiment. Their \(\text{VO}_{2\text{max}}\) was 4.6 ± 0.3 l/min (61.5 ± 2.5 ml·kg\(^{-1}\)·min\(^{-1}\)), and their mean body weight was 75.1 ± 4.0 kg. Subjects were informed of the possible risks involved, and each signed a consent form, approved by the Internal Review Board of The University of Texas at Austin. On two occasions they cycled on an ergometer for 30 min at 84 ± 1% \(\text{VO}_{2\text{max}}\) 1 h after ingesting either carbohydrate alone or in combination with MCT. Two days before each trial the subjects performed the experimental exercise protocol (30 min at 84% \(\text{VO}_{2\text{max}}\)) to familiarize themselves with the procedure and to ensure homogeneity of the last exercise bout. During the day before both trials the subjects did not exercise and consumed a standardized diet.

Experimental procedures. On two occasions, separated by 5–7 days, subjects arrived at the laboratory in the morning after an overnight fast (12 h). On arrival, Teflon catheters were inserted into a forearm vein of both arms, one for isotope infusion, the other for blood sampling, and a heating pad was affixed to the hand and forearm of the sampling arm. Thereafter, they received a primed, constant-rate infusion of \([6,6\text{-d}_2]\text{glucose}\) (0.39 µmol·kg\(^{-1}\)·min\(^{-1}\); prime = 33 µmol/kg) by using a calibrated syringe pump (Harvard Apparatus, South Natick, MA) while resting for at least 1 h. Exactly 1 h before exercise, they ingested one of two test meals: 1) carbohydrate (CHO; 0.72 g sucrose/kg body wt; ~50 g) or 2) MCT + CHO (0.36 g tricaprin/kg body wt; ~25 g; 0.72 g sucrose/kg). CHO was provided as a viscous paste, whereas MCT + CHO was combined into a chewable solid that dissolved at body temperature. Water was ingested with both meals (3.6 ml/kg body wt; ~250 ml). Exactly 1 h after ingestion of the test meal, the subjects cycled for 2 min at ~60% \(\text{VO}_{2\text{max}}\) and then 28 min at 84% \(\text{VO}_{2\text{max}}\) (total of 30 min). The order of the trials was counterbalanced. Muscle biopsies (~40–80 mg) were taken from the vastus lateralis (4) 30 min before and immediately after exercise. The samples were immediately frozen in liquid nitrogen and stored at −80°C for later determination of glycogen concentration. Blood samples were drawn every 10 min at rest after ingestion and at 5-min intervals throughout exercise. \(\text{O}_2\) uptake (\(\text{VO}_2\)) and \(\text{CO}_2\) production (\(\text{VCO}_2\)) were measured from 0–15 and 18–30 min via open-circuit spirometry.

Analytic procedures. Eight milliliters of blood were withdrawn for each sample. Plasma was separated by centrifugation, stored at −80°C, and later analyzed for concentration of glucose (YSI 23a glucose autoanalyzer; Yellow Springs Instruments, Yellow Springs, OH), glycerol (9), FFA (23), lactate (13), \(\beta\)-hydroxybutyrate (36), and insulin (radioimmunoassay; I CN Biomedicals, Costa Mesa, CA). In addition, plasma isotopic enrichment of the aldolitrite acetate derivative of \([6,6\text{-d}_2]\text{glucose}\) (33) was determined via gas chromatography-mass spectrometry (GCMS) for calculations of the rate of appearance (Ra) and Rd of glucose (see below).

Isotope enrichment sample preparation. Plasma samples (1 ml) were deproteinized by adding 1 ml 0.3 N \(\text{Ba(OH)}_2\) and 1 ml 0.3 N \(\text{Zn(SO)}_4\). Each tube was then vortexed and incubated in an ice bath for 20 min. After centrifugation (3,000 rpm for 15 min at 4°C), the supernatant was placed into a clean tube and the water was removed via vacuum centrifugation (Svant Instruments, Farmingdale, NY). The aldolitrite acetate derivative of glucose was prepared by adding 100 µl hydroxylamine-hydrochloride solution (20 mg/ml in pyridine) to the dried sample. After a 30-min incubation at 100°C, 75 µl of acetic anhydride (Supelco, Bellefonte, PA) were then added, and the samples remained incubating for 1 additional hour. Finally, the samples were evaporated under \(\text{N}_2\). Before injection into the GCMS, the samples were reconstituted with ethyl acetate.

Muscle glycogen concentration. The frozen muscle sample was weighed, mechanically homogenized in a glycerol-
\(\text{Na}_3\text{PO}_4\) buffer, hydrolyzed in 2 N \(\text{HCl}\) (2 h), and neutralized with \(\text{NaOH}\). Glucose concentration of the hydrolysate was determined enzymatically (24).

Measurement of gas exchange. Inspired air volume was measured continuously with a Parkinson-Cowan CD4 dry-gas meter (Rayfield Equipment, Waitsfield, VT). The expired gases were constantly sampled from a mixing chamber and analyzed for oxygen (model SA3, Applied Electrochemistry, Ametek, Pittsburgh, PA) and carbon dioxide (model LB-2, Beckman, Schiller Park, IL). These instruments were interfaced with a computer for calculations of the rate of \(\text{VO}_2\), rate of \(\text{VCO}_2\), and respiratory exchange ratio (RER).

Calculations. \(R_a\) glucose and \(R_d\) glucose were calculated by using the non-steady-state equation of Steele (32), modified for use with stable isotopes

\[
R_a \text{ glucose} = \frac{F - V_d \cdot [(C_2 + C_1)/2] [(E_2 - E_1)/(t_2 - t_1)]}{(E_1 + E_2)/2}
\]

\[
R_d \text{ glucose} = R_a - V_d \cdot [(C_2 - C_1)/(t_2 - t_1)]
\]

where \(F\) is the isotope infusion rate, \(V_d\) is the glycolic volume of distribution (estimated to be 100 ml/kg), \(C_1\) and \(C_2\) are the plasma glycerol concentrations at times 1 and 2 (\(t_1\) and \(t_2\)), respectively, and \(E_1\) and \(E_2\) are isotopic enrichment at \(t_1\) and \(t_2\), respectively. Carbohydrate and fat (i.e., triglyceride) oxidations were calculated from \(\text{VO}_2\) and \(\text{VCO}_2\) (10). It has been reported that the calculation of carbohydrate and fat oxidation from \(\text{VO}_2\) and \(\text{VCO}_2\) in trained cyclists exercising at 85% \(\text{VO}_{2\text{max}}\) (identical conditions as in the present study) was the same as that measured by using an alternative method (\(1^\circ\text{C}/^\circ\text{C}\) ratio in breath) that does not rely on \(\text{VCO}_2\) for calculating substrate oxidation (26).

During moderate-intensity exercise (65–75% \(\text{VO}_{2\text{max}}\)) >90% of \(R_d\) glucose is oxidized (5, 17); thus \(R_d\) glucose provides a reasonable representation of blood glucose oxidation. Because carbohydrate oxidation is derived primarily from blood glucose and muscle glycogen, the difference between total carbohydrate oxidation and \(R_d\) glucose is a reasonable measure of the rate of muscle glycogen oxidation in this condition, as we have previously described (27, 28). During high-intensity exercise, however, when lactate accumulates, \(R_d\) glucose may overestimate blood glucose oxidation by the extent to which the blood glucose that disappears from the circulation is not oxidized and is converted to lactic acid. Therefore, the difference between total carbohydrate oxidation and \(R_d\) glucose represents the minimum rate of muscle glycogen oxidation.

Statistical analysis. Data were analyzed by using a two-way ANOVA (treatment by time) for repeated measures with Tukey’s post hoc analysis. Planned comparisons for mean...
values were made by using paired Student's t-tests, with P < 0.05.

RESULTS

The average power output was identical during both trials (286 ± 22 W; 84 ± 1% VO$_2$$\text{max}$). As shown in Table 1, the average (5- to 30-min) energy expenditure, VO$_2$, RER, heart rate, and rating of perceived exertion were also similar during the two trials. Furthermore, carbohydrate oxidation was equally high throughout exercise during both CHO and MCT + CHO (360 ± 15 and 364 ± 17 µmol · kg$^{-1}$·min$^{-1}$, respectively).

Plasma glucose kinetics and concentration. The mean rate of R$_a$ glucose at rest before exercise was greater (P < 0.05) during MCT + CHO compared with CHO (25.4 ± 1.0 vs. 20.8 ± 0.8 µmol · kg$^{-1}$·min$^{-1}$) (Fig. 1A). Similarly, the mean rate of R$_d$ glucose from plasma was also 30% greater (P < 0.05) before exercise during MCT + CHO compared with CHO (26.9 ± 1.5 vs. 20.7 ± 0.7 µmol · kg$^{-1}$·min$^{-1}$) (Fig. 1B). Plasma glucose concentration increased transiently during the 30-min period after ingestion of both meals, and then decreased during the 30- to 60-min period after ingestion as glucose uptake (R$_d$ glucose) exceeded R$_a$ glucose. Immediately before exercise, plasma glucose concentration was lower (P < 0.05) during MCT + CHO compared with CHO (4.4 ± 0.2 and 5.1 ± 0.1 mM, respectively).

During exercise, the mean R$_a$ glucose during MCT + CHO was significantly greater (P < 0.05) than that during CHO (38.0 ± 1.6 vs. 33.4 ± 1.5 µmol · kg$^{-1}$·min$^{-1}$), yet R$_d$ glucose was the same during both trials (Fig. 1B). Although plasma glucose concentration was similar between the two trials during exercise (Fig. 1C), the increase in plasma glucose concentration was greater (P < 0.05) during MCT + CHO compared with CHO (37 ± 10% and 13 ± 9%, respectively).

Plasma insulin concentration. In accordance with R$_a$ glucose, the plasma insulin response, calculated as the integrated area under the insulin vs. time curve at rest, was also significantly greater (P < 0.05) during the hour after ingesting MCT + CHO compared with CHO (1,199 ± 276 and 895 ± 233 µU · min$^{-1}$·ml$^{-1}$, respectively). During exercise, plasma insulin concentration declined to basal levels, and no differences were observed between MCT + CHO and CHO (6.2 ± 1.3 and 6.7 ± 1.1 µU/ml at 30 min of exercise, respectively).

Table 1. Average responses during 30 min of exercise at 84% VO$_2$$\text{max}$

<table>
<thead>
<tr>
<th></th>
<th>CHO</th>
<th>MCT + CHO</th>
</tr>
</thead>
<tbody>
<tr>
<td>Energy expended, kcal</td>
<td>580 ± 33</td>
<td>583 ± 36</td>
</tr>
<tr>
<td>VO$_2$, l/min</td>
<td>3.85 ± 0.22</td>
<td>3.86 ± 0.24</td>
</tr>
<tr>
<td>RER</td>
<td>0.98 ± 0.01</td>
<td>0.99 ± 0.01</td>
</tr>
<tr>
<td>HR, beats/min</td>
<td>167 ± 2</td>
<td>168 ± 3</td>
</tr>
<tr>
<td>RPE</td>
<td>15.3 ± 0.5</td>
<td>15.6 ± 0.4</td>
</tr>
<tr>
<td>CHO oxidation, µmol · kg$^{-1}$·min$^{-1}$</td>
<td>360 ± 15</td>
<td>364 ± 17</td>
</tr>
<tr>
<td>Fat oxidation, µmol · kg$^{-1}$·min$^{-1}$</td>
<td>1.5 ± 0.8</td>
<td>1.2 ± 0.9</td>
</tr>
</tbody>
</table>

Values are means ± SE. VO$_2$$\text{max}$, maximal O$_2$ consumption; CHO, carbohydrate; MCT, medium-chain triglycerides; VO$_2$, O$_2$ uptake; RER, respiratory exchange ratio; HR, heart rate; RPE, rating of perceived exertion.

Plasma substrate concentrations. Plasma FFA and glycerol concentrations decreased during the hour after the ingestion of both meals; however, only the reduction in plasma FFA was statistically significant (P < 0.05), and there were no differences in either plasma FFA or glycerol concentrations between trials (Fig. 2). During exercise, plasma glycerol increased (P < 0.05) above preexercise values, whereas plasma FFA concentration remained low (<150 M). Thirty minutes after ingestion, plasma β-hydroxybutyrate concentration was greater (P < 0.05) during MCT + CHO compared with CHO (40 ± 8 vs. 18 ± 3 mM) (Fig. 3), and it remained more than twofold greater throughout exercise (P < 0.05). Because of the high-intensity exercise, plasma lactate concentration increased (P < 0.05) from ~2 mM at rest to 11.8 ± 13 and 11.8 ± 19 mM at the end of exercise during MCT + CHO and CHO, respectively.

Muscle glycogen. The concentration of muscle glycogen within the vastus lateralis was similar before both
trials (Table 2), and the reduction in glycogen concentration during exercise was not different for CHO and MCT

\[ \text{CHO} = 38.8 \pm 4.0 \text{ mmol/kg wet weight (ww), respectively}. \]

In addition, because both \( R_d \) glucose and carbohydrate oxidation were similar during exercise in both trials, the calculated minimum rate of muscle glycogen oxidation was also similar during CHO and MCT+CHO \( (329 \pm 15 \text{ and } 331 \pm 18 \text{ mmol kg}^{-1} \text{ min}^{-1}, \text{ respectively}) \). Therefore, two methods concur that muscle glycogen utilization was not different during MCT+CHO compared with CHO.

**DISCUSSION**

In previous studies, MCT have not been ingested under conditions where endogenous fat mobilization is very low, and exogenous fat supplementation is known to increase fat oxidation and reduce muscle glycogenolysis. The present study was designed to provide such optimal conditions to determine whether MCT ingestion can potentially reduce muscle glycogen oxidation. First, the combination of preexercise carbohydrate ingestion and high-intensity exercise reduced plasma FFA concentration to very low levels \( (<150 \text{ M}) \). Second, during high-intensity exercise most energy is derived from muscle glycogen \( (27) \). Thus any energy derived from the exogenous MCT would likely be reflected as a reduction in muscle glycogen oxidation. Finally, a high glycolytic flux, such as that observed during high-intensity exercise or during exercise after a preexercise carbohydrate meal, has been shown to decrease LCT oxidation without impairing MCT oxidation \( (6, 31) \). The principal finding of this study, however, was that the addition of \( \approx 25 \text{ g of MCT to a carbohydrate meal did not reduce either net muscle glycogen utilization or calculated glycogen oxidation, even under these theoretically idealized conditions of high-intensity exercise after a carbohydrate feeding.} \)

The addition of MCT to the carbohydrate meal did, however, significantly alter blood glucose kinetics at rest and during exercise. We found that adding MCT to a carbohydrate meal increased glucose availability in plasma throughout the study. It is known that coincesting MCT and carbohydrate increases gastric emptying compared with an equicaloric carbohydrate meal \( (3) \); however, the effect of adding MCT to a given amount of carbohydrate has not been studied. Our findings suggest that MCT may increase gastric emptying and intestinal absorption of the coingested carbohydrate. The resultant elevated plasma insulin response during MCT+CHO caused a greater \( R_d \) glucose at rest during MCT+CHO compared with CHO. During exercise, however, despite an elevated \( R_d \) glucose during MCT+CHO, \( R_d \) glucose and presumably plasma glu-

<table>
<thead>
<tr>
<th>Table 2. Muscle glycogen concentration within the vastus lateralis</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>CHO</strong></td>
</tr>
<tr>
<td>Preexercise muscle glycogen concentration</td>
</tr>
<tr>
<td>Postexercise muscle glycogen concentration</td>
</tr>
<tr>
<td>Net muscle glycogen utilization</td>
</tr>
</tbody>
</table>

Values are means ± SE expressed as mmol/kg wet wt.
cose oxidation were not different during the two trials. Similarly, it has been found that the addition of MCT to carbohydrate feedings during exercise did not alter exogenous carbohydrate oxidation (18). It is likely that the equally high rates of muscle glycogenolysis during MCT+CHO and CHO may have prevented further increase in glucose uptake during MCT+CHO, despite an elevated Rg glucose and a greater preexercise plasma insulin response. Therefore, neither the energy contribution of ingested MCT nor its effect on glucose kinetics altered substrate oxidation during high-intensity exercise.

Unlike fat supplementation via infusion of LCT and heparin, MCT ingestion does not increase plasma FFA concentration (16, 22, 30). However, the absence of a detectable increase in the concentration of plasma FFA does not indicate that the energy from the ingested MCT was not delivered to the systemic circulation. Massicotte et al. (22) reported that nearly 60% of a 13C-labeled MCT meal was oxidized during exercise without an elevation in plasma FFA concentration above control. This may be explained by a very rapid oxidation of medium-chain fatty acids, preventing their accumulation in plasma (1) and/or by the fact that fatty acids derived from MCT are rapidly absorbed within the portal circulation and metabolized to a large extent within the liver, increasing the production of ketone bodies (i.e., acetacetate and β-hydroxybutyrate) (11, 37). In the present study, MCT+CHO ingestion increased plasma β-hydroxybutyrate concentration more than twofold, suggesting that plasma ketones served as an exogenous energy source in the systemic circulation. However, the extent to which an acute elevation in plasma ketone concentration contributes to energy production during exercise is not clear (2, 14). The elevation of plasma ketone concentration in the present study clearly did not reduce muscle glycogen oxidation during high-intensity exercise.

The oxidation of ketone bodies or fatty acids from MCT could potentially reduce the oxidation of a substrate other than muscle glycogen (i.e., endogenous fat or blood glucose). We have previously reported that indirect calorimetry provides a valid measurement of substrate oxidation during high-intensity exercise (80–85% VO2max) (26), and presently we found that fat oxidation was very low during both CHO and MCT+CHO (2–2.5 µmol·kg⁻¹·min⁻¹). Therefore, even if all of the fat oxidized during MCT+CHO was endogenous MCT, thus entirely sparing endogenous fat, the absolute reduction in endogenous fat oxidation would still be very small (<35 kcal) and would account for only a small portion of the ingested MCT (~15%). In addition, MCT ingestion did not alter Rg glucose during exercise, suggesting that blood glucose oxidation was not affected. Because muscle glycogen oxidation accounted for ~90% of the total energy production during the CHO trial, if an appreciable amount of energy was derived from the exogenous MCT during MCT+CHO, it should have been reflected as a reduction in muscle glycogen oxidation, but it did not decline.

The above observations suggest that not enough MCT was oxidized during exercise to result in a measurable sparing of muscle glycogen. Although, if all of the 25 g MCT (~200 kcal) had been oxidized in place of muscle glycogen, muscle glycogen oxidation and the change in muscle glycogen concentration could have been substantially reduced (~125 µmol·kg⁻¹·min⁻¹ and 30 mmol/kg ww, respectively). However, the greatest rate of MCT oxidation previously reported after ingestion of a single dose of MCT was only 12 g/h (30); others have found the rate to be even lower (7–9 g/h) (19, 22). By using the highest reported MCT oxidation rate, this translates to only ~6 g MCT oxidized (~50 kcal) during the 30-min exercise bout in the present study and could account for a reduction in glycogen oxidation of only ~30 µmol·kg⁻¹·min⁻¹ and a decrease in the change in muscle glycogen concentration of only ~7 mmol/kg ww. It is possible that ingesting a greater quantity of MCT may increase the absolute amount of energy derived from MCT. Unfortunately, as we presently observed, as well as had others (7, 16, 22) gastrointestinal distress (i.e., nausea and diarrhea) limited the acute dose of MCT that individuals could tolerate to ~25 g. Therefore, under the present conditions, the energy derived from this tolerable, acute dose of MCT was not enough to reduce muscle glycogen oxidation.

Ingestion of small aliquots of MCT throughout exercise can allow for a greater total amount of MCT to be tolerated. Two recent studies have reported that subjects were able to tolerate ~85 g of MCT by ingesting it over >2-h period of exercise (20, 34). Van Zyl et al. (34) found that, when compared with carbohydrate ingestion alone (65 g CHO/h), the coingestion of ~86 g MCT (~30 g MCT/h) and carbohydrate (65 g CHO/h) during 2 h of cycling at 60% VO2max reduced the calculated rate of muscle glycogen oxidation (20–30 µmol·kg⁻¹·min⁻¹) and slightly improved cycling performance (~3%) during a subsequent simulated 40-km time trial. In contrast, Jukendrup et al. (20) found that the addition of 85 g of MCT to a 10% carbohydrate solution ingested while subjects cycled for 2 h at 60% VO2max did not alter exogenous or endogenous carbohydrate utilization and did not improve cycling performance during a subsequent 15-min cycling time trial. These data suggest that ingesting a relatively large dose of MCT over a prolonged period (2 h) may slightly improve performance during a subsequent exercise bout lasting ~1 h but not during shorter duration exercise bouts (~15 min).

It is possible that several weeks of MCT ingestion and the subsequent chronic exposure to elevated plasma medium-chain fatty acid and ketone concentrations may increase the ability to oxidize medium-chain fatty acids and ketones and thus reduce the reliance on muscle glycogen oxidation during exercise. Mice fed a chronic diet containing MCT for 6 wk increased plasma β-hydroxybutyrate concentration ~100% (12). This resulted in an increase of >20% in the activity of 3-ketoacyl-CoA transferase, an enzyme responsible for allowing muscle to oxidize plasma ketones (12). These
adaptations were associated with a 20% greater muscle glycogen concentration after 30 min of forced swimming compared with that in control mice and a 10% longer swim time to exhaustion (12). Similarly, a 4-wk ketogenic diet in humans, resulting in a chronic resting plasma ketone concentration above 1 mM, has also been reported to reduce the reliance on muscle glycogen oxidation during exercise (25). Because the subjects in the present study were not chronically fed MCT or chronically exposed to high plasma ketone concentrations, their ability to oxidize them may not have been sufficiently enhanced, reducing the potential for MCT ingestion to spare muscle glycogen.

In summary, under conditions in which fat supplementation (i.e., intravenous infusion of LCT and heparin) is known to reduce muscle glycogen oxidation, a tolerable dose of ingested MCT (~25 g) did not reduce muscle glycogen oxidation or attenuate the decline in muscle glycogen concentration. MCT ingestion did, however, increase plasma glucose uptake at rest.

We greatly appreciate the technical support of Dr. Andrew Coggan and Michael Sullivan. We additionally appreciate the assistance of Paul Bellow, Melissa Domenick, Pete Flatten, Ricardo Fritzsche, Patrick Malloix, and the participants in this study.

Address for reprints and other correspondence: J. Horowitz, Washington Univ. School of Medicine, 660 S. Euclid Ave., Box 8127, St. Louis, MO 63110-1093.

Received 25 May 1999; accepted in final form 23 September 1999.

REFERENCES


