Training-induced alterations in fat and carbohydrate metabolism during exercise in elderly subjects

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Sial, Shahid, Andrew R. Coggan, Robert C. Hickner, and Samuel Klein. Training-induced alterations in fat and carbohydrate metabolism during exercise in elderly subjects. Am. J. Physiol. 274 (Endocrinol. Metab. 37): E785–E790, 1998.—Compared with young adults, fat oxidation is lower in elderly persons during endurance exercise performed at either the same absolute or relative intensity. We evaluated the effect of 16 wk of endurance training on fat and glucose metabolism during 60 min of moderate intensity exercise [50% of pretraining maximum oxygen consumption (V\textsubscript{O2peak})] in six elderly men and women (74 ± 2 yr). Training caused a 21% increase in mean V\textsubscript{O2peak}. The average rate of fat oxidation during exercise was greater after (221 ± 28 µmol/min) than before (166 ± 17 µmol/min) training (P = 0.002), and the average rate of carbohydrate oxidation during exercise was lower after (3,180 ± 461 µmol/min) than before (3,937 ± 483 µmol/min) training (P = 0.003). Training did not cause a significant change in glycerol rate of appearance (R\textsubscript{a}), free fatty acid (FFA) R\textsubscript{a}, and FFA rate of disappearance during exercise. However, glucose R\textsubscript{a} during exercise was lower after (1,027 ± 95 µmol/min) than before (1,157 ± 69 µmol/min) training (P = 0.01). These results demonstrate that a 16-wk period of endurance training increases fat oxidation without a significant change in lipolysis (glycerol R\textsubscript{a}) or FFA availability (FFA R\textsubscript{a}) during exercise in elderly subjects. Therefore, the training-induced increase in fat oxidation during exercise is likely related to alterations in skeletal muscle fatty acid metabolism.

ENDOGENOUS FAT is an important fuel for working muscles during endurance exercise. We have recently found that fat oxidation is lower in elderly (66–79 yr old) compared with young adult (20–30 yr old) persons during endurance exercise performed at either the same absolute or relative intensity (34). This phenomenon is presumably related to changes in skeletal muscle itself, because whole body lipolysis and plasma free fatty acid (FFA) availability were not rate limiting. Impairment during exercise performed at the same absolute intensity, fatty acid uptake from plasma was higher but fat oxidation was lower in the elderly compared with the young adults. Impairment of fat oxidation during physical activity could have important clinical implications by decreasing exercise capacity and making it more difficult to decrease body fat mass. Exercise training could have beneficial metabolic effects during exercise in elderly persons. Endurance training has been shown to increase fat oxidation during exercise in young adults (23, 30) and increase resting rates of fat oxidation in elderly persons (31). However, the effect of training on lipid metabolism during exercise has not been studied in elderly persons.

The present study was undertaken to evaluate the effect of endurance training on fat and carbohydrate metabolism during moderate intensity exercise in elderly subjects. We hypothesized that a program of physical training would normalize substrate oxidation by either correcting or compensating for the alterations in skeletal muscle metabolism. Stable isotope tracers and indirect calorimetry were used to assess substrate metabolism at rest and during 60 min of cycle ergometer exercise in elderly subjects before and after 16 wk of cycle ergometer exercise training.

METHODS

Subjects. Six elderly subjects (74 ± 2 yr, 3 men and 3 women; Table 1) participated in this study, which was approved by the Institutional Review Board and the General Clinical Research Center (GCRC) Scientific Advisory Board of The University of Texas Medical Branch. All subjects performed normal daily activities, such as shopping, driving, and walking short distances, but none participated in regular aerobic exercise, such as walking, jogging, or cycling. All subjects were within 10% of ideal body weight according to the 1983 Metropolitan height-weight tables and were considered to be in good health after a comprehensive medical evaluation including history, physical examination, routine screening blood tests, and an oral glucose tolerance test. Subjects with a history of cigarette smoking, cardiovascular disease, diabetes, hypertension, or hyperlipidemia or those taking any medications were excluded. Subjects also completed an exercise stress test, and those with evidence of cardiovascular disease were excluded.

Outpatient studies. Peak oxygen consumption (V\textsubscript{O2peak}) and body composition were determined during two outpatient visits 3–5 days before each isotope infusion protocol, which was performed before and after 16 wk of training. Exercise testing was started with a “warm-up” by having the subjects cycle on a cycle ergometer for 5–10 min. The workload during exercise after this warm-up was increased by 10 W every 2 min in men and by 15 W every 2 min in women until volitional exhaustion. Oxygen consumption (V\textsubscript{O2}) and carbon dioxide production (V\textsubscript{CO2}) were monitored continuously by open-circuit spirometry using a 2900 Metabolic Cart (Sensormedics, Yorba Linda, CA). At least two of the following three criteria were met to establish that V\textsubscript{O2peak} was attained: 1) respiratory exchange ratio (RER) > 1.15, 2) a leveling off of V\textsubscript{O2} and heart rate despite increases in the workload, and 3) attainment of age-predicted maximal heart rate. Fat mass and fat-free mass were determined by dual energy X-ray absorptiometry using Enhanced Whole-Body Software Ver. 5.64 (Hologic QDR 1,000/W, Waltham, MA).

Inpatient studies. Subjects were admitted to the GCRC in the afternoon 1 day before the isotope infusion study. A standard meal and a snack were consumed at 1800 and at...
2100, respectively, on the day of admission containing a total of about 1000 kcal and 175 g of carbohydrate. After subjects fasted overnight, intravenous catheters were inserted in an antecubital vein for infusion of isotope tracers and in a distal forearm vein above the wrist of the contralateral arm, which was heated to obtain arterialized blood samples (25). A primed (19 μmol/kg), constant (0.22 μmol·kg⁻¹·min⁻¹) infusion of [6,6-²H]glucose (99% atom percent enrichment [APE]; Isotec, Miamisburg, OH) dissolved in normal saline was started at 0800 and continued for 120 min using a calibrated syringe pump (Harvard Apparatus, Natick, MA). At 0945 a primed (1.2 μmol/kg), constant (0.08 μmol·kg⁻¹·min⁻¹) infusion of [1,1,2,3,3-²H]glycerol (99% APE, Isotec) dissolved in normal saline and a constant (0.035 μmol·kg⁻¹·min⁻¹) infusion of [1,13C]palmitate (98% APE, Isotec) bound to human albumin were initiated and continued for 135 min. The exact isotope infusion rate was determined for each study by measuring glucose, palmitate, and glycerol concentrations in the infusates. After 120 min of isotope infusion at rest (120 to 0 min), the subjects exercised on a Monarch 8296 cycle ergometer at 50% VO₂peak for 60 min. At the onset of exercise, the isotope infusion rates were increased by 60% to minimize changes in substrate isotopic enrichment. Blood samples were drawn before the start of the isotope infusion to determine background substrate enrichment at -20, -10, and 0 min to measure basal glucose and lipid kinetics and at 10, 15, 20, 25, 30, 35, 40, 45, 50, 55, and 60 min of exercise to determine glucose and lipid kinetics during exercise. Blood samples were drawn for insulin and catecholamine concentrations at the end of the basal (0 min) and exercise (60 min) periods. Blood obtained for the analysis of substrate concentrations and isotopic enrichments was collected in chilled 10-ml glass tubes containing lithium heparin. Plasma was immediately separated by centrifugation at 4°C and frozen at -20°C until further processing. Samples for insulin were collected in tubes containing EDTA and aprotonin. Samples for plasma catecholamine were collected in iced tubes containing reduced glutathione and EGTA. These samples were centrifuged immediately at 4°C and stored at -70°C until analysis. VO₂ and VCO₂ were determined at the end of basal period and every 10 min during exercise using the metabolic cart.

After 16 wk of endurance exercise training, the outpatient and inpatient studies were repeated in all subjects. The isotope infusion study was performed 72 h after the last exercise training session. To avoid the confounding influence of large differences in absolute energy expenditure, the exercise bout during the posttraining isotope infusion protocol was performed at the same absolute intensity as the pretraining study.

Training. All subjects trained by pedaling Monark 818E cycle ergometers during supervised outpatient visits. Initial exercise training bouts were 30 min long and were performed 3 days/wk. The duration of exercise was gradually increased so that after 4 wk of training, each session lasted 45 min. Training frequency was increased to 4 days/wk after 4 wk and finally to 5 days/wk during the last 3 wk of training. Training intensity was monitored with a Polar Unique heart rate watch (Port Washington, NY). Heart rate during exercise was maintained between 70 and 85% of the peak heart rate determined during VO₂peak testing. Absenteeism was rare, and all subjects completed >95% of the scheduled workouts.

Sample analyses. Plasma fatty acid concentrations were determined by gas chromatography (24). Plasma glucose and glycerol concentrations were determined enzymatically by glucose oxidase and glycerol kinase methods, respectively. Plasma insulin concentrations were measured by RIA (11) and plasma catecholamines by a radioenzymatic method (14). Isotopic enrichment of plasma palmitate, glycerol, and glucose in plasma was determined by gas chromatography-mass spectrometry, using electron impact ionization and an MSD 5971 system (Hewlett-Packard, Palo Alto, CA) with capillary column, as described previously (19). FFAs were isolated from plasma and converted to their methyl esters. Ions at mass-to-charge ratios (m/z) of 270.2 and 271.2, representing the molecular ions of unlabeled and labeled methyl esters, respectively, were selectively monitored. Plasma samples were prepared for analysis of glucose and glycerol isotopic enrichment as described previously (19). Plasma proteins were precipitated with barium hydroxide and zinc sulfate. After centrifugation, the supernatant was passed through a mixed cation and anion exchange column. One-half of the sample was used to form a trimethylsilyl derivative of glycerol, and the other one-half was used to form a pentaacetate derivative of glucose. Glycerol enrichment was determined by selectively monitoring ions at m/z values of 205.1 and 208.1. Glucose enrichment was determined by selectively monitoring ions at m/z values of 200.1 and 202.1.

Calculations. Steele’s equation for steady-state conditions (37) was used to calculate substrate (glycerol, palmitate, and glucose) rate of appearance (Ra) and disappearance (Rd) during the last 20 min of the resting (preexercise) period, whereas Steele’s equation for non-steady-state conditions (37) was used to calculate Ra and Rd during exercise. Fatty acid Ra was calculated by dividing palmitate Ra by the percent contribution of palmitate to total FFA concentration. The effective volume of distribution was assumed to be 270 ml/kg for glycerol, 50 ml/kg for palmitate, and 100 ml/kg for glucose.

Triglyceride and carbohydrate oxidation rates were calculated from measurement of VO₂, VCO₂, and estimated urinary nitrogen excretion (8). It was assumed that nitrogen excretion was 80 μg·kg⁻¹·min⁻¹, based on the results of an earlier exercise study (2), and that palmitoyl stearyl oleyl triglyceride (860 g/mol) was a typical triglyceride.

Statistical analysis. All data are expressed as means ± SE. Comparisons between pretreatment and posttraining data were analyzed for statistical significance by using two-way (trial × time) ANOVA for repeated measures, using SigmaStat 2.0 (Jandel Scientific, San Rafael, CA). Where appropriate, significant differences identified by ANOVA were isolated using Tukey’s highly significant difference tests. An α value of 0.05 was used for all significance testing.

RESULTS

Although six subjects participated in this study, plasma hormone concentrations and substrate kinetics are not available for one subject because of technical limitations.
problems in handling the plasma samples. Therefore, the body composition and indirect calorimetry data represent values from six subjects, while plasma hormone and substrate kinetic data represent values from five subjects.

Body composition and $V_{O2peak}$. Training did not cause a change in total body weight (Table 1). However, there was a small increase in fat-free mass ($P < 0.05$), and fat mass tended to be lower ($P = 0.07$) in the trained state. Mean $V_{O2peak}$ increased by 21% as a result of training ($P < 0.01$; Table 1).

Indirect calorimetry. Resting $V_O2$ was the same before (0.214 ± 0.024 l/min) and after (0.198 ± 0.014 l/min) training as was resting $V_{CO2}$ (0.167 ± 0.019 and 0.167 ± 0.016 l/min, respectively). Resting RER was numerically but not statistically significantly greater after (0.824 ± 0.033) than before (0.789 ± 0.011) training because one subject had a high and possibly erroneous resting value after training. Resting energy expenditure was also the same before and after training (0.824 ± 0.033) numerically but not statistically significantly greater after training; average $V_{O2}$ values during 60 min of cycle ergometer exercise before and after training were 0.852 ± 0.090 and 0.847 ± 0.093 l/min, respectively. The RER increased during exercise ($P < 0.001$) during studies performed both before and after training. However, average RER during the exercise bout was lower after (0.858 ± 0.013) than before (0.892 ± 0.006) training ($P = 0.006$).

Substrate oxidation. Fat oxidation increased from 79 ± 11 µmol/min at rest to an average of 166 ± 17 µmol/min during exercise before training ($P < 0.001$) and from 59 ± 12 µmol/min at rest to an average of 221 ± 28 µmol/min during exercise after training ($P < 0.001$; $P = 0.002$ for values obtained during exercise before training compared with values after training; Fig. 1). Carbohydrate oxidation increased from 315 ± 81 µmol/min at rest to an average of 3,937 ± 483 µmol/min during exercise before training ($P < 0.001$) and from 587 ± 190 µmol/min at rest to an average of 3,180 ± 461 µmol/min during exercise after training ($P < 0.001$; $P = 0.003$ for values obtained during exercise before training compared with values after training; Fig. 1).

Plasma hormone concentrations. Before training, plasma epinephrine and norepinephrine concentrations increased two- to threefold during exercise (from 0.30 ± 0.06 and 1.45 ± 0.16 nmol/l, respectively, at rest to 0.94 ± 0.018 and 4.44 ± 0.51 nmol/l, respectively, during exercise; $P < 0.001$). After training, basal plasma epinephrine and norepinephrine concentrations (0.25 ± 0.04 and 1.75 ± 0.38 nmol/l, respectively) were similar to values obtained before training. Plasma epinephrine and norepinephrine concentrations also increased two- to threefold during exercise ($P < 0.001$) after training to values (0.56 ± 0.11 and 6.07 ± 1.81 nmol/l, respectively) that were not significantly different from those observed before training. Mean basal plasma insulin concentrations were the same before (57.4 ± 7.2 pmol/l) and after (57.4 ± 21.5 pmol/l) training. During exercise, plasma insulin concentrations did not change significantly from baseline values either before (43.1 ± 7.2 pmol/l) or after (57.4 ± 14.4 pmol/l) training.

Plasma substrate concentrations. No significant differences in plasma substrate concentrations were observed after training compared with values obtained before training. Plasma FFA concentrations decreased during early exercise but increased as exercise continued so that mean values at the end of the exercise bout were similar to the mean resting values both before training and after training (0.472 ± 0.050 and 0.463 ± 0.039 µmol/ml before and at the end of exercise, respectively, before training; 0.397 ± 0.026 and 0.364 ± 0.020 µmol/ml before and at the end of exercise, respectively, after training). Plasma glycerol concentration increased progressively during exercise, and values obtained at the end of exercise were greater ($P < 0.001$) than resting values both before and after training (0.076 ± 0.006 and 0.137 ± 0.010 µmol/ml before and at the end of exercise before training; 0.054 ± 0.011 and 0.116 ± 0.019 µmol/ml before and at the end of exercise after training). Plasma glucose concentrations did not change during exercise performed either before or after training.
training (5.56 ± 0.25 and 5.54 ± 0.23 µmol/ml before and at the end of exercise after training; 5.45 ± 0.20 and 5.50 ± 0.17 µmol/ml before and at the end of exercise after training).

Substrate kinetics. Fatty acid Ra increased from 379 ± 21 µmol/min at rest to an average of 497 ± 49 µmol/min during exercise before training (P < 0.01) and from 406 ± 42 µmol/min at rest to an average of 559 ± 79 µmol/min during exercise after training (P < 0.01) (Fig. 2). Fatty acid Rd increased from 379 ± 21 µmol/min at rest to an average of 491 ± 47 µmol/min during exercise before training (P < 0.001) and from 406 ± 42 µmol/min at rest to an average of 554 ± 78 µmol/min during exercise after training (P < 0.001). Neither fatty acid Ra nor Rd during exercise was significantly different after training compared with values obtained before training.

Glycerol Ra increased from 161 ± 16 µmol/min at rest to an average of 232 ± 23 µmol/min during exercise before training (P < 0.01) and from 201 ± 22 µmol/min at rest to an average of 288 ± 33 µmol/min during exercise after training (P < 0.01) (Fig. 2). Glycerol kinetics during exercise was not significantly different after training compared with values obtained before training.

Glucose Ra increased from 877 ± 33 µmol/min at rest to an average of 1,157 ± 69 µmol/min during exercise before training (P < 0.001) and from 846 ± 79 µmol/min at rest to an average of 1,027 ± 95 µmol/min during exercise after training (P < 0.001; Fig. 2). Glucose Rd increased from 877 ± 33 µmol/min at rest to an average of 1,168 ± 57 µmol/min during exercise before training (P < 0.001) and from 846 ± 79 µmol/min at rest to an average of 1,015 ± 69 µmol/min during exercise after training (P < 0.001). Glucose kinetics during exercise after training was significantly different from values obtained during exercise before training (P = 0.01).

DISCUSSION

Endogenous fat stores provide an important source of fuel for endurance exercise. We have recently found that elderly persons oxidize less fat than young adults during endurance exercise performed at either the same absolute or relative intensity (34). The decrease in fat oxidation was presumably related to alterations in skeletal muscle metabolism because FFA release from adipose tissue was higher in elderly than young adults during exercise performed at the same absolute intensity. The results of the present study demonstrate that endurance training can correct, or compensate for, the reduced rate of fat oxidation during exercise in elderly persons. Sixteen weeks of supervised exercise training increased the rate of fat oxidation during exercise to values previously observed in young adults exercising at the same absolute intensity (34).

It is well known that endurance training increases fat oxidation during exercise at a given absolute exercise intensity in sedentary young adults. The present study demonstrates that a training-induced shift in substrate oxidation also occurs in elderly subjects. Because endurance training did not cause a significant increase in lipolytic rate (glycerol Ra) or FFA availability (FFA Rd), the increase in fat oxidation was presumably caused by adaptive changes within skeletal muscle itself, most likely related to the training-induced increase in skeletal muscle mitochondrial content. Although muscle mitochondrial respiratory enzyme activities are 25-40% lower in sedentary elderly persons than in sedentary young adults (26, 32), endurance exercise training can increase muscle respiratory capacity by both elderly and young subjects (4, 5, 32). The increase in mitochondrial mass favors the oxidation of fat over carbohydrate (6, 12, 26, 27). Increased muscle respiratory capacity decreases skeletal muscle glycolytic flux (12), which in turn facilitates the oxidation of fatty acids. Although the cellular mechanism(s) responsible for this relationship is not known, it is clear that alterations in skeletal muscle carbohydrate metabolism affect the oxidation of fat. It has recently been shown that decreasing glycolytic flux during exercise by manipulating exercise intensity (35) or dietary intake (7) increases plasma long-chain, but not medium-chain, fatty acid oxidation. These findings suggest that decreased glycolytic flux may enhance long-chain fatty acid transport into skeletal muscle mitochondria. Alternatively, a decrease in glycolytic flux and acetyl-CoA production from pyruvate may simply allow more fatty acid-derived acetyl-CoA to enter the tricarboxylic acid cycle. In either case, it is likely that a training-induced increase in muscle respiratory capacity is in our subjects contributed to the observed increase in fat oxidation.

The source of the additional fatty acids oxidized during exercise after training cannot be directly determined from our study. It is unlikely that plasma triglycerides contributed to the increase in fat oxidation because plasma triglycerides are not normally an important fuel during exercise (28), and training does not increase triglyceride uptake during exercise (17). Although training did not have a significant effect on FFA Rd, it is possible that a greater percentage of FFAs
taken up from plasma were oxidized by muscle. Several factors may enhance the use of plasma FFAs by skeletal muscle in the trained state. Endurance training increases skeletal muscle capillarization (1), fatty acid binding protein content (16), and carnitine palmitoyltransferase activity (27), which together provide a favorable fatty acid concentration gradient from plasma to cytosol to mitochondria for oxidation. It is likely that increased use of nonadipose tissue triglyceride, presumably intramuscular triglyceride, was responsible for a large portion of the increase in fat oxidation. In sedentary subjects, whole body skeletal muscle contains \(~300\) mmol of triglyceride (13), which has the potential to provide \(>2,000\) kcal of energy during exercise. Therefore, a small increase in the percentage of intramuscular triglycerides oxidized can make a considerable contribution to whole body fat oxidation. Training may increase the amount of intramuscular triglycerides used during exercise (13, 23, 30). Previous studies using isotope tracer methodology have indirectly shown that training increases intramuscular fat oxidation during exercise because oxidation of adipose tissue-derived fatty acids could not explain the increased use of fat in trained subjects (15, 23, 30). Moreover, endurance exercise training causes greater depletion of intramuscular triglyceride during moderate intensity exercise performed at the same absolute workload after than before training (13, 29).

To our knowledge, the effect of endurance training on lipid kinetics during exercise in elderly subjects has not been previously evaluated. However, several cross-sectional and longitudinal training studies evaluated the effect of training on glycerol and FFA kinetics during exercise in young adults. Glycerol \(R_a\) during exercise performed at the same absolute intensity is similar in trained and untrained subjects (18, 30) but higher in trained than in untrained subjects during exercise performed at the same relative intensity (20). Two longitudinal training studies found that FFA \(R_a\) during cycle ergometer exercise performed at \(\sim60\)% of the pretraining \(\dot{V}O_2\text{peak}\) was lower after than before training (23, 30). However, the effect of training on FFA kinetics during exercise may only become apparent during more prolonged bouts of exercise than that performed in the present study. During the first 60 min of cycling, the time period evaluated in the present study, FFA \(R_a\) was similar before and after training in one study (30) and was not measured in the other study (23). Therefore, data from the present study are consistent with the observations made in young adults and suggest that a 16-wk period of rigorous cycle ergometer exercise training in elderly subjects does not cause a significant change in either glycerol or FFA \(R_a\) during the first 60 min of exercise performed at the same absolute intensity. Although we observed a trend toward increased glycerol and FFA \(R_a\) during exercise after training, it is unlikely that a true difference was missed because of a type II statistical error. On the basis of the data from the present study, 38 subjects would be needed to demonstrate a significant effect of training on FFA \(R_a\) with a \(\beta\) value of 0.9 and an \(\alpha\) value of 0.05; 19 subjects would be needed to demonstrate a difference in glycerol \(R_a\).

The adaptive changes in carbohydrate metabolism in our subjects were similar to those reported in younger persons. Glucose \(R_a\) and glucose oxidation during 60 min of cycle ergometer exercise decreased significantly after training. Coggan et al. (3) and Phillips et al. (30) found similar changes in young adults after 84 and 31 days of endurance training, respectively.

Our postraining studies were performed 72 h after the last bout of exercise to eliminate the influence of acute exercise. It is possible that fat oxidation rates at rest and during exercise might have been different had we studied our subjects closer to the last exercise session, particularly if glycogen stores were not fully repleted. For example, although we did not observe a training effect on the rate of fat oxidation during resting conditions, Poehlman et al. (31) found that fat oxidation at rest was greater after than before training when elderly subjects were studied \(\sim36\) h after exercise.

The results from our study demonstrate that endurance training can improve athletic performance and cause moderate alterations in body composition in elderly persons. Sixteen weeks of cycle ergometer exercise training increased \(\dot{V}O_2\text{peak}\) by \(21\%\), which is similar to the relative change in body composition reported in younger subjects (5, 21, 23, 36). In addition, we found that total body fat mass tended (\(P = 0.07\)) to be lower and fat-free mass was higher after training compared with values obtained before training. Other longitudinal training studies have reported either no change in body composition after 12 wk of endurance training (26) or a small increase in fat-free mass and a decrease in body fat mass after as much as \(12\) mo of endurance training in elderly persons (10, 22, 33). The small decrease in body fat mass may seem surprising in view of the rigorous training program completed by our subjects. However, alterations in body fat mass reflect alterations in total energy balance. Cycling exercise was performed for only 45 min 3–5 days per week, so most of the day was spent in nonexercise activities. Furthermore, Goran and Poehlman (9) found that endurance training in elderly subjects did not increase total daily energy expenditure, presumably because of a compensatory decrease in physical activity the rest of the day.

In summary, a 16-wk period of endurance training increases fat oxidation and decreases carbohydrate oxidation during exercise in elderly subjects to values similar to those observed in untrained young adults. Training did not cause a significant change in lipolysis (glycerol \(R_a\)) or FFA availability (FFA \(R_a\)) during exercise. Therefore, the training-induced increase in fat oxidation during exercise is likely related to changes within skeletal muscle, possibly an increase in the fractional oxidation of plasma fatty acids taken up by muscle and/or an increase in the use of nonadipose tissue, presumably intramuscular triglycerides.

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REFERENCES


