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Whole-body fat oxidation rate and plasma triacylglycerol concentrations in men consuming an ad libitum high-carbohydrate or low-carbohydrate diet[1–3]

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ABSTRACT

Background: High-carbohydrate diets may increase plasma triacylglycerol concentrations either by increasing production of triacylglycerols or by reducing their clearance.

Objective: We assessed whether the changes in plasma triacylglycerol concentrations induced by dietary interventions were associated with the changes in whole-body fat oxidation rates.

Design: In a parallel study, 37 healthy male subjects [body mass index (in kg/m^2): 28 ± 5, age: 34 ± 11 y ($\bar{x}$ ± SD)] consumed an ad libitum high-carbohydrate (60% of energy; $n = 19$) or low-carbohydrate (46% of energy), high-fat (41% of energy, 23% as monounsaturated fatty acids; $n = 18$) diet for 7 wk. The following variables were measured before and after the dietary interventions: *1*) plasma triacylglycerols before and 2, 4, 6, and 8 h after a meal (containing 40% of daily energy needs and 41% fat); *2*) indirect calorimetry throughout the 8-h test; and *3*) postheparin plasma lipoprotein lipase (phLPL) activity at time 8 h of the test.

Results: The diets induced changes in *1*) body weight: −2.5 ± 2.8 kg ($P < 0.01$) and −1.7 ± 3.1 kg ($P < 0.05$) and *2*) fasting plasma triacylglycerols: 0.0 ± 0.4 mmol/L (NS) and −0.3 ± 0.3 mmol/L ($P < 0.05$) for the high-carbohydrate and the low-carbohydrate diets, respectively. In normoinsulinemic subjects (fasting insulin < 100 pmol/L), dietary changes in postprandial triacylglycerols were significantly predicted by changes in phLPL, body weight, respiratory quotient (or fat oxidation), and the type of diet (stepwise multiple linear regression).

Conclusion: Postprandial plasma triacylglycerol concentrations may depend at least partly on fat oxidation, body weight, and LPL activity. *Am J Clin Nutr* 2003;77:580–6.

KEY WORDS Blood triacylglycerols, high-carbohydrate diet, high–monounsaturated fatty acid diet, indirect calorimetry, fat oxidation rate, men

INTRODUCTION

There is increasing evidence that high plasma triacylglycerol concentrations and a prolonged accumulation of postprandial triacylglycerol-rich VLDLs, chylomicrons, and their remnants are independent risk factors for coronary heart disease (1). The synthesis of VLDLs depends on several factors, such as plasma fatty acid availability, liver fat content, and hepatic de novo lipogenesis (2). In addition to these factors, the macronutrient composition of the diet is known to affect VLDL synthesis (3) and, thereby, plasma triacylglycerol concentrations. It has repeatedly been reported that isocaloric high-carbohydrate diets increase fasting VLDL concentrations (4), probably through their stimulating effect on hepatic lipogenesis (5). Yet, Packard et al (6) recently reported that VLDL clearance is also an important regulator of VLDL concentrations in healthy men. Clearance of VLDLs can occur via 2 main pathways: *1*) storage of triacylglycerols essentially at the adipose tissue level but also at the skeletal muscle level (7) and *2*) oxidation of triacylglycerols mainly by skeletal muscle. However, which pathway plays a predominant role in the regulation of plasma triacylglycerol concentration remains to be investigated.

From plasma triacylglycerol-rich lipoprotein (TRL) arteriovenous difference measurements, it has been estimated that TRLs are mainly cleared at the adipose tissue level and to a lesser extent at the skeletal muscle level (8). This is in accordance with the concept that an excess in fat intake will most likely be stored rather than oxidized (9). Moreover, fat oxidation (FATOX) generally decreases after a meal (10). Interestingly, it was reported that a significant fraction of fatty acids produced by the hydrolysis of TRLs are not stored in situ but rather are released into the blood (11). Therefore, it cannot be excluded that a fraction of TRLs, hydrolyzed at the adipose tissue level, are stored or oxidized or both elsewhere. Feeding high-carbohydrate diets for several days was reported to decrease the FATOX rate, whereas low-carbohydrate, high-fat diets were reported to increase the FATOX rate (12, 13). Therefore, it can be hypothesized that high-carbohydrate diets may modulate TRL concentrations through their action on triacylglycerol clearance (ie, FATOX rate and fat storage) in the fasting and postprandial states.

This hypothesis is in accordance with the observation that postheparin plasma lipoprotein lipase (phLPL; EC 3.1.1.34) activity, which is an index of the whole-body activity of lipoprotein lipase,

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TABLE 1
Physical characteristics and plasma lipid concentrations of the subjects at baseline[1]

	High-carbohydrate diet group (n = 19)	Low-carbohydrate diet group (n = 18)
Age (y)	34 ± 10	34 ± 12
Body weight (kg)	87 ± 11	85 ± 17
Height (cm)	175 ± 6	175 ± 6
BMI (kg/m^2)	28 ± 4	28 ± 6
Fatty acids (mmol/L)	0.31 ± 0.12	0.32 ± 0.13
Plasma glucose (mmol/L)	5.3 ± 0.4	5.1 ± 0.4
Plasma insulin (pmol/L)	60 ± 22	64 ± 28
Postheparin lipoprotein lipase (nmol · min^{-1} · mL^{-1})	71 ± 34	62 ± 36
Fasting plasma triacylglycerols (mmol/L)	1.12 ± 0.49	1.25 ± 0.32
Postprandial plasma triacylglycerols (mmol · min/L)	876 ± 396	889 ± 242

[1] $\bar{x}$ ± SD. There were no statistically significant differences between the groups (one-factor ANOVA).

a key enzyme of plasma triacylglycerol clearance, is inversely related to the area under the curve of postprandial triacylglycerols (14).

The aim of the present study was to assess whether the changes in body weight, phLPL, and FATOX rate induced by ad libitum feeding of a high-carbohydrate diet or a low-carbohydrate diet are determinants of the changes in fasting and postprandial plasma triacylglycerol concentrations induced by these diets. For both diets, the percentage of fat intake accounted for by monounsaturated fatty acids was high (50%). Monounsaturated fatty acids have a known beneficial effect on plasma lipids (15–18).

SUBJECTS AND METHODS

Subjects

Thirty-seven white men [age: 34 ± 11 y; body mass index (in kg/m^2): 28 ± 5 ($\bar{x}$ ± SD)] were recruited in the Québec metropolitan area through advertisement in local newspapers. The participants were nonsmokers, normoglycemic, normolipidemic, and free of any thyroid, endocrine, cardiovascular, hepatic, or renal disorders. Subjects who underwent major surgery within the past 2 months, experienced fluctuations in body weight (> 3 kg) in the 2 mo preceding study onset, had excessive alcohol intake (> 30 g/d), had taken drugs, or had unusual dietary habits were excluded. Physical characteristics and fasting serum lipid concentrations of the subjects at baseline are shown in **Table 1**. After receiving a detailed description of the experimental protocol, all subjects gave their informed consent to participate in the study, which was approved by the Clinical Research Ethical Committee of Laval University.

Dietary intervention

The subjects were randomly assigned to either a high-carbohydrate or low-carbohydrate diet, which they consumed on an ad libitum basis for 7 wk. During the dietary intervention, all the food was provided by the metabolic kitchen of the Department of Food Science and Nutrition of Laval University. The subjects were also instructed to maintain their usual physical activity level throughout the study. On weekdays, the subjects were required to eat their lunch at the research unit under the supervision of a dietitian and were at this time given their packaged breakfast and evening meals to take home. On weekends, all meals were provided by the research unit but were packaged to take home. Multivitamin and mineral supplements and alcohol consumption were discontinued 1 wk before study onset and for the duration of the study.

Before the beginning of the study, each subject completed a 3-d food-intake diary to estimate his usual energy intake. Energy expenditure was also measured in the fasting state, by indirect calorimetry. Daily energy needs were defined as the average between a subject's resting energy expenditure multiplied by 1.5 and his usual daily energy intake calculated with the 3-d dietary record. For some individuals, energy needs may have been underestimated (ie, the factor 1.5 may be low for lean, free-living individuals and for some subjects who may have underreported their energy intake). To ensure that a sufficient amount of food was provided but also to allow for ad libitum consumption of the diets, 150% of the subjects' estimated energy needs were provided during the experimental protocol.

The experimental diets were formulated as 7-d rotating menus and were designed to supply daily allowances of essential nutrients as recommended by Health and Welfare Canada. The nutritional composition of the experimental diets and dietary records was calculated by using the Canadian Nutrient File database (Health Canada, Ottawa, 1997).

The subjects were then instructed to eat their meals on an ad libitum basis, until their habitual satiety was met. All leftovers were returned to the research unit and weighed to determine the quantity of food eaten. The 2 experimental diets contained similar food items and ingredients, which were provided in different proportions and were prepared daily in weighed individual portions. One diet was low in fat (27% of energy; polyunsaturated: saturated fat = 0.89) and high in complex carbohydrates (60% of energy); the other was low in carbohydrates (46% of energy) and high in fat (41% of energy; 23% monounsaturated fatty acids provided mainly as olive oil; polyunsaturated:saturated fat = 0.93). On request and especially for those habituated in eating between meals, participants were provided with snacks prepared in the metabolic kitchen. Each snack contained 837 kJ and had the same macronutrient composition as that of its respective experimental diet. The nutrient composition of the experimental diets is shown in **Table 2**.

Protocol for postprandial studies

Postprandial studies were conducted on days 1 and 49. The subjects were advised to avoid any vigorous or moderate physical exercise during the 3 d preceding each test. On the morning of the postprandial studies, a catheter was introduced into an antecubital vein and a saline perfusion was installed to collect blood samples throughout the day. After the subjects, who had fasted 12 h, rested for 30 min in a supine position, indirect calorimetry measurements were performed for 20 min in the postabsorptive state. Blood samples were collected in the postabsorptive state and 2, 4, 6, and 8 h after consumption of a standard test meal that provided 40% of daily energy needs. The test meal was consumed within 15 min, and, to minimize de novo lipogenesis, was similar in composition to the low-carbohydrate diet (41% energy intake as fat; Table 2).

Blood variables

Fasting and postprandial blood samples were collected into tubes containing disodium EDTA (0.03%). The samples were

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TABLE 2
Nutrient composition of the usual and experimental diets[1]

	High-carbohydrate diet (n = 19)		Low-carbohydrate diet (n = 18)	
	Usual diet	Experimental diet	Usual diet	Experimental diet[2]
Energy (MJ)	12 ± 3.6	12 ± 2.2	13 ± 3.8	13 ± 2.6
Protein				
(g)	98 ± 28	119 ± 21[3]	116 ± 33	119 ± 24
(% of energy)	14 ± 3	16 ± 0[3]	15 ± 3	16 ± 0
Carbohydrate				
(g)	397 ± 135	434 ± 80	366 ± 128	351 ± 70
(% of energy)	54 ± 6	60 ± 0[3]	47 ± 7	46 ± 0
Fat				
(g)	111 ± 35	86 ± 16[3]	130 ± 47	140 ± 28
(% of energy)	34 ± 4	27 ± 0[3]	38 ± 6	41 ± 0[4]
Saturated fatty acids				
(g)	40 ± 14	19 ± 4[3]	46 ± 18	28 ± 6[3]
(% of energy)	12 ± 2	6 ± 0[3]	13 ± 3	8 ± 0[3]
Polyunsaturated fatty acids				
(g)	21 ± 8	17 ± 3[4]	25 ± 10	26 ± 5
(% of energy)	7 ± 2	5 ± 0[4]	7 ± 2	8 ± 0
Monounsaturated fatty acids				
(g)	41 ± 14	43 ± 8	49 ± 20	77 ± 15[3]
(% of energy)	13 ± 2	13± 0	14 ± 3	23 ± 0[3]
Cholesterol (mg/1000 kJ)	25 ± 8	25 ± 0	34 ± 12	26 ± 0[3]
Alcohol				
(g)	4 ± 7	0[4]	5 ± 10	0
(% of energy)	1 ± 2		1 ± 3	
P:S	0.64 ± 0.45	0.89 ± 0[3]	0.56 ± 0.22	0.93 ± 0[3]

[1] $\bar{x}$ ± SD. P:S, ratio of polyunsaturated to saturated fatty cids. The percentage of macronutrients was preset for the experimental diets; therefore, the SDs are close to zero. The SDs for the usual diet are much greater than those for the experimental diet because the proportion of macronutrients was not preset and because subjects tend to selectively underreport intakes of energy and specific macronutrients, making the estimation of diet composition by a 3-d dietary record less accurate. The usual diet was calculated from a 3-d dietary record; the experimental diet was calculated from the weight measurement of all meals given to the subjects during the last 14 d before the test day.

[2] Significantly different from the high-carbohydrate diet, $P < 0.01$, for all nutrients except energy and protein, expressed in grams (ANOVA).

[3,4] Significantly different from the usual diet: [3] $P \leq 0.01$, [4] $P \leq 0.05$.

immediately centrifuged at 4 °C for 10 min at 1500 × g to obtain plasma and were stored at 4 °C with benzamidine (0.03%) until analysis. Total TRLs (chylomicrons and VLDL) were separated by ultracentrifugation (d = 1.006 g/mL) of 4 mL plasma in a 50.3 Beckman rotor (Beckman Instruments, Inc, Fullerton, CA), spun at 93 000 × g (average) at 4 °C for 18 h. Plasma and lipoprotein lipid concentrations were determined enzymatically on an RA-500 Auto-Analyzer (Technicon RA-500 analyzer, Bayer Corporation, Tarrytown, NY), as previously described (19).

Fasting and postprandial plasma glucose concentrations were determined with a glucose oxidase assay from Sigma (St Louis; 20). Plasma insulin concentrations were measured by a commercial double-antibody radioimmunoassay (Linco, St Louis) that shows little cross-reactivity (< 0.02%) with proinsulin (21).

phLPL activity

Eight hours after consumption of the test meal, the subjects received an intravenous injection of heparin (60 IU/kg body weight). Plasma LPL activity was determined in plasma obtained 10 min after the injection of heparin (at time 8 h, 10 min of the indirect calorimetry measurements). The activity was measured by a modification (22) of the method of Nilsson-Ehle and Ekman (23) and expressed in nanomoles of oleic acid released per milliliter of plasma per minute.

Indirect calorimetry

Energy expenditure and substrate utilization were assessed with an open-circuit indirect calorimetry system (SensorMedics Vmax 29; Yorba Linda, CA). The subjects placed their heads in a transparent ventilated box, and analysis of air entering and leaving this box permitted the calculation of oxygen consumption and carbon dioxide production (24). From gas exchanges, energy consumption and substrate utilization were calculated by using each macronutrient's specific respiratory quotient, heat equivalent of oxygen, and energy density (25). Urinary nitrogen excretion was measured the night before and throughout the test to calculate mean protein oxidation. After 20 min of baseline measurements, the ventilated box was removed and the test meal was given. Then indirect calorimetry measurements were performed throughout the day by transferring the ventilated box from one subject to the other every 20 min. The subjects were told to stay in a supine position and to remain awake and motionless throughout the procedure; they were allowed to watch television. Quiet walking was permitted, not to exceed 2 separate periods of 15 min during the entire day.

Statistical analysis

The JMP statistical program (version 3.1.6; SAS Institute Inc, NC) was used to perform statistical analyses. Stepwise multiple linear regressions were used to predict triacylglycerol concentrations. The following independent variables were tested: FATOX,

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TABLE 3
Changes in body weight and blood variables induced by the 7-wk ad libitum diets[1]

	High-carbohydrate diet (n = 19)	Low-carbohydrate diet (n = 18)
Body weight (kg)	−2.5 ± 2.8[2]	−1.7 ± 3.1[3]
Fatty acids (mmol/L)	0.08 ± 0.16[3]	0.08 ± 0.2
Glucose (mmol/L)	−0.2 ± 0.3[3]	−0.0 ± 0.3
Insulin (pmol/L)	−6.0 ± 21.7	6.5 ± 29.7
Postheparin lipoprotein lipase ($nmol \cdot min^{-1} \cdot mL^{-1}$)	−1 ± 18	0 ± 35
Fasting plasma triacylglycerols (mmol/L)	0.0 ± 0.4	−0.3 ± 0.3[2]
Postprandial plasma triacylglycerols (mmol · min/L)	−38 ± 267	−159± 216[2]

[1] $\bar{x}$ ± SD.
[2,3] Significantly different from the beginning of the study: [2] $P \leq 0.01$, [3] $P \leq 0.05$.

fatty acids, LPL activity, and body weight loss. Student's t tests were used to compare the energy expenditure and macronutrient oxidation before and after the dietary intervention. A one-factor analysis of variance was used to calculate the differences between diets. Postprandial triacylglycerol responses were calculated as the area under the 0–8-h triacylglycerol curve.

RESULTS

The composition of the diets before and during the dietary interventions is shown in Table 2. As expected, there was a significant difference in carbohydrate intake between diets. However, although the high-carbohydrate diet provided a greater percentage of energy from carbohydrate than did the habitual diet, the absolute gram amount of carbohydrate consumed during the experimental diets did not differ significantly from that consumed during the subjects' habitual diets.

Consumed ad libitum, both diets led to a significant reduction in body weight (**Table 3**). A significant decrease in fasting and postprandial triacylglycerol concentrations was observed only after the low-carbohydrate diet (Table 3). When subjects from both diet groups were pooled, there was a positive correlation between changes in plasma triacylglycerols and changes in body weight either in the fasting ($r = 0.39$, $P < 0.05$) or in the postprandial ($r = 0.56$, $P < 0.05$) state. In a stepwise multiple linear regression analysis, fasting and postprandial triacylglycerol concentrations were significantly predicted by body weight, the type of diet, and phLPL activity (**Tables 4** and **5**). Four subjects with plasma insulin concentrations > 100 pmol/L were clearly outliers for insulinemia and were considered as hyperinsulinemic. When these subjects were excluded from the analyses, the changes in FATOX were also found to be a good predictor of the postprandial changes in triacylglycerol concentrations, in addition to the type of diet and to changes in body weight and phLPL activity (Table 5). Similar stepwise multiple regression analyses were performed for each diet separately. In this case, changes in plasma triacylglycerols were significantly predicted by changes in phLPL ($P = 0.003$) and respiratory quotient ($P = 0.05$) under the high-carbohydrate diet ($R^2 = 0.48$) and by changes in respiratory quotient ($P = 0.02$) under the low-carbohydrate diet ($R^2 = 0.37$).

Indirect calorimetry results

Indirect calorimetry results are presented in **Table 6**. Changes in indirect calorimetry variables induced by the high-carbohydrate diet did not differ from those induced by the low-carbohydrate diet. Except for fasting energy expenditure that remained unchanged after the high-carbohydrate diet ($P = 0.08$), fasting and postprandial energy expenditure were both significantly decreased after the dietary period ($P < 0.05$). In contrast, the postprandial FATOX rate was significantly decreased after the high-carbohydrate diet ($P < 0.05$) but not after the low-carbohydrate diet. Finally, in the fasting state, the 7-wk dietary periods did not induce significant changes in either carbohydrate or protein oxidation rates.

DISCUSSION

Several studies in addition to ours showed that a high-carbohydrate, low-fat diet, when consumed ad libitum, promotes weight loss (26–28). This effect may be explained by the higher satiating effect (29–31) or the lower energy density (32) of high-carbohydrate diets or a combination of these factors. The resulting drop in energy intake, and thereby body weight, that often follows the consumption of a high-carbohydrate diet is in discordance with the fact that in our study, energy intakes were apparently not reduced under either dietary intervention (Table 2). The most probable explanation for this discrepancy is that, as is often the case in obese subjects (33), our subjects most likely selectively underreported their usual intake of energy and specific nutrients. Hence their intakes of energy and certain macronutrients when consuming their usual diet were probably higher than what was reported in their 3-d food record. We therefore believe that compared with their usual diets, the dietary interventions were most likely hypoenergetic and thereby promoted weight loss.

In accordance with earlier reports (27, 28), ad libitum consumption of a high-carbohydrate diet in the present study resulted in a modest but significant weight loss (Table 3). Surprisingly, the low-carbohydrate, high-fat diet was also associated with a

TABLE 4
Stepwise multiple linear regression to predict triacylglycerol concentrations in the fasting state in normoinsulinemic subjects[1]

Parameter	Estimate	R^2	Probability > F
Intercept (kJ/min)	0.02	0	1.0
Diet (high carbohydrate − low carbohydrate)	0.19[2]	0.28	0.01
Changes in body weight (kg)	0.06	0.37	0.02
Changes in phLPL ($nmol \cdot min^{-1} \cdot mL^{-1}$)	−0.005	0.48	0.02

[1] $n = 33$; $R^2 = 0.48$. Changes in triacylglycerol are expressed in mmol/L. The following independent variables were tested: type of diet, body weight (kg), fatty acids (mmol/L), energy expenditure (kJ/min), fat oxidation (kJ/min), and postheparin lipoprotein lipase activity (phLPL; $nmol \cdot min^{-1} \cdot mL^{-1}$).
[2] For the high-carbohydrate diet, the estimate was +0.19, whereas for the low-carbohydrate diet, the estimate was −0.19.

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TABLE 5
Stepwise multiple linear regression to predict changes in triacylglycerol concentrations in the postprandial state in normoinsulinemic subjects[1]

Parameter	Estimate	R^2	Probability > F
Intercept (kJ/min)	−27.4	0	1.0
Diet (high carbohydrate − low carbohydrate)	−75.7[2]	0.18	0.02
Changes in body weight (kg)	41.2	0.29	0.01
Changes in phLPL (nmol·min^{-1}·mL^{-1})	−3.0	0.43	0.01
Changes in fat oxidation (kJ/min)	−58.4	0.51	0.02

[1] n = 33; R^2 = 0.51. Changes in triacylglycerols are expressed in mmol·min/L. The following independent variables were tested: type of diet, changes in body weight (kg), changes in fatty acids (mmol/L), changes in energy expenditure (kJ/min), changes in fat oxidation (kJ/min), and changes in postheparin lipoprotein lipase activity (phLPL; nmol·min^{-1}·mL^{-1}).
[2] For the high-carbohydrate diet, the estimate was +75.7, whereas for the low-carbohydrate diet, the estimate was −75.7.

significant decrease in body weight (Table 3). Therefore, both diets can be considered to be hypoenergetic. Because our diets were administrated on an ad libitum basis, the weight loss observed can probably be explained by a so-called nonspecific effect of the dietary intervention protocol. For both dietary interventions, the subjects changed their eating habits (eg, taking meals with other participants at the Nutrition Department and eating under the surveillance of dieticians and staff) and were obviously aware that their body weight was closely monitored. These factors may also have influenced total energy intake independently from the macronutrient content of the diets.

As mentioned above, high-carbohydrate diets are known to increase plasma triacylglycerol concentrations when fed under conditions where energy intake is controlled to keep body weight constant (34–36). Interestingly, under ad libitum conditions and associated with weight loss, we found that plasma triacylglycerols did not change significantly after the high-carbohydrate diet. As expected from results published in the literature (37–41), this weight loss appears to be a good predictor of changes in triacylglycerol concentrations in the fasting and postprandial states, as shown by our stepwise linear regression (Tables 4 and 5). It cannot be excluded that the weight loss observed in the present study had beneficial effects on blood lipids that appeared to overcome the increase in plasma triacylglycerols typically seen when such diets are consumed under isoenergetic conditions. This hypothesis is supported by our multiple linear regression results in which both body weight changes and the type of diet were found to predict changes in fasting plasma triacylglycerols (Table 4). From the equation prediction, a high-carbohydrate diet would be expected to increase fasting plasma triacylglycerols by 0.19 mmol/L if body weight was constant. Similarly, a low-carbohydrate diet (which is also rich in fat and monounsaturated fatty acids) is expected to decrease fasting plasma triacylglycerols by 0.19 mmol/L. From our model, the modest weight loss observed after the high-carbohydrate diet (2.5 kg) may have induced a decrease in fasting triacylglycerols (−2.5 kg × 0.06 mmol·L^{-1}·kg^{-1} = −0.15 mmol/L) that partially compensated for the calculated effect of a high-carbohydrate diet. It is also possible that changes in nutrients other than carbohydrate (eg, total fat, polyunsaturated and saturated fatty acids, fiber, etc) may have contributed to the significant dietary effect predicting changes in plasma triacylglycerols. Yet, because the absolute amount of carbohydrate consumed with the high-carbohydrate diet was not significantly greater than what subjects apparently consumed during their usual diet, we cannot exclude the possibility that plasma triacylglycerols might have increased had the difference in carbohydrate intake between the usual and ad libitum high-carbohydrate diet been greater. Our results showing no change in plasma triacylglycerols after the high-carbohydrate diet are nonetheless in general accordance with those of Lichtenstein et al (42), who reported that plasma triacylglycerols are reduced when consumption of a low-fat, high-carbohydrate diet is associated with weight loss.

Both diets were followed by a reduction in energy expenditure. In accordance with earlier reports (43–45), the decrease in energy

TABLE 6
Indirect calorimetry results before and after the 7-wk ad libitum diets and the changes induced by the diets[1]

	High-carbohydrate diet (n = 19)			Low-carbohydrate diet (n = 18)		
	Before diet	After diet	Change	Before diet	After diet	Change
Fasting						
Energy expenditure (kJ/min)	5.62 ± 0.75	5.43 ± 0.69	−0.19 ± 0.43	5.67 ± 0.69	5.30 ± 0.82	−0.37 ± 0.49[2]
Carbohydrate oxidation (kJ/min)	1.23 ± 0.79	0.95 ± 0.83	−0.29 ± 1.16	0.97 ± 0.83	0.87 ± 0.91	−0.09 ± 1.04
Fat oxidation (kJ/min)	2.86 ± 0.77	2.66 ± 1.1	−0.20 ± 1.22	3.17 ± 1.1	2.88 ± 0.76	−0.28 ± 0.89
Protein oxidation (kJ/min)[3]	1.53 ± 0.53	1.83 ± 0.52	0.30 ± 0.71	1.54 ± 0.52	1.55 ± 0.41	0.01 ± 0.51
Respiratory quotient	0.80 ± 0.04	0.80 ± 0.05	0.00 ± 0.06	0.79 ± 0.05	0.79 ± 0.05	0.00 ± 0.05
Postprandial						
Energy expenditure (kJ/min)	6.88 ± 0.62	6.56 ± 0.77	−0.32 ± 0.44[2]	6.76 ± 0.77	6.38 ± 0.76	−0.38 ± 0.4[2]
Carbohydrate oxidation (kJ/min)	1.89 ± 0.71	1.94 ± 0.8	0.05 ± 0.82	1.65 ± 0.8	1.5 ± 0.71	−0.14 ± 0.97
Fat oxidation (kJ/min)	3.46 ± 0.87	2.79 ± 1.04	−0.67 ± 1.02[2]	3.57 ± 1.04	3.33 ± 0.71	−0.25 ± 1.09
Respiratory quotient	0.82 ± 0.03	0.83 ± 0.04	0.01 ± 0.04	0.81 ± 0.04	0.81 ± 0.03	0.00 ± 0.04

[1] $\bar{x}$ ± SD.
[2] Significantly different from zero, $P < 0.05$.
[3] Urine collection was taken throughout the test, and therefore fasting and postprandial periods could not be separated.

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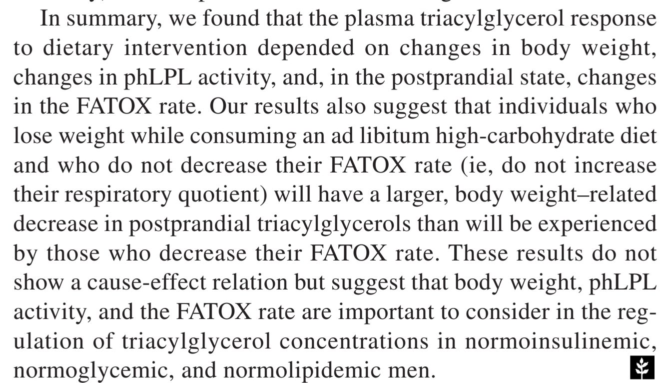
expenditure can be accounted for by the reduction in body weight. When body weight is constant, the oxidation of each macronutrient tends to be equal to its intake (ie, the balance of each macronutrient is equilibrated; 12, 13). In the present study, the subjects were not in energy balance and nutrient oxidation rates were not measured during but after the dietary interventions. Interestingly, under these conditions, the FATOX rate measured after a standard meal (40% fat) remained changed 1 d after the end of the dietary interventions.

In the stepwise regression, the change in phLPL activity induced by the diets was also a significant predictor of the changes in fasting and postprandial triacylglycerol concentrations (Tables 4 and 5). These results are in accordance with those of Taskinen et al (14), who reported an inverse relation between postprandial plasma triacylglycerols and phLPL activity. Interestingly, in the present study, changes in phLPL were not correlated with changes in FATOX ($r = 0.08$; results not shown). At least 3 reasons may explain this absence of a relation: First, factors other than LPL activity (eg, plasma fatty acids, type of diet, etc) may also modulate FATOX. Second, it cannot be excluded that phLPL has a greater effect on fat storage than on FATOX. Finally, phLPL was measured in the fasting state (ie, 8 h after the meal) and is therefore an imperfect index of postprandial LPL activity.

Individuals with insulin resistance (ie, with hyperinsulinaemia) may present a disturbed skeletal muscle fat metabolism with an increased intramuscular fat depot (for a review, *see* 46) and therefore should probably not be included in studies in which FATOX rate or storage are considered. Interestingly, when individuals with an evident hyperinsulinaemia (fasting insulin > 100 pmol/L) were removed from our analyses, changes in FATOX were significantly included into the model to predict changes in plasma triacylglycerols. These findings suggest that individuals who do not increase their FATOX will exhibit the greater increase in postprandial triacylglycerols. Interestingly, when similar multiple regressions were performed for each diet separately, the change in FATOX also tended to predict plasma triacylglycerols ($P = 0.11$; results not shown). Furthermore, in this case, the change in respiratory quotient, which is an index of the relative contribution of FATOX to energy metabolism, still significantly predicted postprandial plasma triacylglycerols. These results are in accordance with those of Parks et al (47), who concluded that a reduced clearance of triacylglycerols from the plasma, rather than an increase in triacylglycerol secretion by the liver, was the primary mechanism responsible for the increase in triacylglycerols induced by a high-carbohydrate diet.

Interestingly, Schrauwen et al (48) reported that in lean subjects, a diet high in monounsaturated fatty acids induces an increase in triacylglycerol-derived oxidation (VLDL or intramuscular triacylglycerols). In accordance with these results, we observed that a low-carbohydrate diet (which was also high in fat and monounsaturated fatty acids) induced a decrease in fasting and postprandial plasma triacylglycerols. These results are compatible with the concept that changes in FATOX, induced by dietary interventions, may have an effect on plasma TRL clearance and concentration.

It can be argued that the FATOX rate is not accurately measured when de novo lipogenesis occurs (49, 50). Yet Hellerstein (5) showed that the importance of de novo lipogenesis to triacylglycerol synthesis is small when humans eat a mixed diet but increases during consumption of a high-carbohydrate diet. In the present study, > 40% of the energy in the test meal consumed during the postprandial studies was supplied by fat. It can therefore be reasonably concluded that our test meal probably induced only minimal de novo lipogenesis, so that this variable probably did not influence our indirect calorimetry results. Moreover, the mean respiratory quotient throughout the postprandial period did not exceed 0.83, which is clearly below 1.0. This indicates that net lipogenesis (which occurs when the respiratory quotient exceeds the unity) was not present under our feeding conditions.



In summary, we found that the plasma triacylglycerol response to dietary intervention depended on changes in body weight, changes in phLPL activity, and, in the postprandial state, changes in the FATOX rate. Our results also suggest that individuals who lose weight while consuming an ad libitum high-carbohydrate diet and who do not decrease their FATOX rate (ie, do not increase their respiratory quotient) will have a larger, body weight–related decrease in postprandial triacylglycerols than will be experienced by those who decrease their FATOX rate. These results do not show a cause-effect relation but suggest that body weight, phLPL activity, and the FATOX rate are important to consider in the regulation of triacylglycerol concentrations in normoinsulinemic, normoglycemic, and normolipidemic men.

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REFERENCES

1. Patsch JR, Miesenbock G, Hopferwieser T, et al. Relation of triglyceride metabolism and coronary artery disease. Studies in the postprandial state. Arterioscler Thromb 1992;12:1336–45.
2. Lewis GF. Fatty acid regulation of very low density lipoprotein production. Curr Opin Lipidol 1997;8:146–53.
3. Francone OL, Kalopissis AD, Griffaton G. Concomitant inhibition of VLDL triglyceride and apoprotein secretion by hepatocytes of rats adapted to a high-fat diet. Adv Exp Med Biol 1991;285:325–8.
4. Chen YD, Coulston AM, Zhou MY, Hollenbeck CB, Reaven GM. Why do low-fat high-carbohydrate diets accentuate postprandial lipemia in patients with NIDDM? Diabetes Care 1995;18:10–6.
5. Hellerstein MK. De novo lipogenesis in humans: metabolic and regulatory aspects. Eur J Clin Nutr 1999;53(suppl):S53–65.
6. Packard CJ, Demant T, Stewart JP, et al. Apolipoprotein B metabolism and the distribution of VLDL and LDL subfractions. J Lipid Res 2000;41:305–18.
7. Oscai LB, Tsika RW, Essig DA. Exercise training has a heparin-like effect on lipoprotein lipase activity in muscle. Can J Physiol Pharmacol 1992;70:905–9.
8. Potts JL, Fisher RM, Humphreys SM, Coppack SW, Gibbons GF, Frayn KN. Peripheral triacylglycerol extraction in the fasting and post-prandial states. Clin Sci (Lond) 1991;81:621–6.
9. Schutz Y, Flatt JP, Jequier E. Failure of dietary fat intake to promote fat oxidation: a factor favoring the development of obesity. Am J Clin Nutr 1989;50:307–14.
10. Elia M, Folmer P, Schlatmann A, Goren A, Austin S. Carbohydrate, fat, and protein metabolism in muscle and in the whole body after mixed meal ingestion. Metabolism 1988;37:542–51.
11. Frayn KN, Coppack SW, Fielding BA, Humphreys SM. Coordinated regulation of hormone-sensitive lipase and lipoprotein lipase in human adipose tissue in vivo: implications for the control of fat storage and fat mobilization. Adv Enzyme Regul 1995;35:163–78.
12. Hill JO, Peters JC, Reed GW, Schlundt DG, Sharp T, Greene HL. Nutrient balance in humans: effects of diet composition. Am J Clin Nutr 1991;54:10–7.
13. Thomas CD, Peters JC, Reed GW, Abumrad NN, Sun M, Hill JO. Nutrient balance and energy expenditure during ad libitum feeding

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of high-fat and high-carbohydrate diets in humans. Am J Clin Nutr 1992;55:934–42.
14. Taskinen M-R, Hilden H, Mero N, Syvänne M. Postprandial lipemia and lipoprotein lipase. Atherosclerosis 1995:758–62.
15. Berry M, Eisenberg S, Friedlander Y, et al. Effects of diets rich in monounsaturated fatty acids on plasma lipoproteins—the Jerusalem Nutrition Study. II. Monounsaturated fatty acids vs carbohydrates. Am J Clin Nutr 1992;56:394–403.
16. Kris-Etherton PM, Pearson TA, Wan Y, et al. High–monounsaturated fatty acid diets lower both plasma cholesterol and triacylglycerol concentrations. Am J Clin Nutr 1999;70:1009–15.
17. Wahrburg U, Martin H, Sandkamp M, Schulte H, Assmann G. Comparative effects of a recommended lipid-lowering diet vs a diet rich in monounsaturated fatty acids on serum lipid profiles in healthy young adults. Am J Clin Nutr 1992;56:678–83.
18. Mata P, Garrido JA, Ordovas JM, et al. Effect of dietary monounsaturated fatty acids on plasma lipoproteins and apolipoproteins in women. Am J Clin Nutr 1992;56:77–83.
19. Rush RF, Leon L, Turrel J. Advances in automated analysis. Miami: Thurman, 1970:503–7.
20. Raabo E, Terkildsen TC. On the enzymatic determination of blood glucose. Scand J Clin Lab Invest 1960;12:402–7.
21. Morgan C, Lazarow A. Immunoassay of insulin—two antibody system: plasma insulin levels in normal, subdiabetic rats. Diabetes 1963; 12:115–26.
22. St-Amand J, Moorjanit S, Lupien PJ, Prud'homme D, Despres JP. The relation of plasma triglyceride, apolipoprotein B, and high-density lipoprotein cholesterol to postheparin lipoprotein lipase activity is dependent on apolipoprotien E polymorphism. Metabolism 1996;45: 261–7.
23. Nilsson-Ehle P, Ekman R. Specific assays for lipoprotein lipase and hepatic lipase activities of post-heparin plasma. Protides Biol Fluid 1978;25:243–6.
24. Jéquier E, Acheson K, Schutz Y. Assessment of energy expenditure and fuel utilization in man. Annu Rev Nutr 1987;7:187–208.
25. Livesey G, Elia M. Estimation of energy expenditure, net carbohydrate utilization, and net fat oxidation and synthesis by indirect calorimetry: evaluation of errors with special reference to the detailed composition of fuels. Am J Clin Nutr 1988;47:608–28. (Published erratum appears in Am J Clin Nutr 1989;50:1475.)
26. Astrup A, Toubro S, Raben A, Skov AR. The role of low-fat diets and fat substitutes in body weight management: what have we learned from clinical studies? J Am Diet Assoc 1997;97:S82–7.
27. Raben A, Jensen ND, Marckmann P, Sandstrom B, Astrup A. Spontaneous weight loss during 11 weeks' ad libitum intake of a low fat/ high fiber diet in young, normal weight subjects. Int J Obes Relat Metab Disord 1995;19:916–23.
28. Siggaard R, Raben A, Astrup A. Weight loss during 12 week's ad libitum carbohydrate-rich diet in overweight and normal-weight subjects at a Danish work site. Obes Res 1996;4:347–56.
29. Blundell JE, Lawton CL, Cotton JR, Macdiarmid JI. Control of human appetite: implications for the intake of dietary fat. Annu Rev Nutr 1996;16:285–319.
30. Rolls BJ. Carbohydrates, fats, and satiety. Am J Clin Nutr 1995; 61(suppl):S960–7.
31. Warwick ZS, McGuire CM, Bowen KJ, Synowski SJ. Behavioral components of high-fat diet hyperphagia: meal size and postprandial satiety. Am J Physiol Regul Integr Comp Physiol 2000;278: R196–200.
32. Golay A, Bobbioni E. The role of dietary fat in obesity. Int J Obes Relat Metab Disord 1997;21(suppl):S2–11.
33. Lichtman SW, Pisarska K, Berman ER, et al. Discrepancy between self-reported and actual caloric intake and exercise in obese subjects. N Engl J Med 1992;327:1893–8.
34. Roche HM. Dietary carbohydrates and triacylglycerol metabolism. Proc Nutr Soc 1999;58:201–7.
35. Kris-Etherton PM. AHA Science Advisory. Monounsaturated fatty acids and risk of cardiovascular disease. American Heart Association. Nutrition Committee. Circulation 1999;100:1253–8.
36. Yagalla MV, Hoerr SL, Song WO, Enas E, Garg A. Relationship of diet, abdominal obesity, and physical activity to plasma lipoprotein levels in Asian Indian physicians residing in the United States. J Am Diet Assoc 1996;96:257–61.
37. Dattilo AM, Kris-Etherton PM. Effects of weight reduction on blood lipids and lipoproteins: a meta-analysis. Am J Clin Nutr 1992; 56:320–8.
38. Shintani TT, Beckham S, Brown AC, O'Connor HK. The Hawaii Diet: ad libitum high carbohydrate, low fat multi-cultural diet for the reduction of chronic disease risk factors: obesity, hypertension, hypercholesterolemia, and hyperglycemia. Hawaii Med J 2001;60:69–73.
39. Purnell JQ, Kahn SE, Albers JJ, Nevin DN, Brunzell JD, Schwartz RS. Effect of weight loss with reduction of intra-abdominal fat on lipid metabolism in older men. J Clin Endocrinol Metab 2000;85: 977–82.
40. Nakanishi N, Nakamura K, Suzuki K, Matsuo Y, Tatara K. Relation of body weight change to changes in atherogenic traits; a study of middle-aged Japanese obese male office workers. Ind Health 2000; 38:233–8.
41. McLaughlin T, Abbasi F, Kim HS, Lamendola C, Schaaf P, Reaven G. Relationship between insulin resistance, weight loss, and coronary heart disease risk in healthy, obese women. Metabolism 2001;50: 795–800.
42. Lichtenstein AH, Ausman LM, Carrasco W, Jenner JL, Ordovas JM, Schaefer EJ. Short-term consumption of a low-fat diet beneficially affects plasma lipid concentrations only when accompanied by weight loss. Hypercholesterolemia, low-fat diet, and plasma lipids. Arterioscler Thromb 1994;14:1751–60.
43. Heshka S, Yang MU, Wang J, Burt P, Pi-Sunyer FX. Weight loss and change in resting metabolic rate. Am J Clin Nutr 1990;52:981–6.
44. Leibel RL, Rosenbaum M, Hirsch J. Changes in energy expenditure resulting from altered body weight. N Engl J Med 1995;332:621–8. (Published erratum appears in N Engl J Med 1995;333:399.)
45. Ballor DL, Harvey-Berino JR, Ades PA, Cryan J, Calles-Escandon J. Decrease in fat oxidation following a meal in weight-reduced individuals: a possible mechanism for weight-recidivism. Metabolism 1996;45:174–8.
46. Kraegen EW, Cooney GJ, Ye J, Thompson AL. Triglycerides, fatty acids and insulin resistance—hyperinsulinemia. Exp Clin Endocrinol Diabetes 2001;109(suppl):516–26.
47. Parks EJ, Krauss RM, Christiansen MP, Neese RA, Hellerstein MK. Effects of a low-fat, high-carbohydrate diet on VLDL-triglyceride assembly, production, and clearance. J Clin Invest 1999;104: 1087–96.
48. Schrauwen P, Wagenmakers AJ, van Marken Lichtenbelt WD, Saris WH, Westerterp KR. Increase in fat oxidation on a high-fat diet is accompanied by an increase in triglyceride-derived fatty acid oxidation. Diabetes 2000;49:640–6.
49. Elia M, Livesey G. Theory and validity of indirect calorimetry during net lipid synthesis. Am J Clin Nutr 1988;47:591–607.
50. Simonson DC, DeFronzo RA. Indirect calorimetry: methodological and interpretative problems. Am J Physiol 1990;258:E399–412.

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