Postprandial effects of dietary *trans* fatty acids on apolipoprotein(a) and cholesteryl ester transfer[1–3]

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ABSTRACT

Background: The consumption of *trans* fatty acids adversely affects fasting plasma lipoprotein concentrations.

Objective: This study aimed to investigate whether postprandial lipoprotein metabolism is affected by the consumption of *trans* fatty acids.

Design: In a randomized crossover study, 19 healthy men consumed fatty meals that were identical except that 10% of energy was provided as *trans* 18:1 acids in the *trans* meal and as oleic acid in the *cis* meal.

Results: The meals induced similar responses in plasma lipids. Cholesteryl ester transfer (CET) was activated after consumption of both meals ($P < 0.0001$); however, it was 28% higher after the *trans* meal than after the *cis* meal (280 ± 129 compared with 219 ± 116 nmol cholesteryl ester/mL plasma · 6 h; time × diet interaction: $P < 0.0001$). Plasma apolipoprotein(a) [apo(a)] concentrations remained constant; however, triacylglycerol-rich lipoproteins formed 4 h after ingestion of the *trans* meal contained a higher concentration of apo(a) than did those formed after ingestion of the *cis* meal (48.9 ± 6.6 compared with 39.6 ± 5.4 U/L; $P < 0.02$). The change in CET and in the proportion of plasma apo(a) in the triacylglycerol-rich lipoprotein fractions correlated with indexes of alimentary lipemia.

Conclusions: Consumption of meals high in *trans* fatty acids results in higher CET and postprandial lipoprotein concentrations enriched in apo(a) than does consumption of meals free of *trans* fatty acids. This study highlights the importance of double-bond configuration in determining postprandial lipoprotein composition. *Am J Clin Nutr* 2003;77:1119–24.

KEY WORDS Postprandial lipemia, *trans* fatty acids, apolipoprotein(a), cholesteryl ester transfer, men

INTRODUCTION

Partial hydrogenation techniques to convert some of the *cis* fatty acids in oils and marine fats into *trans* fatty acids (TFA) or saturated fatty acids (SFAs) have dramatically increased the availability of TFAs in the food supply. Ecologic studies (1–5) suggest that the consumption of TFAs is positively associated with ischemic heart disease (IHD) risk, and increasing public health concerns (6) have prompted the production of margarines with minimal TFA concentrations. Despite efforts to reduce the amount of TFAs in the food supply, partially hydrogenated fats continue to feature in the production of many foods, particularly baked and fast-food products.

Studies in humans (7–16) and animals (17) suggest that the increased risk of IHD associated with TFA intake involves elevations in both apolipoprotein(a) [apo(a)] concentrations and the ratio of LDL to HDL cholesterol. High concentrations of apo(a) (18, 19) and LDL cholesterol (20, 21) and low concentrations of HDL cholesterol (20, 22) in fasting plasma are important independent predictors of IHD risk; however, only a small proportion of the day is spent in the fasting state. The typical Western diet is characterized by the regular consumption of energy-dense meals; therefore, the metabolically postprandial state usually predominates.

The idea that postprandial lipoproteins play a significant role in the progression of atherosclerotic lesions is not new (23, 24); however, triacylglycerol-rich lipoproteins (TRLs) were previously considered too large to penetrate arterial tissue. Chylomicron remnants can diffuse through arterial tissue in a rapid nonspecific manner and become preferentially trapped within the subendothelial space as concentrated focii (25). In addition, there is a growing number of reports that provide strong evidence that postprandial TRLs are involved in atherogenesis (26–29).

Although the fatty acid composition of individual meals has been shown to be a determinant of the plasma TRL response (30), the postprandial effects of consuming high-TFA meals are poorly understood. Therefore, this study aimed to compare the acute effects of ingesting meals high in TFAs with the effects of meals high in oleic acid on aspects of postprandial lipoprotein metabolism. Particular attention was directed toward differential effects on postprandial plasma and TRL lipid and apo(a) concentrations and cholesteryl ester transfer (CET).

SUBJECTS AND METHODS

Subjects

Volunteers were screened to exclude persons with the apolipoprotein *E2/E2* genotype, plasma apo(a) concentrations

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<30 mg/L, diabetes mellitus, abnormal liver function, and a body mass index (in kg/m^2) >30 and those persons taking medications or nutritional supplements known to affect lipoprotein metabolism. Nineteen volunteers with a mean (±SD) age of 29.0 ± 7.8 y and a body mass index of 24.8 ± 2.8 were accepted into the study. The subjects' fasting baseline lipid and lipoprotein concentrations (mmol/L) were as follows: triacylglycerol, 1.2 ± 0.3; total cholesterol, 4.8 ± 0.8; HDL cholesterol, 1.2 ± 0.3; and LDL cholesterol, 3.2 ± 0.8. The median apo(a) concentration was 130 mg/L (range: 37–634 mg/L). The distribution of apo E genotypes among the subjects was as follows: *E3/E3* (n = 9), *E3/E4* (n = 6), and *E2/E3* (n = 4). The volunteers accepted into the study were requested to maintain their habitual diet and exercise regimens. The protocol was approved by The Sydney University Human Ethics Review Committee.

Study design

A randomized crossover design was used to compare aspects of the postprandial response to a challenge meal containing TFAs (*trans* meal) with those to a control meal containing *cis* fatty acids (*cis* meal). On 2 occasions ≈2 wk apart, the subjects reported in a fasting (12 h) state to a metabolic unit, where a baseline (0 h) blood sample was collected. The subjects were then provided with either the *trans* or *cis* meal and were requested to consume the entire amount within 10 min. Additional blood samples were collected 4, 6, and 8 h postprandially. The subjects remained sedentary during the tests and were allowed water only.

Test meals

The test meals provided 49.4 kJ/kg body wt and contained 75% of total energy from fat, 20% from carbohydrate, and 5% from protein. The test meal provided 0.14 mg cholesterol/kg body wt and 1 g fat/kg body wt. The meals were identical in composition, except that 10% of energy was provided as *trans* 18:1 fatty acids in the *trans* meal and as oleic acid in the *cis* meal. The TFA was a commercially available TFA-containing margarine (Gold'n Canola; Meadow Lea Foods, Mascot, Australia), whereas the *cis* fatty acid was a blend of canola, olive, and palm oils (Meadow Lea Foods). The fat content of the meals was almost exclusively (99.5%) derived from test fats. The ratio of SFAs to monounsaturated fatty acids (MUFAs) to polyunsaturated fatty acids (PUFAs) in the meals was 0.69:3.08:1.00 and 0.62:2.87:1.00 in the *cis* and *trans* meals, respectively. The *cis* meal contained 62.4% of fatty acids as oleic acid (*cis*-18:1) and was devoid of *trans* 18:1 fatty acids, whereas the *trans* meal contained 51.7% of fatty acids as oleic acid and 9.9% as *trans* 18:1. Both fats contained small amounts of *trans* 16:1 (<0.01% total fatty acids) and *trans* 18:2 isomers (<0.50% total fatty acids). In calculating the ratio of fatty acid classes, *trans* fatty acids were included with the monounsaturates.

Meals were prepared by combining an amount of oil blend containing 1 g/kg fat with 2.96 mL/kg skim milk (Dairy Farmers, Sydney) with 0.43 g/kg condensed skim milk (Carnation Inc, Bathurst) and 0.43 g/kg chocolate topping (Mynor Chocolate Topping; Schweppes Cottee's, Melbourne) in a blender and presented to the subjects as a warm chocolate-flavored beverage.

Blood collection and processing

The subjects rested in a seated position for 15 min before each blood sample was obtained. Between blood samplings, the subjects were allowed to walk within a restricted area of the Metabolic Unit, read, or watch videos. Blood was drawn into EDTA-coated tubes, and plasma was recovered immediately by centrifugation (1000 × g, 15 min, 4 °C). The rate of CET was determined in fresh plasma supplemented with sodium azide, Trasylol (Bayer AG, Leverkusen, Germany), and Paraoxan (Sigma, St Louis) at final concentrations of 1 mmol/L, 50 U/mL, and 2 mmol/L, respectively.

Lipid and apolipoprotein(a) measurements

The concentrations of total cholesterol, free cholesterol, and triacylglycerol in plasma and the d (density) <1.006 (TRL) and >1.006 g/mL fractions were determined with the use of enzymatic techniques: cholesterol by CHOD-PAP and triacylglycerol with Unimate 5 (Roche, Basel, Switzerland) and free cholesterol with a method developed by Boehringer Mannheim, Mannheim, Germany. Cholesteryl ester (CE) concentrations were calculated by difference. HDL-cholesterol concentrations were measured after the precipitation of apo B–containing lipoproteins (31). Apo(a) was measured by radioimmunoassay (Mercodia, Uppsala, Sweden), and apo E genotyping was performed by restriction fragment length polymorphism gel electrophoresis. The CV for all assays was <5%.

Lipoprotein isolation

TRLs (d < 1.006 g/mL) were isolated by ultracentrifugation (200 000 × g, 16 h, 4 °C) in a 50.4 rotor (Beckman, Palo Alta, CA) on 2 separate occasions. First, lipoprotein fractions for lipids and CET assays were obtained by ultracentrifugation of fresh (unfrozen) plasma. Second, ultracentrifugation of a frozen aliquot was carried out for the analysis of apo(a). All samples obtained from an individual subject were assayed in the same run; >95% (n = 19) of total cholesterol and triacylglycerol were recovered from plasma.

Net cholesteryl ester transfer to triacylglycerol-rich lipoproteins

The net mass transfer of CE from lipoprotein fractions with a d >1.006 g/mL to TRLs was measured in plasma collected at 0 and 6 h as described previously (32). Briefly, duplicate aliquots (4 mL) of plasma were either kept on ice (control tubes) or incubated (6 h, 37 °C, pH 7.4) in a shaking water bath to activate the CET protein reaction. After ultracentrifugation (200 000 × g, 16 h, 4 °C, 50.4 rotor), both TRL fractions were assayed in triplicate for total cholesterol and free cholesterol. The TRL-CE value obtained from the control tube (incubated at 4 °C) was subtracted from the TRL-CE value incubated at 37 °C, and the results were expressed as nmol CE transferred/mL plasma in a 6-h incubation (nmol/mL plasma · 6 h). The CV of the 2 methods (cholesterol and free cholesterol concentrations) is <3%. In pilot studies, we showed that CET is linear over 6 h at baseline triacylglycerol concentrations in the range of 1.05–5.40 mmol/L.

Apolipoprotein(a) in the d < 1.006 and d > 1.006 g/mL fractions

The total plasma concentration and distribution of apo(a) in the d < 1.006 and d > 1.006 g/mL fractions were determined at 0 and 4 h. Aliquots (4 mL) of plasma were ultracentrifuged as described above, and the d < 1.006 g/mL fractions were recovered. The analysis of apo(a) concentrations was performed in duplicate.

Statistical analyses

Comparisons between test meal data were carried out by using a two-factor repeated-measures general linear model with Greenhouse-Geisser adjustments for asphericity where necessary.

TABLE 1
Plasma lipid concentrations in the fasting and postprandial states[1]

Variable and test meal	Time			
	0 h	4 h	6 h	8 h
Triacylglycerol[2]				
cis Meal	1.60 ± 0.50	2.74 ± 0.96	2.38 ± 1.00	1.77 ± 0.57
trans Meal	1.55 ± 0.32	2.80 ± 0.81	2.50 ± 0.86	1.73 ± 0.54
Total cholesterol[3]				
cis Meal	4.74 ± 0.99	4.87 ± 1.02	4.88 ± 1.05	4.86 ± 0.83
trans Meal	4.73 ± 0.81	4.84 ± 0.81	4.88 ± 0.91	4.75 ± 0.90
Cholesteryl ester[4]				
cis Meal	3.45 ± 0.61	3.58 ± 0.67	3.56 ± 0.66	3.46 ± 0.65
trans Meal	3.11 ± 0.74	3.30 ± 0.75	3.24 ± 0.80	3.31 ± 0.69
HDL cholesterol				
cis Meal	1.48 ± 0.37	1.46 ± 0.40	1.49 ± 0.43	1.51 ± 0.40
trans Meal	1.48 ± 0.37	1.46 ± 0.41	1.47 ± 0.43	1.48 ± 0.37

[1] $\bar{x}$ ± SD; $n = 19$.
[2–4] Significant time effect: [2] $P < 0.004$, [3] $P < 0.02$, [4] $P < 0.001$.

TABLE 2
Triacylglycerol-rich lipoprotein (TRL) triacylglycerol and TRL-cholesterol concentrations in the fasting and postprandial states[1]

	TRL-triacylglycerol[2]		TRL-cholesterol[2]	
Value	*cis* Meal	*trans* Meal	*cis* Meal	*trans* Meal
0 h				
(mmol/L)	0.71 ± 0.35	0.81 ± 0.31	0.24 ± 0.17	0.27 ± 0.13
(%)	49 ± 11	54 ± 8	5.02 ± 2.79	5.55 ± 2.35
6 h				
(mmol/L)	1.64 ± 1.01	1.94 ± 0.92	0.36 ± 0.22	0.42 ± 0.21
(%)	67 ± 14	71 ± 11	7.85 ± 4.78	8.23 ± 3.57

[1] $\bar{x}$ ± SD; $n = 19$.
[2] Significant time effect, $P < 0.001$.

P values for the effects of diet, time, and time × diet interaction were obtained. When a significant time × treatment effect was detected, specific effects were located by pairwise comparisons with a Bonferroni adjustment for multiple comparisons. Apo(a) data were analyzed with the use of Wilcoxon's matched-pairs signed-rank test. Correlations between variables were assessed with the use of Pearson's correlation coefficients. Analyses were performed with SPSS for WINDOWS (version 10; SPSS Inc, Chicago), and significance was set at $P < 0.05$. The data are presented as means ± SDs, except where noted otherwise.

RESULTS

All subjects who qualified for entry completed the study. The change in body weight between visits was an increase of 1.0 ± 0.1 kg.

Plasma and TRL concentrations

The subjects' fasting total cholesterol, HDL-cholesterol, CE, and triacylglycerol concentrations were not significantly different before the *cis* and *trans* test meals (**Table 1**). The meals elicited significant postprandial responses in plasma total cholesterol ($P < 0.02$), CE ($P < 0.001$), and triacylglycerol ($P < 0.004$) concentrations. HDL-cholesterol concentrations were not affected significantly. Plasma triacylglycerol was highest at 4 h, with concentrations being ≈2 times greater than fasting, and then decreased slightly to ≈1.5 times fasting concentrations by 6 h and then decreased to nearly fasting concentrations by 8 h. Plasma TRL concentrations are shown in **Table 2**. TRL-cholesterol and TRL-triacylglycerol concentrations were measured in fasting and 6-h postprandial plasma samples. Baseline concentrations were not significantly different, and both test meals resulted in increases in TRL-cholesterol ($P < 0.001$) and TRL- triacylglycerol ($P < 0.001$) concentrations.

Cholesteryl ester transfer

Rates of CET from lipoproteins in the $d > 1.006$ g/mL fraction to those in the $d < 1.006$ g/mL fraction were determined in fasting (0 h) and postprandial (6 h) samples. Fasting CET rates were similar in the *cis* and *trans* groups (147 ± 77 compared with 148 ± 73 nmol CE/mL · 6 h, respectively). Rates of CET from lipoproteins in the $d > 1.066$ g/mL fraction to TRLs were significantly higher 6 h after consumption of the *cis* and *trans* test meals than at baseline (219 ± 27 and 280 ± 30 nmol CE/mL · 6 h, respectively; $P < 0.0001$; **Figure 1**). The extent of the increase after the *trans* meal was significantly greater than that after the *cis* meal, as indicated by a significant time × diet interaction ($P < 0.0001$).

CET was closely correlated with indexes of plasma lipemia (**Table 3**). CET correlated with plasma triacylglycerol and TRL- triacylglycerol in both the fasting and postprandial states. At 6 h after ingestion of the meals, the percentage increase in CET correlated positively with the percentage increase in plasma triacylglycerol and TRL- triacylglycerol. CET did not correlate with plasma total cholesterol or TRL-cholesterol concentrations.

Apo(a) in plasma TRL and the $d > 1.006$ g/mL fraction

TRL-apo(a), expressed as the percentage change from baseline, correlated significantly with plasma triacylglycerol ($r = 0.60$,

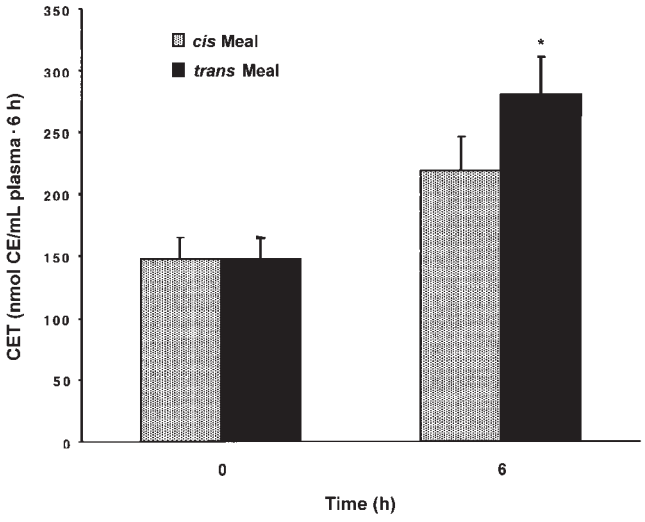

FIGURE 1. Mean (±SE) cholesteryl ester transfer (CET) from lipoproteins with a density > 1.006 g/mL to triacylglycerol-rich lipoproteins (density < 1.006 g/mL) in the fasting state and after the consumption of meals in which 10% of energy was provided as *trans* 18:1 acids (*trans* meal) or as oleic acid (*cis* meal). $n = 19$ healthy men. Significant time ($P < 0.0001$) and time × diet interaction ($P < 0.0001$). *Significantly different from the *cis* meal, $P < 0.05$.

TABLE 3
Relation between cholesteryl ester transfer (CET) (nmol CE/mL plasma · 6 h) and plasma triacylglycerol and triacylglycerol-rich lipoprotein triacylglycerol concentrations in the fasting and postprandial states[1]

Variable and test meal	CET 0 h	CET 6 h	↑ CET
			%
Plasma triacylglycerol (mmol/L)			
0 h			
cis Meal	0.53[2]	0.54[2]	−0.32
trans Meal	0.75[3]	0.34	−0.18
6 h			
cis Meal	0.71[3]	0.88[3]	0.30
trans Meal	0.55[4]	0.89[3]	0.38
TRL-triacylglycerol (mmol/L)			
0 h			
cis Meal	0.88[3]	0.74[4]	−0.32
trans Meal	0.91[3]	0.62[5]	−0.31
6 h			
cis Meal	0.70	0.84[3]	0.20
trans Meal	0.54[2]	0.87[3]	0.32
↑ Plasma triacylglycerol (%)			
cis Meal	0.10	0.48[2]	0.59[5]
trans Meal	0.13	0.64[2]	0.60[5]
↑ TRL-triacylglycerol (%)			
cis Meal	−0.19	0.18	0.76[3]
trans Meal	−0.10	0.41	0.65[5]

[1] Values are *r*; $n = 19$ for each meal.
[2] $P \leq 0.05$.
[3] $P \leq 0.0001$.
[4] $P < 0.001$.
[5] $P < 0.007$.
[6] $P = 0.0005$.

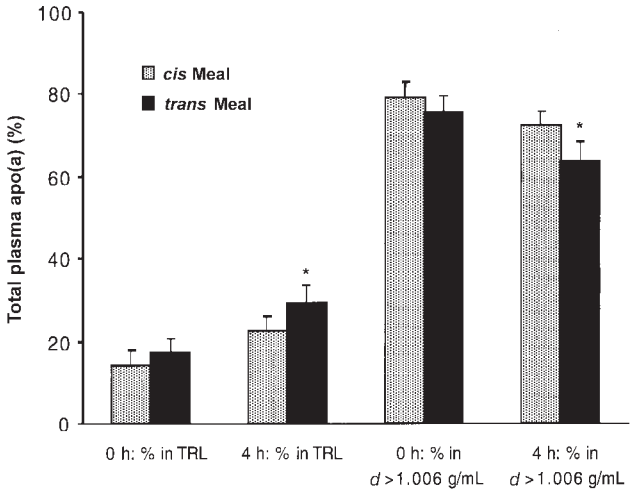

FIGURE 2. Mean (±SE) percentage of total plasma apolipoprotein(a) [apo(a)] in triacylglycerol-rich lipoprotein [TRL; density (*d*) < 1.006 g/mL] and in plasma fractions with a $d > 1.006$ g/mL in the fasting state and after the consumption of meals in which 10% of energy was provided as *trans* 18:1 acids (*trans* meal) or as oleic acid (*cis* meal). $n = 19$ healthy men. *Significantly different from the *cis* meal at same time, $P < 0.05$.

$P < 0.0001$), TRL-triacylglycerol ($r = 0.77$, $P < 0.0001$), and the percentage increase in plasma triacylglycerol ($r = 0.69$, $P < 0.0001$) at 4 h. Ingestion of the test meals altered the distribution of apo(a) within the plasma compartment. In fasting plasma, TRL-apo(a) expressed as a percentage of the plasma apo(a) concentration was not significantly different between the *cis* and *trans* meal groups. After consumption of the test meals (4 h), the percentage distribution of apo(a) in TRL increased significantly in the *trans* meal group compared with the *cis* meal group ($P = 0.005$; **Figure 2**). This redistribution was confirmed by a significant reduction in the concentration of apo(a) in the $d > 1.006$ g/mL fraction ($P < 0.02$; Figure 2). Together, these results indicate that the consumption of the *trans* meal resulted in a greater apo(a) redistribution from the $d > 1.006$ g/mL fraction to the TRL fraction than did the consumption of the *cis* meal.

DISCUSSION

Research into the mechanisms underlying the increased risk of IHD associated with consumption of high-TFA diets suggests that the effects are multifactorial. Two key factors have been identified. First, the consumption of TFA-rich diets increases the fasting plasma CET protein activity relative to other major dietary fatty acids (17, 33–35). Although many other factors, such as lipoprotein receptor activity and rates of lipoprotein secretion, could be involved, studies showing increased fasting ratios of LDL to HDL cholesterol after short-term consumption of high-TFA diets (7–10, 12–17) support a role for TFA in regulating CET protein activity. Second, diets rich in TFAs have been shown to increase plasma apo(a) compared with diets containing similar amounts of oleic acid (11, 13, 17), stearic acid (1), palmitic acid (13, 17), or SFA combinations (11, 13, 17). The findings of the present study show that an increase in CET and an enrichment of TRL with apo(a) occurs in the postprandial state to a greater extent after a meal that contains fat in the *trans* than in the *cis* configuration.

Postprandial lipemia induces the formation of TRLs with elevated rates of CET (36–38) and elevated apo(a) concentrations (39–41). The current study was designed to investigate the acute effects of meals high in either TFAs (*trans* meal) or oleic acid (*cis* meal) on lipid concentrations, CET, and the apo(a) content of TRLs. The timing of blood collection was designed to take advantage of the maximal remodeling of plasma lipoproteins 3–6 h after an oral fat load. The results suggest that ingestion of TFA-rich meals induces a greater postprandial increase in CET and TRL-apo(a) concentrations than do meals in which TFAs are replaced with oleic acid. Postprandial increases in CET and the proportion of total plasma apo(a) contained TRLs correlated closely with postprandial increases in plasma and TRL-triacylglycerol. This highlights the importance of double-bond configuration in determining the composition of postprandial lipoproteins and suggests that the increased risk of IHD associated with high TFA intakes includes adverse effects on postprandial lipoprotein metabolism.

The test meals used in the current study provided 1 g fat /kg body wt, which represents a serving of fat easily achieved in real-life settings. Ingestion of the *cis* and *trans* meals elicited similar postprandial responses in plasma triacylglycerol, TRL-triacylglycerol, total cholesterol, HDL cholesterol, and CE concentrations (Table 1). Peak plasma triacylglycerol and TRL-triacylglycerol concentrations were observed at 4 h, with concentrations increasing by ≈2-fold. Plasma triacylglycerol and TRL-triacylglycerol concentrations remained elevated at 6 h but approached fasting

concentrations by 8 h. The postprandial increases in plasma and TRL-triacylglycerol observed in the current study are comparable with those observed in previous reports (36, 40, 41).

Fasting rates of CET from lipoproteins with a $d > 1.006$ g/mL to TRLs were not significantly different; however, ingestion of the *trans* meal resulted in significantly higher rates of CET in postprandial plasma than did the *cis* meal (increases of $102 \pm 68\%$ and $68 \pm 52\%$, respectively; Figure 1). The postprandial elevations in CET are similar to the elevations observed in previous reports in healthy (37) and hypercholesterolemic (36) subjects fed similar oral fat loads. CET was correlated with plasma triacylglycerol and TRL-triacylglycerol in both the fasting and postprandial states (Table 3). Postprandially, the percentage increase in CET was most closely correlated with the percentage increase in plasma triacylglycerol and TRL-triacylglycerol (Table 3). These findings agree with those of previous studies, ie, the plasma triacylglycerol concentration is the major factor determining the extent of postprandial CET activation (36–38), whereas the fatty acid composition of TRL has less of an effect (37).

Increases in the plasma CETP concentration have also been implicated in both the postprandial stimulation of CET (38) and in elevated fasting plasma CETP activity after the consumption of TFA-rich diets (34); however, this was not investigated in the current study. The increase in postprandial CET after ingestion of the *trans* meals in the current study is comparable with increases in fasting CET activities reported in other short-term feeding trials (33, 34). The similar plasma triacylglycerol and TRL-triacylglycerol responses to the *cis* and *trans* meals together with the lack of an association of CET with the concentration of TFA in TRL support the notion that increased CETP mass may account for increases in CETP activity.

Total plasma apo(a) concentrations in fasting and postprandial plasma were not significantly different after the *cis* or *trans* meals; however, consumption of the oral fat loads altered the distribution of apo(a) within the lipoprotein fractions. The percentage of total plasma apo(a) in the TRL fraction in fasting plasma was also similar; however, ingestion of the *trans* meal resulted in the formation of a TRL fraction containing a significantly higher ($P < 0.005$) proportion of total plasma apo(a) relative to the *cis* meal. Similarly, reciprocal changes in apo(a) were detected in the $d > 1.006$ g/mL lipoprotein fraction. Together, these data suggest that elevations in TRL-apo(a) concentrations after an oral fat load are due to the redistribution of apo(a) or lipoprotein(a) from lipoproteins with a $d > 1.006$ g/mL to TRLs rather than to an increase in the production of apo(a). These data corroborate similar findings from previous work in which the acute effects of equivalent oral fat loads were investigated (40, 41). In addition, the findings of the current study provide new evidence suggesting that the consumption of TFA-containing meals results in TRLs that contained more apo(a) than did the consumption of TFA-free meals.

The percentage of total plasma apo(a) in TRLs and the percentage increase in TRL-apo(a) were closely correlated with 4-h plasma triacylglycerol and TRL-triacylglycerol concentrations and with the percentage increase in plasma triacylglycerol and TRL-triacylglycerol. In contrast, the correlations between plasma total apo(a) and TRL-apo(a)—expressed as the absolute concentration or the change in concentration 4 h postprandially—were much weaker ($r \leq 0.37$, $P < 0.05$). Postprandial increases in TRL-apo(a) did not correlate significantly with increases in CET, suggesting that many factors may be involved in the 2 processes.

Marcoux et al (42) showed that postprandial TRLs contained a much smaller proportion (≈5%) of total plasma apo(a) than observed in the current study and in other studies (40, 41). These differences may have been due to the smaller fat load administered, to the earlier timing of blood collection, or to the different method of preparing the TRL fraction. Despite these differences, characterization of 3-h postprandial TRLs showed apo(a) to be associated with lipoproteins intermediate in size between VLDLs and LDLs, consistent with it being apo(a) (42). Apo(a) was also easily dissociated from TRL lipids, suggesting that increases in TRL-apo(a) are the result of noncovalent binding of lipoprotein(a) to TRL during alimentary lipemia.

In addition to being associated with TRLs, apo(a) has also been isolated from human atherosclerotic plaque (43–46), possibly in association with proteoglycans (46). This could allow for the accumulation of lipoprotein(a) at the site of vessel injury, where it may undergo oxidative modification and become a ligand for the scavenger receptor on macrophages (47), thereby contributing to foam cell formation (48). The elevated concentration of apo(a) in TRLs after meals enriched in TFAs may therefore enhance the involvement of TRLs in atherogenesis.

In summary, our data provide insight into the role of TFAs in regulating lipoprotein metabolism. The consumption of meals in which *cis* fatty acids (oleic acid) are replaced with *trans* fatty acids results in elevations in CET and in the formation of TRLs, which are relatively enriched in apo(a). The findings of the current study suggest that frequent ingestion of foods that contain TFAs has deleterious consequences on the composition of postprandial lipoprotein particles, which may enhance their atherogenicity.

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