Postprandial lipaemia is associated with increased levels of apolipoprotein A-IV in the triacylglycerol-rich fraction and decreased levels in the denser plasma fractions

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Apolipoprotein (apo) A-IV is primarily associated with HDL or with the lipoprotein-free fraction of plasma, and in small amounts with chylomicrons and VLDL. The aim of the present study was to assess the effect of a fatty meal on the postprandial variation in plasma apo A-IV and on its distribution among lipoprotein fractions following absorption of fat. Twenty healthy male subjects participated in the study. After an overnight fast, subjects were given a fatty breakfast containing 1 g fat/kg body weight (% energy: fat 65, carbohydrate 20, protein 15). Blood samples were taken every hour during the next 10 h. Apo A-IV was measured by ELISA. Postprandial lipaemia was associated with a moderate, although significant, increase in the plasma levels of apo A-IV. Apo A-IV increased from the median baseline value of 0·15 g/l to 0·165 g/l (median +17 %; $P < 0·01$) 5 h after fat ingestion. The postprandial peak of apo A-IV occurred 1 h after the triacylglycerol peak. There were no statistically significant correlations between baseline lipids, baseline apo A-IV and postprandial changes in apo A-IV levels, or between postprandial changes in lipids and apo A-IV at any time. To assess apo A-IV distribution among lipoproteins, plasma was fractionated by fast performance liquid chromatography at baseline and 3, 6 and 10 h postprandially. There was a substantial heterogeneity in the apo A-IV distribution among lipoproteins following the fatty meal. At 3 h after fat ingestion, apo A-IV levels increased in the triacylglycerol-rich lipoprotein (TRL) fraction and decreased in the denser plasma fraction. At 6 h after the fatty meal, apo A-IV was still present in the TRL but was decreased in the HDL fractions. The findings of the present study support the concept that apo A-IV particles transfer from the denser plasma fraction to TRL during postprandial lipaemia.

Postprandial metabolism: Apolipoprotein A-IV: Lipids

Human apolipoprotein (apo) A-IV is a 46 kDa glycoprotein (Beisiegel & Utermann, 1979) of known amino acid structure (Elshourbagy *et al.* 1986) that is synthesized in the intestine (Beisiegel & Utermann, 1979; Green *et al.* 1979, 1980; Utermann & Beisiegel, 1979). In plasma, apo A-IV is found primarily associated with HDL or in the lipoprotein-free fraction (Bisgaier *et al.* 1985; Ohta *et al.* 1985; Weinberg & Spector, 1985; Lagrost *et al.* 1989). Small amounts of apo A-IV are found associated with chylomicrons and VLDL (Lagrost *et al.* 1989). The primary function of apo A-IV is not known. Apo A-IV has been reported to activate lecithin-cholesterol acyltransferase (*EC* 2.3.1.43; LCAT) (Steinmetz *et al.* 1985) and to favour plasma cholesterol-ester transfer activity among lipoproteins (Barter *et al.* 1988). *In vitro*, apo A-IV potentializes activation of lipoprotein lipases by apo C-II (Goldberg *et al.* 1990). In addition, apo A-IV complexed with liposomes promotes cholesterol efflux from cultured cells (Stein *et al.* 1986). Recent studies have demonstrated that intravenous and cerebro-ventricular injections of apo A-IV in the rat are associated

with a significant reduction in feed intake (Fujimoto *et al.* 1992, 1993). This suggests that apo A-IV may act in rats as a physiological signal for satiation. However, other experiments using transgenic mice overexpressing human apo A-IV were unable to reproduce the anorectic effect of apo A-IV (Aalto-Setälä *et al.* 1994).

Most of the evidence concerning apo A-IV postprandial metabolism comes from poorly standardized studies involving small numbers of subjects (Green *et al.* 1979; Bisgaier *et al.* 1985; Seishima *et al.* 1988; Zaiou *et al.* 1993). Accordingly, an increase in plasma apo A-IV level at a single point in time after a fatty meal was demonstrated (Green *et al.* 1979; Bisgaier *et al.* 1985; Zaiou *et al.* 1993). After a fatty meal, an increase in apo A-IV mRNA in the enterocytes is followed by secretion of the protein. Human apo A-IV thus secreted is associated with chylomicrons (Green *et al.* 1979). *In vitro* experiments suggest that on entering into the plasma compartment, apo A-IV is displaced from chylomicrons by other transferable apolipoproteins (Weinberg & Spector, 1985). However, *in vivo* the distribution of human apo A-IV among lipoproteins has not been properly documented following fat ingestion. This is because ultracentrifugation, the most common method used to separate plasma lipoproteins, dissociates apo A-IV from the surface of the lipoproteins. To avoid this problem we used gel filtration chromatography to analyse the distribution of apo A-IV among lipoproteins following a fatty meal. The results of the present study support the concept that apo A-IV particles transfer from the denser plasma fraction to triacylglycerol-rich lipoproteins (TRL) during postprandial lipaemia.

METHODS

Subjects

Twenty healthy male subjects participated in the study after signing an informed written consent. None of them had diabetes, liver, renal or thyroid disease. All participants were consuming their habitual diet at the time of the experiment. The subjects were admitted to the hospital (Centre d'Investigation Clinique, CHR and U de Lille, Lille, France) on the morning of the study and remained hospitalized for 10 h. The protocol was reviewed by an INSERM ethical board and approved by the local ethics committee (Comité Consultatif de Protection des personnes dans la Recherche Biomedicale de Lille, Centre Hospitalier Régional, 1 place de Verdun, 59045 Lille Cedex) according to French regulations.

Oral fat meal

After an overnight fast (12 h), subjects were given a fatty breakfast. This was prepared according to the subject's weight with white bread (3·5 slices), sugar (20 g), butter (40 g), fresh double cream (100 ml), powdered milk (50 g) and strawberries (100 g). The fatty meal (65% energy as fat, 20 % as carbohydrates and 15 % as protein) contained 1 g fat/kg body weight. It contained 80 kJ energy and 3 mg cholesterol per kg body weight. This breakfast was ingested in 15 min beginning between 07.45 and 08.15 hours. After the meal the subjects remained fasting for 10 h, but were allowed to drink as much water as desired. The meal was well tolerated by all subjects.

Lipid measurements

Blood was collected in tubes containing EDTA to reach a final concentration of 1 mg/ml. Plasma was separated by centrifugation (3300 ***g***) for 20 min at 4°. Lipoproteins were separated using a standard procedure (Lipid Research Clinics Program, 1974) by a

combination of ultracentrifugation (at density (d) 1·006 g/ml) and phosphotungstate precipitation. HDL-cholesterol was measured after precipitation with phosphotungstate using commercially available reagents (Cholesterol HDL, CHOD/PAP, Boehringer Mannheim, Mannheim, Germany). VLDL were separated by ultracentrifugation (Traber *et al.* 1987), using a Beckman TL100 centrifuge (Beckman Instrument France SA, Gagny, France), from 0·5 ml plasma by a single spin at d 1·006 g/ml. NaCl (9 g/l; 0·5 ml) was added to 0·5 ml plasma and spun in a polycarbonate tube (435 700 ***g***, 20°) in a Beckman 100.2 Ti rotor. The tube was sliced and the remaining 0·5 ml infranatant was analysed for lipids.The TRL ($d < 1·006$ g/ml) fraction was measured by subtracting infranatant values from plasma values and LDL was quantified by subtracting HDL values from infranatant values. Triacylglycerols (TG) (Triglycerides GPO-PAP, Boehringer Mannheim) and cholesterol (Cholesterol C System, Boehringer Mannheim) were determined enzymically.

Gel filtration chromatography

Gel filtration chromatography (fast performance liquid chromatography; FPLC) was performed using a Superose 6 HR 10/30 column (Pharmacia LKB Biotechnology, S-751 82 Uppsala, Sweden). The column was allowed to equilibrate with phosphate-buffered saline (PBS; 10 mmol/l) containing 1 mmol/l EDTA; 130 μl plasma was eluted with the buffer at room temperature at a flow rate of 0·2 ml/min. The elution profile was monitored at 280 nm and recorded by an analogue-recorder chart tracing system (Pharmacia LKB Biotechnology). The effluents were collected in 0·26 ml fractions. Calibration was carried out with VLDL ($d < 1·006$ g/ml), LDL ($1·019 < d < 1·063$ g/ml), HDL ($1·063 < d < 1·21$ g/ml) and bovine albumin Fraction V (Sigma Chemical Co., St Louis, MO, USA).

Apolipoprotein A-IV measurements

Human apolipoproteins were measured by a non-competitive ELISA (sandwich ELISA). Briefly, rabbit polyclonal antibodies were prepared in our laboratory using human apo A-IV. Polystyrene microtitre plates were coated with the affinity-purified polyclonal antibodies (1 mg/ml). Duplicate plasma samples were diluted 1:10 000 with PBS (100 mmol/l) containing 10 g albumin/l. The samples were added to the wells along with the standards and controls. The samples were incubated for 2 h at 37°. After incubation, the plates were washed four times with PBS (100 mmol/l) and apo A-IV antibodies conjugated to peroxidase (*EC* 1.11.1.7) were added. The plates were incubated for 2 h at 37° and then washed. Colour development was performed in 30 min by the addition of peroxidase substrate (o-phenylenediamine dihydrochloride; Sigma). The plates were read at 492 nm on an automated microplate reader model EL340 (Bio-Tek Instruments, Inc., Winooski, VT, USA).

Statistical analysis

Results are expressed as means and standard deviations, median and range. Overall differences among mean lipid and apolipoprotein values were tested with one-way ANOVA with repeated measures (time after fatty meal). Whenever a statistically significant main effect ($P < 0·05$) was found, post hoc analysis was performed with the Dunnett test for comparison with baseline. In addition, the Wilcoxon test for paired samples was used to test the effect of the fatty meal on non-parametric data. Pearson's correlation coefficients were used to assess the relationship between two variables.

RESULTS

Plasma lipid and lipoprotein levels

The clinical and biochemical characteristics of the twenty subjects under study are presented in Table 1. The mean age and BMI were, respectively, 23 (SD 1·5) years and 22·5 (SD 2·1) kg/m^2. Plasma cholesterol (range 2·77–6·34 mmol/l) and plasma TG (range 0·65–1·70 mmol/l) were within normal values. Apo A-IV levels varied between 0·09 and 0·26 g/l with a mean of 0·16 (SD 0·04) g/l and median of 0·15 g/l which correspond to normal levels. The mean values of plasma lipid and lipoprotein responses to the fatty meal are summarized in Table 2. Mean plasma TG levels increased progressively to reach a peak 4 h after the ingestion of the fat-rich meal. This was followed by a decrease in the mean TG level, returning to the baseline value 7 h after the fatty load. Mean TG levels further decreased to reach the lowest plasma value 10 h after the fatty meal. VLDL-TG followed the same response pattern, whereas mean VLDL-cholesterol reached a plateau 3 h after breakfast and decreased progressively to the baseline value 10 h postprandially. Other lipid variables changed only slightly.

Plasma apolipoprotein A-IV levels

Mean, median and range of plasma apo A-IV values in response to the fatty meal are summarized in Table 2. Mean apo A-IV concentration remained fairly stable up to 4 h after the meal. It was significantly higher than the baseline value 5 h postrandially and decreased progressively. Fig. 1 illustrates the median percentage changes in plasma TG, VLDL-TG and apo A-IV concentrations. The median percentage changes in plasma TG (+60 %; $P < 0{\cdot}001$) and VLDL-TG (+110 %; $P < 0{\cdot}001$) were the highest 3 h postprandially and decreased slowly for 7 h after the meal. In contrast, median apo A-IV was fairly stable and increased significantly (+17 %; $P < 0{\cdot}001$) only at the time point 5 h after the fat-rich meal. The response to this meal was heterogeneous. One third of the subjects presented a modest (< 0 %) median increase in plasma apo A-IV between fasting and 5 h after the fatty meal.

Table 1. *Clinical and biological characteristics of the twenty male subjects participating in this study*

	Mean	SD	Median	Range
Age (years)	23·5	1·5	24	20–26
Weight (kg)	73·3	9·1	71·5	62–99
BMI (kg/m^2)	22·5	2·1	22	19·6–28
Cholesterol (C) (mmol/l)	4·31	0·92	4·15	2·77–6·34
LDL-C (mmol/l)	2·51	0·92	2·56	0·71–1·88
HDL-C (mmol/l)	1·35	0·50	1·21	0·74–2·67
Triacylglycerols (TG) (mmol/l)	1·09	0·33	1·07	0·65–1·70
VLDL-TG (mmol/l)	0·69	0·30	0·64	0·29–1·33
VLDL-C (mmol/l)	0·45	0·21	0·5	0·10–0·79
Apo B (g/l)	0·65	0·22	0·64	0·16–1·0
Apo A-I (g/l)	1·17	0·21	1·14	0·90–1·58
Apo A-II (g/l)	0·29	0·06	0·27	0·19–0·41
Apo A-IV (g/l)	0·16	0·04	0·15	0·09–0·26

Table 2. *Plasma lipid, lipoprotein and apolipoprotein (apo) A-IV levels according to time after a fatty meal in twenty male subjects*‡

(Mean values and standard deviations, median values and range)

Time after meal (h) ...		Baseline	1	2	3	4	5	6	7	8	9	10	P§
Cholesterol (C) (mmol/l)	Mean	4·30	4·04***	4·04***	4·15*	4·12*	4·20	4·26	4·15	4·18	4·18	4·31	0·0001
	SD	0·92	0·87	0·92	0·90	0·87	0·99	1·00	1·03	1·00	1·00	0·95	
Triacylglycerols (TG) (mmol/l)	Mean	1·09	1·23	1·52***	1·84***	1·95***	1·73***	1·42*	1·12	0·94	0·83	0·85	0·0001
	SD	0·33	0·42	0·56	0·78	0·90	0·77	0·51	0·27	0·24	0·20	0·25	
VLDL-TG (mmol/l)	Mean	0·69	0·86	1·09***	1·39***	1·47***	1·26***	0·97*	0·68	0·53	ND	0·47	0·0001
	SD	0·30	0·39	0·53	0·72	0·86	0·71	0·51	0·28	0·22		0·24	
VLDL-C (mmol/l)	Mean	0·45	0·55	0·63*	0·71***	0·69**	0·61	0·61	0·58	0·55	ND	0·45	0·0002
	SD	0·21	0·21	0·29	0·32	0·29	0·26	0·26	0·26	0·26		0·26	
Apo A-IV (g/l)	Mean	0·160	0·155	0·156	0·155	0·155	0·181**	0·165	0·156	0·151	0·155	0·157	0·0005
	95% CI	0·080–0·240	0·095–0·215	0·096–0·216	0·095–0·215	0·095–0·215	0·101–0·261	0·085–0·245	0·096–0·216	0·091–0·211	0·075–0·235	0·097–0·217	
	Median	0·150	0·150	0·158	0·158	0·158	0·165†	0·163	0·163	0·148	0·155	0·153	
	Range	0·09–0·26	0·09–0·25	0·10–0·22	0·11–0·20	0·10–0·22	0·13–0·26	0·11–0·27	0·09–0·22	0·10–0·20	0·08–0·23	0·10–0·24	

ND, not determined.

Mean values were significantly different from baseline: *$P < 0·05$, **$P < 0·01$, ***$P < 0·001$ (Dunnett test, post hoc analysis).

†Median value was significantly different from baseline, $P < 0·05$ (Wilcoxon test for paired samples).

‡For details of subjects and procedures, see Table 1 and pp. 214–215.

§For ANOVA with repeated measures.

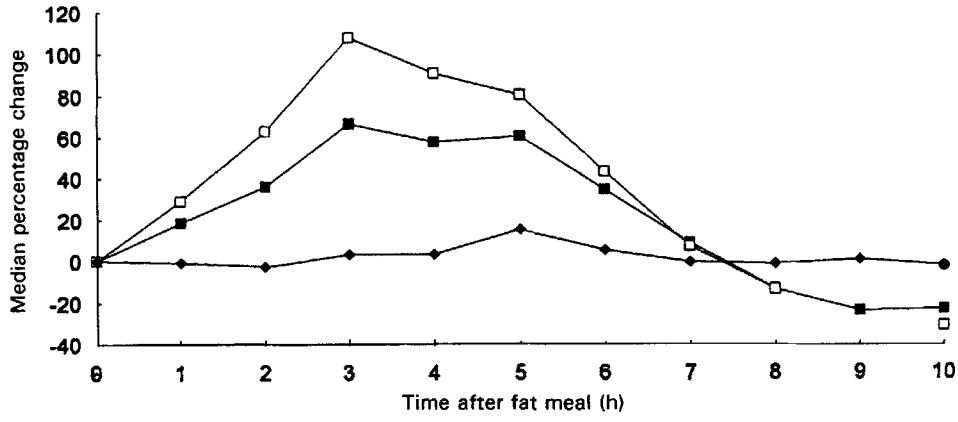

Fig. 1. Percentage changes in plasma triacylglycerol (■), VLDL-triacylglycerol (□) and apolipoprotein A-IV (◆) concentrations after intake of a fatty meal. Values are medians for twenty subjects. For details of subjects and procedures, see Table 1 and pp. 214–215.

Another third had a moderate increase ranging between 0% and +25% and in the last third median apo A-IV values increased between 25% and 90%.

In order to evaluate a possible relationship between TG and apo A-IV secretion, mean and median apo A-IV levels were calculated at TG peak and the subsequent hours (Table 3). Mean levels of apo A-IV at the peak of TG were not statistically significantly different from the baseline values. At 1 h after the postprandial TG peak, mean apo A-IV concentration was significantly higher than the baseline value and decreased progressively to reach the fasting value 3 h after the TG peak. Correlation analysis did not demonstrate any statistically significant ($P < 0.05$) relationship between the fasting values of apo A-IV and the fasting levels of cholesterol (r 0·12; NS), TG (r 0·25; NS) and VLDL-TG (r 0·23; NS). There was no significant correlation between fasting apo A-IV and changes in apo A-IV (r 0·32; NS). There was no significant correlation between changes in plasma apo A-IV and changes in plasma TG (r 0·13; NS) or VLDL-TG (r 0·13; NS).

Plasma apolipoprotein A-IV distribution among lipoproteins after the fatty meal

The changes in plasma apo A-IV were associated with changes in both TRL and denser plasma fractions. The median apo A-IV level in each FPLC fraction from plasma collected at baseline and 3, 6 and 10 h after the fatty meal is illustrated in Fig. 2. In fasting samples (baseline value), only a minimal amount of apo A-IV was recovered with VLDL. In contrast, apo A-IV increased in the TRL fractions 3 h after the fatty meal. The increased levels of apo A-IV in the TRL fraction were associated with lower values in the denser plasma fraction. At 6 h after the fatty meal, TRL-apo A-IV remained above the the baseline value although not as elevated as 3 h after the fatty meal and was associated with lower values in the HDL size range. At 10 h after the meal apo A-IV distribution among lipoprotein fractions was similar to that of fasting samples.

Table 3. *Plasma apolipoprotein (apo) A-IV levels in twenty male subjects according to time after the postprandial triacylglycerol (TG) peak*‡

(Mean values and standard deviations)

	Baseline		Peak TG		Peak TG + 1 h		Peak TG + 2 h		Peak TG + 3 h		
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	*P*§
TG (mmol/l)	1·09	0·33	2·06***	0·85	1·67***	0·71	1·29	0·48	1·01	0·29	0·0001
VLDL-TG (mmol/l)	0·69	0·30	1·59***	0·80	1·18***	0·66	0·81	0·44	0·59	0·24	0·0001
Apo A-IV (g/l)											
Mean	0·16		0·158		0·176*		0·17		0·157		0·01
95% CI	0·08–0·24		0·098–0·218		0·096–0·256		0·07–0·27		0·097–0·257		
Median	0·155		0·168		0·170†		0·165		0·157		

Mean values were significantly different from baseline: $*P < 0·05$, $***P < 0·001$ (Dunnett test, pest hoc analysis).

† Median value was significantly different from baseline, $P < 0·05$.

‡For details of subjects and procedures, see Table 1 and pp. 214–215.

§For ANOVA with repeated measures.

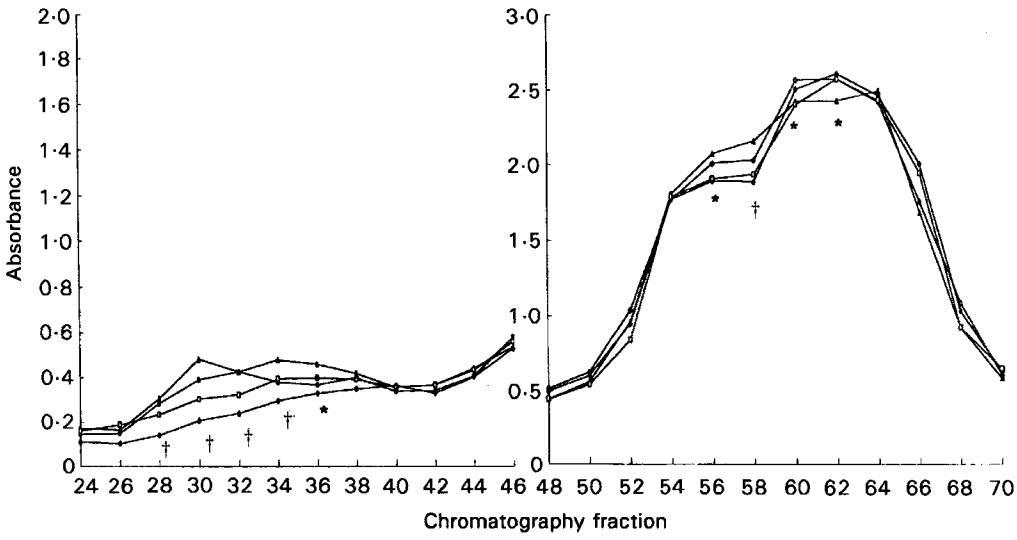

Fig. 2. Distribution of apolipoprotein A-IV among lipoproteins after gel filtration chromatography. Apolipoprotein A-IV concentration was measured in each sample collected by gel filtration chromatography. Chromatography fractions (from fraction 28 to fraction 70) are presented on the X axis. Apo A-IV concentrations are expressed as absorbance values on the Y axis. Values are medians for eighteen subjects at baseline (◇), and 3 h (▲), 6 h (●), and 10 h (□) postprandially. Two scales are used: (1) left panel: chylomicrons from fraction 28 to 30; VLDL from fraction 28 to 34; Intermediate density lipoproteins from fraction 32 to 36; LDL from fraction 34 to 44, (2) right panel: HDL from fraction 52 to 60; lipoprotein-free medium from fraction 60 to 70. One-way ANOVA with repeated measures was used to test for differences among times: $*P < 0{\cdot}05$, $\dagger P < 0{\cdot}01$.

DISCUSSION

The results of the present study indicate that plasma apo A-IV levels rise moderately although significantly after fat ingestion. The median increase reached 117% of the fasting baseline value and peaked 5 h after the meal. This result is in agreement with those of previous studies (Green *et al.* 1980; Bisgaier *et al.* 1985; Seishima *et al.* 1988). Initial observations by Green *et al.* (1980) demonstrated a modest (+16%) elevation of apo A-IV levels after a fatty meal in five normal volunteers. Bisgaier *et al.* (1985) confirmed the increase (+31%) in apo A-IV levels 4 h after ingestion of 40 g fat by five healthy subjects. In another investigation, Seishima *et al.* (1988) found in eight healthy normolipidaemic subjects a moderate increase (mean +14%) in plasma apo A-IV concentration 4 h after the ingestion of 55 g butter. In contrast with these studies, Zaiou *et al.* (1993) did not find a consistent elevation in plasma apo A-IV concentration following fat ingestion. This was possibly due to the small amount of fat in the test meal (13 g lipids) in the study. The findings of the present study, as well as the results of published studies, indicate that fat ingestion is associated with a moderate and transient accumulation of plasma apo A-IV. The restoration of apo A-IV concentration to the basal levels 10 h after fat ingestion indicates that plasma apo A-IV is cleared to the baseline level or that its synthesis is not stimulated in the late absorptive state.

The mean plasma apo A-IV level peaked 1 h after plasma- and VLDL-TG supporting the concept of a time discrepancy between chylomicron and apo A-IV postprandial secretion. One study in men (Green *et al.* 1980) demonstrated that the secretion of apo A-IV was delayed compared with that of chylomicrons. Green *et al.* (1980) have shown in two chyluric patients that urine apo A-IV accumulation followed the appearance of TG. Triacylglyceroluria was maximal between 3 and 6 h after a fatty meal whereas urine apo

A-IV peaked between 6 and 9 h. In the present study each subject received 1 g lipid/kg body weight resulting in a significant increase in plasma TG and VLDL-TG. There was, among the subjects, a great variability in the degree of the plasma apo A-IV response to the fat load, but it was not related to basal apo A-IV or TG levels or to postprandial TG changes. This suggests that factors other than TG intestinal secretion contribute to the postprandial variation of plasma apo A-IV.

Apo A-IV FPLC elution profile showed, in the fasting samples, that apo A-IV was present almost exclusively in the denser plasma fraction. This is in agreement with the observations of other authors who found only small amounts of apo A-IV in the TRL fraction (Bisgaier *et al.* 1985; Lagrost *et al.* 1989). In the present study we demonstrated that significant, though small, amounts of apo A-IV associate with TRL in the bloodstream following a fatty meal. This association is not specific to apo A-IV since apo A-I and apo A-II had a similar response pattern (results not shown). Several lines of evidence indicate that apo A-IV is secreted with chylomicrons. First, apo A-IV is synthesized by intestinal cells (Swift *et al.* 1984). Second, chylomicrons from chyluric men or experimental animals contain apo A-IV as one of their apolipoproteins (Beisiegel *et al.* 1979; Green *et al.* 1979, 1980; Utermann & Beisiegel, 1979). Third, intestinal malabsorption and parenteral nutrition result in a significant reduction in plasma apo A-IV levels (Sherman & Weinberg, 1988). These pieces of evidence support the concept that at least part of the elevation in TRL-associated apo A-IV following a fatty meal is secondary to an induction of intestinal apo A-IV secretion.

Several subjects did not show an increase in TRL apo A-IV concentration. The most likely explanation is that they were not sensitive to the amount of fat that they received. In agreement with this observation, among the five healthy individuals that were studied postprandially by Bisgaier *et al.* (1985) one subject did not show an elevation of apo A-IV levels, indicating a substantial heterogeneity in the range of response to the fat load. Another explanation could be that the TRL increase occurred at a time other than 3, 6 or 10 h postprandially. In favour of this explanation we found an evident heterogeneity in the postprandial timing of the apo A-IV peak. Thus, in these subjects the apo A-IV association with TRL might have been missed. Finally, in some subjects the very fast clearance of chylomicrons and the apo A-IV attached to their surface could also result in the absence of a detectable elevation of apo A-IV in TRL.

Apo A-IV decreased in the HDL fraction during the absorptive state. Two major reasons may account for this finding. First, HDL apo A-IV may be cleared individually or in association with HDL during postprandial metabolism. According to this hypothesis, apo A-IV secreted with chylomicrons during fat absorption would transfer to the higher density fractions (Ohta *et al.* 1985) where it would be subsequently catabolized. Second, apo A-IV may transfer from the denser plasma fractions to TRL on entry of chylomicrons into the blood vessels. Indeed, several studies have demonstrated that other apolipoproteins (apo E and apo C-III) shift from HDL to TRL during postprandial lipaemia (Havel *et al.* 1973; Blum, 1982; Annuzi *et al.* 1989). The current concept is that this shift results in the removal of apo A-IV from chylomicrons (Weinberg & Spector, 1985). Conversely, our findings suggest that chylomicrons can accommodate apo C and apo E as well as apo A-IV. It also explains the reciprocal change in TRL and HDL apo A-IV levels during the absorptive state.

In conclusion, the results of the present study demonstrated that plasma apo A-IV levels rose moderately in TRL after fat ingestion. This elevation was associated with a reciprocal reduction in the denser plasma fraction. Among apolipoproteins, apo A-IV has the lowest surface exclusion pressure (Weinberg *et al.* 1992) which makes it very sensitive

to any change in the water–lipid interface. This property may explain the complex changes that occur among lipoproteins during postprandial lipaemia. *In vitro* studies have demonstrated that apo A-IV acts on the fine tuning of plasma lipolytic enzymes (Goldberg *et al.* 1990) and lipid-transfer proteins (Barter *et al.* 1988). Thus, our findings of a transient increase in TRL apo A-IV in the postprandial state support the concept that apo A-IV has a potential role in TG metabolism.

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