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Metabolic Heterogeneity Underlying Postprandial Lipemia among Men with Low Fasting High Density Lipoprotein Cholesterol Concentrations*

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ABSTRACT

The high triglyceride (TG) and low high density lipoprotein (HDL) cholesterol dyslipidemia has been associated with increased postprandial lipemia. Although fasting TG is a powerful predictor of postprandial hyperlipidemia, the role of hypoalphalipoproteinemia in postprandial TG metabolism is uncertain. We have studied postprandial lipemia among 63 men with low fasting plasma HDL cholesterol concentrations (<0.9 mmol/L), but with either low (<2.0 mmol/L) or high (>2.0 mmol/L) fasting plasma TG levels. A significant relationship was noted between postprandial TG response and fasting HDL cholesterol concentration ($r = -0.43$; $P < 0.0005$). We also found that men with high TG/low HDL dyslipidemia (high TG and low HDL cholesterol; n = 16) were characterized by abdominal obesity as well as increased visceral adipose tissue accumulation, whereas normolipidemic controls (low TG and high HDL cholesterol; n = 26) and men with isolated low HDL cholesterol concentrations (low TG and low HDL cholesterol; n = 17) were not characterized by features of the insulin resistance syndrome (visceral obesity, hyperinsulinemia, and hypertriglyceridemia). Although controls and men with isolated low HDL cholesterol levels had similar postprandial lipemic responses, men with the high TG/low HDL dyslipidemia had a marked increase in their postprandial TG responses to the fat load compared with the other subgroups ($P < 0.001$). Men with the high TG/low HDL dyslipidemia were also characterized by higher concentrations of apolipoprotein (apo) B-48 and B-100 particles (chylomicron remnants and very low density lipoproteins, respectively) before and during the postprandial period compared with the other subjects. These results suggest that low HDL cholesterol concentration is a heterogeneous metabolic phenotype that it is not associated with postprandial hyperlipidemia unless accompanied by other features of the insulin resistance syndrome. (*J Clin Endocrinol Metab* **85:** 4575–4582, 2000)

A REDUCED fasting plasma high density lipoprotein (HDL) cholesterol concentration has been shown to be predictive of an increased risk of coronary heart disease (CHD) (1, 2). Although a role in reverse cholesterol transport has been proposed, the physiological mechanism by which low HDL cholesterol level increases CHD risk remains a matter of debate. Interestingly, hypoalphalipoproteinemia is often accompanied by elevated plasma triglyceride (TG) concentrations in the fasting state (3, 4). For instance, the high TG and low HDL cholesterol phenotype is frequently observed in type 2 diabetic patients (5) or abdominally obese, insulin-resistant individuals, and these subjects are at increased risk for CHD (6).

Twenty years ago, Zilversmit (7) put forward the hypothesis that the development of atherosclerosis could be the result of a postprandial phenomenon. Since then, postprandial lipoprotein metabolism has received more attention, and it has been reported that dietary fat tolerance is affected by numerous factors, such as age (8, 9), gender (8, 10, 11), obesity (12), body fat distribution (13–16), diet (17), physical activity (18–21), and type 2 diabetes (22, 23). In addition, fasting lipoprotein-lipid alterations have been associated with disturbances of plasma TG clearance during the postprandial period. Thus, fasting hypertriglyceridemia has been identified as a powerful predictor of postprandial hyperlipidemia (24–26). On the other hand, it has been reported that subjects with reduced fasting plasma HDL cholesterol levels, especially in the HDL_2 subfraction, were characterized by increased postprandial lipemia (27), which has led some to suggest that reduced HDL cholesterol concentrations may be a surrogate for inefficient clearance of TG-rich lipoproteins (TRL). In contrast to these latter observations, a normal (28) and even decreased (29) postprandial TG response to a fat meal has also been reported in normotriglyceridemic men

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with hypoalphalipoproteinemia, suggesting that low HDL cholesterol could also be associated with a heterogeneous postprandial lipoprotein phenotype. Thus, the contribution of decreased HDL cholesterol concentrations to postprandial hyperlipidemia remains uncertain. The present study therefore examined the relationship of reduced fasting plasma HDL cholesterol levels to postprandial lipemia among men showing either normal or elevated fasting plasma TG levels.

Subjects and Methods

Subjects

Sixty-three men (mean age ± SD, 45 ± 10 yr) were recruited through the media and selected to cover a wide range of body fatness values. Subjects gave their written consent to participate in the study, which was approved by the medical ethics committee of Laval University. Subjects were all nonsmokers, and those with diabetes or coronary heart disease were excluded from the study. The apolipoprotein E genotype was not available in these subjects. None of the subjects was taking medication known to affect insulin action or plasma lipoprotein levels. With the exception of not consuming alcohol 48 h before the test meal, no other dietary recommendations were made to the subjects before the study.

Anthropometry, body composition, and body fat distribution

Body weight, height, as well as waist and hip circumferences were measured following standardized procedures (30), and the waist to hip ratio was calculated. Body density was measured by the hydrostatic weighing technique (31). The mean of six measurements was used in the calculation of percent body fat from body density using the equation of Siri (32). Fat mass was obtained by multiplying body weight by percent body fat. Visceral adipose tissue (AT) accumulation was assessed by computed tomography, which was performed on a Siemens Somatom DRH scanner (Erlagen, Germany) using previously described procedures (33, 34). Briefly, the subjects were examined in the supine position with both arms stretched above the head. The scan was performed at the abdominal level (between L4 and L5 vertebrae) using an abdominal scout radiograph to standardize the position of the scan to the nearest millimeter. The total AT area was calculated by delineating the abdominal scan with a graph pen and then computing the AT surface with an attenuation range of −190 to −30 Hounsfield units (33–35). The abdominal visceral AT area was measured by drawing a line within the muscle wall surrounding the abdominal cavity. The abdominal sc AT area was calculated by subtracting the visceral AT area from the total abdominal AT area.

Oral lipid tolerance test

After a 12-h overnight fast, an iv catheter was inserted into a forearm vein for blood sampling. Each participant was given a test meal containing 60 g fat/m^2 body surface area as previously described (13). The meal (total kilocalories between 1800–2200 depending on body surface area) consisted of eggs, cheese, toasts, peanut butter, peaches, whipped cream, and milk and provided 64% of calories from fat, 18% from carbohydrates, and 18% from protein. The test meal was well tolerated by all subjects, and they were not allowed to eat for the next 8 h, but were given free access to water. Blood samples were drawn before the meal and every 2 h after the meal over an 8-h period.

Fasting and postprandial plasma lipoprotein concentrations

Plasma was separated immediately after blood collection by centrifugation at 3000 rpm for 10 min at 4 C. TG and cholesterol concentrations in total plasma were determined enzymatically on a RA-500 analyzer (Bayer Corp., Tarrytown, NY), as previously described (36). Each plasma sample (4 mL) was then subjected to a 12-h ultracentrifugation (50,000 rpm) in a Beckman Coulter, Inc. 50.3Ti rotor (Palo Alto, CA) at 4 C in 6-mL Beckman Coulter, Inc. Quickseal tubes, which yielded two fractions: the top fraction contained TG-rich lipoproteins (total-TRL; density, <1.006 g/mL), and the bottom fraction consisted of TG-poor lipoproteins (density, >1.006 g/mL). Using the distilled water layering technique and modified method of Ruotolo *et al.* (37), the total TRL fraction was further separated by a 5-min spin (40,000 rpm) at 4 C, using the same tubes and rotor, into three subclasses of TRL, namely, large, medium, and small. A small volume (100 mL) of a 1.019 g/mL density saline solution was added to the total TRL fraction to facilitate water layering. The large TRL fraction was collected by tube slicing and made up to a final volume of 1 mL with 0.15 mol/L NaCl. The next 3 mL of the middle layer were collected by aspiration as medium TRL, and the final 2 mL were considered the small TRL fraction. Large TRL consist of lipoproteins of Svedberg flotation rate (S_f) more than 400, whereas the medium and small TRL are within a spectrum of particles of S_f 20–400 (37). HDL particles were isolated from the bottom fraction (density, >1.006 g/mL) after precipitation of apo B-containing lipoproteins with heparin and $MnCl_2$ (38). The TG and cholesterol contents of each fraction, *i.e.* large, medium, and small TRL as well as HDL, were quantified on the autoanalyzer. All lipoprotein isolation procedures were completed within 2–3 days of the fat load test. Plasma free fatty acid (FFA) levels were also measured at 0, 2, 4, 6, and 8 h using an enzymatic method (39). Fasting total and LDL apo B as well as apo A-I concentrations were measured in plasma by the rocket immunoelectrophoretic method (40). The lyophilized serum standard for apo B measurement was prepared in our laboratory and calibrated with reference standards obtained from the Centers for Disease Control and Prevention (Atlanta, GA).

Postprandial apo B-48 and B-100 measurements

Apo B-48 and B-100 concentrations were quantified in the total TRL fraction by densitometry scanning of apo bands separated by electrophoresis in 3–10% SDS-polyacrylamide slab gels and stained with Coomassie blue, as previously described (41, 42).

Postheparin plasma lipoprotein lipase activity

Plasma lipoprotein lipase (LPL) and hepatic lipase (HL) activities were also measured on one occasion in subjects after a 12-h overnight fast, 10 min after an iv injection of heparin (60 IU/kg BW). The activity was measured using a modification of the method of Nilsson-Ehle and Ekman (43), as previously described (44), and expressed as nanomoles of oleic acid released per mL plasma/min.

Glucose and insulin concentrations

Fasting and postprandial plasma glucose concentrations were determined using the glucose oxidase assay (Sigma, St. Louis, MO) (45). Plasma insulin levels were measured by a commercial double antibody RIA (Linco Research, Inc., St. Louis, MO) that shows little cross-reactivity (<0.02%) with proinsulin (46).

Statistical analysis

Pearson product-moment correlation coefficients were used to quantify associations between variables. Men were divided into four subgroups according to fasting plasma TG and HDL cholesterol concentrations: normolipidemic controls (low TG and high HDL cholesterol; n = 26), men with isolated low HDL cholesterol levels (low TG and low HDL cholesterol; n = 17), men with isolated hypertriglyceridemia (high TG and high HDL cholesterol; n = 4), and men with the high TG/low HDL dyslipidemia (high TG and low HDL cholesterol; n = 16). Cut-points used for TG and HDL cholesterol were 2.0 and 0.9 mmol/L, respectively (3). As the isolated hypertriglyceridemia phenotype had a relatively low frequency in the present cohort (n = 4), this subgroup of men was not included in the comparative analyses. Differences between men with different fasting lipoprotein-lipid phenotypes were tested for significance using the general linear regression model procedure. The different areas under the curve of TG, glucose, insulin, FFA, as well as HDL cholesterol and HDL TG concentrations were determined by the trapezoid method. All analyses were conducted with the SAS statistical package (SAS Institute, Inc., Cary, NC).

Results

The association between fasting plasma HDL cholesterol and the postprandial plasma TG response is shown in Fig. 1.

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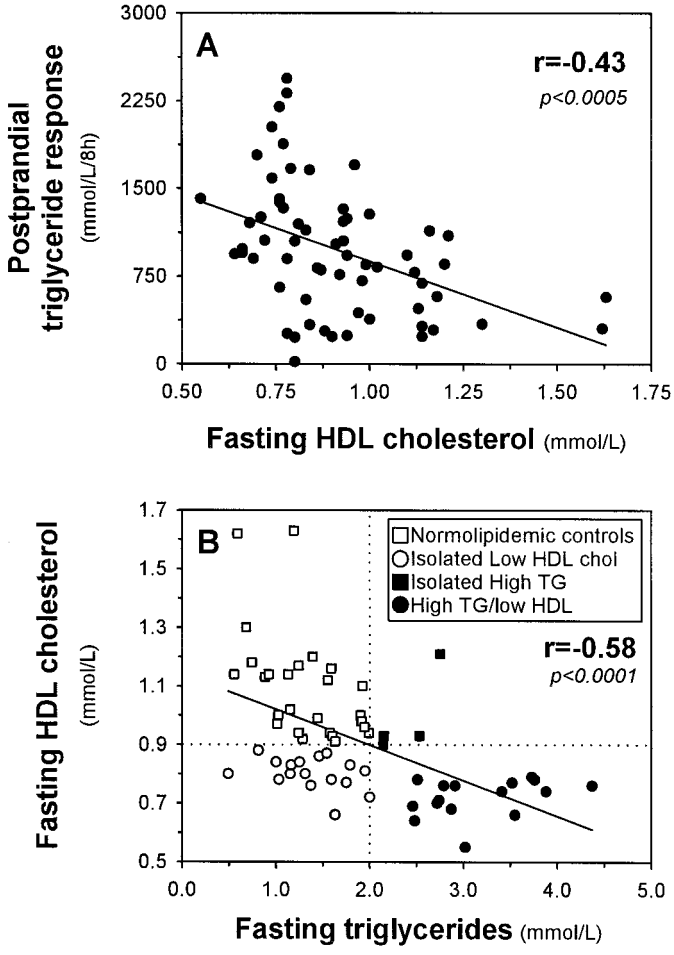

FIG. 1. A, Association between fasting plasma HDL cholesterol and the postprandial plasma TG response (calculated as the incremental area under the 0–8 h TG curve); B, association between fasting plasma HDL cholesterol and TG concentrations in the 63 men included in the study. Subjects were divided on the basis of 4 fasting plasma lipoprotein-lipid phenotypes: normolipidemic controls (n = 26) as well as men with isolated low HDL cholesterol (n = 17), men with isolated high TG (n = 4), and men with high TG/low HDL dyslipidemia (n = 16). *Dotted lines* indicate the cut-off points of HDL cholesterol (0.90 mmol/L) and TG (2.00 mmol/L) that were used to create the subgroups.

We found that HDL cholesterol was significantly and negatively related ($r = -0.43$; $P < 0.0005$) to the postprandial plasma TG response. To identify individuals with hypoalphalipoproteinemia but with either low or high fasting TG levels, we used the association between fasting plasma TG and HDL cholesterol concentrations (Fig. 1). As expected, we noted a negative relationship between both variables. Using cut-off points of 2.0 and 0.9 mmol/L for TG and HDL cholesterol, respectively (3), we were able to identify subgroups of men with different fasting lipoprotein-lipid phenotypes, *i.e.* normolipidemic controls (low TG and high HDL cholesterol), men with isolated low HDL cholesterol levels (low TG and low HDL cholesterol), as well as men with the high TG/low HDL dyslipidemia (high TG and low HDL cholesterol).

Adiposity and body fat distribution indexes among men with different fasting lipoprotein-lipid phenotypes are presented in Table 1. Men with the high TG/low HDL dyslipidemia had increased overall adiposity compared with normolipidemic controls and men with isolated low HDL cholesterol levels. Men with high TG/low HDL dyslipidemia were also characterized by abdominal obesity, as evidenced by larger waist circumference, higher waist to hip ratio, and greater visceral AT accumulation compared with the other subgroups.

Table 2 compares the fasting metabolic profile among the three groups of men. As expected, men with the high TG/low HDL dyslipidemia showed the most disturbed profile. Indeed, in addition to elevated fasting TG levels in plasma and in all TRL subfractions (data not shown), men with high TG/low HDL dyslipidemia were characterized by higher fasting apo B and LDL apo B concentrations as well as a markedly increased total/HDL cholesterol ratio compared with both normolipidemic controls and men with isolated low HDL cholesterol levels. Compared with normolipidemic controls, men with the high TG/low HDL dyslipidemia had lower HDL cholesterol and HDL apo A-I concentrations as well as increased insulin levels. Although men with isolated low HDL cholesterol were also characterized by decreased HDL apo A-I levels compared with controls, they did not show any other metabolic alterations compared with normolipidemic subjects. Furthermore, there was no significant

TABLE 1. Physical characteristics of the subjects

	Controls	Isolated low HDL cholesterol	High TG/low HDL dyslipidemia
No. of subjects	26	17	16
Age (yr)	46 ± 11	45 ± 11	44 ± 7
BW (kg)	84.5 ± 10.4	83.3 ± 10.2	97.4 ± 14.0[a]
Body mass index (kg/m^2)	28.0 ± 3.8	27.5 ± 2.9	32.3 ± 4.5[a]
% Body fat	26.1 ± 7.6	26.8 ± 5.1	29.9 ± 5.6
Fat mass (kg)	22.6 ± 8.5	22.6 ± 6.4	29.8 ± 9.2[a]
Waist circumference (cm)	96.2 ± 9.1	94.3 ± 8.9	105.3 ± 9.7[a]
Waist to hip ratio	0.94 ± 0.05	0.91 ± 0.06	0.99 ± 0.05[a]
Abdominal adipose tissue areas (cm^2)			
Visceral	129 ± 49	135 ± 53	195 ± 71[a]
sc	254 ± 114	244 ± 86	331 ± 100[a]

Values are the mean ± SD.
[a] Significantly different from controls and significantly different from men with isolated low HDL cholesterol levels.

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difference in postheparin plasma lipase activities between normolipidemic controls and men with hypoalphalipoproteinemia with or without elevated fasting TG levels. However, a tendency was noted for normolipidemic subjects to have slightly higher LPL and lower HL activities compared with the other individuals, which resulted in a significantly lower HL/LPL ratio in controls compared with that in men with high TG/low HDL dyslipidemia.

Increases in large, medium, and small TRL TG concentrations after fat meal ingestion were noted in all subgroups of men (Fig. 2). Although no difference was noted in postprandial responses of normolipidemic controls *vs.* men with isolated low HDL cholesterol levels, men with the high TG/low HDL dyslipidemia were characterized by substantially higher TRL-TG levels at all times during the postprandial period compared with the other subgroups. These increased postprandial TRL-TG concentrations in men with the high TG/low HDL dyslipidemia led to higher postprandial TG responses in all TRL subfractions compared with subjects with isolated low HDL cholesterol levels and normolipidemic controls. Figure 3 illustrates the postprandial changes in total TRL apo B-48 and B-100 concentrations in the three subgroups of men. As for TG, men with high TG/low HDL dyslipidemia were characterized by increased apo B-48 and B-100 levels in the total TRL fraction throughout the entire postprandial period compared with normolipidemic controls and men with isolated low HDL cholesterol concentrations. In contrast, normolipidemic controls and men with isolated low HDL cholesterol did not show any difference in apo B-48 and B-100 levels over the 8-h postprandial period.

TABLE 2. Fasting metabolic profile of the subjects

	Controls	Isolated low HDL cholesterol	High TG/low HDL dyslipidemia
No. of subjects	26	17	16
Triglycerides (mmol/L)	1.31 ± 0.44	1.37 ± 0.41	3.17 ± 0.58[a,b]
HDL cholesterol (mmol/L)	1.10 ± 0.19	0.80 ± 0.06[a]	0.72 ± 0.06[a]
Cholesterol (mmol/L)	5.10 ± 0.82	4.71 ± 0.75	5.41 ± 0.64[b]
LDL cholesterol (mmol/L)	3.41 ± 0.85	3.12 ± 0.66	3.29 ± 0.57
Apolipoprotein B (g/L)	1.00 ± 0.19	1.01 ± 0.20	1.23 ± 0.16[a,b]
LDL apolipoprotein B (g/L)	0.90 ± 0.17	0.91 ± 0.18	1.05 ± 0.16[a,b]
HDL apolipoprotein A-I (g/L)	1.30 ± 0.15	1.16 ± 0.10[a]	1.18 ± 0.13[a]
Total/HDL cholesterol	4.77 ± 1.07	5.90 ± 1.05[a]	7.57 ± 1.05[a,b]
Glucose (mmol/L)	5.09 ± 0.41	4.82 ± 0.59	5.32 ± 0.75[b]
Insulin (pmol/L)	74.2 ± 27.4	100.8 ± 64.3	125.6 ± 57.7[a]
Postheparin plasma lipase activities (nmol/mL·min)[c]			
Lipoprotein lipase	55.8 ± 24.3	50.1 ± 37.3	34.3 ± 20.4
Hepatic lipase	166.0 ± 67.8	212.6 ± 74.9	219.8 ± 81.0
HL/LPL	4.0 ± 3.6	8.0 ± 7.8	10.0 ± 9.6[a]

Values are the mean ± SD.
[a] Significantly different from controls.
[b] Significantly different from men with isolated low HDL cholesterol levels.
[c] Number of subjects for PHLA: controls, n = 19; isolated low HDL cholesterol, n = 15; high TG/low HDL dyslipidemia, n = 10.

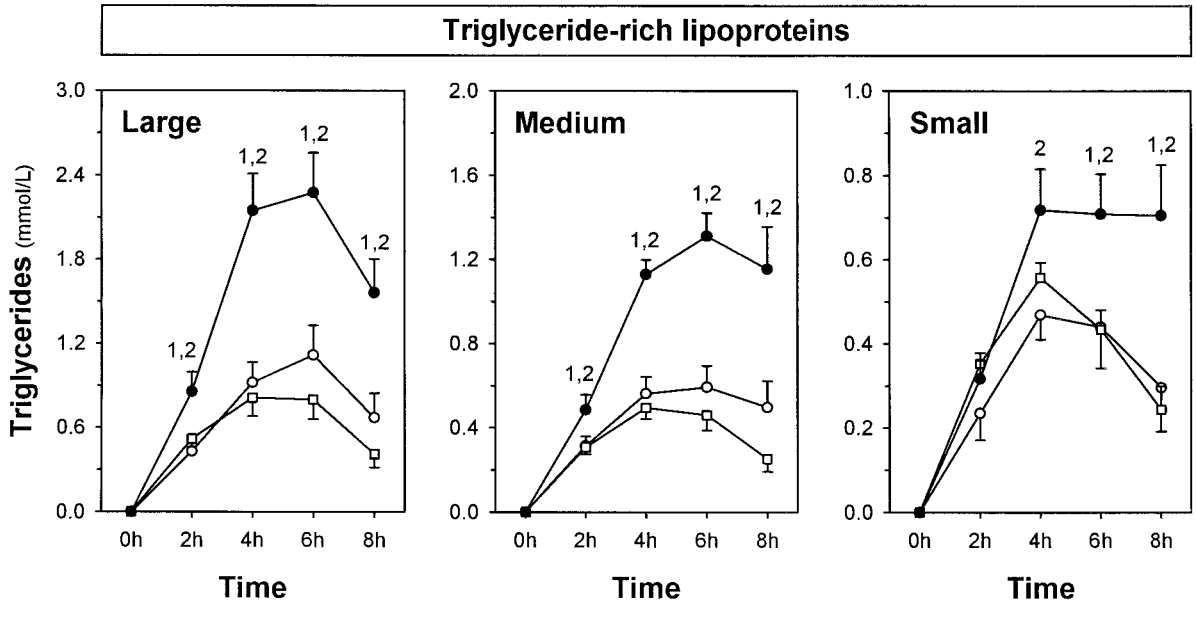

FIG. 2. Postprandial TRL TG concentrations in normolipidemic controls (n = 26; □) as well as in men with isolated low HDL cholesterol levels (n = 17; ○) or the high TG/low HDL dyslipidemia (n = 16; ●). Data are presented as the mean ± SEM. 1, Significantly different from controls; 2, significantly different from men with isolated low HDL cholesterol levels.

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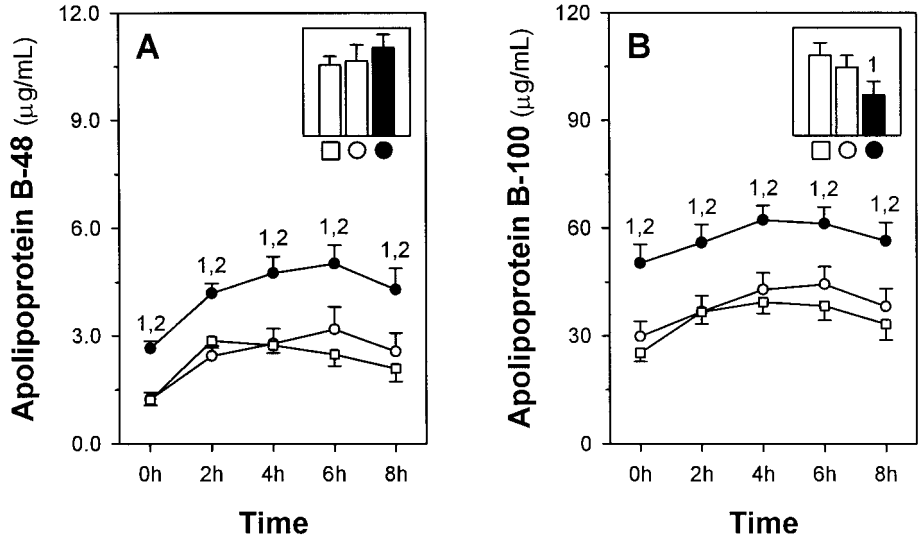

FIG. 3. Postprandial TRL. Apo B-48 (A) and B-100 (B) concentrations in normolipidemic controls (n = 26; □) as well as in men with isolated low HDL cholesterol levels (n = 17; ○) or high TG/low HDL dyslipidemia (n = 16; ●). Data are presented as the mean ± SEM. 1, Significantly different from controls; 2, significantly different from men with isolated low HDL cholesterol levels.

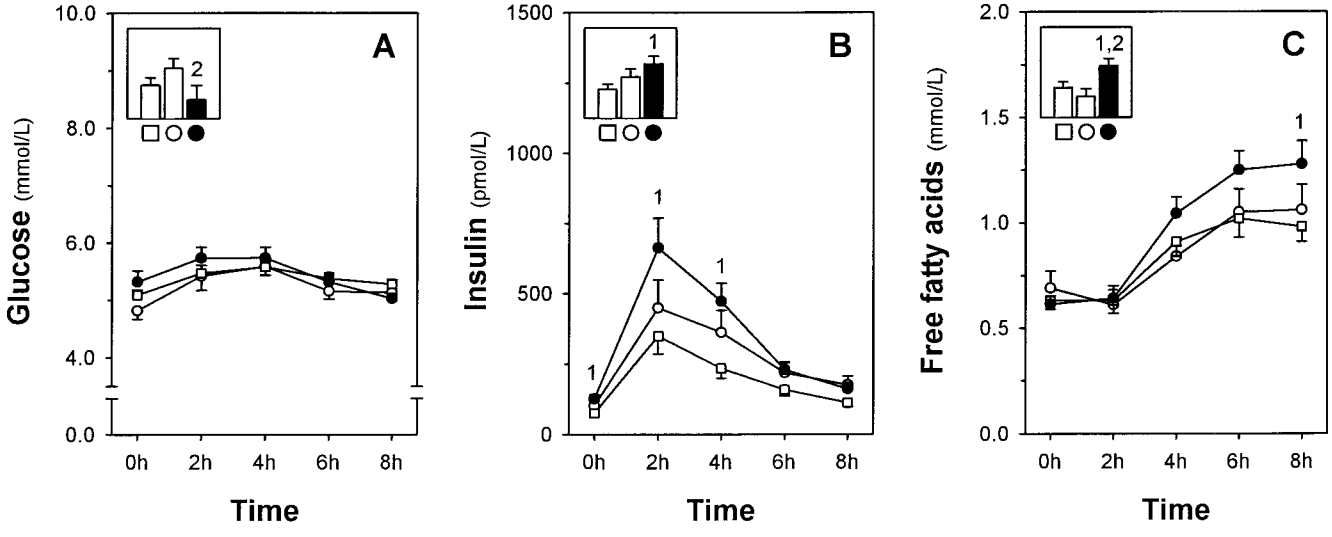

FIG. 4. Postprandial plasma glucose (A), insulin (B), and FFA (C) concentrations in normolipidemic controls (n = 26; □) as well as in men with isolated low HDL cholesterol levels (n = 17; ○) or high TG/low HDL dyslipidemia (n = 16; ●). *Bars* represent the area under the 8-h incremental curve. Data are presented as the mean ± SEM. 1, Significantly different from controls; 2, significantly different from men with isolated low HDL cholesterol levels.

Although men with high TG/low HDL dyslipidemia showed a higher postprandial insulin response compared with the other subgroups of individuals, the difference only reached statistical significance when compared with normolipidemic controls (Fig. 4). However, compared with men with high TG/low HDL dyslipidemia, lower postprandial FFA responses were noted in both normolipidemic controls and men with isolated low HDL cholesterol levels (Fig. 4).

Finally, Fig. 5 illustrates postprandial HDL cholesterol and HDL TG levels in all subgroups of men. Men with low fasting HDL cholesterol concentrations, either as an isolated phenomenon or in the presence of elevated fasting TG levels, displayed significantly decreased HDL cholesterol concentrations throughout the entire postprandial period compared with normolipidemic controls. In addition, a tendency was observed for normolipidemic controls to have greater changes in postprandial HDL cholesterol levels compared with men with low HDL cholesterol (isolated or with hypertriglyceridemia), but the difference did not reach statistical significance. On the other hand, men with high TG/low HDL dyslipidemia were characterized by a greater postprandial HDL TG response compared with the other subgroups of men, but the difference only reached statistical significance when compared with men with isolated low fasting HDL cholesterol concentrations (Fig. 5).

Discussion

In the present study we found a significant association between the magnitude of the postprandial TG response and fasting plasma HDL cholesterol concentrations. Similar results had been published showing that elevated HDL cholesterol levels were associated with reduced postprandial TG levels (27, 47–49). However, in the study by Patsch *et al.* (27),

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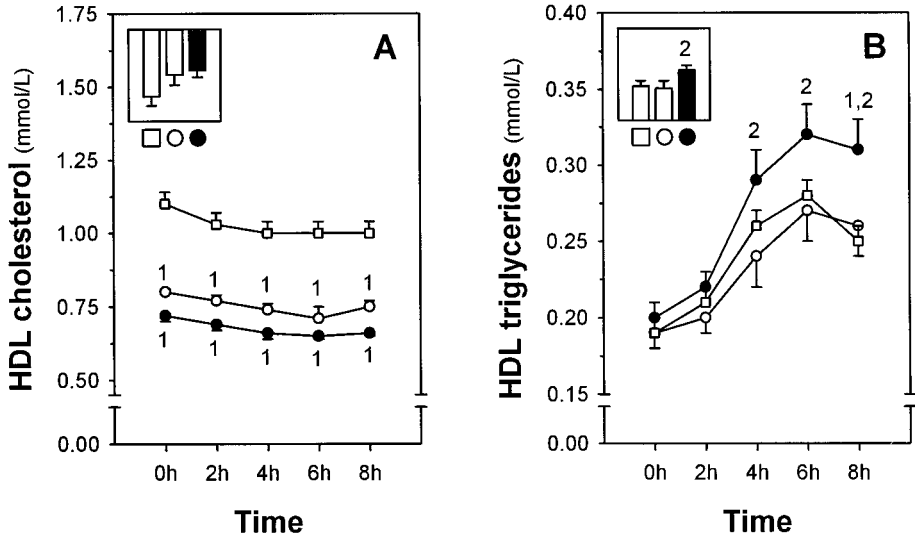

FIG. 5. Postprandial plasma HDL cholesterol (A) and HDL TG (B) concentrations in normolipidemic controls (n = 26; □) as well as in men with isolated low HDL cholesterol levels (n = 17; ○) or high TG/low HDL dyslipidemia (n = 16; ●). *Bars* represent the area under the 8-h incremental curve. Data are presented as the mean ± SEM. 1, Significantly different from controls; 2, significantly different from men with isolated low HDL cholesterol levels.

subjects had normal fasting TG levels (~0.9 mmol/L), whereas individuals included in our study showed a wide range of fasting TG concentrations (0.5–4.4 mmol/L). As the importance of fasting triglyceridemia in postprandial hyperlipidemia is well documented (24–26), the aim of the present study was to examine the relationship between low fasting HDL cholesterol levels, with or without concomitant hypertriglyceridemia, to postprandial lipemia.

The high TG and low HDL cholesterol phenotype has been frequently reported in abdominal obese individuals (50, 51), especially among those with increased visceral AT accumulation (52, 53). Our results are in accordance with these previous observations, as men with high TG/low HDL dyslipidemia showed increased overall adiposity and a preferential accumulation of fat in the abdominal region compared with both normolipidemic controls and men with isolated low HDL cholesterol levels. Furthermore, men with high TG/low HDL dyslipidemia were characterized by higher visceral AT accumulation compared with the other subgroups of men.

In addition to increased fasting plasma TG and low HDL cholesterol levels, men with high TG/low HDL dyslipidemia were also characterized by numerous metabolic alterations compared with normolipidemic controls and men with isolated low HDL cholesterol concentrations. Indeed, men with high TG/low HDL dyslipidemia displayed other features of the insulin resistance syndrome (54–56), *i.e.* elevated fasting plasma apo B levels and hyperinsulinemia compared with the other subjects. In contrast, a low HDL cholesterol concentration observed in the absence of high TG levels was not associated with the expected features of the insulin resistance dyslipidemic syndrome.

After ingestion of the fat-rich meal, important differences were noted in the postprandial TRL-TG responses among men with low HDL cholesterol levels depending upon the presence or absence of fasting hypertriglyceridemia. Thus, men with high TG/low HDL dyslipidemia were characterized by an exaggerated postprandial TG response in large, medium, and small TRL compared with both normolipidemic controls and men with isolated low HDL cholesterol levels. Our results reinforce the idea that fasting hypertriglyceridemia is an important determinant of postprandial hyperlipidemia (49) especially when accompanied by abdominal obesity and hyperinsulinemia (13). In addition to increased postprandial triglyceridemia, men with high TG/low HDL dyslipidemia appeared to have slower removal of TRL from the circulation compared with both normolipidemic controls and men with isolated low HDL cholesterol levels. Indeed, men with high TG/low HDL dyslipidemia showed higher levels of apo B-48 and apo B-100 throughout the postprandial period, suggesting the presence of an increased number of both chylomicron remnants and very low density lipoprotein (VLDL) particles. Our results raise the possibility of impaired TRL particle removal (both VLDL and remnant particles) in men with high TG/low HDL dyslipidemia. This, however, needs to be further examined.

HDL particle formation is closely associated with TRL catabolism, especially that of chylomicrons (25). Accordingly, Patsch *et al.* (27) had proposed that low HDL cholesterol levels could result from impaired TRL lipolysis, a condition that would favor an exaggerated postprandial lipemia, in subjects with hypoalphalipoproteinemia. In the present study no difference was found in the postprandial TRL-TG response of normolipidemic controls and men with low HDL cholesterol in the absence of elevated plasma TG concentrations in the fasting state. We also measured postheparin plasma HL and LPL activities and found no difference in lipase activities between normolipidemic controls and men with isolated low HDL cholesterol levels. Although men with high TG/low HDL dyslipidemia had lower LPL activity compared with the two other subgroups of men, this difference did not reach statistical significance. In light of this observation, it seems that a difference in lipolytic activity was not a major factor in the postprandial hyperlipidemia observed in the present study (shared variance between the two variables, ~10%). However, we found that the HL/LPL ratio was significantly higher in men with high TG/low HDL cholesterol dyslipidemia compared with normolipidemic controls. We previously used the HL/LPL ratio as an index of the balance of lipolytic activities of HL and LPL (57, 58). As increased HL and decreased LPL activities have both been

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associated with disturbed lipoprotein-lipid concentrations, the increased HL/LPL ratio in men with the high TG/low HDL dyslipidemia suggests that the combination of both lipases favors the deterioration of the lipoprotein-lipid profile.

Whereas LPL activity *per se* does not seem to play a major role in the postprandial hyperlipidemia of men with high TG/low HDL dyslipidemia, it is likely that the exaggerated postprandial lipemia noted in these individuals may result from the competition of intestinally and hepatically derived TRL for LPL (59), leading to saturation of the lipolytic pathway. To support this hypothesis, men with high TG/low HDL dyslipidemia were characterized by higher fasting and postprandial apo B-48 (chylomicron remnants) and B-100 (VLDL) concentrations compared with normolipidemic controls and men with isolated low HDL cholesterol levels. Another study demonstrated that subjects with isolated hypoalphalipoproteinemia were characterized by lower postprandial TG levels compared with normolipidemic subjects (29). Our results do not support this observation.

The lively lipolytic activity of visceral adipocytes, which is poorly inhibited by insulin (60), has been proposed as a major factor in the hypertriglyceridemic state commonly found in visceral obese individuals (61, 62). In response to an increased FFA availability, resulting from the lipolysis of adipose cells, an increased esterification of FFA and a reduced hepatic degradation of apolipoprotein B could lead to an increased synthesis and secretion of VLDL particles. We have reported that visceral obese subjects have impaired postprandial FFA metabolism (13). In the present study men with high TG/low HDL dyslipidemia who had greater visceral AT accumulation compared with the other subjects were also characterized by an increased postprandial FFA response compared with normolipidemic controls and men with isolated low HDL cholesterol levels. Furthermore, there was no difference in the postprandial FFA response between the two normotriglyceridemic groups regardless of HDL cholesterol levels. Thus, these altered postprandial FFA levels in men with high TG/low HDL dyslipidemia may have contributed to the elevation of fasting TG through the stimulation of hepatic VLDL TG secretion long after meal ingestion. This phenomenon can be associated in our study with the increase in small TRL TG concentrations and higher levels of apo B-100 in the late stages of the postprandial period in subjects with high TG/low HDL dyslipidemia.

Men with high TG/low HDL dyslipidemia also had an increased postprandial HDL TG response, suggesting that the hypertriglyceridemic state during the postprandial period in these subjects may have contributed to the TG enrichment of HDL particles through the activity of cholesterol ester transfer protein (63). Furthermore, it has been demonstrated that TG-enriched HDL particles are more susceptible to hydrolysis by HL (64, 65), generating smaller HDL particles that are cleared more rapidly from the circulation than larger HDL particles (66). In men with isolated low HDL cholesterol levels, an increase in postprandial HDL TG concentrations was noted, but it was not different from the TG enrichment observed in normolipidemic controls. Thus, it appears that an exaggerated TG response, leading to a greater TG enrichment of HDL, could contribute to further reduce HDL cholesterol concentrations in men with high TG/low HDL dyslipidemia. It is therefore suggested that the etiology of low HDL cholesterol levels may differ according to an individual's fasting TG levels.

In summary, the results of the present study indicate that fasting hypertriglyceridemia is required to see the exaggerated postprandial TG response in men with low fasting plasma HDL cholesterol concentrations. Furthermore, differences in postprandial HDL metabolism are noted in men with low HDL cholesterol levels with either low or high fasting TG concentrations. Indeed, men with high TG/low HDL dyslipidemia were characterized by greater TG enrichment of HDL during the postprandial period compared with normolipidemic controls and men with isolated low HDL cholesterol levels. Further studies should address the physiological relevance of, and processes responsible for, the reduction of HDL cholesterol concentrations as well as investigate the potential alterations of HDL particle density (or diameter) in subjects with low HDL cholesterol levels with either low or high fasting TG concentrations. From a clinical standpoint, these results emphasize the metabolic heterogeneity underlying low HDL cholesterol levels. Indeed, hypoalphalipoproteinemia, when observed as an isolated condition, is not predictive of an exaggerated postprandial TG response to a high fat meal.

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