# Change in dietary saturated fat intake is correlated with change in mass of large low-density-lipoprotein particles in men[1–3]

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**ABSTRACT** We tested whether nutrient intakes estimated from 4-d diet records were associated with plasma lipoprotein subclasses in 103 men who were randomly assigned to a low-fat (24% fat) and a high-fat (46% fat) diet for 6 wk each in a crossover design. Postheparin plasma lipoprotein lipase (LPL) and hepatic lipase (HL) activities were also determined in a subset of 43 men. Changes in intake (ie, high fat minus low fat) of total saturated fatty acids, as well as myristic (14:0) and palmitic (16:0) acids, were positively correlated ($P < 0.01$) with increases in mass of large LDL particles [measured by analytic ultracentrifugation as mass of lipoproteins of flotation rate ($S_f^o$) 7–12] and with LDL peak particle diameter and flotation rate, but not with changes in LDL-cholesterol concentration. Changes in total saturated fatty acids as well as myristic and palmitic acids were also inversely associated with changes in HL activity ($P < 0.05$). With the high-fat diet only, variation in dietary total saturated fatty acid intake was inversely correlated ($P < 0.01$) with concentrations of small, dense LDL of $S_f^o$ 0–5. This correlation was significant specifically for myristic acid ($P < 0.001$). Stearic acid (18:0), monounsaturates, and polyunsaturates showed no significant associations with lipoprotein concentrations. These data indicate that a high saturated fat intake (especially 14:0 and 16:0) is associated with increased concentrations of larger, cholesterol-enriched LDL and this occurs in association with decreased HL activity. *Am J Clin Nutr* 1998;67:828–36.

**KEY WORDS** Diet, saturated fat, low-density lipoprotein subfractions, high-density lipoprotein, lipoprotein lipase, hepatic lipase, high-fat diet, low-fat diet, men

## INTRODUCTION

Cross-cultural and metabolic ward studies provide evidence that dietary nutrients influence plasma lipids and lipoproteins (1, 2). Saturated fat feeding has been reported to increase LDL cholesterol and HDL cholesterol (1, 2). On the other hand, monounsaturates and polyunsaturates do not increase LDL cholesterol when added to a low-fat diet, but do increase HDL cholesterol, the latter effect being less marked than for saturated fat (1, 3). Dietary saturates, monounsaturates, and polyunsaturates all reportedly decrease plasma triacylglycerol concentrations, relative to carbohydrates, to about the same extent (3). However, many early cross-sectional studies in free-living populations (4–7) failed to show such relations, perhaps because of the inability to assess the usual nutrient intakes of individuals accurately or the inability to perform detailed measurements of lipoprotein components. In addition, most studies of the effects of dietary fat on plasma lipoproteins have not reported the intakes of individual dietary fatty acids. More recent cross-sectional reports using multiple-day diet records and lipoprotein subfraction concentration measurements describe significant correlations between intakes of dietary fat and carbohydrate with concentrations of LDL and HDL subclasses (8–11). Also, experimental evidence (12) shows associations of LDL-subclass distributions with changes in dietary fat and carbohydrate intake.

Among the numerous metabolic influences on plasma lipoproteins that may mediate dietary effects are lipoprotein lipase (LPL) and hepatic lipase (HL). Previous reports showed in humans (13–15) and monkeys (16, 17) that an increase in dietary fat is associated with increases in both LPL and HL. LPL hydrolyzes triacylglycerol in chylomicrons and VLDL (18). LPL activity was shown to correlate negatively with VLDL and positively with HDL (13, 19). HL has been associated with the metabolism of VLDL and intermediate-density lipoproteins (IDLs) and in the conversion of $HDL_2$ to $HDL_3$ (20–22). An inverse correlation was found between HL and HDL concentrations (19, 23). Both LPL and HL have been implicated in lipoprotein metabolism leading to the formation of LDL. LPL deficiency results in reductions in LDL cholesterol and low HL is associated with larger, more buoyant LDL particles (20–22, 24).

The objective of the present study was to use detailed nutritional analyses and refined lipoprotein measurements to assess the relations of plasma lipids, lipoproteins, and lipoprotein-subclass

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[2] Supported in part by a grant from the National Dairy Promotion and Research Board and administered in cooperation with the National Dairy Council, and by NIH Program Project grant HL-18574 from the National Heart, Lung, and Blood Institute through the US Department of Energy under contract no. DE-AC03–76SF00098.

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Received November 31, 1996.

Accepted for publication November 19, 1997.

 

mass concentrations to nutrient intakes in 103 nonobese men consuming standardized low-fat and high-fat diets. In addition, this report describes the relation of nutrient intakes to postheparin LPL and HL in a subset of 43 subjects consuming these diets.

## SUBJECTS AND METHODS

### Subjects

The subjects participated in an outpatient crossover study of low- and high-fat diets, the details of which were reported previously (12). We recruited healthy, nonsmoking men > 20 y of age through newspaper and radio announcements, fliers, and direct mail. Subjects were selected if they had been free of chronic disease during the past 5 y and were not taking medication likely to interfere with lipid metabolism. In addition, they were required to have plasma total cholesterol < 6.74 mmol/L (260 mg/dL), triacylglycerol < 5.65 mmol/L (500 mg/dL), resting blood pressure < 160/105 mm Hg, and body weight < 130% of ideal (25).

The Committee for the Protection of Human Subjects at Ernest Orlando Lawrence Berkeley National Laboratory, University of California, Berkeley, approved the study protocol and each participant signed a consent form and participated in a medical interview. One hundred five men completed the study (12). Their mean (± SD) age and body mass index (BMI; kg/m$^2$) were 48.9 ± 11.1 y (range: 28.0–79.0 y) and 25.5 ± 3.0 (range: 17.4–35.1), respectively. Two subjects were eliminated from the present analyses (one who did not complete food records and another who did not participate in the diet protocols).

### Dietary protocol

As described previously (12), the subjects were randomly assigned to outpatient treatment with diets of either low or high fat content (described below) for 6 wk each. The subjects then switched to the alternate diet for an additional 6 wk. The participants were not provided with food, but were instructed on the experimental diets by registered dietitians and were given 2-wk cycle menus showing the number and size of servings. The subjects abstained from alcohol throughout the study and were counseled to keep weight and exercise patterns constant between the two diets. There were no significant diet-induced changes in mean body weight between the low-fat and high-fat diets (12).

Dietary information on the subjects following each experimental diet was collected at the end of the sixth week of each diet by registered dietitians using 4-d (Thursday to Sunday) food records of measured and weighed food intake (26). Nutrient intakes were calculated by using the Minnesota Nutrition Data System (NDS) software (version 2.1), developed by the Nutrition Coordinating Center, University of Minnesota, Minneapolis (27, 28). The subjects recorded any dietary deviations from the menu daily as another measure of compliance with the experimental diets. If the daily dietary deviations averaged > 5% of total energy, the subject was considered noncompliant and his data were not included in the analyses. Only one subject was eliminated for noncompliance.

Because the subjects were free-living and consuming prescribed diets, there was no external verification of food consumed other than that reported in the diet record. Grocery store receipts were obtained to verify that the study food was purchased. Because food consumed on only 4 of 14 d of the diet was recorded, these analyses assume that the intakes seen in the 4-d diet record reflect of the rest of the dietary period.

The reported dietary intake of selected nutrients ($\bar{x}$ ± SD) for the sample of 103 men following the experimental diets is shown in **Table 1**. Nutrients are expressed as a percentage of total energy except for dietary cholesterol (mg/kJ) and dietary fiber (g/kJ). The low-fat diet contained 24% of energy as fat (6% saturated, 12% monounsaturated, and 4% polyunsaturated) and 59% as carbohydrate, with equal amounts of simple and complex carbohydrates. The high-fat diet contained 46% of energy as fat (18% saturated, 13% monounsaturated, and 12% polyunsaturated) and 39% as carbohydrate. Palmitic acid (16:0) was the primary dietary saturated fatty acid in both diets, followed by stearic (18:0) and myristic (14:0) acids, which are representative of the major saturated fatty acids in most human diets (3). In the high-fat diet, the largest increase in saturated fat was palmitic acid. Although prescribed dietary proportions of total protein (16%), cholesterol (0.030–0.036 mg/kJ), the ratio of polyunsaturated fat to saturated fat (P:S, 0.7), and dietary fiber (0.96–1.20 g/kJ) were not significantly different in the two diets, differences in reported intakes of these nutrients were observed.

The nutrients that make up the present analyses are the following: total protein, total carbohydrate, total fat, total saturated fatty acids, myristic acid, palmitic acid, stearic acid, total monounsaturated fatty acids, oleic acid (18:1), total polyunsaturated fatty acids, linoleic acid (18:2), cholesterol, and dietary fiber. Other individual fatty acids supplied a negligible percentage of total energy intake and therefore were not included in the analyses. Mean nutrient intake as estimated from the reported 4-d food records indicated good group compliance with the experimental diets (12). However, the individual variability in dietary compliance enabled us to examine associations of nutrient intake with lipoproteins and lipase activities for both the low-fat and high-fat diets. For example, the distribution of reported dietary intake of saturated fat, monounsaturated fat, and polyunsaturated fat is shown in **Figure 1** in the 103 men following the low- and high-fat diets. The change in dietary fatty acids (high-fat diet minus low-fat diet) is shown in **Figure 2**. The distributions of reported intakes of myristic, palmitic, and stearic acids for the low- and high-fat diets were similar to that of total dietary saturated fatty acid (data not shown).

### Laboratory procedures

The subjects reported to our clinic in the morning after the sixth week of each experimental diet, having abstained for 12–14 h from all food and vigorous activity. Blood samples for lipid analyses were first collected in tubes containing disodium EDTA (1.4 g/L). Blood samples for HL and LPL analyses were then obtained 10 min after intravenous injection of heparin (75 U heparin/kg). Blood and plasma were kept at 4 °C until processed. Postheparin plasma was stored at −70 °C for lipase analyses.

Plasma total cholesterol and triacylglycerol were determined in our laboratory by enzymatic procedures on a Gilford Impact 400E analyzer (Ciba Corning Diagnostics Corp, Oberlin, OH). These measurements and measurement error were consistently within limits set by the CDC standardization program. HDL cholesterol was measured after heparin-manganese precipitation of plasma (29). LDL cholesterol was calculated from the formula of Friedewald et al (30), unless triacylglycerol concentrations were > 4.51 mmol/L (400 mg/dL), in which case, LDL cholesterol was measured by direct beta quantitation in the ultracentrifugal plasma fraction with density ($d$) > 1006 g/L. Apolipoprotein (apo) A-I and apo B concentrations in plasma were determined by maximal radial immunodiffusion (31, 32).

**TABLE 1**
Reported (4-d food record) mean daily nutrient intake for 103 middle-aged men consuming low-fat and high-fat diets[1]

| Nutrient | Low-fat diet | High-fat diet | Change |
|---|---|---|---|
| Protein (% of energy) | 16.6 ± 1.9 | 16.3 ± 0.9 | −0.2 ± 1.8 |
| Carbohydrate (% of energy) | 59.0 ± 2.9 | 38.8 ± 2.3 | −20.2 ± 3.7[2] |
| Fat (% of energy) | 24.2 ± 3.0 | 45.5 ± 2.3 | 21.3 ± 3.4[2] |
| Saturated fat (% of energy) | 5.9 ± 1.0 | 18.4 ± 1.2 | 12.5 ± 1.6[2] |
| 4:0 (butyric) | 0.0 ± 0.0 | 0.7 ± 0.1 | 0.7 ± 0.1[2] |
| 6:0 (caproic) | 0.0 ± 0.0 | 0.4 ± 0.1 | 0.4 ± 0.1[2] |
| 8:0 (caprylic) | 0.0 ± 0.0 | 0.2 ± 0.1 | 0.2 ± 0.1[2] |
| 10:0 (capric) | 0.0 ± 0.0 | 0.5 ± 0.1 | 0.5 ± 0.1[2] |
| 12:0 (lauric) | 0.1 ± 0.0 | 0.5 ± 0.3 | 0.5 ± 0.2[2] |
| 14:0 (myristic) | 0.3 ± 0.1 | 2.3 ± 0.3 | 2.1 ± 0.3[2] |
| 16:0 (palmitic) | 3.7 ± 0.5 | 9.0 ± 0.5 | 5.4 ± 0.7[2] |
| 18:0 (stearic) | 1.5 ± 0.3 | 4.0 ± 0.3 | 2.3 ± 0.4[2] |
| Monounsaturated fat (% of energy) | 11.8 ± 1.7 | 12.5 ± 1.0 | 0.7 ± 1.9[2] |
| 16:1 (palmitoleic) | 0.4 ± 0.1 | 0.8 ± 0.1 | 0.5 ± 0.1[2] |
| 18:1 (oleic) | 11.7 ± 1.7 | 11.7 ± 1.0 | 0.0 ± 1.9 |
| 20:1 (eicosenoic) | 0.1 ± 0.0 | 0.0 ± 0.0 | 0.0 ± 0.0[2] |
| Polyunsaturated fat (% of energy) | 4.2 ± 0.9 | 11.8 ± 1.6 | 7.5 ± 1.9[2] |
| 18:2 (linoleic) | 3.9 ± 0.8 | 10.8 ± 1.6 | 7.2 ± 1.9[2] |
| 18:3 (linolenic) | 0.3 ± 0.1 | 0.6 ± 0.1 | 0.4 ± 0.1[2] |
| 20:4 (arachidonic) | 0.1 ± 0.0 | 0.0 ± 0.0 | 0.0 ± 0.0[2] |
| Cholesterol (mg/kJ) | 0.033 ± 0.007 | 0.037 ± 0.005 | 0.004 ± 0.007[2] |
| P:S | 0.7 ± 0.1 | 0.6 ± 0.1 | −0.1 ± 0.2[2] |
| Fiber (g/kJ) | 1.17 ± 0.14 | 1.10 ± 0.14 | −0.12 ± 0.65[3] |

[1] $\bar{x}$ ± SD. P:S, ratio of polyunsaturated to saturated fat.
[2,3] Significant difference: [2] $P < 0.001$, [3] $P < 0.05$.

Lipoproteins were analyzed by analytic ultracentrifugation, which measures mass of lipoproteins as a function of Svedberg flotation rate [$S_f^o$ $d$ < 1063 g/L; and $F^0_{1.2}$ $d$ < 1210 g/L]. Mass concentrations were determined for VLDL ($S_f^o$ 20–400), IDL ($S_f^o$ 12–20), and for four major LDL subclasses: LDL-I ($S_f^o$ 7–12), LDL-II ($S_f^o$ 5–7), LDL-III ($S_f^o$ 3–5), and LDL-IV ($S_f^o$ 0–3) (33). For LDL, this procedure provides a measurement of peak flotation rate ($S_f^o$) as well as density (g/L) of the peak LDL for each subject (34). In addition, mass was determined for concentrations of two major HDL subclasses: $HDL_2$ ($F^0_{1.2}$ 3.5–9) and $HDL_3$ ($F^0_{1.2}$ 0–3.5) (34).

Nondenaturing polyacrylamide gradient gel electrophoresis, which separates LDL particles by size and shape, was used to identify the major LDL peak particle diameters, measured in nm (33). Electrophoresis of whole plasma was performed by using Pharmacia PAA 2% to 16% gradient gels (Uppsala, Sweden), as described previously (33, 35). Stained gels were scanned with a Transidyne RFT Scanning Densitometer (Transidyne Corp, Ann Arbor, MI), and LDL peak particle diameters were calculated from calibration curves by using standards of known size (33).

Lipase activities were determined by the method of selective inhibition with protamine sulfate as described previously (13, 36). All determinations were in triplicate and a control sample was included with each batch of test samples. Between-assay and within-assay CVs for a control sample were 8.1% and 2.8%, respectively. Lipase activities were expressed in mmol fatty acid $\cdot L^{-1} \cdot h^{-1}$.

### Statistical analyses

The strengths of the relations between amounts of nutrients and plasma lipoprotein concentrations and amounts of nutrients and LPL and HL were measured by Spearman's correlation coefficients ($r_s$). These procedures were repeated for the low-fat and high-fat diets and for changes (high-fat minus low-fat values). Spearman's correlation coefficients provide a nonparametric test for significant association, have high efficiency when the data are in fact normal and are robust to outliers. For all of the nutrient-lipid correlations, a $P$ value < 0.01 was considered significant. Because HL and LPL analyses were carried out in only 43 subjects, correlations with a $P$ value < 0.05 were considered significant for these variables. The computer program StatView 4.0 (Abacus Concepts, Inc, Berkeley, CA) was used for the analyses.

## RESULTS

The subjects in the present study were healthy, nonsmoking men with normal lipid and lipoprotein concentrations at screening ($\bar{x}$ ± SD, mmol/L): triacylglycerol, 1.37 ± 0.69; total cholesterol, 5.39 ± 0.76; LDL cholesterol, 3.52 ± 0.69; and HDL cholesterol, 1.23 ± 0.23. Plasma concentrations of lipids, lipoproteins, and major lipoprotein subfractions in all subjects consuming the two diets were reported elsewhere (12, 37) and summarized in **Table 2**. Activities of LPL and HL during the two diets were also published previously (15) and are shown in Table 2.

### Correlations of dietary fat with plasma lipoproteins

During the low-fat and high-fat diets, dietary protein, carbohydrate, cholesterol, and fiber did not correlate with plasma lipoproteins (data not shown). Changes in these dietary variables also did not correlate with changes in plasma lipoproteins (data not shown). The correlations of dietary total fat and total saturated fat with plasma lipoproteins during the low-fat and high-fat diets, as well as correlations of the changes in these variables are shown in **Table 3**. During the low-fat diet, dietary total fat was correlated negatively with $HDL_3$ mass. Although not shown in Table 3, HDL-cholesterol concentrations were positively associ-

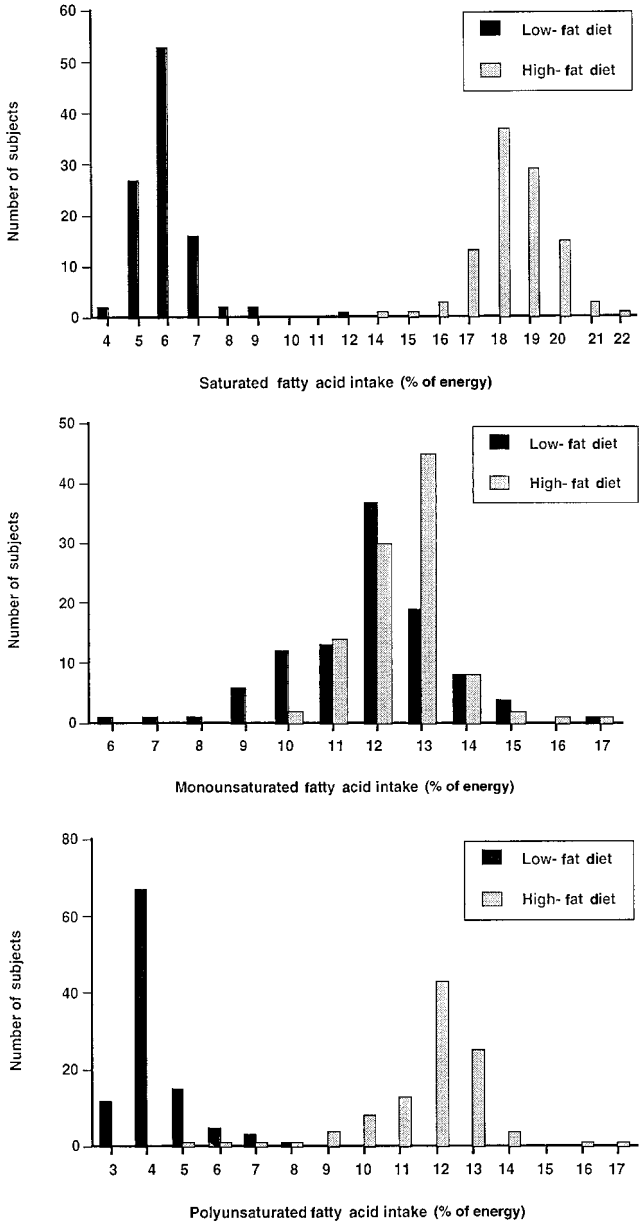


**FIGURE 1.** Distribution of dietary saturated, monounsaturated, and polyunsaturated fatty acid intake as a percentage of total energy in 103 men consuming low-fat and high-fat diets.

ated with changes in total saturated fatty acids ($r_s$ = 0.20, $P$ < 0.05) and inversely associated with changes in total carbohydrate ($r_s$ = 0.19, $P$ = 0.06). During the high-fat diet, saturated fat was correlated negatively with mass of smaller LDL particles ($S_f^o$ 0–5). Changes in total fat and saturated fat were associated positively with change in large LDL mass ($S_f^o$ 7–12). Change in saturated fat was also associated positively with LDL diameter and flotation rate, indicating increased size of LDL particles. Total monounsaturated fat (and oleic acid) and total polyunsaturated fat (and linoleic acid) did not significantly correlate with plasma lipoproteins during the low-fat and high-fat diets, nor were there associations with dietary change (data not shown). P:S also did not significantly correlate with plasma lipoproteins (data not shown).

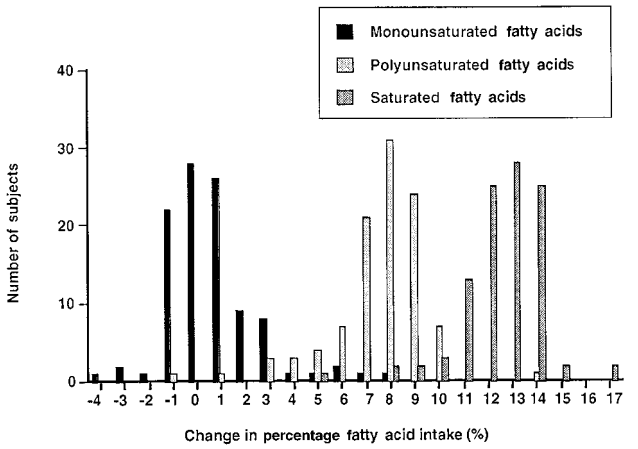


**FIGURE 2.** Distribution of change in fatty acid intake as a percentage of total energy in 103 men consuming high-fat and low-fat diets (high-fat minus low-fat).

### Correlations of individual saturated fatty acids with plasma lipoproteins

Significant correlations of individual saturated fatty acids with plasma lipoproteins during the low-fat and high-fat diets were found for myristic and palmitic acids. During the high-fat diet, myristic acid correlated negatively ($P$ < 0.001) with mass of LDL-III ($r_s$ = −0.38) and LDL-IV ($r_s$ = −0.33) and positively ($P$ < 0.01) with LDL flotation rate ($r_s$ = 0.27). Change in myristic acid correlated positively ($P$ < 0.01) with LDL-I ($r_s$ = 0.28), and LDL diameter ($r_s$ = 0.31) and flotation rate ($r_s$ = 0.32). Change in palmitic acid correlated positively ($P$ < 0.01) with LDL-I ($r_s$ = 0.29) and LDL diameter ($r_s$ = 0.29). Stearic acid was not significantly correlated with plasma lipoproteins during either the low-fat or high-fat diet or during dietary change.

### Correlations of dietary nutrients with postheparin hepatic and lipoprotein lipase activities

During both the low-fat and high-fat diets, dietary protein, carbohydrate, monounsaturated fat, polyunsaturated fat, cholesterol, P:S, and fiber, did not correlate with LPL or HL activity (data not shown). There also were no significant correlations between changes in these dietary variables with LPL or HL activity (data not shown). The correlations between dietary total saturated fat, myristic, palmitic, and stearic acids with LPL and HL during the low-fat and high-fat diets are shown in **Table 4**. During the high-fat diet, total saturated fat, as well as myristic and palmitic acids, were correlated inversely with HL activity. Changes in dietary saturated fat and myristic acid were also associated inversely with HL activity. There were no significant correlations between saturated fatty acids and LPL activity during either the low-fat or high-fat diets, nor were the changes in these variables correlated.

## DISCUSSION

We describe here associations of dietary nutrient intake with plasma lipoproteins and lipoprotein subclasses in healthy men. The results indicate significant associations of dietary saturated fat intake with plasma LDL-particle distributions. Change in dietary saturated fat was associated positively with mass of larger LDL particles and with peak LDL particle diameter and LDL flotation rate. These results suggest, therefore, that feeding

**TABLE 2**
Plasma lipoprotein concentrations in all subjects[1]

| | Low-fat diet | High-fat diet |
|---|---|---|
| Triacylglycerol (mmol/L) | 1.59 ± 0.09 | 1.12 ± 0.05[2] |
| LDL cholesterol (mmol/L) | 3.26 ± 0.08 | 3.70 ± 0.09[2] |
| HDL cholesterol (mmol/L) | 1.08 ± 0.02 | 1.27 ± 0.03[2] |
| Apolipoprotein A-I (mmol/L) | 40.87 ± 0.53 | 44.84 ± 0.60[2] |
| Apolipoprotein B (mmol/L) | 1.98 ± 0.04 | 2.00 ± 0.05 |
| Lipoprotein mass (g/L) | | |
| VLDL | 127.30 ± 8.84 | 75.91 ± 6.10[2] |
| IDL | 33.49 ± 1.66 | 32.86 ± 1.64 |
| LDL | | |
| LDL-I ($S_f^o$ 7–12) | 92.44 ± 3.91 | 131.83 ± 4.56[2] |
| LDL-II ($S_f^o$ 5–7) | 106.70 ± 3.48 | 122.57 ± 3.81[2] |
| LDL-III ($S_f^o$ 3–5) | 81.26 ± 3.98 | 59.82 ± 3.76[2] |
| LDL-IV ($S_f^o$ 0–3) | 17.99 ± 1.52 | 10.95 ± 1.02[2] |
| $HDL_2$ | 24.64 ± 2.41 | 36.94 ± 3.39[2] |
| $HDL_3$ | 181.98 ± 3.06 | 190.73 ± 3.26[3] |
| LDL peak particle | | |
| Diameter (nm)[4] | 25.86 ± 0.08 | 26.48 ± 0.07[2] |
| Flotation rate ($S_f^o$) | 5.30 ± 0.10 | 6.11 ± 0.10[2] |
| Lipoprotein lipase (mmol fatty acids · $L^{-1}$ · $h^{-1}$) ($n$ = 43) | 4.09 ± 0.40 | 4.86 ± 0.48[5] |
| Hepatic lipase (mmol fatty acids · $L^{-1}$ · $h^{-1}$) ($n$ = 43) | 15.36 ± 0.81 | 16.65 ± 0.84[2] |

[1] $\bar{x}$ ± SEM; $n$ = 103 unless otherwise noted. $S_f^o$, Svedberg flotation rate.
[2,3,5] Significantly different from low-fat diet: [2] $P < 0.0001$, [3] $P < 0.01$, [5] $P < 0.05$.
[4] Determined by gradient-gel electrophoresis.

saturated fat is associated with increased mass of larger LDL. This association was found with the long-chain saturated fatty acids myristic and palmitic acids, but not with stearic acid.

The present results accord with cross-sectional correlations that show a positive association between diets high in saturated fat and elevations in larger LDL particles (8, 9). The increase in concentrations of larger LDLs is also consistent with results from studies in monkeys indicating that diets high in saturated fat increase LDL particle size (38).

In this study, the association between small LDL and saturated fat was significant with the high-fat diet but not with the low-fat diet. This may be accounted for by somewhat greater variability in dietary adherence to the high-fat diet than the low-fat diet. Alternatively, because there is evidence that LDL subclasses are affected by genetic factors (39–42) as well as nongenetic influences (12, 37, 43, 44), an interaction between a high-fat diet and other determinants of the LDL-particle size distribution may have contributed to the significant associations reported here.

Although increased concentrations of the largest, most buoyant LDL particles have been found in subgroups of patients with coronary artery disease (CAD) (45, 46), it is currently unknown whether increased concentrations of large LDL particles in a healthy population are associated with increased CAD risk. Studies of the relation between LDL subclasses and CAD have, in contrast, established that a predominance of small, dense LDL particles (LDL subclass pattern B) is associated with increased risk of myocardial infarction (47, 48) and angiographically documented CAD (48–50). Some studies have also shown that small LDL particles are potentially more atherogenic than larger LDL because of increased susceptibility to oxidation (51, 52) and increased promotion of intracellular cholesterol ester accumulation (53). In addition, reductions in small LDL particles, not in larger LDL particles, have been associated with decreased CAD progression (54, 55).

An increase in dietary saturated fat has been associated with the progression of CAD independent of LDL-cholesterol concentrations (56), and in cross-cultural studies, higher intakes of dietary saturated fat are associated with higher prevalence rates of CAD (57). This association of increased dietary saturated fat

**TABLE 3**
Spearman's correlations of percentage total dietary fat and saturated fat with plasma lipids, lipoproteins, and LDL peak particle diameter and flotation rate in 103 men consuming low-fat and high-fat diets[1]

| | Total fat | | | Saturated fat | | |
|---|---|---|---|---|---|---|
| | Low-fat diet | High-fat diet | Change | Low-fat diet | High-fat diet | Change |
| Triacylglyerol | −0.06 | −0.12 | 0.01 | 0.04 | −0.10 | −0.09 |
| LDL cholesterol | −0.10 | −0.07 | 0.11 | −0.01 | −0.14 | 0.08 |
| HDL cholesterol | −0.11 | 0.08 | 0.18 | −0.10 | 0.13 | 0.20 |
| Apolipoprotein A-I | −0.11 | 0.00 | 0.09 | −0.04 | 0.03 | 0.12 |
| Apolipoprotein B | −0.05 | −0.05 | 0.09 | −0.01 | −0.18 | 0.02 |
| Lipoprotein mass | | | | | | |
| VLDL | −0.03 | −0.12 | −0.01 | 0.04 | −0.12 | −0.09 |
| IDL | 0.06 | −0.08 | 0.11 | 0.12 | −0.10 | −0.05 |
| LDL | | | | | | |
| LDL-I ($S_f^o$ 7–12) | 0.01 | 0.11 | 0.29[2] | 0.12 | 0.08 | 0.30[2] |
| LDL-II ($S_f^o$ 5–7) | −0.16 | −0.06 | 0.00 | −0.02 | −0.18 | −0.08 |
| LDL-III ($S_f^o$ 3–5) | −0.02 | −0.18 | −0.17 | 0.04 | −0.31[2] | −0.19 |
| LDL-IV ($S_f^o$ 0–3) | −0.02 | −0.12 | −0.08 | 0.04 | −0.26[2] | −0.02 |
| $HDL_2$ | −0.13 | 0.08 | 0.10 | −0.11 | 0.11 | 0.18 |
| $HDL_3$ | −0.27[2] | −0.17 | −0.08 | −0.14 | −0.22 | −0.14 |
| LDL peak particle | | | | | | |
| Diameter[3] | −0.02 | 0.10 | 0.17 | −0.02 | 0.16 | 0.31[2] |
| Flotation rate | −0.03 | 0.19 | 0.10 | −0.05 | 0.22 | 0.28[2] |

[1] $S_f^o$, Svedberg flotation rate.
[2] $P < 0.01$.
[3] Determined by gradient-gel electrophoresis.

**TABLE 4**
Spearman's correlations of percentage dietary saturated fatty acid (SFA) intake compared with lipoprotein and hepatic lipase activities for low-fat and high-fat diets and change (high-fat minus low-fat diet) in 43 men

| | Total SFA | | | Myristic acid | | | Palmitic acid | | | Stearic acid | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Low-fat diet | High-fat diet | Change | Low-fat diet | High-fat diet | Change | Low-fat diet | High-fat diet | Change | Low-fat diet | High-fat diet | Change |
| Lipoprotein lipase | −0.14 | 0.11 | 0.17 | −0.04 | 0.16 | 0.17 | −0.15 | 0.15 | 0.13 | −0.14 | −0.04 | −0.01 |
| Hepatic lipase | 0.24 | −0.33[1] | −0.26 | 0.11 | −0.36[1] | −0.33[1] | 0.22 | −0.32[1] | −0.23 | 0.20 | −0.12 | −0.08 |

[1] $P < 0.05$.

with CAD, however, may be limited to a subset of normolipidemic individuals whose lipoprotein changes differ from those reported in the general population (12, 37). For example, we showed previously that in the minority of subjects studied here with LDL-subclass pattern B following the high-fat diet, concentrations of both small and large LDL particles were higher than for the low-fat diet (37). In contrast, in most subjects with predominantly large LDL (pattern A) following the high-fat diet, concentrations of large LDL particles were higher but small LDL particles concentrations were lower than during the low-fat diet. Therefore, genetic and environmental factors may contribute to such interindividual variation in dietary response and promote variable increases in large LDL particles and more atherogenic small LDL particles with a high-saturated-fat diet (58).

The present study extends information on the relation between changes in diet, lipoproteins, and the lipolytic enzymes (13–15). An increase in dietary saturated fat (specifically 14:0) was associated with increases in large LDL particles ($S_f^o$ 7–12) and with decreases in HL, suggesting that diet-induced changes in HL may contribute to the regulation of large, buoyant LDL particles. This inference is consistent with other reports showing that buoyant LDL particles accumulate in patients with HL deficiency (21, 59) and after inhibition of HL activity in the cynomolgus monkey (60). In addition, more recent reports (61, 62) have shown an inverse relation between buoyant LDL particles and HL.

The distribution of lipoprotein mass among LDL particles is a result of a variety of metabolic events including interconversions that accompany the loss of triacylglycerol during lipolysis (63). In the present study, an increase in large LDL particles was associated with a decrease in plasma triacylglycerol ($r_s = -0.33$, $P < 0.001$) (DM Dreon and RM Krauss, unpublished observations, 1997), consistent with the known inverse relation between triacylglycerol concentration and LDL particle size (63–65). Thus, the catabolism of triacylglycerol-rich lipoproteins is closely linked to LDL subclasses such that decreased triacylglycerol concentrations may promote the production of larger LDL particles (66). Alternatively, plasma concentrations of larger LDL particles may reflect nutritional influences on LDL receptors that regulate different forms of LDL (67).

In the present study, correlation analyses revealed significant positive relations of change in intake of the long-chain saturated fatty acids myristic and palmitic acids with change in plasma concentrations of large LDL particles. These findings are consistent with studies showing that, of the long-chain saturated fatty acids, myristic and palmitic are the most hypercholesterolemic (1–3, 68–73). Also, it was reported that lauric acid (12:0), another long-chain saturated fatty acid, is hypercholesterolemic (70, 71), but the negligible amount of lauric acid in our experimental diets did not allow us to evaluate the magnitude of its cholesterolemic effects. In contrast with the significant association of myristic and palmitic acids with large LDL particles, there were no significant correlations of stearic acid with LDL. This finding is consistent with the results of studies (68, 69, 73–76) showing that, in men, stearic acid is not hypercholesterolemic compared with the other long-chain saturated fatty acids.

In the present study, monounsaturated and polyunsaturated fatty acids did not show associations with plasma lipoprotein concentrations, a finding that differs from reports showing that unsaturated fatty acids are hypocholesterolemic (1, 71). Our unexpected finding may be explained by several factors: *1*) the amounts of monounsaturated and polyunsaturated fatty acids in the diets were lower than those used by other investigators reporting hypocholesterolemic effects of unsaturated fatty acids (1, 77–81), *2*) the P:S was held constant, and *3*) the variance in the range of intakes of unsaturated fats was not large enough to detect associations with lipoprotein concentrations.

Lipoproteins other than LDL were less strongly correlated with dietary variables. Although of marginal significance, the correlations we observed of change in HDL cholesterol with total saturated fatty acid ($r_s = 0.20$, $P < 0.05$) and total carbohydrate ($r_s = -0.19$) were similar to those shown in a meta-analysis with greater numbers of subjects in controlled feeding environments (1). Although changes in triacylglycerol were also reported to occur with changes in both dietary fat and carbohydrate (1), the small number of subjects studied here may have limited the power to detect significant correlations.

In summary, the present study showed that changes in dietary saturated fat are associated with changes in LDL subclasses in healthy men. An increase in saturated fat, and in particular, myristic acid, was associated with increases in larger LDL particles (and decreases in smaller LDL particles). LDL particle diameter and peak flotation rate were also positively associated with saturated fat, indicating shifts in LDL-particle distribution toward larger, cholesterol-enriched LDL. This study also showed that increases in dietary saturated fat were associated with decreases in HL activity. This finding, together with our previous cross-sectional analyses that revealed significant inverse relations of HL activity with LDL peak flotation rate (15), suggests an inverse association of HL activity with concentrations of buoyant LDL particles. Although there is a possibility that a subset of large LDL particles may be atherogenic (46), earlier results (37) point to a differential benefit of low-saturated-fat diets on LDL concentrations in individuals who have an atherogenic lipoprotein profile denoted by a predominance of small LDL particles.

We thank Adelle Cavanaugh and the staff of the Cholesterol Research Center at Ernest Orlando Lawrence Berkeley National Laboratory for assistance in carrying out the dietary protocol, and Laura Holl, Joseph Orr, and the staff of the Lipoprotein Analysis Laboratory at Donner Laboratory for performing

the laboratory analyses.

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