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Low Fat–Monounsaturated Rich Diets Containing High-Oleic Peanuts Improve Serum Lipoprotein Profiles[1]

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ABSTRACT: Postmenopausal hypercholesterolemic women are at risk for cardiovascular disease and are encouraged to follow low-fat (LF) (≤30% energy) diets. However, these diets may have undesirable effects on high density lipoprotein cholesterol (HDL-C), apolipoprotein A-I (apo A-I) and triglycerides, whereas diets high in monounsaturated fats do not. Twenty postmenopausal hypercholesterolemic women previously consuming high-fat diets (34% energy) were placed on a low fat–monounsaturated rich diet (LFMR: 26%, 14% energy, respectively) for 6 mon. Sixteen women already eating LF diets (24% energy) were also followed to monitor variations in serum lipids due to seasonal variations. Twenty-five women successfully completed the study (LFMR = 12, LF = 13). Serum cholesterol decreased 10% (264 to 238 mg/dL, $P \leq 0.01$) and low density lipoprotein cholesterol (LDL-C) decreased 12% (182 to 161 mg/dL, $P \leq 0.01$) in the LFMR group, but did not change in the LF group. The reduction in serum cholesterol in the LFMR group was greater than estimated by predictive formulas. Serum triglycerides and apo A-I did not change in the LFMR group. A modest decrease in HDL-C, HDL_3-C, and apolipoprotein B (apo B) occurred in both groups, but only the LFMR group showed a trend toward beneficial changes in LDL-C/HDL-C and apo A-I/apo B ratios. Overall, the LFMR diet was well tolerated and resulted in an improved serum lipid and apolipoprotein profile. *Lipids 32*, 687–695 (1997).

Coronary heart disease (CHD) is the leading cause of death for women over the age of 40 yr (1). The incidence of CHD in women is low prior to menopause; however, after the onset of menopause, it increases to approximately that of men. In the United States, the mean total serum cholesterol for women prior to age 45 is 200–215 mg/dL (5.12–5.56 mmol/L) but rises to 240–260 mg/dL (6.20–6.72 mmol/L) between the ages of 45–54 (2). Currently, the initial treatment for hypercholesterolemia is the Step 1 diet (≤30% energy from fat, ≤10% energy from saturated fat, ≤300 mg cholesterol/d), which generally results in significant reductions in CHD risk factors such as serum cholesterol, low density cholesterol (LDL-C), and apolipoprotein B (apo B). However, low-fat (LF) diets often reduce high density lipoprotein cholesterol (HDL-C) and apolipoprotein A-I (apo A-I), and elevate serum triglycerides (3–5). These changes in the serum profile may be particularly detrimental for women, since serum levels of HDL-C, triglycerides, and the ratio of apo A-I/apo B may be more important in defining the risk of heart disease in this population (6–8). In contrast, diets low in saturated fatty acids (SFA) but high in monounsaturated fatty acids (MUFA) have resulted in reductions in serum cholesterol and LDL-C concentrations without adversely affecting HDL-C, apo A-I, or triglycerides (9–12). Most of the high MUFA diets studied to date, however, are also high in overall fat content (35–40% energy), and are therefore not recommended for treating hypercholesterolemia. Short-term (3–4 wk) controlled studies using diets moderate in fat but relatively high in MUFA have lowered serum cholesterol and LDL-C, but have had inconsistent effects on HDL-C and apo A-I in hypercholesterolemic men and women (13–16). At the time the present study was initiated, it could not be assumed that similar effects would be achieved in a free-living population. Furthermore, it was unclear if postmenopausal women are responsive to dietary treatment, or if diet modification may adversely alter the serum lipid profile. No long-term intervention study using a LF diet rich in MUFA has been conducted exclusively on postmenopausal women.

Most experimental diets have used olive oil, canola oil, or high-oleic sunflower oil as the source of MUFA, but it is also feasible to use nuts containing high amounts of oleic acid (17–19). A high-oleic acid peanut cultivar has been developed at the University of Florida in which 76–80% of the lipid content is MUFA (20), approximately 60–70% more oleic acid than most peanut cultivars. There are several advantages of using the high-oleic peanut as the MUFA source. The low lysine/arginine ratio of peanuts may promote serum cholesterol reduction and other physiological changes which

[1]A portion of this material was presented earlier at the annual meeting of the American Oil Chemists' Society and in abstract form (O'Byrne, D.J., Shireman, R.B., and Knauft, D., 1993. The effects of a low-fat/high-oleic acid diet on lipoproteins in postmenopausal hypercholesterolemic women. *INFORM 4(4)*, 553, #SS7).

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Abbreviations: apo, apolipoprotein; BMI, body mass index; CHD, coronary heart disease; HDL, high density lipoprotein; HDL-C, high density lipoprotein cholesterol; LDL, low density lipoprotein; LDL-C, low density lipoprotein cholesterol; LF, low fat; LFMR, low fat–monounsaturated rich; MUFA, monounsaturated fatty acid; PUFA, polyunsaturated fatty acid; SFA, saturated fatty acid; UF, unsaturated fat.

protect against atherosclerosis (21,22). Frequent consumption of nuts, including peanuts, has been associated with a lower incidence of CHD (23). Peanuts are widely accepted, versatile, and convenient to eat, which may enhance long-term compliance to this LF diet in a free-living population.

The purpose of this study was to determine if a LF diet rich in MUFA from high-oleic peanuts would result in an improved serum lipid and apolipoprotein profile in free-living postmenopausal hypercholesterolemic women.

SUBJECTS AND METHODS

Design. This study was designed to be a 6-mon diet intervention using free-living hypercholesterolemic postmenopausal women who switched from a typical American diet to a LF–monounsaturated rich diet (LFMR). Results were compared to a cohort. Serum lipids and apolipoproteins, body composition, health status, physical activity, and diet composition were measured before initiation of the study and after 6 mon of the diets. The University of Florida Institutional Review Board approved the screening and experimental protocol for this study.

Subjects. Healthy postmenopausal women (50–65 yr of age) with elevated serum cholesterol (220–300 mg/dL; 5.68–7.76 mmol/L) were recruited from the region. To minimize the probability of genetic hyperlipidemia or secondary hyperlipidemias, prospective subjects were eliminated for the following reasons: family history of premature death from heart disease coupled with a serum cholesterol >300 mg/dL (7.76 mmol/L); obesity; serum triglyceride >200 mg/dL; endocrine disorders; hypertension (>140/90 mm Hg); cigarette smoking; consumption of >3 alcoholic beverages per day; hormone replacement therapy; and taking medications that alter blood lipids. Over 350 potential participants were interviewed, and 36 met the criteria to participate in the study. Subjects were unpaid volunteers who gave informed consent to participate in the study. All vitamin/mineral supplements were discontinued 3 mon prior to initiation of the study.

Twenty women who habitually consumed a typical American diet (34% fat, 11% SFA) were assigned to the LFMR diet. It was desirable to have a cohort to control for the seasonal variation in serum lipids and lipoproteins, which has been reported in some long-term studies (24,25). However, having a cohort continue on a high-fat diet posed an ethical dilemma; allowing hypercholesterolemic women to continue eating high-fat diets during a long-term study would continue placing the group at risk for CHD and would be comparable to denying necessary medical treatment. As an alternative, the cohort was constituted from the other 16 hypercholesterolemic women; they were already following self-selected LF diets (LF:20–30% fat, <10% SFA, <300 mg cholesterol). The LF cohort group was instructed to continue following their LF diet. Eight women from the LFMR group and three women from the LF group were unable to complete the study due to injury, illness, schedule conflicts, or noncompliance with the study protocol. The results of the subjects who successfully completed the study are reported (LF = 13, LFMR = 12).

Diets. All participants were taught how to weigh, measure, and record all foods and beverages consumed. Participants completed Seven-Day Diet Records prior to the initiation of the study, and the energy level for weight maintenance was determined by computer analysis (Professional Dietitian, Wellsource, Clackamas, OR) of each subject's baseline diet record. This database contains the nutrient content of approximately 3000 foods and beverages. Information was obtained from the United States Department of Agriculture (USDA) Handbook 8 series (26–33), USDA Handbook 456 (34), Pennington and Church (35), and manufacturers. The nutrient database was expanded by D.J. O'Byrne to include specific processed foods and information on the dietary fiber content of frequently eaten foods (26–33, 36–38, manufacturers' information).

A registered dietitian instructed all participants on their diet protocols. Because subjects were free-living, Daily Eating Plans were given to provide standard guidelines for food selections that would conform to the energy requirements and diet assignment. The LF and LFMR diets had energy distributions of <30% fat, 50–60% carbohydrate, and 15–20% protein. Dietary SFA was restricted to <10% energy, and dietary cholesterol was limited to <300 mg/d. Monounsaturated fat constituted between 50–60% of the fat in the LFMR diet; the main source was high-oleic peanuts. Subjects assigned to the LFMR diet received prepackaged daily rations of dry-roasted high-oleic peanuts. Depending upon energy requirements, LFMR subjects consumed 35–68 g peanuts per day. The peanuts replaced an average of 1 oz (28 g) of cooked lean meat and 3–4 servings of oil or margarine (equivalent of 15–20 g of fat) in the diet.

All participants received educational materials and monthly nutrition/cooking classes to ensure compliance with assigned diets. Subjects were asked to record their food and beverage intake for seven consecutive days each month of the study and to maintain their weight and activity level. Compliance was determined by monthly telephone conversations and evaluation of subject's body weight and Seven-Day Diet Records. A detailed nutrient analysis of each subject's initial and final Seven-Day Diet Record was performed by computer.

Physical measurements. The following measurements were made on each subject prior to the beginning of the diet period and at the end of the 6-mon dietary period: weight, body mass index (BMI) (39), and percentage body fat based on the skinfold thickness of seven anatomical sites (40). Subjects completed a questionnaire on physical activity prior to initiation of the diet and after completion of the study. Weight was measured monthly.

Laboratory methods. Blood samples were drawn after a 12-h fast. Subjects refrained from vigorous exercise and alcohol consumption for 24 h prior to donating blood. Three blood samples were obtained from each subject at 1-wk intervals prior to the beginning of the study and again after 6 mon of dietary treatment. Serum lipid concentrations were measured in triplicate from each sample using microplate methods (41) with reagents from enzymatic kits (Stanbio Enzymatic Triglycerides Procedure No. 2000, Stanbio Enzymatic Cholesterol Procedure No. 1010, and Stanbio Enzymatic HDL-Cho-

lesterol Procedure No. 0599; Stanbio, Houston, TX). Reference sera were included in each assay (Fischer Diagnostics, Orangeburg, NJ). Serum HDL_3 was isolated from total HDL by precipitation with 1.5 M $MgCl_2$ in aqueous 1% dextran sulfate as described by Patsch *et al.* (42). The concentration of HDL_3-C was determined in a similar manner as HDL-C (Stanbio Enzymatic HDL-Cholesterol Procedure No. 0599), except that the dilution correction factor used to take into account the precipitating reagents was 1.21 rather than 1.1. Serum HDL_2-C was calculated by subtracting the concentration of HDL_3-C from HDL-C. The concentration of LDL-C was calculated by the Friedewald formula (43). Freshly isolated serum from each subject was flushed with nitrogen and stored at −70°F (−57°C) until used for apolipoprotein analysis at the end of the study. The serum concentrations of apo A-I, A-II, and B were measured in triplicate from one blood sample taken from each subject prior to initiation of the study and after 6 mon of following the diet. Serum concentrations were determined by a microplate method (41) using turbidimetric test kit reagents and standards (Boehringer Mannheim Biochemica, Indianapolis, IN).

Statistical analysis. Preliminary measurements of serum cholesterol were made on volunteers for the study. Forty-three of 75 prospective subjects had mean serum cholesterol concentrations between 5.68–7.76 mmol/L. Of this group, the mean concentration was 6.55 mmol/L and the sample variance was 10.04 mmol/L. This study was designed to detect a change in serum cholesterol of at least 10% of the sample mean (approximately 0.655 mmol/L). The sample size for each group was calculated using the following formula: $n = 2\sigma^2 [(z_\alpha + z_\beta)^2/\Delta^2]$ (44). In this formula, n = number of subjects in each group; σ^2 = estimated sample variance; $z_\alpha = 1.64$, which corresponds to a one-sided test with $\alpha = 0.05$; $z_\beta = 1.28$, which corresponds with the power = 0.9; and Δ = anticipated change in serum cholesterol. Using the above formula, it was determined that at least 10 subjects were needed in each group in order to have a sufficient sample size. Results are expressed as the mean ± standard deviation. Because subjects were not randomly assigned to the diet groups, Levene's Test for Variance Homogeneity (45) was performed to determine if the sample distribution was similar in both groups. The significance level was set at $P = 0.05$. The Levene's Test showed significant variance for several dietary factors, and log transformations were performed on these data. For variables that had similar sample distribution, an analysis of variance with repeated measures was used to test for significant differences "within" and "between" the two groups ($P = 0.05$). If a significant interaction was detected, a follow-up *t*-test was conducted. A nonparametric test (46) was used on variables in which data transformation did not successfully reduce the sample variance. Analyses were performed using the Statistical Analysis System software (SAS Institute, Inc., Cary, NC).

Correlations between the mean change in variables selected *a priori* were performed to assess the impact of specific dietary components on serum lipids and apolipoproteins and to identify potential confounding factors. These statistical analyses were performed using Microsoft Excel® 4.0 (Microsoft Corporation, Redmond, WA) statistical program.

RESULTS

Diets. Subjects following the LFMR diet tolerated the daily ration of peanuts without difficulties. Initially, some subjects complained of gastrointestinal bloating and cramping, but this subsided with increased fluid intake and consumption of peanuts throughout the day rather than at one time.

The LF and LFMR diets were designed to maintain weight and meet the subjects' nutritional requirements. Dietary energy level was intended to be the same as baseline, but subjects in both groups reduced energy intake (Time Effect, $P \leq 0.01$) by approximately 812–1011 kJ (Table 1). An examination of diet records showed that subjects in each group

TABLE 1
Calculated Daily Energy and Nutrient Intake at Baseline and While Subjects Followed the Low-Fat (LF) or Low Fat–Monounsaturated Rich (LFMR) Diets[a]

	LF (n = 13)		LFMR (n = 12)	
	Before	After	Before	After
Energy (kJ/d)[b,**]	7063 ± 1594	6054 ± 1351	7736 ± 1749	6925 ± 1381
%Fat[c]	23 ± 6	17 ± 4**	34 ± 5	26 ± 3**
%SFA[c]	7 ± 3	5 ± 1**	11 ± 2	5 ± 1**
%MUFA[d,**]	7 ± 2[a]	6 ± 2[a]	11 ± 2[b]	14 ± 1[c]
%PUFA[d,*]	4 ± 2[a]	2 ± 1[b]	6 ± 2[c]	2 ± 1[b]
%Protein[b,**;e,**]	19 ± 3	22 ± 3	15 ± 2	20 ± 2
%Carbohydrate[b,**;e,**]	60 ± 7	63 ± 5	50 ± 7	55 ± 5
%Alcohol	0 ± 1	1 ± 3	2 ± 4	1 ± 3
Cholesterol (mg)[b,**]	182 ± 87	129 ± 36	222 ± 68	130 ± 52
Fiber (g)[d,**]	14 ± 5[a,b]	17 ± 4[b]	11 ± 4[a]	22 ± 8[c]

[a]Mean ± standard deviation, calculated from 7 d of recorded food and beverage intake prior to initiation of the study and after 6 mon of following the assigned diets. *$P \leq 0.05$, **$P \leq 0.01$.
[b]Time effect; analysis of variance (ANOVA).
[c]Data for each group were analyzed by nonparametric tests. The LF and LFMR groups could not be compared.
[d]Significant ANOVA interaction between diet and time; group means that are statistically significant have different letter superscripts.
[e]Group effect, ANOVA. SFA = saturated fatty acids; MUFA = monounsaturated fatty acids; PUFA = polyunsaturated fatty acids.

TABLE 2
Calculated Nutrient Ratios at Baseline and While Subjects Followed the LF or LFMR Diets[a]

	LF (n = 13)		LFMR (n = 12)	
Ratios	Before	After	Before	After
SFA/MUFA[b]	0.95 ± 0.20	0.90 ± 0.30	0.98 ± 0.20	0.39 ± 0.06**
SFA/UFA[b]	0.62 ± 0.16	0.61 ± 0.19	0.64 ± 0.12	0.33 ± 0.04**
PUFA/MUFA[c,**]	0.57 ± 0.16[a]	0.45 ± 0.12[a]	0.54 ± 0.22[a]	0.18 ± 0.04[b]
SFA/fat[c,**]	0.29 ± 0.06[a]	0.28 ± 0.05[a]	0.32 ± 0.04[a]	0.21 ± 0.02[b]
MUFA/fat[c,**]	0.31 ± 0.04[a]	0.34 ± 0.10[a]	0.33 ± 0.05[a]	0.54 ± 0.03[b]
PUFA/fat[c,d,**]	0.18 ± 0.05[a]	0.15 ± 0.02[a]	0.17 ± 0.04[a]	0.10 ± 0.02[b]
Lysine/arginine[c,**]	1.42 ± 0.12[a]	1.48 ± 0.09[a]	1.48 ± 0.34[a]	0.97 ± 0.17[b]

[a]Mean ± standard deviation, calculated from 7 d of recorded food and beverage prior to initiation of the study and after 6 mon of following the assigned diets. **$P \leq 0.01$.
[b]Data for each group were analyzed by nonparametric tests. The LF and LFMR groups could not be compared.
[c]Significant ANOVA interaction between diet and time; group means that are statistically significant have different letter superscripts.
[d]Log transformation performed prior to ANOVA. Nontransformed data are shown. UFA = unsaturated fatty acids; see Table 1 for other abbreviations.

began selecting specific food items that were lower in fat and energy than foods eaten at baseline. This may have accounted for the slight decrease in energy intake. The final diets of all subjects provided at least 75% of the Recommended Dietary Allowance for major vitamins and minerals (data not shown). The LFMR group altered their diet to meet the experimental guidelines by increasing %MUFA ($P \leq 0.01$) and lowering %fat ($P \leq 0.01$), %SFA ($P \leq 0.01$), % polyunsaturated fatty acids (PUFA) ($P \leq 0.05$), and cholesterol ($P \leq 0.01$). Subjects in the LF group were already following LF diets at the beginning of the study; thus their baseline diets were significantly different from the LFMR group. The LF group participated in nutrition and cooking classes with the LFMR subjects, which may have inadvertently influenced LF subjects to further restrict %fat ($P \leq 0.01$), %SFA ($P \leq 0.01$), %PUFA ($P \leq 0.05$), and dietary cholesterol ($P \leq 0.01$). Because dietary fat was reduced in both groups, the proportion of energy derived from protein and carbohydrates increased (time effects, $P \leq 0.01$). However, the LF group consistently consumed a diet higher in percentage protein and percentage carbohydrate (Group Effects, $P \leq 0.01$). Dietary fiber increased in both groups, but this was only significant for the LFMR group ($P \leq 0.01$).

The most notable difference between the LF and LFMR diets was the MUFA and fatty acid composition of the diet. Subjects in the LFMR group increased dietary MUFA and ate more than twice the proportion of energy as MUFA compared to the LF group. Fatty acid ratios were similar in the LF and LFMR groups at baseline and did not change in the LF group (Table 2). In contrast, the following dietary fatty acid ratios were reduced ($P \leq 0.01$) in the LFMR group: SFA/MUFA, SFA/UFA, PUFA/MUFA, SFA/fat, and PUFA/fat. The MUFA/fat ratio increased significantly ($P \leq 0.01$) so that LFMR subjects were consuming more than half of all dietary fat as MUFA.

Baseline diets contained similar ratios of lysine to arginine (Table 2). Even though the LF group ate more protein, the ratio of lysine to arginine did not change. Because peanuts are high in arginine, the LFMR diet resulted in a significantly lower lysine/arginine ratio ($P \leq 0.01$).

Physical measurements. Figure 1 shows the monthly weight of subjects. There was a trend toward weight loss during the last month of the study, but the LFMR group experienced a gradual and continuous trend toward weight loss during the entire study. After following the LFMR diet for 6 mon, subjects lost approximately 3 kg ($P \leq 0.01$) while the LF group maintained their weight (Table 3). Four of the LFMR subjects experienced weight loss in excess of 3.6 kg. Reported physical activity did not change in either group (data not shown). The subjects who lost the most weight expressed difficulty in consuming all the required food. When their data were eliminated from the group mean, the mean weight loss for the LFMR group was only 2.1 kg. As a consequence of the weight loss, BMI decreased ($P \leq 0.01$) and body fat was slightly lower in the LFMR group.

Serum lipid and apolipoprotein profile. The baseline serum lipid concentrations for cholesterol, LDL-C, and cholesterol ratios (Table 4) were higher in the LFMR group compared to the LF group. After 6 mon of following the LFMR diet, serum cholesterol and LDL-C fell by approximately 10% and 12%,

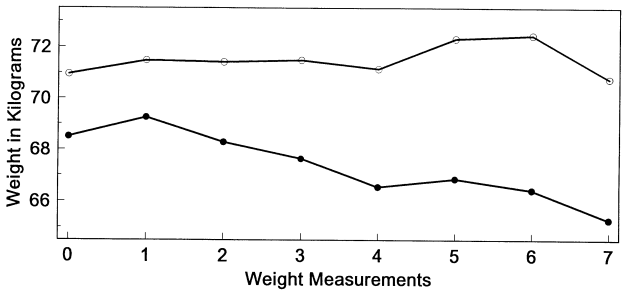

FIG. 1. Mean weight in kilograms, of the postmenopausal hypercholesterolemic women in the low-fat (LF) -o- (n = 13) and low fat–monounsaturated rich (LFMR) -●- (n = 12) group at baseline (0), and at seven time points during the 6-mon dietary period.

TABLE 3
Characteristics of Subjects Following the LF Diet and the LFMR Diet[a]

Physical measurement	LF (n = 13)		LFMR (n = 12)	
	Before	After	Before	After
Weight (kg)[b,**]	71.0 ± 10.5[a]	70.8 ± 11.0[a]	68.6 ± 6.2[b]	65.3 ± 6.5[c]
% Body fat[c,*]	34.5 ± 3.6	34.0 ± 5.5	34.6 ± 3.6	31.5 ± 3.5
Body mass index[b,**]	26.4 ± 3.3[a]	26.3 ± 3.6[a]	26.2 ± 3.8[a]	24.9 ± 3.8[b]

[a]Mean ± standard deviation, obtained prior to initiation of the study and after 6 mon of following the assigned diets. *$P \leq 0.05$, **$P \leq 0.01$.
[b]Significant ANOVA interaction between diet and time; group means that are statistically significant have different letter superscripts.
[c]Time effect. See Table 1 for abbreviations.

TABLE 4
Concentrations of Serum Lipids and Lipid Ratios in Subjects Before and After Following the LF and LFMR Diets (for 6 mon)[a]

Serum lipids	LF (n = 13)		LFMR (n = 12)	
	Before	After	Before	After
	mg/dL	mg/dL	mg/dL	mg/dL
Triglyceride	120 ± 43	134 ± 42	157 ± 67	156 ± 72
Cholesterol[b,**]	247 ± 19[a]	241 ± 22[a]	264 ± 25[b]	238 ± 24[c]
LDL cholesterol[b,**]	170 ± 17[a]	166 ± 21[a]	182 ± 20[b]	161 ± 19[c]
HDL cholesterol[c,**]	52 ± 11	48 ± 10	50 ± 8	46 ± 9
HDL_2 cholesterol	11 ± 10	12 ± 8	8 ± 7	10 ± 7
HDL_3 cholesterol[c,**]	41 ± 4	36 ± 4	43 ± 4	36 ± 4
Total-C/HDL-C[b,*]	4.92 ± 0.97[a]	5.20 ± 1.10[b]	5.37 ± 0.77[b]	5.32 ± 0.94[b]
LDL-C/HDL-C[b,*]	3.42 ± 0.78[a]	3.61 ± 0.91[a,b]	3.69 ± 0.44[b]	3.58 ± 0.58[b]

[a]Mean ± standard deviation. The mean concentration is the average value of three fasting serum samples; each sample was measured in triplicate. Lipid ratios are calculated from mean serum lipid concentrations.
*$P \leq 0.05$, **$P \leq 0.01$.
[b]Significant ANOVA interaction between diet and time; group means that are statistically significant have different letter superscripts.
[c]Time effect, ANOVA. Total-C/HDL-C = ratio of serum total cholesterol to serum high density lipoprotein cholesterol. LDL-C/HDL-C = ratio of serum low density lipoprotein cholesterol to serum high density lipoprotein cholesterol. See Table 1 for other abbreviations.

respectively ($P \leq 0.01$), and triglyceride levels were stable. Serum cholesterol and LDL-C did not change in the LF group, but triglycerides rose by 14% ($P = 0.056$). Both groups experienced a 4 mg/dL (0.10 mmol/L) decrease in HDL-C (time effect, $P \leq 0.01$). This modest reduction was due to changes in the cholesterol content of the HDL_3 subfraction (time effect, $P \leq 0.01$). The ratios of total cholesterol/HDL-C and LDL-C/HDL-C increased in the LF group ($P \leq 0.05$, $P = 0.058$, respectively) but were lowered by 0.05–0.11 in the LFMR group.

A reduction in serum apo A-I (time effect, $P \leq 0.01$) and apo B concentrations (time effect, $P \leq 0.05$) occurred in both groups (Table 5). Although results from the analysis of variance indicated an effect of time on the concentration of apo A-I, this was primarily due to the 13% decrease in serum values in the LF group ($P \leq 0.01$). In contrast, the LFMR group experienced a small but nonsignificant reduction in apo A-I concentration. Apo B concentrations were lowered to a similar extent in both groups, and the final mean values were within the normal range of 0.60–1.00 g/L. As a result of the changes in apo A-I and apo B concentrations, the ratio of apo A-I/apo B increased slightly in the LFMR group but decreased in the LF group.

DISCUSSION

The LFMR diet resulted in significant reductions in serum cholesterol and LDL-C. These results are in line with short-term studies in which controlled LF diets relatively high in MUFA reduced serum cholesterol by 7–15% and LDL–C by 11–16% in hyperlipidemic males and females (13–15). A seasonal effect on these variables was discounted since the LF group had no reduction in serum cholesterol or LDL-C. Our study demonstrates that free-living postmenopausal women are responsive to diet therapy, and that the LFMR diets elicit reductions in serum cholesterol levels similar to more controlled diets.

The hypocholesterolemic effects of the LFMR diet were underestimated by established predictive equations (47–50). These equations estimated a 3.4–4.0% decrease in serum cholesterol compared to the 10% reduction observed. Yet, when applied to the LF group, these formulas accurately predicted

TABLE 5
Concentrations of Serum Apolipoproteins in Subjects Before and After Following the LF and LFMR Diets (for 6 mon)[a]

	LF (n = 13)		LFMR (n = 12)	
	Before	After	Before	After
Apo A-I (g/L)[b,**]	1.90 ± 0.28	1.62 ± 0.28	1.70 ± 0.24	1.60 ± 0.37
Apo A-II (g/L)	0.48 ± 0.08	0.46 ± 0.12	0.43 ± 0.11	0.42 ± 0.09
Apo B (g/L)[b,*]	1.09 ± 0.18	0.98 ± 0.25	1.08 ± 0.16	0.99 ± 0.17
Apo A-I/Apo B	1.81 ± 0.53	1.75 ± 0.50	1.59 ± 0.26	1.61 ± 0.24

[a]Mean ± standard deviation. The mean concentration of each apolipoprotein was determined on a fasting serum sample and measured in triplicate. *$P \leq 0.05$, **$P \leq 0.01$.
[b]Time effect, ANOVA. Apo = apolipoprotein. See Table 1 for other abbreviations.

the reduction in serum cholesterol (1.8% vs. 1.4–1.5%, respectively). It is important to point out that the predictive equations account only for the influence of dietary cholesterol, SFA, and PUFA on serum cholesterol. Other components of the LFMR diet may have had an additional impact on serum cholesterol. Significant correlations were detected in the LFMR group between the change in serum cholesterol and changes in the amount of carbohydrate (r = –0.842, $P < 0.05$), % fat (r = 0.619, $P < 0.05$), amount of protein (r = –0.603, $P < 0.05$), and MUFA/fat (r = –0.572, P = 0.055). These correlations are largely consistent with the known cholesterol-lowering effects of a LF diet and of replacing SFA with MUFA. Additional factors such as the arginine, phytosterol, and fiber content of the LFMR diet were also analyzed to determine their possible influence on serum cholesterol. The low lysine/arginine ratio of the LFMR diet was expected to promote cholesterol-lowering, but the change in this ratio was not correlated with changes in serum cholesterol (r = –0.195) or LDL-cholesterol (r = –0.085). Phytosterols have been shown to lower serum cholesterol levels, presumably by inhibiting cholesterol absorption (51,52). The phytosterol content of foods has not been thoroughly studied; therefore, the nutrient database used in this study does not contain sufficient information to provide more than a crude approximation of the amount of phytosterols in subjects' diets. Based on information available, the phytosterol content of the LFMR diet appeared to increase (71 ± 42 vs. 147 ± 29 mg/d, $P < 0.001$), whereas the amount in the LF diet did not change (55 ± 40 vs. 41 ± 16 mg/d). It is doubtful whether the small increase in phytosterols influenced serum levels in the LFMR group, since other studies have shown the addition of 500–3400 mg/d of phytosterols is required to elicit significant reductions in serum cholesterol and LDL-C (51,52). Furthermore, no correlation was found between the change in dietary phytosterol content and the change in serum total cholesterol (r = –0.251) and LDL-C (r = 0.199) in the LFMR group. The fiber content in the LFMR diet also increased from 11 to 22 g/d. Peanuts contributed 2.4–4.5 g of dietary fiber to the LFMR diet, but <0.2 g was soluble fiber (38). Dietary fiber has been found to lower serum cholesterol when consumed in excess of 49 g/d as part of a LF diet, or when diets have been supplemented with 12–45 g of purified soluble fiber (53,54). The modest increase in dietary fiber in the LFMR diet did not correlate with changes in serum cholesterol (r = –0.365).

Participants in the study were free-living and as a consequence, food intake could not be strictly controlled. Both groups lowered energy intake below their baseline diets. The reduced energy intake by the LFMR group might account for their weight loss. It is interesting to note that both groups had similar reductions in energy intake, but only the LFMR group lost weight. Serum lipids can be influenced by weight loss, and a significant correlation was seen between changes in weight and cholesterol in the pooled data (r = 0.483). When the LFMR group was analyzed separately, no significant correlations were found between the changes in serum cholesterol and changes in weight (r = 0.545), even though final weights ranged from +2.0 to −5.5 kg of baseline. The influence of weight on serum cholesterol should not be dismissed entirely since the correlation was approaching statistical significance, but of more clinical relevance is the lack of significant correlation between changes in weight and serum LDL-C in the LFMR group (r = 0.397). Nevertheless, it is possible that an interaction between the LFMR diet and weight loss elicited the hypocholesterolemic effects. A linear regression was performed on the pooled data of both groups, and no interaction was found between the LFMR diet and weight change (P = 0.839). The main effect of the LFMR diet on changes in serum total cholesterol was significant (P = 0.045), but the effect of weight change was not (P = 0.185). With the relatively small sample size in this study, it is difficult to separate out the potentially confounding effects of modest weight loss, and it is possible that changes in weight had a slight effect.

Long-term consumption of the LFMR diet resulted in apo B levels within the normal range. Of interest in our experiment was the trend toward lower apo B values even in the LF group. Since the LFMR and LF groups reduced dietary fat, SFA, and cholesterol, the influence of diet modifications probably explains the similar changes in apo B, but seasonal variations cannot be ruled out.

The high MUFA content of the LFMR diet was expected to prevent an increase in serum triglycerides and a decrease in HDL-C and apo A-I, when total dietary fat and saturated fat were reduced. Serum triglycerides and apo A-I did remain stable in the LFMR group, but were adversely affected in the LF group. This suggests that the MUFA content of the LFMR diet attenuated the changes in serum triglycerides and apo A-I that are usually associated with LF-high carbohydrate diets.

This was also evidenced by the slight increase in apo A-I/apo B ratios in the LFMR group, in contrast to the downward trend in the LF group. The modest reduction in HDL-C after the LFMR diet is consistent with that reported for short-term controlled studies of LF diets containing 14–16% MUFA (13–16). It was expected that subjects would consume 16–19% MUFA, but the calculated content of the LFMR diet was only 14%. This was due to inconsistent consumption of canola and olive oils, and overall restriction of dietary fat. One study has shown that a LF diet containing approximately 17% MUFA from olive oil prevented reductions in HDL-C (15). If the LFMR subjects had consumed a higher proportion of MUFA, HDL-C levels might have been spared. Although a reduction in HDL-C is not desirable, this change was a reflection of the lower cholesterol concentration in the HDL_3 subfraction, rather than HDL_2. Epidemiological and clinical data indicate that the inverse relationship seen between HDL-C and premature atherosclerosis is stronger for HDL_2-C than for HDL_3-C (55,56). Because the concentrations of HDL_2-C and apo A-I did not change and the ratio of LDL-C/HDL-C showed a beneficial downward trend, the protective role of HDL was probably not compromised by the LFMR diet.

In summary, the LFMR diet was well tolerated and the high-oleic peanuts were easily incorporated into each subject's daily diet. This diet resulted in significant reductions in serum cholesterol and LDL-C and a trend toward improved lipid and apolipoprotein ratios. The hypocholesterolemic effects of the LFMR diet were greater than expected by predictive equations, which suggests that the use of high-oleic peanuts as the primary source of MUFA may be more advantageous than typical high-oleic oils or other vegetable oils. Furthermore, serum triglycerides, HDL_2-C, and apo A-I were not adversely affected by the LFMR diet. This study documents that free-living postmenopausal women can achieve improved serum lipid and apolipoprotein levels on self-selected LF diets high in MUFA.

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