EFFECT OF A DIET ENRICHED WITH MONOUNSATURATED OR POLYUNSATURATED FATTY ACIDS ON LEVELS OF LOW-DENSITY AND HIGH-DENSITY LIPOPROTEIN CHOLESTEROL IN HEALTHY WOMEN AND MEN

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Abstract Polyunsaturated fatty acids are thought to lower the serum cholesterol level more effectively than monounsaturated fatty acids. It is unclear whether the difference — if any — is due to a lowering of the level of high-density lipoprotein (HDL) or low-density lipoprotein (LDL) cholesterol. We therefore placed 31 women and 27 men on a mixed natural diet rich in saturated fat (19.3 percent of their daily energy intake from saturated fat, 11.5 percent from monounsaturated fat, and 4.6 percent from polyunsaturated fat) for 17 days. For the next 36 days, they received a mixed diet with the same total fat content, but enriched with olive oil and sunflower oil ("monounsaturated-fat diet": 12.9 percent saturated fat, 15.1 percent monounsaturated fat, and 7.9 percent polyunsaturated fat) or with sunflower oil alone ("polyunsaturated-fat diet": 12.6 percent saturated fat, 10.8 percent monounsaturated fat, and 12.7 percent polyunsaturated fat).

The serum LDL cholesterol level decreased by 17.9 percent in those on the monounsaturated-fat diet and by 12.9 percent in those on the polyunsaturated-fat diet (95 percent confidence interval for the difference between the effects of the two unsaturated-fat diets, −9.9 percent to 0.0 percent). In men, the HDL cholesterol level fell slightly but not significantly with both diets. In women, the HDL cholesterol level did not change with either.

We conclude that a mixed diet rich in monounsaturated fat was as effective as a diet rich in (n−6)polyunsaturated fat in lowering LDL cholesterol. Both diets lowered the level of HDL cholesterol slightly in men but not in women. (N Engl J Med 1989; 321:436-41.)

THE risk of coronary heart disease rises continuously as serum total and low-density lipoprotein (LDL) cholesterol concentrations increase and falls with increasing levels of high-density lipoprotein (HDL) cholesterol.[1,2] It is generally accepted that a reduction in the intake of saturated fat will lower the level of LDL cholesterol, but there is disagreement over the type of nutrient that should replace it. Keys et al.[3] and Hegsted et al.[4] found that replacing saturated fat with (n−6)polyunsaturated fat in the form of linoleic acid caused a larger decline in total serum cholesterol levels than monounsaturated fatty acids, carbohydrates, or protein. Health authorities in many countries therefore recommend increasing the intake of polyunsaturated fat to 10 percent of energy intake[5,6] from the usual 4 to 8 percent. However, LDL and HDL lipoprotein fractions were not studied separately in the early trials, and it has been suggested that part of linoleic acid's cholesterol-lowering action consists of lowering the level of HDL cholesterol.[7] Indeed, Mattson and Grundy showed that HDL cholesterol levels were reduced by regular safflower oil, which is rich in linoleic acid, as compared with safflower oil that was high in the monounsaturated fatty acid oleic acid.[8] Their experiment has been criticized because the amount of linoleic acid in the diet it studied was unrealistically high (28 percent of total energy intake). In addition, their study and others[9,10] have involved mostly men, even though the HDL cholesterol level is also predictive of coronary risk in women,[11] and the effect of diet on HDL cholesterol levels may differ in men and women.[12,13]

We therefore tested the effects of two diets on the levels of serum lipoproteins. In one, saturated fatty acids were replaced principally by monounsaturated fatty acids, and in the other, by polyunsaturated fatty acids. To ensure that any biologically important differences in the effects of the two diets on LDL or HDL cholesterol levels would be detected, both men and women were enrolled in the study, and their diets were strictly controlled.

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METHODS

Design and Statistical Analysis

The trial had a parallel design and consisted of two consecutive periods. In the first, all participants were placed on a diet high in saturated fat (19.3 percent of total energy sources; Table 1), and the base-line levels of relevant variables were determined after the serum lipids had stabilized. The subjects were then randomly assigned to one of two test diets (Table 1). One group received a diet rich in oleic acid (the "monounsaturated-fat diet"), and the other group a diet rich in linoleic acid (the "polyunsaturated-fat diet"). After another period of stabilization, the serum lipid levels were measured again. The outcome variables consisted of the changes in lipoprotein levels between the end of the base-line period (mean of days 14 and 17) and the end of the test period (mean of days 50 and 53). For the group as a whole, such changes may have been biased by seasonal effects or other drifts with time. Therefore, the absolute changes observed simultaneously in subjects on both diets may in theory have been artifacts. The study's design allowed the unbiased detection of differences only between the effects of the monounsaturated-fat and polyunsaturated-fat diets on the outcome variables. A two-sided t-test was used to examine these differences in the changes among those following the two diets and to examine differences in the responses of women and men within each diet group.[14] To reduce the skewness of the data, the responses of serum lipids, lipoproteins, and apolipoproteins were expressed as a percent rather than an absolute change.

Subjects

Eighty-seven women and men, most of them students, applied for enrollment in the study. One man was on a cholesterol-lowering diet, and two men and one woman did not like dairy products. These four were excluded. The remaining 83 had no history of atherosclerotic disease, and all were apparently healthy, as indicated by a medical questionnaire. None had anemia, glycosuria, proteinuria, or hypertension, and none were taking any medication known to affect serum lipids. Because the study had been designed for only 60 participants, we accepted all 28 eligible men in order to obtain a nearly equal number of men and women. We then added 3 women who were married to participants and 29 other women selected at random. Nine women were taking oral contraceptive agents.

The protocol and the aim of the study were fully explained to the subjects, who gave their written consent. Approval for the study had been obtained from the ethics committee of the Department of Human Nutrition.

During the first week of the study, one man and one woman withdrew. Thus, data from 58 subjects were analyzed. Their fasting levels of serum lipids before the experiment began ranged from 3.68 to 6.12 mmol per liter (mean, 4.81 mmol per liter [186 mg per deciliter]) for total cholesterol, from 0.76 to 2.31 mmol per liter (mean, 1.34 mmol per liter [52 mg per deciliter]) for HDL cholesterol, and from 0.24 to 3.19 mmol per liter (mean, 0.99 mmol per liter [88 mg per deciliter]) for triglycerides. One man had mild hypertriglyceridemia (3.19 mmol per liter). The men were between 20 and 48 years old (mean, 25 years). They weighed between 63 and 94 kg (mean, 74 kg), and their body-mass indexes ranged from 18.3 to 27.5 (mean, 21.9). The women were between 19 and 45 years old (mean, 24). They weighed between 53 and 79 kg (mean, 62), and their body-mass indexes (weight [in kilograms] divided by height [in meters] squared) ranged from 19.1 to 26.6 (mean, 21.3). Seven participants smoked: one man and two women on the monounsaturated-fat diet, and two men and two women on the polyunsaturated-fat diet.

Diets

Before the study began, the participants weighed and recorded their habitual diet for two working days and one weekend day to allow us to estimate their energy and nutrient intake. The food records were coded and the composition of the diets was calculated with the use of the Netherlands Nutrient Data Base.[15]

The diets consumed during the study consisted of conventional solid foods, and the menus changed daily. All the participants consumed a control diet high in saturated fat (19.3 percent of total energy intake) for 17 days. They were then divided according to sex and, among the women, according to their use of oral contraceptive agents. Half of each group was randomly assigned to the monounsaturated-fat diet (actually a diet enriched with both monounsaturated and polyunsaturated fats), and the others to the polyunsaturated-fat diet. For the next 36 days (days 18 to 53), the control diet was changed: 6.5 percent of the total energy intake, which had previously consisted of saturated fat, now consisted of either monounsaturated and (n−6)polyunsaturated fats together or (n−6)polyunsaturated fat alone (Table 1). The monounsaturated-fat diet was enriched with olive oil and the polyunsaturated-fat diet with sunflower oil. In addition, subjects on both diets used a margarine high in linoleic acid. The diets were formulated at 23 levels of energy intake ranging from 5.5 to 16.5 MJ per day. All the bread for the monounsaturated-fat group and some for the polyunsaturated-fat group contained 8 g of olive oil per 100 g. In the monounsaturated-fat group, olive oil alone contributed 40 percent of the monounsaturated fatty acids; the other 60 percent was provided by the rest of the diet. The intake of other nutrients was kept meticulously constant throughout the study.

All food stuffs were supplied to the participants individually, as described.[12,16] However, the participants were allowed to choose a limited number of items, free of fat and cholesterol, which provided 9 to 10 percent of their total daily energy intake. They were urged not to change their selection of these free-choice items between study periods.

The participants were asked to maintain their usual patterns of activity, their smoking habits, and their use of oral contraceptive agents. They recorded in diaries any signs of illness, medications used, the foodstuffs they had chosen, and any deviations from their diets.

Duplicate portions of each diet for an imaginary participant with a daily energy intake of 10 MJ (2390 kcal) were collected, pooled according to diet, and analyzed. The values thus obtained were combined with the values for the free-choice items (Table 1).

Table 1. Mean Daily Intake of Energy and Nutrients of Subjects on Habitual, Control, and Monounsaturated-Fat or Polyunsaturated-Fat Diets.*

ENERGY/NUTRIENT	DIET			
	HABITUAL† (N = 58)	CONTROL‡ (N = 58)	MONOUNSATURATED-FAT (N = 29)	POLYUNSATURATED-FAT (N = 29)
Energy				
MJ/day	10.1±2.5	11.7	11.8	11.9
kcal/day	2423±602	2796	2820	2844
Protein	14.3±1.8	13.1	13.4	13.1
Fat	35.8±5.6	36.7	37.4	37.6
Saturated fatty acids	14.6±2.9	19.3	12.9	12.6
C12:0 + C14:0 + C16:0§		13.7	8.9	8.4
Monounsaturated fatty acids	12.4±2.2	11.5	15.1	10.8
Polyunsaturated fatty acids	6.3±1.9	4.6	7.9	12.7
Polyunsaturated/saturated ratio	0.45±0.2	0.21	0.61	1.00
Carbohydrates	48.6±6.0	49.1	47.8	48.5
Alcohol	1.7±2.1	1.2¶	1.5	1.0
Cholesterol (mg/MJ)‖	31.4±12.6	33.4	35.8	35.3
Dietary fiber (g/MJ)‖	3.1±0.9	4.0	4.1	4.1

*Unless otherwise indicated, values are expressed as percentages of total energy intake.

†Values were calculated from three-day weighed inventories before the experiment began, and they are means ±SD.

‡Based on the chemical analysis of duplicate diets during the high-saturated-fat base-line period. The standard deviations for energy intake during the study were 2.7 MJ in the subjects on the control diet, 2.8 MJ on the monounsaturated-fat diet, and 2.3 MJ on the polyunsaturated-fat diet. Analysis of ancillary duplicate diets providing 6.5, 10, and 15 MJ per day that were collected during one week of the study showed that the variation between subjects in the composition of the study diets was negligible; therefore, no standard deviations are given for the nutrients.

§Values indicate saturated fatty acids with chain lengths of 12, 14, or 16 carbon atoms. There were no reliable figures for them in the food-composition table used.

¶Value represents 1.3 percent for those on the monounsaturated-fat diet and 1.1 percent for those on the polyunsaturated-fat diet.

‖To convert values for the intake of cholesterol to milligrams and dietary fiber to grams per 1000 kcal, multiply by 4.184.

Body weights without heavy clothing were recorded twice a week, and energy intake was adjusted when necessary. Over the 53 days of the study, average body weight increased by 0.2±1.3 (±SD) kg (range, −3.2 to 2.4) in the monounsaturated-fat group and by 0.2±1.0 kg (range, −1.8 to 2.2) in the polyunsaturated-fat group. Pearson's correlation coefficients, calculated for each diet group separately for the relation between changes in weight and changes in all relevant variables, ranged from −0.26 ($P = 0.165$) for apolipoprotein B in the polyunsaturated-fat group to 0.30 ($P = 0.119$) for total cholesterol in the monounsaturated-fat group.

Blood Sampling and Analysis

Venous blood was sampled after an overnight fast on days 1, 14, and 17 (control period), and on days 23, 30, 44, 50, and 53 (test period). Serum was obtained by low-speed centrifugation within one hour of venipuncture, stored at −80°C, and analyzed enzymatically at the end of the study to determine the levels of total and HDL cholesterol and triglycerides.[17-19] Before the study began, all the subjects were assigned a random number that was then used in labeling their blood and serum tubes. In this way, the technicians who performed the analyses were blinded as to the subjects' diets. All the samples from each subject were analyzed within a single run. The coefficient of variation of control serum samples within one run was 1.4 percent for total cholesterol, 2.5 percent for HDL cholesterol, and 1.9 percent for triglycerides. Accuracy was checked by the analysis of four serum pools of known value provided by the U.S. Centers for Disease Control and, for HDL cholesterol only, of three pools produced by the North-West Lipid Research Clinic.[20] The mean bias with regard to target values of the Centers for Disease Control was 0.01 mmol per liter for total cholesterol, −0.07 mmol per liter for HDL cholesterol, and −0.05 mmol per liter for total triglycerides. Bias with regard to the North-West Lipid Research

Clinic's target value for HDL cholesterol was −0.02 mmol per liter. We calculated the LDL cholesterol concentration using the Friedewald equation.[21]

For each subject, the fatty-acid composition of serum cholesterol esters was determined in a pool of two serum samples obtained at the end of the control period (days 14 and 17) and in another pool of two samples obtained at the end of the test period (days 50 and 53), as described earlier.[22] Results were expressed as a proportion by weight of all fatty acids detected. The same pooling procedure was used for apolipoprotein analysis. Apolipoprotein A-I was measured twice and apolipoprotein B three times in whole serum, as described.[16] For each subject, samples from the control and test periods were analyzed on the same plate. The coefficient of variation of control serum samples within one run was 3.2 percent for apolipoprotein A-I and 4.5 percent for apolipoprotein B.

Results

The total fat and cholesterol intake of the participants did not change during the study (Table 1). Our previous experience had suggested that the actual amount of energy needed to maintain body weight would exceed the amount reported before the experiment by about 15 percent. Therefore, the amount of energy provided at the beginning of the study was already 15 percent higher than the energy intake the participants reported as typical.

Adherence to the diets was confirmed by a lower proportion of oleic acid and a higher proportion of linoleic acid in the serum cholesterol esters of those on the polyunsaturated-fat diet than of those on the monounsaturated-fat diet (Table 2). The mean (±SD) ratio of oleic (C18:1n−9) to linoleic (C18:2n−6) acid in the serum cholesterol esters decreased from 0.33±0.04 to 0.29±0.05 in the monounsaturated-fat group and from 0.33±0.04 to 0.21±0.03 in the polyunsaturated-fat group.

The courses of the serum lipid values over time are shown in Figure 1, and the values at the end of each period are shown in Table 3. The total cholesterol level fell by 14.1 percent (0.72 mmol per liter [28 mg per deciliter]) in those on the monounsaturated-fat diet, which was more than the decrease of 9.7 percent (0.51 mmol per liter [20 mg per deciliter]) in those on the polyunsaturated-fat diet (95 percent confidence interval for the difference in percent changes between the diet groups, −8.6 to −0.3 percent). The LDL cholesterol level fell by 17.9 percent (0.59 mmol per liter [23 mg per deciliter]) in those on the monounsaturated-fat diet and by 12.9 percent (0.46 mmol per liter [17 mg per deciliter]) in those on the polyunsaturated-fat diet (95 percent confidence interval for the difference, −9.9 to 0.0 percent). The changes in the level of LDL cholesterol were similar in women and men. Because total and LDL cholesterol levels in the participants on the polyunsaturated-fat diet dipped on day 44 of the study, we also calculated the response to the test diets as the change between the end of the control period and day 44. The 95 percent confidence interval for the difference in percent changes between the monounsaturated-fat and polyunsaturated-fat diets was then −3.9 to 7.5 percent for total cholesterol and −4.5 to 9.1 percent for LDL cholesterol. Thus, even the deliberate selection of the most favorable data point did not make (n−6)polyunsaturated fats more efficacious than monounsaturated fats in lowering cholesterol levels.

During the test period, the level of HDL cholesterol fell slightly but not significantly in the men on both diets, but it remained virtually unchanged in the women. The difference between the sexes in the change was significant for both the monounsaturated-fat and the polyunsaturated-fat groups (P<0.05).

The diets' effects on the levels of triglycerides were slight and did not differ between the monounsaturated-fat and polyunsaturated-fat groups (Table 3). The ratio of HDL to LDL cholesterol increased by 14.0 percent in the subjects on the monounsaturated-fat diet and by 11.9 percent in those on the polyunsaturated-fat diet.

As with the LDL cholesterol level, the decline (13.6 percent) in the serum apolipoprotein B level in those on the monounsaturated-fat diet was greater than the decline (7.4 percent) in those on the polyunsaturated-fat diet (95 percent confidence interval for the difference, −11.1 to −1.2 percent; Table 4). The changes in the level of apolipoprotein A-I paralleled those in the level of HDL cholesterol. The ratio of apolipoprotein A-I to apolipoprotein B increased by 11.2 percent in subjects on the monounsaturated-fat diet and by 4.4 percent in those on the polyunsaturated-fat diet.

In the final two weeks of the study, two men and one woman following the monounsaturated-fat diet and two men following the polyunsaturated-fat diet reported that they had an influenza-like illness, which lasted from one to three days and was accompanied by a lack of

Table 2. Changes in the Fatty-Acid Composition of Serum Cholesterol Esters.*

Fatty Acid	Monounsaturated-Fat Group (N = 29)			Polyunsaturated-Fat Group (N = 29)		
	Control Diet	Test Diet	Change	Control Diet	Test Diet	Change
	grams per 100 g of fatty acid					
C14:0	1.2±0.3	0.7±0.2	−0.5±0.3	1.1±0.4	0.6±0.1	−0.5±0.3
C16:0	10.9±0.6	10.0±0.8	−0.8±0.7	10.7±0.7	9.7±0.6	−1.1±1.0
C16:1 n−7	4.1±0.6	2.7±0.6	−1.4±0.7	4.0±0.5	2.4±0.4	−1.6±0.6
C18:0	0.8±0.2	0.7±0.1	−0.1±0.2	0.8±0.2	0.7±0.1	−0.1±0.2
C18:1 n−9	17.9±1.2	17.2±2.0	−0.8±1.9	17.9±1.2	13.3±1.6	−4.6±1.6†
C18:2 n−6	54.8±2.5	59.0±3.6	4.2±3.3	54.6±2.9	63.4±2.7	8.7±3.3†
C18:3 n−3	0.8±0.2	0.4±0.2	−0.4±0.3	0.9±0.2	0.4±0.1	−0.5±0.2
C18:3 n−6	0.7±0.4	0.6±0.3	−0.1±0.4	0.8±0.4	0.7±0.3	−0.2±0.5
C20:4 n−6	5.9±0.9	6.5±1.2	0.6±1.0	6.2±1.1	6.7±1.3	0.5±1.3
Other	2.8±0.5	2.2±0.6	−0.6±0.7	3.0±0.9	2.2±0.5	−0.8±0.7

*Values are means ±SD.

†Denotes a significant difference in changes between diet groups (P<0.0001).

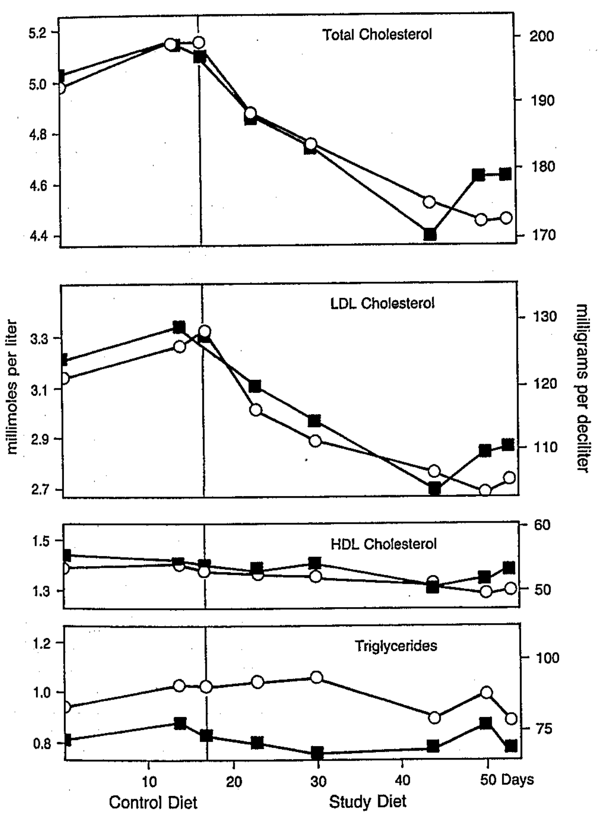

Figure 1. Mean Serum Concentrations of Total, LDL, and HDL Cholesterol and Triglycerides during the Experiment.

All 58 subjects received a diet high in saturated fatty acids for 17 days. For the next 36 days, 29 subjects received a diet enriched with both monounsaturated and (n−6)polyunsaturated fatty acids (O), and 29 subjects received a diet enriched with polyunsaturated fatty acids alone (■).

appetite. In these subjects, the level of HDL cholesterol had fallen between the end of the base-line period and the end of the test period by 27.9 percent (range, 23.2 to 39.8 percent) and the level of LDL cholesterol by 24.8 percent (range, 11.1 to 32.1 percent). When these subjects were excluded from the analyses, the 95 percent confidence interval for the difference in percent changes between the monounsaturated-fat and polyunsaturated-fat groups was −8.3 to −0.5 percent (N = 53) for total cholesterol, −10.6 to −0.6 percent for LDL cholesterol, and −11.6 to −0.9 percent for apolipoprotein B. The mean decrease in the HDL cholesterol level was then 9.3 percent in the 12 men on the monounsaturated-fat diet and 6.0 percent in the 11 men on the polyunsaturated-fat diet.

Discussion

In this controlled study with 58 volunteers, we did not find that linoleic acid was superior to oleic acid in lowering levels of cholesterol. The amount of polyunsaturated fat in our monounsaturated-fat diet (7.9 percent of total energy intake) represents approximately the upper limit of what is currently consumed by most people. The amount in the polyunsaturated-fat diet (12.7 percent) would represent a substantial increase.

Keys et al. have concluded from a large series of studies in middle-aged men that polyunsaturated fatty acids are more effective in decreasing serum cholesterol levels than either monounsaturated fatty acids or carbohydrates.[3] Their findings, as summarized in Keys' formula,[3] predict that in our study the decrease in the serum total cholesterol level in subjects on the polyunsaturated-fat diet should have exceeded that in subjects on the monounsaturated-fat diet by 0.18 mmol per liter. Hegsted and coworkers summarized the results of their experiments[4] in another formula, which predicts a difference in change between the two diets of 0.23 mmol per liter. Our results do not support these conclusions; at the end of our study the decrease in serum total and LDL cholesterol levels was greater in those on the monounsaturated-fat diet than in those on the polyunsaturated-fat diet. Changes in the level of apolipoprotein B paralleled those in the level of LDL cholesterol. The original data of Hegsted et al.[4] include one experiment in which olive oil and safflower oil produced the same total cholesterol level. More recently, Mattson and Grundy showed that in patients whose level of triglycerides was normal, oleic acid and linoleic acid were equally effective in reducing the LDL cholesterol level.[8] However, the fatty-acid composition of the liquid-formula diets used by Mattson and Grundy[8] was very extreme: the ratio of polyunsaturated to saturated fat was as high as 2.1 in the diet rich in monounsaturated fat and 6.5 in the diet rich in polyunsaturated fat. We have shown that their conclusion is also valid for mixed solid diets with a more realistic composition of fatty acids.

The polyunsaturated-fat diet did not reduce the levels of HDL cholesterol or apolipoprotein A-I more effectively than the monounsaturated-fat diet. This finding is in contrast to the results of Mattson and Grundy,[8] but it agrees with a large body of experimental evidence[23-25] suggesting that different classes of fatty acids have comparable effects on the level of HDL cholesterol. In the studies that demonstrated a decline in the HDL cholesterol level, the intake of polyunsaturated fat was very high, and the ratio of polyunsaturated to saturated fat ranged from 2.0 to 6.5.[8,26-28] In addition, some of the studies involved other changes in diet, such as an increase in carbohydrates, a decrease in cholesterol, or both — all of which are known to lower the HDL cholesterol level.[29-31] We therefore conclude that increasing the intake of (n−6)polyunsaturated fatty acids, as compared with oleic acid, in the quantities recommended by some health agencies does not have an unfavorable effect on HDL cholesterol levels.

Previous studies of dietary fatty acids and lipoproteins have been limited largely to men. We studied both women and men because coronary heart disease

Table 3. Effects of the Monounsaturated-Fat and Polyunsaturated-Fat Diets on Serum Lipid and Lipoprotein Levels.*

	Men		Women		All	
	Monounsaturated-Fat Diet (N = 14)	Polyunsaturated-Fat Diet (N = 13)	Monounsaturated-Fat Diet (N = 15)	Polyunsaturated-Fat Diet (N = 16)	Monounsaturated-Fat Diet (N = 29)	Polyunsaturated-Fat Diet (N = 29)
Total cholesterol (mmol/liter)						
Control period	4.78±1.01	5.27±0.74	5.47±0.59	4.99±0.72	5.14±0.88	5.11±0.73
Test period	4.03±0.95	4.59±0.75	4.78±0.67	4.61±0.62	4.42±0.89	4.60±0.67
Percent change	−15.8±7.9	−12.8±8.1	−12.6±6.7	−7.1±7.8	−14.1±7.4	−9.7±8.3
95% confidence interval	−9.4 to 3.3		−10.8 to 0.0†		−8.6 to −0.3†	
LDL cholesterol (mmol/liter)						
Control period	3.05±0.79	3.62±0.68	3.53±0.65	3.09±0.61	3.30±0.75	3.33±0.68
Test period	2.52±0.73	3.06±0.66	2.89±0.58	2.73±0.52	2.71±0.67	2.87±0.60
Percent change	−17.7±8.1	−15.3±9.1	−18.1±7.6	−11.0±12.1	−17.9±7.7	−12.9±10.9
95% confidence interval	−9.2 to 4.4		−14.6 to 0.4		−9.9 to 0.0†	
HDL cholesterol (mmol/liter)						
Control period	1.25±0.30	1.27±0.24	1.51±0.29	1.50±0.37	1.38±0.32	1.41±0.34
Test period	1.08±0.25	1.15±0.25	1.47±0.27	1.52±0.40	1.28±0.32	1.35±0.38
Percent change	−12.6±14.5‡	−9.0±12.3‡	−1.5±11.1	1.2±7.0	−6.9±13.8	−3.4±10.9
95% confidence interval	−14.3 to 7.1		−9.5 to 4.1		−10.0 to 3.0	
HDL/LDL cholesterol ratio						
Control period	0.43±0.15	0.37±0.11	0.45±0.14	0.50±0.14	0.44±0.15	0.44±0.14
Test period	0.46±0.15	0.40±0.13	0.53±0.15	0.58±0.19	0.49±0.15	0.50±0.19
Percent change	6.3±14.9‡	7.7±11.1	21.2±17.9	15.4±15.7	14.0±17.9	11.9±14.2
95% confidence interval	−11.9 to 9.1		−6.6 to 18.1		−6.4 to 10.5	
Triglycerides (mmol/liter)						
Control period	1.05±0.64	0.84±0.42	0.94±0.28	0.87±0.24	0.99±0.48	0.86±0.33
Test period	0.95±0.52	0.84±0.53	0.93±0.36	0.80±0.21	0.94±0.43	0.82±0.38
Percent change	−2.5±25.2	−2.8±16.9	1.9±39.3	−5.5±20.2	−0.2±32.7	−4.3±18.5
95% confidence interval	−16.9 to 17.4		−15.3 to 30.1		−9.9 to 18.0	

*Values are means ±SD. Because of the skewness of the data, the difference between the means of the control (days 14 and 17) and test (days 50 and 53) periods does not always equal the mean of the percent change. To convert values for total, HDL, and LDL cholesterol to milligrams per deciliter, multiply by 38.67. To convert values for triglycerides to milligrams per deciliter, multiply by 88.54.

†Denotes a significant difference in changes between diet groups (P<0.05). ‡Denotes a significant difference in changes between women and men within a diet group (P<0.05).

is not exclusively a disease of men. We found no evidence that fluctuations in lipid levels during the menstrual cycle made women less suitable subjects. In our study, the systematic effects of the menstrual phase on serum lipid levels tended to be offset by the fact that each woman was in a different phase of the cycle at any given stage of the experiment. Also, in spite of the menstrual cycle, lipid levels varied no more in the women than in the men: the standard deviations of the mean responses observed in the women were similar to those in the men (Tables 3 and 4). When saturated fat was removed from the diet, the levels of HDL cholesterol and apolipoprotein A-I decreased in the men as compared with the women. This effect was observed in those following both test diets. In the 23 men who were free of intercurrent illness, the absolute decline in both diet groups was between −0.07 and −0.11 mmol per liter (−2.7 to −4.3 mg per deciliter). Such a

Table 4. Effects of the Monounsaturated-Fat and Polyunsaturated-Fat Diets on Serum Apolipoprotein A-I and Apolipoprotein B Levels.*

	Men		Women		All	
	Monounsaturated-Fat Diet (N = 14)	Polyunsaturated-Fat Diet (N = 13)	Monounsaturated-Fat Diet (N = 15)	Polyunsaturated-Fat Diet (N = 16)	Monounsaturated-Fat Diet (N = 29)	Polyunsaturated-Fat Diet (N = 29)
Apolipoprotein A-I (mg/liter)						
Control period	1247±144	1240±121	1329±144	1389±202	1289±147	1322±184
Test period	1090±109	1127±139	1343±119	1379±211	1221±171	1266±220
Percent change	−11.8±10.1†	−8.9±8.6†	1.5±7.2	−0.6±6.6	−4.9±10.9	−4.3±8.5
95% confidence interval	−10.4 to 4.5		−3.0 to 7.1		−5.8 to 4.5	
Apolipoprotein B (mg/liter)						
Control period	1010±248	1087±217	1081±153	1001±147	1047±204	1040±183
Test period	872±253	1002±226	942±171	927±157	908±214	960±191
Percent change	−14.3±8.0	−7.8±7.4	−12.9±9.4	−7.0±12.3	−13.6±8.6	−7.4±10.2
95% confidence interval	−12.6 to −0.4‡		−13.9 to 2.2		−11.1 to −1.2‡	
Apolipoprotein A-I/B ratio						
Control period	1.31±0.36	1.19±0.31	1.26±0.26	1.42±0.29	1.28±0.31	1.32±0.31
Test period	1.35±0.43	1.19±0.37	1.47±0.29	1.53±0.35	1.41±0.36	1.38±0.39
Percent change	3.8±16.9†	−0.7±11.7	18.0±16.9	8.6±15.1	11.2±18.1	4.4±14.3
95% confidence interval	−7.0 to 16.2		−2.4 to 21.1		−1.8 to 15.3	

*Values indicated are ±SD. Because of the skewness of the data, the difference between the means of the control (days 14 and 17) and test (days 50 and 53) periods does not always equal the mean of the percent change.

†Denotes a significant difference in changes between women and men within a diet group (P<0.05). ‡Denotes a significant difference in changes between diet groups (P<0.05).

change may have been caused in part by factors outside the experiment; we cannot conclude that it was specifically due to the removal of saturated fat from the diet. However, the difference in the change between men and women cannot be explained by baseline drift. We have earlier observed that the effects of diet on HDL levels may be sex-specific,[12] and this reinforces the need for more dietary studies in women.

Although we compared olive oil and sunflower oil, there is no reason to limit our conclusions to these sources of fat. The triglycerides of a limited number of fatty acids make up about 99 percent of the weight of most vegetable oils, and in the amounts consumed in our experiment, the minor components of olive and other oils do not have major effects on serum lipid levels.[32]

Our findings suggest that as far as lipoprotein levels are concerned, it is immaterial whether saturated fatty acids are replaced by a mixture of monounsaturated and polyunsaturated fats or by polyunsaturated fats alone; both diets will lower the level of LDL cholesterol, and both will have the same effect on the HDL cholesterol level, as long as extremely large amounts of polyunsaturated fats (i.e., more than 13 percent of total energy intake) are avoided. We must note, however, that our conclusion that polyunsaturated fats are not superior to monounsaturated fats in lowering total cholesterol levels disagrees with the outcomes of many trials conducted in the 1950s and 1960s by various investigators.[3,4] The findings of more recent studies, though suggestive, are not yet sufficient to reject this mass of earlier data.

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