Changes in Plasma Lipoprotein Concentrations and Composition in Response to a Low-Fat, High-Fiber Diet Are Associated With Changes in Serum Estrogen Concentrations in Premenopausal Women

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We have investigated the effects of a low-fat, high-fiber diet on plasma lipid and lipoprotein levels and serum sex hormone concentrations in 22 normal premenopausal women (mean age, 25.8 ± 3.8 years). Participants consumed a baseline diet for 4 weeks (40% of calories as fat, 16% as saturated fatty acids, 8% as polyunsaturated fatty acids, 400 mg/d cholesterol, and 12 g/d dietary fiber) and then a low-fat, high-fiber diet for 8 to 10 weeks (16% to 18% of calories as fat, 4% as saturated fatty acids, 4% as polyunsaturated fatty acids, 150 mg/d cholesterol, and 40 g/d fiber). Blood samples for determination of plasma lipids and serum hormones were obtained during the follicular and luteal phases of the menstrual cycle during both diets. Compared with the baseline diet, the low-fat, high-fiber diet resulted in significant decreases in total cholesterol (TC), low-density lipoprotein (LDL) cholesterol, and high-density lipoprotein (HDL) cholesterol concentrations during both the follicular and luteal phases (TC, −14% and −16%; LDL cholesterol, −14% and −17%; and HDL cholesterol, −15% and −18%, respectively). During the follicular phase but not the luteal phase on the low-fat, high-fiber diet, women exhibited significant increases in plasma triglyceride ([TG] 22%) and very–low-density lipoprotein (VLDL)-TG (36%) concentrations. During the follicular phase, serum estrone sulfate concentrations decreased by 25% ($P < .0001$) when subjects were fed the low-fat, high-fiber diet. During this phase of the low-fat, high-fiber diet relative to the baseline diet, changes in HDL cholesterol levels were significantly and positively associated with changes in estrone levels ($r = .49$, $P < .02$), and the ratio of TC to HDL cholesterol was inversely associated with the changes in estradiol and free estradiol levels ($r = -.47$ and $r = -.43$, $P < .05$, respectively). Our data are consistent with the concept that in premenopausal women, low-fat, high-fiber diets reduce estrone sulfate levels and both LDL cholesterol and HDL cholesterol levels without affecting the TC to HDL cholesterol ratio. Moreover, changes in estrone and estradiol levels are associated with changes in HDL cholesterol and HDL-TG levels.

THE ASSOCIATION BETWEEN plasma cholesterol levels and the risk of coronary heart disease (CHD) is clearly established in epidemiologic studies.[1-4] Some of these studies have also demonstrated that a decrease in plasma cholesterol levels induced by drug intervention is accompanied by a reduction in the rate of CHD.[3,4] Evidence that the composition of the diet plays a major role in determining plasma cholesterol levels, and therefore, indirectly, the risk of CHD, came as early as the 1950s from the cross-country ecologic studies of Keys et al.[5-7] They showed that relatively high intakes of dietary cholesterol and fat, such as were observed in the higher socioeconomic strata of the populations, were associated with increased morbidity and mortality from CHD.

The National Cholesterol Education Program (NCEP) Expert Panel has defined elevated plasma levels of low-density lipoprotein ([LDL] ≥160 mg/dL) and low levels of high-density lipoprotein ([HDL] <35 mg/dL) as independent risk factors for CHD in both men and women.[8] Increased intakes of dietary saturated fatty acids increase LDL cholesterol levels, whereas substitution of polyunsaturated fatty acids for saturated fatty acids reduces both LDL and HDL cholesterol levels.[6,9-11] The majority of these diet studies have primarily focused on the effect of different diets on plasma lipid levels in men. This is probably due to the fact that until recently, diet intervention in healthy young women with low plasma cholesterol levels had little clinical relevance. However, it has now been recommended that the general population consume diets containing less than 30% fat, less than 10% saturated fat, and less than 300 mg/d cholesterol to reduce heart disease risk (NCEP Step 1 diet).[8]

Recent observations indicate that a change from the average American diet high in fat and low in fiber to a low-fat, high-fiber diet is accompanied by changes in serum sex hormone levels in young healthy women.[12-14] Both endogenous and exogenous estrogens have been shown to be strong determinants of plasma lipoprotein levels and metabolism in women.[15-17] In addition, the use of exogenous estrogens has been implicated in the development of endometrial cancer and possibly breast cancer (in high-risk individuals).[18-20]

The purpose of this study was to determine the effects of consuming a diet meeting NCEP Step 2 diet criteria (≤30% total fat, <7% saturated fat, and <200 mg/d

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cholesterol, ie, a low-fat, high-fiber diet)[8] on lipoprotein and sex hormone levels in healthy premenopausal women. Our results indicate that modification of plasma lipoprotein levels and composition by adhering to the low-fat, high-fiber diet are associated with changes in sex hormone levels.

SUBJECTS AND METHODS

Subjects

Twenty-two premenopausal women (mean ± SD: age, 25.8 ± 3.8 years; body mass index, 22.2 ± 2.0 kg/m^2) were recruited for this study through newspaper advertisements. They were all nulliparous and reported normal menses. None of the women were taking medications known to alter plasma lipid metabolism or oral contraceptives. The study was approved by the Human Investigation Review Committees of New England Medical Center and Tufts University. All subjects provided informed consent before beginning the study.

Study Design

Before enrollment onto the study, subjects were interviewed by a nutritionist to assess the composition of their average diet, to ensure that it conformed to the typical American diet (~40% of calories as fat). Subjects who were on a diet to lose or gain weight, had an eating disorder, or were vegetarians were not included in the study. Each woman started a 4-week period on a baseline control diet, similar to the usual American diet (Table 1), 1 week before they expected their menstrual period. Women were then provided the low-fat, high-fiber diet (Table 1) for a minimum of 8 weeks to a maximum of 10 weeks, depending on the length of their menstrual cycle. The nutrient composition of the diets was assessed from food tables based on the revised US Department of Agriculture Handbook No. 8.[21] All meals were prepared by the Metabolic Research Unit of the US Department of Agriculture Human Nutrition Research Center on Aging at Tufts University and were consumed at the Metabolic Unit during weekdays. Weekend meals were prepared at the Metabolic Unit and packaged for home consumption. A nutritionist met with each subject at least once per week to assess and enforce compliance with the diet. During this visit, each subject's weight was also measured. Energy intakes were adjusted when necessary to keep body weight constant (±1.3 kg) throughout the study period.

Each woman was instructed to use a commercial kit (First Response Ovulation Predictor; Carter-Wallace, Cranbury, NJ) for determination of the time of ovulation for all menstrual cycles. The follicular phase was defined as the period from the first day of the menstrual cycle to the day of the luteinizing hormone surge, and the luteal phase was defined as the period from the day after the luteinizing hormone surge to the day before the onset of menstruation.

Table 1. Composition of Baseline and Low-Fat, High-Fiber Diets

	Baseline Diet	Low-Fat, High-Fiber Diet
Carbohydrate (%)*	44	65-66
Protein (%)*	16	17-18
Fat (%)*	40	16-18
Saturated fatty acid (%)*	16	4
Polyunsaturated fatty acid (%)*	8	4
Monounsaturated fatty acid (%)*	13	6-8
Cholesterol (mg/d)	400	150
Fiber (g/d)	12	40

*Percent of total calories.

Plasma Lipid Measurements

On one day between days 3 to 7 (follicular phase) and days 21 to 23 (luteal phase) of the menstrual cycle, after a 12-hour fast, blood was drawn into tubes containing EDTA at a final concentration of 1 mg/mL during both the baseline diet and the second cycle on the low-fat, high-fiber diet. Plasma was separated by centrifugation at 2,500 rpm for 20 minutes at 4°C. Plasma HDL cholesterol levels were measured after precipitation of apolipoprotein B–containing lipoproteins with dextran sulfate–Mg^{2+} as previously described.[22] Plasma samples were subjected to ultracentrifugation in a Beckman 50.3-Ti rotor (Beckman Instruments, Fullerton, CA) at 39,000 rpm for 18 hours at 4°C, at a density of 1.006 g/mL. Levels of cholesterol and triglycerides (TG) in total plasma, HDL, and the 1.006-g/mL infranate were measured by automated enzymatic techniques with an Abbott Diagnostics ABA-200 bichromatic analyzer (Irving, TX) and Abbott A-Gent enzymatic reagents.[23] Plasma very–low-density lipoprotein (VLDL) and LDL cholesterol levels were calculated as follows: VLDL cholesterol = total cholesterol (TC) − 1.006-g/mL infranate cholesterol; LDL cholesterol = 1.006-g/mL infranate cholesterol −HDL cholesterol; and similar formulas were applied to obtain VLDL- and LDL-TG levels.

Our laboratory is standardized according to the Centers for Disease Control–National Heart, Lung, and Blood Institute Lipid Standardization Program and also serves as one of the nine network laboratories in the Centers for Disease Control Cholesterol Method Laboratory Network. Coefficients of variation for plasma lipid measurements were less than 5%.

Serum Hormone Measurements

Serum samples for determination of hormone levels were collected on 2 or 3 consecutive days during the early follicular phase (days 3 to 7) and the luteal phase (days 21 to 23) of the menstrual cycle during both the baseline diet and the second cycle on the low-fat, high-fiber diet. On some occasions, serum samples were also obtained during the third cycle on the low-fat, high-fiber diet. Serum samples were stored at −70°C until hormone measurement. Serum levels of estrone, estrone sulfate, estradiol, free estradiol, progesterone, testosterone, and androstenedione were determined by radioimmunoassay as previously described.[24,25] Coefficients of variation for the estrone, estrone sulfate, estradiol, testosterone, and androstenedione assays were 8.9%, 3.1%, 8.2%, 7.3%, and 9.5%, respectively. Sex hormone-binding globulin was measured by the DEAE-cellulose filter technique.[26,27]

Statistical Analyses

The plasma lipid portion of the study involved a single measurement taken during the early follicular and midluteal phases of the baseline and low-fat, high-fiber diet. Because the diet-related changes in plasma lipid levels were not normally distributed, the nonparametric Wilcoxon signed-rank test[28] was used to assess the intrasubject difference in plasma lipid levels between the baseline and the low-fat, high-fiber diet. The percent change in plasma lipid levels was expressed as the geometric mean percent difference. The hormone portion of the study involved multiple measurements taken during approximately 3 days of the early follicular and midluteal phases of the cycle on the baseline and low-fat, high-fiber diet. Therefore, a repeated-measures regression analysis was used to test for differences in serum hormone and sex hormone-binding globulin levels between the two diets.[29] Between-subject differences in age and body mass index were adjusted for in this analysis. Because distributions of the hormone values were skewed, a logarithmic transformation was applied when the repeated-measures regression analysis, which requires normality of the

residuals for valid statistical inference, were implemented. The percent change in hormone levels was obtained from the regression slope, β, as $100 \cdot (e^{\beta} - 1)$, where e is the natural logarithm base.

Associations between intrasubject changes in plasma lipid and lipoprotein values and intrasubject changes in serum hormone values between the baseline and the low-fat, high-fiber diet were assessed by Spearman correlation analysis.

RESULTS

The composition of the baseline and low-fat, high-fiber diets is listed in Table 1. The baseline diet provided a high percentage of calories from fat and saturated fatty acids and a high-cholesterol, low-fiber content. The difference in the percentage of calories from fat in the low-fat, high-fiber diet was compensated for by an increase in the percentage of calories from carbohydrate.

Table 2 lists plasma lipid levels measured during the early follicular phase of the menstrual cycle for both the baseline diet and the low-fat, high-fiber diet. During the follicular phase of the cycle, consumption of the low-fat, high-fiber diet was associated with a significant decrease in plasma TC levels, due to decreases in both LDL and HDL cholesterol (Table 2). The ratio of TC to HDL cholesterol did not change significantly. Plasma TG levels were significantly increased in total plasma and in VLDL during this phase (Table 2). A significant increase in the TG to cholesterol ratio was observed in all lipoprotein fractions during consumption of the low-fat, high-fiber diet relative to the baseline diet.

Plasma lipid and lipoprotein levels were also measured during the luteal phase of the menstrual cycle in 17 of 22 women participating in the study (Table 3). During the luteal phase, plasma TC levels decreased significantly during the low-fat, high-fiber diet, as did the cholesterol content in LDL and HDL. The increase in TG levels in total plasma and in the VLDL fraction was not significant. TG levels increased significantly only in LDL (Table 3). These changes resulted in a significant increase in the TG to cholesterol ratio in VLDL and LDL.

During the low-fat, high-fiber diet relative to the baseline diet, women experienced a significant decrease in serum estrone sulfate and androstenedione levels measured during the follicular phase of the cycle (Table 4). Even though mean serum levels of other estrogens did not differ significantly between the two diets, individual variability in response to the low-fat, high-fiber diet was marked, as indicated by the large standard deviations of the changes (Table 4). During the luteal phase of the cycle, only testosterone levels were significantly affected by the diet, with a 22% increase during the low-fat, high-fiber diet (Table 5).

Table 6 shows that during the follicular phase of the cycle, the change in plasma HDL-TG levels observed during the low-fat, high-fiber diet relative to the baseline diet was inversely and significantly associated with changes in estrone, estradiol, and free estradiol. An opposite trend, statistically significant only for the change in estrone, was observed for changes in HDL cholesterol levels. The association between changes in serum estrone and estradiol levels and plasma HDL cholesterol and HDL-TG levels is shown in Fig 1. Associations between the change in LDL cholesterol levels and the change in estradiol and free estradiol were negative (nonsignificant). In addition, the change in the TC to HDL cholesterol ratio was inversely and significantly associated with changes in total and free estradiol. During the luteal phase of the cycle, in contrast to what was observed during the follicular phase, changes in HDL-TG levels were positively and significantly associated

Table 2. Effects of a Low-Fat, High-Fiber Diet on Plasma Lipid and Lipoprotein Levels Measured During the Follicular Phase of the Cycle in Premenopausal Women

Parameter	Diet		Change	P*	% Change†
	Baseline	Low-Fat, High-Fiber			
Cholesterol (mg/dL)					
Total	169 ± 18	146 ± 21	−23 ± 14	.0001	−14
VLDL	20 ± 6	17 ± 6	−3 ± 8	.16	−20
LDL	92 ± 19	80 ± 17	−12 ± 11	.0001	−14
HDL	58 ± 14	49 ± 12	−9 ± 9	.0001	−15
TG (mg/dL)					
Total	55 ± 12	68 ± 18	13 ± 18	.001	22
VLDL	30 ± 9	42 ± 14	12 ± 17	.006	36
LDL	9 ± 8	11 ± 6	2 ± 5	.09	51
HDL	17 ± 5	17 ± 5	0 ± 5	.72	−2
Ratios					
TC/HDL-C	3.1 ± 0.7	3.1 ± 0.7	0.0 ± 0.4	.99	1
VLDL-TG/VLDL-C	1.49 ± 0.48	3.81 ± 6.66	2.32 ± 6.66	.0002	58
LDL-TG/LDL-C	0.10 ± 0.08	0.14 ± 0.08	0.04 ± 0.07	.02	74
HDL-TG/HDL-C	0.30 ± 0.10	0.36 ± 0.13	0.06 ± 0.12	.04	16

NOTE. Values are the means ± SD in 22 subjects, with the exception of plasma and lipoprotein TG levels, which have been measured in 20 subjects.

Abbreviation: C, cholesterol.

*Wilcoxon signed-rank test on the paired within-subject baseline diet and low-fat, high-fiber diet differences.

†Geometric mean of the percent change.

Table 3. Effects of a Low-Fat, High-Fiber Diet on Plasma Lipid and Lipoprotein Levels Measured During the Luteal Phase of the Cycle in Premenopausal Women

Parameter	Diet		Change	P*	% Change†
	Baseline	Low-Fat, High-Fiber			
Cholesterol (mg/dL)					
Total	165 ± 18	138 ± 18	−27 ± 18	.0001	−16
VLDL	19 ± 7	14 ± 5	−5 ± 9	.06	−26
LDL	88 ± 18	74 ± 15	−14 ± 23	.02	−17
HDL	58 ± 13	48 ± 11	−10 ± 5	.0001	−18
TG (mg/dL)					
Total	54 ± 18	59 ± 13	5 ± 14	.08	14
VLDL	29 ± 14	33 ± 11	4 ± 14	.09	22
LDL	8 ± 5	11 ± 4	3 ± 6	.02	68
HDL	17 ± 6	14 ± 7	−3 ± 7	.11	−18
Ratios					
TC/HDL-C	3.0 ± 0.6	3.0 ± 0.6	0.0 ± 0.3	.43	2
VLDL-TG/VLDL-C	1.69 ± 0.88	2.54 ± 0.76	0.85 ± 1.06	.003	64
LDL-TG/LDL-C	0.09 ± 0.06	0.16 ± 0.06	0.07 ± 0.08	.0001	102
HDL-TG/HDL-C	0.30 ± 0.11	0.31 ± 0.14	0.01 ± 0.13	.85	0

NOTE. Values are the mean ± SD in 17 subjects.
*Wilcoxon signed-rank test on the paired within-subject baseline diet and low-fat, high-fiber diet differences.
†Geometric mean of the percent change.

with changes in serum estradiol and free estradiol levels (Table 7).

DISCUSSION

The decreases in plasma LDL and HDL cholesterol levels attributable to the consumption of a low-fat, high-fiber diet that we observed in the premenopausal women participating in our study are in agreement with previous studies conducted in both men and women.[9-11,30-32] Differences in plasma lipid levels during the follicular and luteal phases of the cycle in women have been reported.[33,34] However, seldom has the time of the menstrual cycle been taken into consideration when assessing the effect of diets on plasma lipid levels in women.[35] Moreover, to our knowledge, no study has attempted to relate the lipoprotein response to diet to alterations in serum hormone levels. Our study design avoided the confusion derived from the fluctuation of endogenous sex hormones and their effect on plasma lipid levels.

Plasma TG levels increased during the low-fat, high-fiber diet. Such increases in TG levels during low-fat diets have been reported in several studies.[36,37] It has been shown that under isocaloric conditions, the compensatory increase in the percentage of caloric intake from carbohydrates in low-fat diets leads to liver secretion of VLDL particles enriched in TG.[38] This is in agreement with the increased TG to cholesterol ratio our subjects exhibited in VLDL during both the follicular and luteal phases of the cycle while on the low-fat, high-fiber diet. A change in the composition of LDL particles, as assessed by the TG to cholesterol ratio in these particles, was also observed. LDL particle size and composition are strongly associated with plasma TG levels, so that subjects with elevated TG levels have small, dense, cholesterol-poor, TG-enriched LDL particles.[39,40] In addition, modifications in plasma TG levels have been associated with changes in LDL particle size.[41,42] These studies are in agreement with the change in LDL composition exhibited by our subjects during the low-fat diet, and with the observation that populations with high carbohydrate intake have smaller LDL particles than populations on the usual American diet.[43]

In our subjects, the change from a high-fat, low-fiber diet to a low-fat, high-fiber diet was associated with highly variable individual changes in serum estrogen levels (es-

Table 4. Effects of a Low-Fat, High-Fiber Diet on Serum Sex Hormone Levels Measured During the Follicular Phase of the Cycle in Premenopausal Women

Parameter	Diet		Change	P*	% Change†
	Baseline	Low-Fat, High-Fiber			
Estrone (pg/mL)	50 ± 26	49 ± 28	−1 ± 32	.28	−6
Estrone sulfate (pg/mL)	520 ± 295	423 ± 373	−97 ± 363	.0001	−25
Estradiol (pg/mL)	57 ± 40	64 ± 58	7 ± 61	.68	3
Free estradiol (pg/mL)	0.8 ± 0.5	0.9 ± 0.6	0.1 ± 0.7	.63	−4
Testosterone (ng/mL)	0.4 ± 0.2	0.3 ± 0.1	−0.1 ± 0.2	.09	−13
Androstenedione (ng/mL)	1.2 ± 0.5	1.1 ± 0.5	−0.1 ± 0.5	.02	−12
Sex hormone-binding globulin (μg/dL)	2.0 ± 1.0	1.6 ± 0.7	−0.4 ± 0.7	.34	−6

NOTE. Values are the means ± SD in 22 subjects.
*Repeated-measures regression analysis using logarithmic-transformed values and adjusted for age and body mass index.
†Expressed as $100 \cdot (e^{\beta} - 1)$, where β is the regression slope.

Table 5. Effects of a Low-Fat, High-Fiber Diet on Serum Sex Hormone Levels Measured During the Luteal Phase of the Cycle in Premenopausal Women

Parameter	Diet		Change	P *	% Change†
	Baseline	Low-Fat, High-Fiber			
Estrone (pg/mL)	91 ± 26	94 ± 31	3 ± 33	.14	9
Estrone sulfate (pg/mL)	1,341 ± 518	1,264 ± 565	−77 ± 629	.43	−6
Estradiol (pg/mL)	107 ± 36	109 ± 32	2 ± 42	.59	3
Free estradiol (pg/mL)	1.8 ± 0.7	1.8 ± 0.7	0.0 ± 1.0	.30	8
Testosterone (ng/mL)	0.3 ± 0.1	0.4 ± 0.2	0.1 ± 0.2	.005	22
Androstenedione (ng/mL)	1.3 ± 0.5	1.4 ± 5.2	0.1 ± 0.5	.92	1
Progesterone (pg/mL)	17.8 ± 4.7	16.2 ± 8.5	−1.6 ± 7.9	.92	0

NOTE. Values are the mean ± SD in 18 subjects.

*Repeated-measures regression analysis using logarithmic-transformed values and adjusted for age and body mass index.

†Expressed as $100 \cdot (e^{\beta} - 1)$, where β is the regression slope.

trone, estrone sulfate, estradiol, and free estradiol), as indicated by the high standard deviation of the change for these hormones. In a study of 48 premenopausal women, we recently reported a greater effect of a low-fat, high-fiber diet on serum estrone and estradiol levels (−9.2% and −10.5%, respectively) than was observed in this study.[14] The greater number of subjects in the former study may likely be responsible for the difference in the magnitude of the hormonal change caused by the diet. It has recently been reported that postmenopausal women participating in the Women's Health Trial (WHT) experienced a significant decrease in serum estradiol levels and no change in estrone sulfate levels after consuming a low-fat diet for 10 to 22 weeks.[44] The difference in results between the WHT and our study may be due to differences in characteristics of the study subjects (ie, menopausal status) and in the study design. Women in the WHT study lost an average of 3.4 kg during the low-fat diet phase, whereas our subjects' body weight was kept constant throughout the study. In addition, it is possible that low-fat diets decrease serum estradiol levels only after several weeks of intervention, as previously suggested.[45]

During the follicular phase of the cycle, we found a significant and inverse association of the change in the plasma TC to HDL cholesterol ratio and the TG content in HDL with the change in serum estradiol levels. It is known that exogenous estrogens increase HDL cholesterol levels and apolipoprotein A-I synthesis rates in women.[17,46,47] Brinton et al[48] have recently shown that one of the mechanisms responsible for the reduction in HDL cholesterol levels during a low-fat diet is the decrease in the apolipoprotein A-I transport rate. Other steps in the metabolism of HDL are also influenced by estrogens: hepatic lipase activity is inhibited by estrogens and enhanced by androgens,[49,50] and it has been proposed recently that cholesterol ester transfer protein activity is modulated by estrogens.[51] Based on these observations, our results may indicate that in premenopausal women consuming a low-fat, high-fiber diet, changes in HDL levels and composition may be modulated in part by the diet-induced changes in sex hormone levels.

During the luteal phase of the cycle, the association between the change in HDL cholesterol and HDL-TG and the change in estrone and estradiol levels was in the opposite direction. This apparently contradictory result may be explained by the complex interaction of sex hor-

Table 6. Spearman Correlation Coefficients Between Changes in Plasma Lipid Levels and Changes in Serum Sex Hormone Levels That Occurred After a Low-Fat, High-Fiber Diet, Measured During the Follicular Phase of the Cycle in Premenopausal Women

	ΔE1	ΔE1S	ΔE2	ΔE2-free	ΔT	ΔA	ΔSHBG
Cholesterol							
ΔTotal	.23	.08	.01	.08	−.12	.19	−.16
ΔVLDL	.04	.21	.02	.16	−.20	.32	−.29
ΔLDL	.12	.10	−.26	−.37	.16	−.10	−.02
ΔHDL	.49†	.10	.32	.30	−.03	.17	−.08
TG							
ΔTotal	−.02	−.17	−.34	−.27	.12	−.14	.00
ΔVLDL	−.07	−.12	−.25	−.12	.04	.04	.00
ΔLDL	.27	.27	.28	.21	−.06	.31	.12
ΔHDL	−.52†	−.24	−.45*	−.45*	−.29	−.46*	−.25
Ratios							
ΔTC/HDL	−.18	−.03	−.47*	−.43*	.15	−.11	−.05
ΔVLDL-TG/VLDL-C	−.02	−.34	.00	−.01	.14	−.26	.08
ΔLDL-TG/LDL-C	.26	.15	.24	.19	−.02	.37	.18
ΔHDL-TG/HDL-C	−.40	−.22	−.49*	−.52†	−.07	−.45*	−.10

Abbreviations: E1, estrone; E1S, estrone sulfate; E2, estradiol; T, testosterone; A, androstenedione; SHBG, sex hormone-binding globulin.

*$P < .05$.

†$P < .02$.

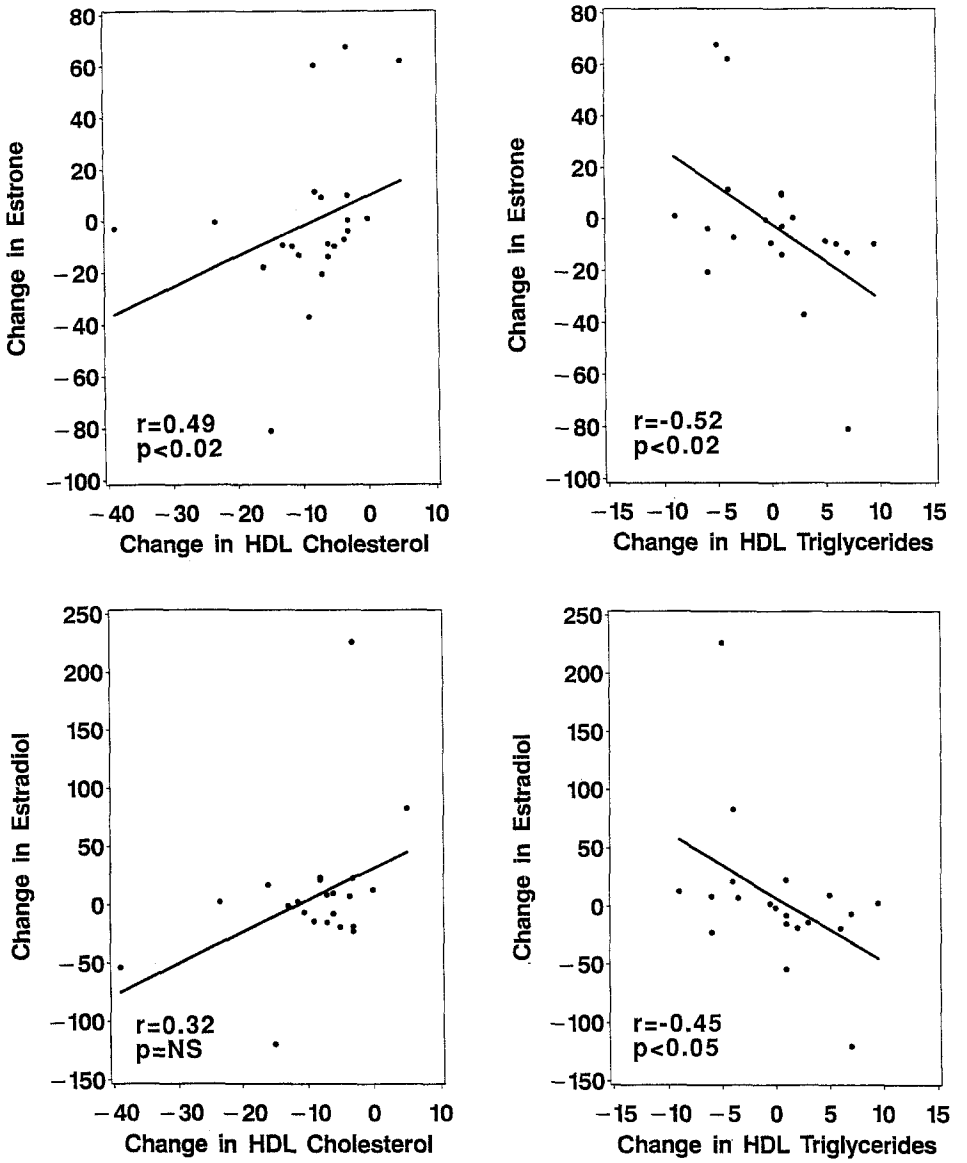

Fig 1. Correlations between diet-induced changes in serum estrone and estradiol levels and changes in plasma HDL cholesterol and triglyceride levels in premenopausal women.

Table 7. Spearman Correlation Coefficients Between Changes in Plasma Lipid Levels and Changes in Serum Sex Hormone Levels After a Low-Fat, High-Fiber Diet, Measured During the Luteal Phase of the Cycle in Premenopausal Women

	ΔE1	ΔE1S	ΔE2	ΔE2-free	ΔT	ΔA	ΔP
Cholesterol							
ΔTotal	.27	.19	−.17	−.40	−.17	−.14	.05
ΔVLDL	−.22	−.08	.13	.21	−.11	.24	−.45
ΔLDL	.07	.04	−.20	−.39	−.20	−.25	.26
ΔHDL	.36	.20	.01	−.30	−.25	.12	.33
TG							
ΔTotal	.09	.07	.14	.11	.11	.29	.06
ΔVLDL	−.11	.25	−.07	.02	.17	.33	.21
ΔLDL	.05	−.46	−.22	−.22	.09	−.50	−.27
ΔHDL	.48	.19	.54*	.38	−.13	.40	.54*
Ratios							
ΔTC/HDL	.02	−.15	.08	.01	−.01	−.15	−.40
ΔVLDL-TG/VLDL-C	.03	−.07	−.23	−.33	.23	−.04	.42
ΔLDL-TG/LDL-C	−.07	−.49	−.18	−.04	.24	−.41	−.39
ΔHDL-TG/HDL-C	.44	.17	.64†	.56†	−.02	.39	.37

Abbreviations: E1, esterone; E1S, estrone sulfate; E2, estradiol; T, testosterone; A, androstenedione; P, progesterone.

*$P < .05$.

†$P < .02$.

mones having estrogenic or androgenic activity during the follicular and luteal phases of the menstrual cycle. Progesterone levels are known to be higher during the luteal phase than during the follicular phase of the cycle. Furthermore, the significant increase in testosterone levels observed after the low-fat diet in our subjects during the luteal phase but not the follicular phase may have affected the estrogen-HDL relationship.

Several studies have recently indicated that diet may affect serum sex hormone levels in women.[12-14] The mechanism responsible for diet-induced changes in sex hormone levels in women appears to be related to the presence in high-fiber diets of naturally occurring substances with weak estrogenic activity, capable of competing and inhibiting the activity of more potent endogenous estrogens such as estradiol.[52-54] In addition, fiber has the ability to interfere with the enterohepatic circulation of estrogens and thereby prevent reabsorption from the intestine.[55] It is known that women in populations consuming diets low in total fat and cholesterol and high in fiber have a lower risk of CHD and breast cancer than women in populations consuming higher-fat diets.[53,54] Our data indicate that such low-fat diets may exert a beneficial effect on CHD risk by decreasing LDL cholesterol, and that the changes in serum estrone and estradiol levels associated with these diets may, in part, modulate the changes in HDL cholesterol levels.

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