Plasma lipids and lipoproteins in hypercholesterolemic men fed a lipid-lowering diet containing lean beef, lean fish, or poultry[1–3]

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ABSTRACT

Background: To reach desirable lipid and lipoprotein concentrations, patients with hypercholesterolemia are often told to replace the consumption of beef with that of fish and poultry.

Objective: The objective of this study was to compare the effects on lipoprotein profiles in hypercholesterolemic men of the incorporation of lean beef, poultry (without skin), and lean fish into an American Heart Association diet with a high polyunsaturated-to-saturated fatty acid ratio and a high fiber content.

Design: Three groups of subjects each rotated in a crossover design through 3 experimental periods that lasted 26 d each. The diets were planned to provide 11 713 kJ/d, of which 18% came from protein, 53% from carbohydrate, and 30% from lipids (polyunsaturated-to-monounsaturated-to-saturated fatty acid ratio: 1.0:1.1:1.0); 268 mg cholesterol/d; and 29 g fiber/d.

Results: The lean beef, lean fish, and poultry diets reduced plasma total and LDL cholesterol by 5–9%, LDL apolipoprotein B by 16–19%, VLDL triacylglycerols by 22–31%, and the ratio of total cholesterol to HDL cholesterol by 6–11%; they also increased the ratio of LDL cholesterol to apolipoprotein B by 18–28%. No significant difference was found in these lipid variables between the 3 experimental diets. However, the lean fish diet increased HDL_2 cholesterol significantly more ($P < 0.05$) than did the lean beef diet and the ratio of HDL_2 to HDL_3 cholesterol significantly more ($P < 0.05$) than did the lean beef and poultry diets.

Conclusion: The results indicate that an American Heart Association diet with a high polyunsaturated-to-saturated fatty acid ratio and high fiber content induced numerous favorable changes in coronary artery disease risk factors in hypercholesterolemic men, regardless of the protein source. *Am J Clin Nutr* 2003;77:587–93.

KEY WORDS Plasma lipids, plasma lipoproteins, beef, poultry, fish, hypercholesterolemic men, American Heart Association diet

INTRODUCTION

Normalization of the plasma lipid profile is the goal of nutritional intervention to prevent or reduce the development of atherosclerosis. To reach this goal, expert groups, including the 2001 National Cholesterol Education Program Adult Treatment Panel III (1), the American Heart Association (AHA; 2), and the Canadian Working Group on Hypercholesterolemia and Other Dyslipidemia (3), recommended replacing saturated fats with unsaturated fats rather than with carbohydrates. According to the AHA diet (2), the proportion of saturated lipids should be reduced to ≤ 10% of total energy and the cholesterol consumption limited to < 300 mg/d; in addition, according to the Canadian Working Group on Hypercholesterolemia and Other Dyslipidemia (3), fiber intake should be > 25 g/d.

Patients with hypercholesterolemia are often told to adopt diets in which either fish or poultry replaces red meats because of the lower saturated fat content of fish and poultry. In this respect, Scott et al (4), using isoenergetic low-fat diets with a high ratio of polyunsaturated to saturated fatty acids (P:S), showed that the replacement of lean beef with chicken produced similar reducing effects on plasma total and LDL cholesterol in hypercholesterolemic subjects. Furthermore, Wolmarans et al (5) compared the effects of the consumption of red meat or fatty fish on plasma lipids in free-living men and women. They found lower plasma total, VLDL, and LDL cholesterols and lower plasma total and VLDL triacylglycerols in those who ate fatty fish than in those who ate red meat. From that study, the reduction in plasma total, VLDL, and LDL cholesterols has been ascribed to lower levels of saturated fats in the fatty fish, and the decrease in total and VLDL triacylglycerols has been ascribed to higher levels of n–3 polyunsaturated fatty acids in the fatty fish diet than in the red meat diet.

The effects of beef and other animal protein sources, such as pork, veal, eggs, and milk, were also compared with those of lean white fish in normolipidemic men (6) and in premenopausal (7) and postmenopausal (8) women fed a well-controlled, low-fat (30%), high-P:S (1:1) diet. In those studies (6–8), the consumption

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TABLE 1
Physical characteristics and lipid profile of the study subjects[1]

Age (y)	50.1 ± 3.3
Body weight (kg)	81.4 ± 3.4
BMI (kg/m^2)	26.5 ± 0.9
Cholesterol (mmol/L)	
Total	6.06 ± 0.16
LDL	4.41 ± 0.15
HDL	0.93 ± 0.03
Total:HDL	6.55 ± 0.23
Total triacylglycerols (mmol/L)	1.75 ± 0.13

[1] $\bar{x}$ ± SEM; n = 17.

TABLE 2
Assessment of coronary artery disease risk among study subjects according to the 2001 National Cholesterol Education Program Adult Treatment Panel III classification of LDL-cholesterol concentrations[1]

LDL cholesterol (mmol/L)	Coronary artery disease risk	Subjects
<2.6	Optimal	0
2.6–3.3	Near or above optimal	0
3.4–4.1	Borderline high	7
4.15–4.9	High	7
>4.92	Very high	3

[1] As given in reference 1.

of beef and other animal protein sources induced lower concentrations of plasma LDL apolipoprotein B (apo B) than did the consumption of lean white fish. It is interesting that the lean whitefish protein maintained the concentration of plasma LDL apo B despite the presence of a high P:S. Because the effects of variations in plasma lipids in terms of coronary artery disease (CAD) risk are greater in hypercholesterolemic subjects, we were interested in determining whether the beneficial effects of lean meat on plasma lipoproteins in normolipidemic subjects, compared with those of lean fish, would also be observed in hypercholesterolemic subjects. On the basis of previous studies cited above, our general hypothesis was that the AHA diet incorporating either lean beef or poultry results in a more favorable lipid profile than does the AHA diet containing lean fish. The objective was to compare the effects of lean beef, poultry (without skin), and lean fish incorporated into a high-P:S and high-fiber AHA diet on plasma lipids and lipoproteins in hypercholesterolemic men.

SUBJECTS AND METHODS

Subjects

Volunteers were recruited from the Québec City area by means of advertisements in local newspapers and by announcements at Laval University. After a physical examination and blood and urine analysis, 18 white men aged 21–73 y with hypercholesterolemia (familial or polygenic, with total cholesterol > 5.2 mmol/L, LDL cholesterol > 3.4 mmol/L, or both) were selected for this study. Exclusion criteria were dyslipidemia other than high total and/or LDL cholesterol, previous vascular incident, and any other health problem that could affect lipid metabolism (eg, diabetes, renal or hepatic disease, and thyroid dysfunction). Those who had undergone major surgery within the previous 3 mo, those who had gained or lost a significant amount of weight within the previous 6 mo, and those who were smokers were also excluded. Subjects did not have food allergies, nor did they present with contraindications to the intake of calcium or vitamin D supplements. Subjects who initially took medication for the regulation of the lipid profile were required to cease taking the medication ≥ 5 wk before the beginning of the study and to obtain authorization for this step from their physician. One subject withdrew from the study for personal reasons, and his data have been deleted from this report. The physical and clinical characteristics of the subjects before the study are shown in **Table 1**. According to the 2001 National Cholesterol Education Project Adult Treatment Panel III classification (1), the CAD risk in our subjects ranged from borderline high to very high (**Table 2**). Each participant gave written informed consent after the study protocol was fully explained. The study was approved by the Clinical Research Ethical Committee of Laval University.

Study design

Subjects were asked to consume a noncontrolled diet close to their usual food consumption, without alcohol, for 2 wk before each experimental period. A crossover design for 3 experimental periods (9) was used to compare the effects of lean beef with those of lean poultry and lean fish. The 18 subjects were randomly assigned to begin the study with either the lean beef diet, the lean fish diet, or the poultry diet. Then the 3 groups of men each rotated through the 3 experimental periods that lasted 26 d each. Participants switched back to the preexperimental diet for a washout period of 6 wk after each experimental period to remove the possible residual effects of the preceding experimental diet on the blood variables tested.

Diets

Experimental diets were built as 7-d rotating menus and were formulated to meet the nutrient specifications of a lipid-lowering AHA diet (2). Diets supplied daily allowances of all essential nutrients as recommended by Health and Welfare Canada (10). A 3-d food intake diary was kept by each participant before the study to facilitate the formulation of menus reflecting the subjects' preferences and usual energy intake. Participants were also asked to keep dietary records for 3 d before each experimental period to monitor their preexperimental food consumption. The nutritional composition of the experimental diets and dietary records was calculated with the use of computer-assisted analysis of the Canadian Nutrient File database (11). Because the nutrient intake was similar for the 3 preexperimental periods, the nutrient data have been pooled together and identified as the preexperimental diet.

The 3 experimental diets had no differences in food composition with the exception of the protein source tested, which was lean beef (lean ground beef, exterior round, sirloin tip) for diet 1, skinless chicken and ground turkey for diet 2, or fish (pollack, cod, sole, and haddock) with < 1% fat for diet 3. A proportion of 69% of daily proteins came from beef, fish, or poultry, and the remaining proportion was from a vegetable source. Because no milk products were allowed during experimental periods to avoid casein consumption, subjects were given daily calcium (600 mg) and vitamin D (125 IU) supplements. The nutrient compositions of the preexperimental and experimental diets are shown in **Table 3**. When compared with the preexperimental diet of the participants, the experimental diets had a higher P:S (1.0:1 compared with 0.5:1 for the preexperimental diet) as well as a higher ratio

TABLE 3
Nutrient composition of preexperimental and experimental diets[1]

	Diet			
	Preexperimental	Lean beef	Lean fish	Poultry
Energy (kJ)	11 999 ± 560[2]	11 636 ± 403	11 790 ± 332	11 713 ± 415
Protein (% of energy)	17	18	17	18
Carbohydrate (% of energy)	53	52	53	52
Lipids (% of energy)	30	30	30	30
Polyunsaturated fatty acids (g)	19 ± 2[3]	30 ± 1	31 ± 1	31 ± 1
Monounsaturated fatty acids (g)	43 ± 4[3]	34 ± 1	34 ± 1	34 ±
Saturated fatty acids (g)	37 ± 3[3]	30 ± 1	30 ± 1	30 ± 1
P:M:S[4]	0.5:1.2:1.0[3]	1.0:1.1:1.0	1.0:1.1:1.0	1.0:1.1:1.0
(P+M):S[5]	1.7:1[3]	2.1:1	2.2:1	2.2:1
Cholesterol (mg)	351 ± 32[3]	253 ± 8	258 ± 7	263 ± 8
Total fiber (g)	23.5 ± 1.9[3]	30.1 ± 1.0	28.2 ± 0.6	28.8 ± 0.9

[1] $n = 17$.
[2] $\bar{x}$ ± SEM.
[3] Significantly different from the experimental diets, $P < 0.05$ (Tukey's test).
[4] Ratio of polyunsaturated to monounsaturated to saturated fatty acids.
[5] Ratio of polyunsaturated + monounsaturated fatty acids to saturated fatty acids.

of (polyunsaturated + monounsaturated)-to-saturated fatty acid [(P+M):S; 2.2:1 compared with 1.7:1 for the preexperimental diet], higher fiber content, and lower content of cholesterol to meet the AHA diet guidelines (2, 3). Energy and other nutrients not differ significantly between preexperimental and experimental diets.

A sample 1-d menu of the lean beef, lean fish, and poultry 11 760-kJ diets is presented in **Table 4**. Subjects began the study at the energy level nearest to their usual intake, as calculated from the 3-d dietary record. Six energy levels were established for each diet (9200, 10 450, 11 760, 13 400, 14 650, and 16 750 kJ). Body weight was taken every 2 d. Because subjects had to maintain their body weight (a maximum variation of 2 kg was allowed within each experimental period), they were moved from one level to another when they reached a body weight variation of ≥ 1 kg. Subjects were informed that they had to avoid alcohol consumption and that they should maintain the same activity level throughout the study. They were also asked to consume nothing besides the prepared meals they were given or the foods included on the breakfast and snack lists.

All lunches and dinners were prepared in our food experimentation laboratory by 3 registered dietitians and 1 dietary technician. Subjects consumed their breakfasts and snacks at home from an approved food list including types and quantities of foods to be consumed. They ate their lunches at our food experimentation laboratory under the supervision of registered dietitians and took their prepared dinners

TABLE 4
Sample 1-d menu for the experimental diets[1]

	Lean beef diet	Lean fish diet	Poultry diet
Breakfast	263 g Orange juice	263 g Orange juice	263 g Orange juice
	48 g Sliced whole-wheat bread	48 g Sliced whole-wheat bread	48 g Sliced whole-wheat bread
	15 g Margarine	8 g Margarine	15 g Margarine
	40 g Strawberry jam	40 g Strawberry jam	40 g Strawberry jam
	11 g Peanut butter	11 g Peanut butter	11 g Peanut butter
Lunch	Beef stew	270 g Pollack fillets (with Italian spices)	Chicken cacciatore
	180 g Beef	130 g White rice	180 g Chicken (dark)
	318 g Vegetables	100 g Green beans	110 g Sauce
	150 g Baked potato	118 g Oatmeal squares with prune filling	150 g Baked potato
	144 g Green beans		100 g Green beans
	8 g Margarine		8 g Margarine
	118 g Oatmeal squares with prune filling		118 g Oatmeal squares with prune filling
Dinner	200 g Beef tournedos	225 g Cod fillets	225 g Chicken tournedos
	37 g Pepper sauce	72 g Barbecue sauce	37 g Barbecue sauce
	137 g Tomato linguine	137 g Spinach linguine	137 g Tomato linguine
	6 g Safflower oil	14 g Safflower oil	8 g Olive oil
	90 g Cauliflower	9 g Olive oil	90 g Cauliflower
	22 g Leeks	90 g Cauliflower	22 g Leeks
	84 g Apple cake	22 g Leeks	8 g Margarine
		8 g Margarine	84 g Apple cake
		84 g Apple cake	
Snacks	269 g Fruit (2 medium-sized)	269 g Fruit (2 medium-sized)	269 g Fruit (2 medium-sized)
		22 g Oatmeal cookies (2 cookies)	22 g Oatmeal cookies (2 cookies)

[1] Second day of the 11 760-kJ/d diets.

TABLE 5
Plasma lipid, lipoprotein, and apolipoprotein concentrations before and after the dietary treatments[1]

	Lean beef diet	Lean fish diet	Poultry diet
Total cholesterol			
Before treatment (mmol/L)	5.9 ± 0.2[2]	5.9 ± 0.2	6.0 ± 0.2
After treatment (mmol/L)	5.4 ± 0.2	5.6 ± 0.2	5.5 ± 0.2
Percentage of change (%)	−8	−5	−8
Total triacylglycerol			
Before treatment (mmol/L)	1.6 ± 0.1	1.5 ± 0.1	1.6 ± 0.1
After treatment (mmol/L)	1.3 ± 0.1	1.2 ± 0.1	1.2 ± 0.1
Percentage of change (%)	−19	−20	−25
VLDL cholesterol			
Before treatment (mmol/L)	0.63 ± 0.06	0.62 ± 0.06	0.62 ± 0.06
After treatment (mmol/L)	0.50 ± 0.05	0.42 ± 0.05	0.44 ± 0.06
Percentage of change (%)	−21	−32	−29
LDL cholesterol			
Before treatment (mmol/L)	4.3 ± 0.1	4.4 ± 0.2	4.4 ± 0.1
After treatment (mmol/L)	4.0 ± 0.2	4.2 ± 0.2	4.0 ± 0.2
Percentage of change (%)	−7	−5	−9
HDL cholesterol			
Before treatment (mmol/L)	0.96 ± 0.03	0.96 ± 0.04	0.96 ± 0.04
After treatment (mmol/L)	0.95 ± 0.04	0.98 ± 0.05	1.01 ± 0.04
Percentage of change (%)	−1	2	5
HDL_2 cholesterol			
Before treatment (mmol/L)	0.28 ± 0.02	0.27 ± 0.03	0.29 ± 0.02
After treatment (mmol/L)	0.29 ± 0.03	0.34 ± 0.04[3]	0.32 ± 0.04
Percentage of change (%)	4	26	10
HDL_3 cholesterol			
Before treatment (mmol/L)	0.68 ± 0.02	0.69 ± 0.03	0.67 ± 0.03
After treatment (mmol/L)	0.66 ± 0.02	0.64 ± 0.02	0.68 ± 0.03
Percentage of change (%)	−3	−7	1
VLDL triacylglycerol			
Before treatment (mmol/L)	1.04 ± 0.10	0.98 ± 0.10	1.02 ± 0.12
After treatment (mmol/L)	0.81 ± 0.09	0.68 ± 0.10	0.73 ± 0.11
Percentage of change (%)	−22	−31	−28
LDL triacylglycerol			
Before treatment (mmol/L)	0.31 ± 0.02	0.32 ± 0.02	0.32 ± 0.02
After treatment (mmol/L)	0.29 ± 0.02	0.29 ± 0.02	0.27 ± 0.02
Percentage of change (%)	−6	−9	−16
HDL triacylglycerol			
Before treatment (mmol/L)	0.22 ± 0.01	0.23 ± 0.01	0.22 ± 0.01
After treatment (mmol/L)	0.22 ± 0.01	0.21 ± 0.01	0.21 ± 0.01
Percentage of change (%)	0	−9	−5
Apo B			
Before treatment (g/L)	1.32 ± 0.03	1.33 ± 0.05	1.36 ± 0.03
After treatment (g/L)	1.13 ± 0.04	1.13 ± 0.03	1.11 ± 0.04
Percentage of change (%)	−14	−15	−18
VLDL apo B			
Before treatment (g/L)	0.16 ± 0.04	0.12 ± 0.01	0.14 ± 0.02
After treatment (g/L)	0.11 ± 0.02	0.10 ± 0.01	0.13 ± 0.02
Percentage of change (%)	−31	−17	−7
LDL apo B			
Before treatment (g/L)	1.21 ± 0.03	1.21 ± 0.04	1.22 ± 0.04
After treatment (g/L)	1.01 ± 0.04	1.01 ± 0.04	0.99 ± 0.04
Percentage of change (%)	−17	−16	−19
HDL apo A-I			
Before treatment (g/L)	1.27 ± 0.03	1.28 ± 0.03	1.28 ± 0.04
After treatment (g/L)	1.15 ± 0.02	1.13 ± 0.02	1.18 ± 0.02
Percentage of change (%)	−9	−12	−8

[1] $n = 17$. Apo, apolipoprotein.
[2] $\bar{x}$ ± SEM.
[3] Significantly different from the lean beef diet, $P < 0.05$ (ANOVA for crossover design with >2 periods (9), followed by Tukey's test.

and weekend meals home with them. Food preparation procedures were strictly standardized, and foods were precisely measured and weighed. Subjects were asked to report any deviation from the menu or any intake of medication during the experimental periods.

Blood analysis

One blood sample was taken early in the morning after a 12-h fast before the beginning of experimental periods and after the end of the experimental periods. Blood (7 mL) from the antecubital vein was collected in tubes with EDTA to obtain plasma. Blood samples were centrifuged immediately for 10 min at 1500 × *g* at 4 °C to separate plasma, which was thereafter stored at 4 °C and analyzed for lipid determinations within 5 d at the Lipid Research Unit of the University Medical Center of Québec City. An analyzer (RA-500; Bayer Corporation, Tarrytown, NY) was used to measure plasma triacylglycerol and cholesterol concentrations in the plasma and in the lipoprotein subfractions, and enzymatic reagents were obtained from Randox (Mississauga, Canada). Lipoprotein fractions (VLDL, LDL, and HDL) were separated by combined ultracentrifugation (256 000 × *g* at 11 °C for 9 h 53 min) and heparin-manganese precipitation (12, 13). The cholesterol content of the infranatant fraction was measured before and after the precipitation step for the measurement of LDL and HDL cholesterol levels. HDL_2 and HDL_3 subfractions were separated with the use of dextran-sulfate precipitation (14). Apolipoproteins were assessed with the use of rocket immunoelectrophoresis (15).

Statistical analysis

The SAS software, version 6.12 (SAS Institute Inc, Cary, NC) was used to perform statistical analysis. Results are presented as means ± SEMs. Tukey's test was used to compare the nutrient intakes of the preexperimental, lean beef, lean fish, and poultry diets. The general linear model (GLM) procedure of SAS was used for an analysis of variance for crossover design with >2 periods (9), and, when P was < 0.05, the GLM procedure was followed by Tukey's test to compare the effects of the lean beef, lean fish, and the poultry diets. Because no residual effect of the first experimental period during the second experimental period or of the second experimental period during the third experimental period was seen on any lipid variable, the data for dietary treatment, experimental period, and sequence of treatment were pooled.

RESULTS

Body weight and body mass index

There were no significant differences between the mean body weights before the lean beef (81.4 ± 3.3 kg), lean fish (81.4 ± 3.3 kg), and poultry (81.7 ± 3.4 kg) diets. Moreover, there were no significant differences between the mean body mass indexes (BMI; in kg/m^2) before the lean beef (26.6 ± 0.9), lean fish (26.5 ± 0.9), and poultry (26.5 ± 1.0) diets. No significant changes in these values were observed after the experimental periods, which indicates that neither body weight nor BMI had an effect on the lipid profile.

Plasma lipids and lipoproteins

Mean concentrations of plasma lipids, lipoproteins, and apolipoproteins before and after the lipid-lowering lean beef, lean fish, and poultry diets are shown in **Table 5**. The lean beef diet

TABLE 6
Plasma lipid ratios before and after the dietary treatments[1]

Ratio	Lean beef diet	Lean fish diet	Poultry diet
LDL cholesterol:LDL apo B[2]			
Before treatment	1960 ± 34[3]	1983 ± 36	1983 ± 33
After treatment	2367 ± 77	2335 ± 82	2531 ± 70
Percentage of change (%)	21	18	28
Total:HDL cholesterol			
Before treatment	6.23 ± 0.22	6.30 ± 0.28	6.25 ± 0.21
After treatment	5.83 ± 0.25	5.81 ± 0.27	5.54 ± 0.27
Percentage of change (%)	−6	−8	−11
HDL_2:HDL_3 cholesterol			
Before treatment	0.42 ± 0.03	0.40 ± 0.03	0.43 ± 0.03
After treatment	0.43 ± 0.04	0.52 ± 0.05[4]	0.47 ± 0.07
Percentage of change (%)	2	30	9

[1] $n = 17$. Apo, apolipoprotein.
[2] To obtain similar units for lipoprotein lipid (cholesterol) and apo B values, the LDL apo B concentrations (in g/L) were divided by 550 g/mmol, which is the apo B molecular weight. LDL cholesterol:LDL apo B was calculated as follows:
[LDL cholesterol (mmol/L)]/{[LDL apo B (g/L)]/550 g/mmol}
[3] $\bar{x}$ ± SEM.
[4] Significantly different from the lean beef and poultry diets, $P < 0.05$ (ANOVA for crossover design with >2 periods (9), followed by Tukey's test.

reduced plasma total and LDL cholesterol by 7–8%, the lean fish diet reduced them by 5%, and the poultry diet by 8–9%; no significant differences were observed in plasma total and LDL-cholesterol concentrations among the lean beef, lean fish, and poultry diets.

The lean beef diet decreased plasma total triacylglycerols by 19%, the lean fish diet decreased it by 20%, and the poultry diet by 25%. VLDL triacylglycerols and cholesterol were reduced by 21–22%, 31–32%, and 28–29% after the consumption of the lean beef, lean fish, and poultry diets, respectively. Therefore, no significant differences were observed in plasma total and VLDL triacylglycerols and VLDL cholesterol when the lean beef, lean fish, and poultry diets were compared together.

The lean beef diet decreased plasma total and LDL apo B by 14–17%, the lean fish diet decreased them by 15%, and the poultry diet by 18–19%, whereas HDL apolipoprotein A-I was reduced by 9%, 12%, and 8% after the lean beef, the lean fish, and the poultry diets, respectively. No significant differences were thus observed in plasma total and LDL apo B concentrations and HDL apolipoprotein A-I concentrations among the 3 experimental diets.

Notably, the lean fish diet increased HDL_2 cholesterol by 26% and reduced HDL_3 cholesterol by 7%, whereas the lean beef and poultry diets maintained these variables close to their initial levels. Consequently, the lean fish diet increased HDL_2 cholesterol significantly more ($P < 0.05$) than did the lean beef diet.

Mean plasma lipid ratios before and after the consumption of the 3 lipid-lowering experimental diets are shown in **Table 6**. Greater reduction in LDL apo B than of LDL cholesterol resulted in a plasma LDL cholesterol-to-apo B ratio that increased by 21%, 18%, and 28% after the lean beef, lean fish, and poultry diets, respectively. The lean beef diet decreased the total to HDL cholesterol ratio by 6%, the lean fish diet decreased it by 8%, and the poultry diet by 11%. Therefore no significant differences were observed in either the LDL cholesterol:apo B or the total:HDL cholesterol among the 3 experimental diets. However, the 26% increase in HDL_2 cholesterol concomitant with the 7% decrease in HDL_3 cholesterol with the lean fish diet resulted in an HDL_2:HDL_3 cholesterol greater than that seen with the lean beef and poultry diets.

DISCUSSION

These results indicate that the consumption of a lean beef, lean fish, or poultry lipid-lowering diet induced reductions in plasma total and LDL cholesterol, and the magnitude of decrease depended on the diet consumed. After 26 d of dietary intervention, the lean beef and the poultry diets reduced plasma total and LDL-cholesterol concentrations by about 8%, and the lean fish diet reduced them by 5%. In general, short-term controlled-feeding studies showed that the AHA diet decreased plasma total and LDL cholesterol by ≈7–9% from the concentrations seen with the average American diet (16). These results indicate that higher P:S and lower cholesterol intake together with a higher fiber intake without a modification of total energy and fat intake can be effective in helping to reduce plasma total and LDL cholesterol. The present effects of lean beef and poultry diets are in good agreement with those reported in a short-term controlled study conducted by Scott et al (4) and a long-term (36-wk) study conducted by Davidson et al (17), which showed the cholesterol-lowering effects of lean red and white meats incorporated into AHA diet. In the present study, although there was some range in the response to the 3 diets, no significant differences were observed in total and LDL cholesterol among the lean fish, lean beef, and poultry groups. These results agree with those of our previous study (6) that found no significant difference between the plasma total and LDL-cholesterol concentrations in normolipidemic men fed a lean fish diet and in those fed a nonfish diet with a high P:S and high fiber content. However, it would be of interest to test whether varying the source of dietary protein would induce changes in LDL cholesterol when more atherogenic, controlled diets are consumed.

The present results show that the 3 diets had the beneficial effect of lowering plasma VLDL triacylglycerols and cholesterol by 20–30%, regardless of the protein source used. In controlled-feeding studies in which body weight is maintained, low-fat diets are generally associated with increases in plasma triacylglycerols and decreases in HDL cholesterol (18). These effects are likely due to the fact that total and saturated fats are often replaced by carbohydrates in those diets. Incidentally, Scott et al (4) showed that an AHA diet containing lean beef or chicken, which was low in total and saturated fats and cholesterol and high in total carbohydrates and fibers, induced reductions in plasma total, LDL, and HDL cholesterol but no change in triacylglycerols or body weight over a 5-wk intervention period in hypercholesterolemic subjects. It appears from that study that the hypertriacylglycerolemic response to a high-carbohydrate diet was prevented by the high fiber content of those diets. More recently, a high-fiber (50 g/d) diet has been shown to reduce the area under the curve for 24-h plasma glucose and insulin concentrations and for plasma cholesterol, triacylglycerol, and VLDL cholesterol concentrations in patients with type 2 diabetes (19). Earlier studies (20, 21) support the concept that an increase in fiber, mainly of the soluble type, in the diet decreases plasma glucose and lipid responses. In the present AHA diets, both dietary P:S and the fiber content were increased and the dietary cholesterol was decreased, whereas

dietary total lipids and carbohydrates remained unchanged. Therefore, the present results suggest that the plasma triacylglycerol-lowering effect of the experimental AHA diets containing either lean beef, lean fish, or poultry could be attributed to an increase in the fiber content (20, 21) of these diets. Because our subjects' weight did not change, there is a possibility that dietary fibers reduced plasma total and VLDL triacylglycerols by improving glycemic control (19).

The 3 experimental diets also decreased LDL apo B by about 17% and increased LDL cholesterol:LDL apo B by 18–28%, which indicates the presence of less dense LDL particles. Scientific evidence from basic studies showed that, particle for particle, the larger, more cholesterol-rich LDL particles are less atherogenic than the smaller, denser LDL particles (22, 23). Moreover our data are in good agreement with those of Nydahl et al (24) who showed that high dietary P:S is associated with a decrease in plasma cholesterol and apo B. It is well established that an increase in the dietary P:S and the removal of dietary cholesterol can decrease LDL particle levels by increasing LDL receptor activity (25). Also in the present study, higher fiber consumption could have been a factor in the reductions in LDL cholesterol and apo B (20). The underlying mechanism could be an increase in the excretion of fecal acidic sterol and a decrease in the gastrointestinal absorption of cholesterol (19).

In normolipidemic men (6) and premenopausal (7) and postmenopausal (8) women, the AHA nonfish diet consisting of mixed animal proteins (beef, pork, eggs, and milk products) reduced plasma LDL apo B, whereas the AHA lean fish diet maintained these concentrations. On the other hand, our results indicate that, in hypercholesterolemic subjects, the AHA diet containing lean fish, rather than failing to reduce plasma LDL apo B as in normolipidemic subjects, was as effective as the lean beef and poultry diets in reducing LDL apo B. These results are of great clinical interest, because a basic principle of CAD prevention is that the intensity of risk-reduction therapy should be adjusted to a person's risk status (1). In light of the present study and previous studies (6–8), the hypercholesterolemic subjects who are known to be at high risk for CAD could be advised to include lean fish as well as lean beef or poultry without skin in an AHA diet to reduce their LDL apo B concentrations. The normolipidemic subjects who do not need to reduce their already-normal plasma LDL apo B can also incorporate lean fish in an AHA diet because lean fish has been shown not to affect their plasma LDL apo B concentrations (6). However, it would be of scientific interest to determine by kinetic studies the mechanisms accounting for the discrepancies between the responses to lean fish intake in normolipidemic and hypercholesterolemic subjects.

In the present study, there was a favorable effect of the lean fish diet on HDL_2 cholesterol, the most protective HDL subfraction, and on HDL_2:HDL_3 cholesterol. Lacaille et al (6) conducted a study comparing the effects of a lean fish diet and of a nonfish diet in normolipidemic men and also observed a favorable effect of a lean fish diet on HDL_2 cholesterol. The present effect on HDL_2 cholesterol could be attributed to the presence of small quantities of n–3 polyunsaturated fatty acids in lean fish. There is published evidence that the addition to the diet of fatty fish containing high amounts of n–3 polyunsaturated fatty acids can increase HDL_2 cholesterol (26). Abbey et al (27) showed that fish oil can inhibit cholesterol ester transfer protein, which prolongs the stay of cholesterol esters in HDL and accounts for the increase in HDL_2 cholesterol. There is also a possibility that the presence of another constituent of fish—namely, its protein—may contribute to an increase in HDL_2-cholesterol concentrations. Bergeron et al (28) reported an increase in HDL cholesterol in rabbits fed fish protein, which was accompanied by a parallel increase in plasma lipoprotein lipase activity after heparin administration and in a reduction in VLDL triacylglycerols. These beneficial effects observed in rabbits and the increase in HDL_2 cholesterol observed in the present study could partly result from an improvement in insulin sensitivity. There is indeed increasing evidence in animal studies that fish protein can increase insulin sensitivity (29, 30). Differences in the arginine content of dietary proteins have been proposed to mediate the protein-dependent changes in glucose and insulin (31, 32) and in blood lipid concentrations (32). Finally, the total:HDL cholesterol currently used as an indicator of CAD risk (33) was reduced after the consumption of any of the 3 experimental diets, which supports the concept that incorporating either lean beef, lean fish, or poultry into the AHA diet can be beneficial in reducing CAD risk in patients with hypercholesterolemia.

In conclusion, with respect to CAD risk, an AHA diet with a high P:S and high fiber content, regardless of the protein source, induced numerous favorable changes such as reductions in plasma total and LDL cholesterol and apo B, total and VLDL triacylglycerols, and total:HDL cholesterol in hypercholesterolemic men, and it overlapped the effects of protein sources on LDL apo B previously observed in normocholesterolemic subjects. The lean fish diet had the added benefit of improved HDL_2 cholesterol.

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