Lack of an effect of dairy protein (casein) and soy protein on plasma cholesterol of strict vegetarians. An experiment and a critical review

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Abstract In animals, ingestion of casein, the principal protein in milk, causes hypercholesterolemia, whereas in humans this effect has not been documented. We added 27 g of casein (the amount in 1.1 liters of skim milk and nearly twice the average U.S. intake) for 20 days, and 27 g of soy protein for an additional 20 days to the daily diet of 13 strict vegetarians who consumed no other animal protein during the study period. The protein supplementation increased the ad libitum daily protein intake from 59 g to 82 g. Levels of plasma LDL, HDL, and total cholesterol were not significantly affected by either the casein or the soy supplementation. Over the 40 days of protein supplementation, there were progressive decreases in VLDL cholesterol (VLDL-C) and increases in triglycerides (TG) from pre-study levels, demonstrated by an overall change in the VLDL-C/TG ratio from 0.30 to 0.17 (P = 0.003). Caloric intake and body weight did not change significantly. From the literature on dietary protein and blood lipid levels and from the present data, it appears that neither the amount of protein in the diet nor whether the protein comes from animal or vegetable sources has an important effect on plasma LDL and HDL levels in humans when consumed in physiologic amounts.—**Sacks, F. M., J. L. Breslow, P. G. Wood, and E. H. Kass.** Lack of an effect of dairy protein (casein) and soy protein on plasma cholesterol of strict vegetarians. An experiment and a critical review. *J. Lipid Res.* 1983. **24:** 1012–1020.

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In many animal species hypercholesterolemia occurs when semisynthetic, cholesterol-free diets are substituted for laboratory chow (1, 2). For the hypercholesterolemic effect to occur, animal protein in the formula diets is necessary. Proteins from beef, egg yolk, and milk elevate serum cholesterol levels, but vegetable proteins such as soy, wheat, and sunflower do not.

In humans, it is not at all certain that dietary protein, either in type or quantity, can significantly influence plasma lipid levels. Strict vegetarians who consume no animal protein have lower serum cholesterol levels than lactovegetarians. They, in turn, have lower serum cholesterol levels than nonvegetarians who consume unrestricted amounts of animal protein (3–6). Not only is there a gradient of increasing animal protein consumption from strict vegetarian to nonvegetarian diets, but also the total protein intake is elevated in nonvegetarian groups. However, vegetarians and nonvegetarians consume different amounts of nutrients such as fat and fiber that affect serum cholesterol levels. Controlled studies in which the dietary protein content was modified while other nutrients were held constant have yielded inconclusive results. Although one group observed 15–20% reductions in total and LDL cholesterol when animal protein was replaced by textured soy protein in the diets of hyperlipidemic patients (7, 8), most other studies of the diets of normal and hyperlipidemic subjects have demonstrated slight (9–12) or no significant effects on serum cholesterol after changing either the amount or source of dietary protein (13–18).

In the current study, we tested the two hypotheses that the level of dietary protein, per se, influences plasma lipids, and that casein, which comprises 80% of the protein in milk, is relatively hypercholesterolemic in comparison to soy protein when consumed in physiologic amounts. We added 27 g of casein, equivalent to 1.1 liters of skim milk (19) and nearly twice the average United States intake per day (20), and 27 g of soy protein to the diets of 13 strict vegetarians and measured lipid and lipoprotein levels for each subject on his or her regular diet, after 20 days of casein and after 20 days of soy supplementation. No significant differences were observed in the effects of the two proteins on plasma total cholesterol or its major components.

Abbreviations: LDL, low density lipoproteins; HDL, high density lipoproteins; C, cholesterol; VLDL, very low density lipoproteins; TG, triglyceride.

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SUBJECTS AND METHODS

Subjects

Strict vegetarians were recruited from the student body at the Kushi Institute, a center for teaching the macrobiotic diet and philosophy in Brookline, MA, and from the staff of a nearby macrobiotic publication and grocery. Other strict vegetarians were located through a notice at the grocery. Eighteen vegetarians were enrolled into the study. Data from five subjects were not analyzed. Four subjects left the protocol at the halfway point, two due to changes in a travel itinerary and two because of dislike of the protein preparations. One additional subject contracted a viral illness during the last 2 weeks of the protocol with resulting anorexia and weight loss of 2.7 kg, and left the study. Thus data on the 13 strict vegetarians who adhered to the protocol form the basis of this report. There were nine men and four women, mean age 31 with range 21–40 years. All subjects had been adhering to a strict vegetarian diet for at least 11 months prior to the onset of the protocol. Subjects were healthy and were taking no medicines.

Design of the study

The protocol consisted of three phases: a 1-week preintervention period for baseline observations was followed by two 20-day intervention periods during which each subject consumed in random sequence 27 g per day of casein and soy protein. During the baseline period, the subjects were observed while consuming their usual strict vegetarian diet. The original group of 18 subjects was randomly divided into two equal groups who received the soy and casein in opposite order during the study. Of the 13 persons in the final study group, 8 were in the soy-casein sequence and 5 were in the casein-soy sequence. Subjects who lived or worked together were randomized in subgroups in order to avoid direct comparison of the two proteins by the subjects who were kept unaware of the identity of the protein preparations.

Vitamin-free casein and soy protein isolate were purchased from BioServe, Frenchtown, NJ. The protein composition of the casein and soy isolate was 98.1% and 93% of dry weight, respectively, and the percentage of solids by weight in the preparations was 91% and 94%, respectively. Thirty grams of the protein isolate per day cooked in either muffins or oatmeal, was given to the subjects and supplied approximately 27 g per day of the pure test protein. The muffins were prepared by a cook trained in macrobiotic cuisine. In accordance with the macrobiotic dietary guidelines and the preferences of the subjects, unrefined grains including millet, cracked wheat, and cornmeal were used in the recipes, and corn oil and sugars in the form of barley malt syrup were added in very small amounts. The daily ration of the muffins and oatmeal had similar nutrient composition. Based upon actual records of consumption, the average amount of nutrients supplied daily by these foods was protein, 7.9 g; fat, 2.4 g; and carbohydrate 74.5 g, exclusive of the casein and soy protein added. The daily ration consisted of two muffins or one 12-ounce container of oatmeal, and replaced other sources of cereal products in the diet. Aside from the test foods, which supplied 457 kcal per day, the subjects adhered to their usual strict vegetarian diet throughout the study. Muffins and oatmeal were distributed to the subjects twice per week, and at those times the 13 subjects were questioned regarding their consumption of the previously delivered batch. Except on rare occasions, the subjects consumed the allotted foods.

Subjects were weighed during the baseline phase, and after each 20-day period on one portable scale.

Diet assessment

The principal foods in the macrobiotic diet are unrefined cereal products, legumes, and vegetables, supplemented by fruits (21). Fish, dairy products, and eggs are consumed once per week or less, and poultry and meat seldom or never. Sugars including honey, molasses, and maple syrup are avoided. Dietary patterns of the group are stable over time, reflecting the narrow range and similar nutrient content of foods acceptable to these vegetarians.

Dietary histories were obtained from each subject during the baseline assessment period and at the end of the period of protein supplementation. Initially, participants answered a comprehensive questionnaire of food intake. This questionnaire listed 143 foods or groups of similar foods that were prevalent in the vegetarians' diets. The specific foods were chosen from detailed dietary records completed by other macrobiotic vegetarians and from discussions with several macrobiotic persons. A typical portion size was listed with each item of food along with nine categories of frequency of consumption ranging from "never" to "6+ times/day" of the designated portion of food. Thus, for each food a subject would check the frequency category approximating his/her usual consumption of the specified portion. Nutrient composition of each listed portion was derived from standard tables (22–25). In several cases, responses to the questionnaires were clarified by the results of a dietary history. The responses of two persons on the final diet questionnaires were not sufficiently quantitative for accurate nutrient analysis, and these subjects were not available for further information. The nutrient content of the diet was thus calculated in 11 of the 13 subjects who completed the protocol.

Plasma lipid determination

Plasma samples were coded before being sent to the laboratory. All personnel involved with the lipid measurements were unaware of the dietary phase or subject identification number of each sample.

A fasting blood sample was taken with the subject in the sitting position on the last 2 days of each of the three assessment periods. The subjects had been sitting for about 10 min before the venipuncture took place. Venous blood was drawn into evacuated 7-ml glass tubes containing 10.5 mg of solid EDTA. Specimens were kept in ice water until centrifugation (1500 *g* for 30 min at 4°C) which took place within 3 hr after venesection. Lipoprotein separation and lipid measurements were performed at the Metabolism Division, Children's Hospital Medical Center, Boston, according to methods specified by the Lipid Research Clinics Program (26). The Metabolism Division Laboratory is standardized for cholesterol, HDL-C, and triglyceride measurements by the Lipid Standardization Laboratory of the Centers for Disease Control. Plasma was centrifuged at its own density for 18 hr at 143,000 *g*, and the infranate, containing LDL and HDL, was isolated by tube-slicing. LDL was precipitated from the infranate by the addition of heparin, 183 U/ml, and, 92 μM $MnCl_2$. Cholesterol was measured by the LRC method in a Technicon Autoanalyzer II system in whole plasma, the HDL + LDL infranate, and the HDL supernate, deriving values for LDL and VLDL by difference (26). Triglycerides were measured by fluoronephelometry and results were corrected for free glycerol as measured in each sample.

Analysis of data

Since each person served as his/her own control, the two-tailed paired *t*-test was used to assess the significance of mean differences in lipid levels between the baseline soy and casein periods. The average of the two lipid determinations for each dietary phase was used in the analysis.

The sensitivity or power of this study to detect a 10% difference in LDL or HDL levels between the soy and casein diets was calculated from the following equation (27):

$$\text{power } (1 - \beta) \times 100\% = \Phi\left[\frac{\Delta\sqrt{n}}{s} - Z_{1-\alpha/2}\right]$$

Where Φ is the normal distribution function, Δ is 7.5 mg/dl for LDL and 4 mg/dl for HDL representing 10% changes in the subjects' mean lipoprotein levels, s is the mean intra-individual standard deviation for differences in LDL of 8.9 mg/dl and in HDL of 4.6 mg/dl, and $Z_{1-\alpha/2}$ is the number of standard deviations in a normal distribution corresponding to a two-sided *P* value (α) of 0.05. Thus the power in this protocol to detect the 10% changes in plasma lipids was 86% for LDL and 88% for HDL.

This study was approved by the human experimentation committees at Brigham and Women's Hospital, and Children's Hospital Medical Center.

RESULTS

During the study, nutrient intake, aside from protein, varied only slightly and conditions were nearly isocaloric (**Table 1**). Dietary histories during the baseline period indicated a mean daily consumption of 1686 kcal. The principal foods in the diet of the subjects were unchanged by the protocol. The subjects consumed a macrobiotic vegetarian diet during the entire study. This diet allows a much narrower range of foods, and a more rigidly specified proportion of major nutrients than the customary omnivorous American diet (21). During the periods of protein supplementation, the subjects reduced their intake of self-selected foods by a mean of 334 kcal per day to compensate for the test foods, which added 457 kcal/day. The mean difference in calories between baseline and protein phases was 122 ± 199 (SE) and was not significant ($P > 0.50$). The subjects reported that the protein-enriched muffins and oatmeal replaced other breakfast cereals and snack foods that were composed primarily of complex carbohydrate with no animal products, in accordance with the adherence to a strict vegetarian diet. The test proteins increased the daily protein intake by 42%, and comprised 33% of the total protein in the experimental periods. Mean body weight did not change significantly during the study (**Table 2**).

There were no significant differences in total, LDL, and HDL cholesterol levels at the end of the baseline, soy, and casein periods (Table 2). Baseline levels of these lipids were similar to the low levels found in an earlier population survey of macrobiotic vegetarians (5). There was a tendency toward decreased VLDL cholesterol (VLDL-C) and increased total triglyceride levels when either protein was added to the vegetarian diet. This trend was more pronounced during casein supplementation (Table 2). Data from the two groups of subjects who received the casein and soy protein in opposite sequence were analyzed separately, and the results from each group reflected the overall results. The changes in lipid levels in men and women analyzed separately were similar to those reported for the entire group. No individual subject showed an increase in LDL during the casein period of more than 13% over the LDL levels of the soy period.

TABLE 1. Daily nutrient intake in 11 strict vegetarians before and during protein supplementation[a]

		Supplementation Period	
	Baseline Period[b]	Self-selected[b] Intake	Total Intake[c]
Protein (g)	59 ± 4.5[d]	47 ± 6.0	82 ± 6.0
Fat (g)	30 ± 4.2	27 ± 5.1	30 ± 5.1
Saturated (g)	5 ± 0.8	5 ± 1.1	5 ± 1.1
Polyunsaturated (g)	11 ± 1.4	10 ± 2.0	11 ± 2.0
Carbohydrate (g)	295 ± 27.0	230 ± 30.0	304 ± 30.0
Cholesterol (mg)	12 ± 4.1	30 ± 4.1	30 ± 4.1
Kcal	1686 ± 148.0	1349 ± 173.0	1809 ± 173.0

[a] Intake of calories and nutrients, aside from protein, during baseline and protein supplementation (total intake) was not significantly different by paired *t*-test ($P > 0.1$).
[b] Data derived from food frequency questionnaires.
[c] Total intake = self-selected intake + test foods containing casein and soy protein.
[d] Mean ± SEM.

To look for a cumulative effect of the added protein over the 40 days of observation, the data were grouped and analyzed according to the actual time sequence of the study rather than by the specific protein consumed. There were no sequential trends in LDL and HDL levels. VLDL-C and TG levels in the baseline, first, and second protein supplementation periods, respectively, were the following (mg/dl): VLDL-C: 15.1, 13.4, 11.2 ($P = 0.025$ for baseline − period 2 difference); TG: 53, 65, 67 ($P = 0.06$ for baseline − period 1, $P = 0.03$ for baseline − period 2). The VLDL-C/TG ratio decreased during the study from 0.30 to 0.17 ($P = 0.003$). The results are thus consistent with a progressive effect over 40 days of dietary protein supplementation on VLDL and TG levels regardless of the source of the protein.

DISCUSSION

We added 27 g of casein or of soy protein sequentially to the diet of 13 strict vegetarians for 20-day periods. This amount of protein supplement increased the usual protein intake of the vegetarians by 42%, and comprised 33% of the total protein intake during the intervention. The 27 g of casein is nearly twice the average daily consumption of adults in the USA (20), and is the amount contained in approximately 1.1 liters of skim milk (19). The feeding of these proteins produced no significant changes in LDL or HDL cholesterol from baseline levels, and the soy and casein did not differ in their effects on any of the lipids or lipoproteins studied.

There is no way of knowing whether the vegetarian diet of the subjects somehow protected them from the possible effects of the protein supplements. However, the cholesterol levels of macrobiotic vegetarians and other vegetarians were responsive to changing the saturated fat and cholesterol content of the diet (28, 29), suggesting that constitutional dietary insensitivity is not an explanation for the current findings.

In view of these results, and those of others, what can be stated about the effect of dietary protein on blood lipid levels?

TABLE 2. Plasma lipid levels and body weight in 13 strict vegetarians before and after casein and soy protein supplementation

	Baseline	Casein	Soy
Cholesterol (mg/dl)			
Total	129 ± 5.5*	125 ± 5.5	126 ± 5.4
LDL	75 ± 3.3	74 ± 4.0	74 ± 4.0
HDL	38 ± 2.2	39 ± 1.8	40 ± 2.9
VLDL	15 ± 1.8[a]	12 ± 1.1[a1]	13 ± 1.5
Triglycerides (mg/dl)	53 ± 5.6[b]	68 ± 5.5[b1]	63 ± 6.6[b2]
VLDL-C/TG	0.30 ± 0.04[c]	0.18 ± 0.02[c1]	0.22 ± 0.03[c2]
Body weight (kg)	62.5 ± 2.4	62.5 ± 2.4	62.9 ± 2.5

Differences between dietary periods were analyzed by paired *t*-test, and unless noted, were not significant ($P > 0.1$). * Mean ± SEM.
[a,b,c] Comparisons of a and a^1, $P = 0.06$; b and b^1, $P = 0.02$; b and b^2, $P = 0.09$; c and c^1, $P = 0.005$; c and c^2, $P = 0.07$.

Animal vs. human studies

First, the nutritional conditions of neither the present study nor of most other studies of dietary protein in humans are analogous to experiments in animals that demonstrated such profoundly hypercholesterolemic effects of animal protein (1, 2). The animal studies usually used formula diets in young animals in which the test protein supplied the majority of the protein or was the only protein in the diet. Generally, in human studies, investigators derived the experimental diets from foods rather than formula, and altered the amount of test protein within a mixture of several proteins consistent with the dietary habits of free-living persons. One study directly compared the serum lipid responses of juvenile rabbits and adult humans to soy and casein diets composed of natural ingredients. The soy and casein diets produced no divergent effects on the cholesterol levels of the humans, whereas aliquots of the casein diet greatly increased the serum cholesterol levels of the rabbits relative to the effects of the soy diet (11). In a study of hospitalized human infants treated with formula diets for malnutrition, serum total cholesterol was 36% lower when the sole source of protein was wheat gluten rather than casein in the otherwise isocaloric, isonitrogenous formula diets (30). Thus it is possible that under extreme nutritional conditions in young patients, as in the protocols in animals, the source of dietary protein may have an influence on levels of human plasma lipoproteins.

Level of dietary protein and serum cholesterol (Table 3)

Low protein diets. When the total protein in the diet falls below minimum requirements, serum cholesterol levels decline. In nine adults housed on a metabolic ward, a reduction of protein from 100 g of animal protein to 25 g of vegetable protein per day with calories

TABLE 3. Review of the literature concerning dietary protein and serum cholesterol.

Test protein	Time on Diet	Subjects	Results	Comment	Ref.
I. Studies testing the quantity of protein in the diet					
A. Protein-deficient diets					
1. 100 g Animal vs. 25 g vegetable	1–2 wk	9 Adults	TC ↓ 14% on 25 g protein	Fiber, P/S ratio not reported	31
2. 21 g Milk, 21 g chick pea supplement	1 year	46 Malnourished children; 32 Controls	TC ↑ 18% on either supplement vs unsupplemented controls		32
3. 50–75 g Animal supplement	3 wks	12 Malnourished adults	TC ↑ 88%		33
B. Diets with adequate protein levels					
1. 33 g Mixed vs. 100 g egg white	4 wk	7 Men	TC unchanged		15
2. 60 g, 105 g, 160 g Mixed	6 wk	10 Men	TC unchanged		34
3a. 85 g Mixed ± 47 g milk protein	4 wk	17 Men	Response of TC and β + pre βLP to fat same on high or low protein diets		13
3b. 65 g, 130 g Mixed	4 wk	25 Men	TC unchanged		13
4. 93 g Mixed ± 31 g ± 62 g milk protein	17 days	24 Men	TC unchanged		16
5. 55 g Mixed ± 36 g animal	4 wk	6 Women	TC ↓ 28% on 55 g protein		35
II. Animal vs. vegetable protein					
A. Normal humans					
1. 45–50 g Animal vs. vegetable	6 wk	6 Women	TC ↓ 17% animal protein TC ↓ 25% vegetable protein	Fiber content not controlled	9
2a. 50 g Animal + 21 g vegetable 67 g soy 50 g Animal + 21 g vegetable	24 days 36 days 13 days	6 Women	TC ↓ 19% TC unchanged TC ↑ 15%	See Fig. 1	10
2b. 42 g Animal + 28 g vegetable vs. 75 g textured soy	40 days	10 Women	TC ↓ 6% on soy		10
3. 45 g Total: 30 g milk vs. 30 g wheat	25 days	7 Men	TC unchanged		14
4. 120 g Total: 60 g egg white vs. 60 g wheat	28 days	11 Men	TC unchanged		17

TABLE 3. *(Continued)*

Test protein	Time on Diet	Subjects	Results	Comment	Ref.
5a. 81 g Total: 55 g casein vs. 55 g soy, 26 g mixed vegetable	28 days	25 Adults	TC, HDL, VLDL unchanged; Δ LDL-C ↓ 7%, apoB ↑ 6% on soy vs. casein	Loss of weight accounted for half of LDL-C decrease	11
5b. 85 g Total: 51 g casein vs. 55 g soy isolate vs. 55 g soy concentrate, remainder mainly vegetable	28 days	17–20 Adults	Soy isolate: HDL ↑ 4%, LDL no difference vs. casein; soy concentrate: no difference vs. casein	Loss of weight occurred	36
B. Hyperlipidemic patients					
1. 90 g Total: 60 g textured soy + 25 g other veg + 5 g animal (approx.)	3 wk	12 Type II inpatients	TC ↓ 14%, LDL ↓ 18%	Lipid intake constant (protocol A2) low fat, high P/S	7
2. 90 g Total: approx 80% soy, followed by 90 g total: 72 g animal/18 g vegetable	8 wk 6 wk	127 Type II	TC ↓ 24%, LDL ↓ 30% on soy TC ↑ 8%, LDL ↑ 17% on animal	Incomplete reversal of effects of soy by low lipid animal protein diet	8
3. 122 g Total: 91 g soy vs. 91 g animal, 31 g vegetable	6 wk	12 Type II	Soy: LDL + apoB ↓ 18%; animal: LDL + apoB↓ 12%		12
4a. 69 g Total: ²/₃ animal/¹/₃ vegetable vs. ¹/₃ animal/²/₃ vegetable	4 wk	7 Type II 5 Type IV	Hypolipidemic response same on animal and vegetable diet	All diets low in cholesterol with high P/S ratio	18
4b. 86 g Total: 62 g meat vs. 62 g soy, 24 g vegetable	3 wk	5 Type II 5 Type IV	Same as 4a		18
5. 89 g Total: 58 g animal vs. 55 g soy, remainder mixed vegetable	6 wk	13–14 Young men Mean TC = 240	Same as 4a		39

[a] Unless otherwise noted, the test proteins were introduced isocalorically into the diet and replaced other proteins in the diet (isonitrogenous conditions). In the studies on the amount of dietary protein, the test proteins replaced an equivalent amount of carbohydrate. TC, total cholesterol.

and fat remaining constant produced a 14% reduction in total cholesterol (31). Protein supplements given to malnourished patients raise the serum cholesterol. In malnourished children, 21 g of milk protein or chick pea protein were equally effective over 1 year of observation in raising the serum cholesterol 17–18% above levels of children who did not receive the protein. Serum albumin nearly doubled after the supplementation (32). In malnourished adults consuming 15–30 g of protein daily, the isocaloric replacement of polysaccharide with 50–75 g of animal protein per day caused serum cholesterol levels to increase 88% over 3 weeks. Seventy percent of the increase occurred after the first week of supplementation and no further increase was observed after the third week, whereas the body weight slowly increased throughout (33). It is possible that the hypocholesterolemia of protein-deficient diets is a reflection of the overall depression of anabolic capacity. Whether dietary protein affects the serum lipid levels of persons consuming nutritionally adequate diets is a separate problem.

Diets supplying adequate protein. There are five reports concerning the effects on serum cholesterol of adults when the amount of dietary protein was altered within adequate nutritional levels without changes in total daily calories, fat, and cholesterol. No differences in serum cholesterol were observed when *1)* 100 g of egg white protein was added for 4 weeks to a diet replacing 33 g of protein from animal and vegetable sources (15); *2)* basal protein levels of 105 g per day were increased to 160 g or decreased to 60 g for 6 weeks (34); *3)* 47 g of milk protein was added to an 85-g mixed animal and vegetable protein diet (13); *4*) protein was increased from 65 g to 130 g per day for 4 weeks (13); and *5*) protein was sequentially increased from 92.5 to 124 g and 155 g per day using milk supplements for 17 days (16). On the other hand, serum cholesterol levels in college women were 28% lower on a 55-g protein diet compared with a 91-g protein diet, with fat, fiber, and calories held constant (35).

Animal vs. vegetable protein and serum cholesterol (Table 3)

Normal subjects. Changes in serum cholesterol resulting from exchange of animal and vegetable proteins in the diet of normal subjects have been either small or absent. Twelve college women were divided into two equal groups, one receiving a diet containing animal protein, and the other vegetable protein for 6 weeks. Serum cholesterol decreased 17% and 25% on the animal and vegetable protein diets, respectively (9). The increased dietary fiber in the vegetable diet may have contributed to this difference.

In a subsequent study in college women, replacement of all animal protein in a mixed animal and vegetable protein diet with analogues made of soy protein yielded inconsistent results (10). Six women were fed a mixed animal and vegetable protein diet for 24 days during which time serum cholesterol levels steadily declined. No further decrement in serum cholesterol occurred after the soy analogues were introduced for 36 days; but when the animal protein was re-introduced, serum cholesterol increased 15%. In a second experiment using a two-group crossover design, serum cholesterol levels were 5% higher during the mixed protein period than during the soy protein period (10).

Studies in which wheat protein replaced animal protein showed no change in serum cholesterol. No effects on serum cholesterol were found when 30 g of milk protein and wheat protein were interchanged in a 45-g protein diet in seven men age 53–70 (14), or when 60 g of 120 g of protein per day was supplied by either egg white or wheat protein in young men (17).

Van Raaij and coworkers (11, 36) reported two experiments in normal subjects comparing the effects of casein and soy protein on plasma lipoproteins, using diets in which the test proteins supplied most of the total protein. Although the interpretation of the results of both studies is complicated by significant loss of weight during the experimental periods, there were no consistent differential effects of soy vs casein on LDL or HDL cholesterol.

Hyperlipidemic patients. A subgroup of severely hypercholesterolemic patients, who were not improved by a low lipid diet or by a trial of hypolipidemic drugs, responded to a diet in which textured soy protein replaced nearly all the animal protein in the diet (7, 8). The soy diet necessitated the removal of foods such as meat, poultry, and eggs which contain saturated fat and cholesterol, and as a general policy, polyunsaturated fats were used to replace dairy and other saturated fats in the soy diet. When the soy and animal protein diets were compared on a metabolic ward, with fat content held constant, total cholesterol and LDL-C decreased by 14% and 18%, respectively (7:protocol A2). Also, over half of the reduction in serum cholesterol levels that occurred in outpatients who were transferred from a low lipid diet to the soy diet was preserved when the patients returned to their baseline low-lipid animal protein diets (8). Thus some of the 20–30% decrements in total and LDL cholesterol in patients who changed from a self-selected low-lipid diet to a rigorously specified low-fat soy diet were probably due to the alterations in dietary fat content and/or increased compliance to the fat modification. There is reason to think that even the residual hypolipidemic effect of the soy diet was not caused by the soy protein itself. First, according to these researchers, only textured soy protein (50% protein) and not soy isolate (90% protein) or other forms of soy protein were effective (37, 38). The textured soy protein must supply over 20% of the daily calories and, at these high levels, many subjects experienced gastrointestinal discomfort that was prevented by pretreatment of the soy with pepsin (7). Most subjects lost weight while on the soy diet despite adequate caloric intake. Perhaps the textured soy product when consumed in large quantities is not fully digested and acts as dietary fibers in lowering serum lipids.

Carefully controlled studies from three other groups of investigators fail to clarify whether soy protein exerts hypocholesterolemic effects. One study reported that a low lipid diet with soy as the major protein caused 18% reductions in LDL-C and apolipoprotein B, whereas the same diet but with animal protein replacing the soy caused 12% decreases (12). But in two additional dietary trials, a low lipid diet caused the same degree of hypocholesterolemia whether the protein in the diet was from animal products or soy (18, 39).

In conclusion, total protein, when consumed in a range above minimum requirements, has not been found to affect plasma lipid levels. Secondly, the dramatic hypercholesterolemic response to animal protein observed in animals has not been found in adult humans under similar dietary conditions. Controlled studies have reported either no effect or a very modest hypolipidemic effect of replacing most of the animal protein in the diet with vegetable protein. Specifically, casein, in amounts common to American diets, has not been shown to modify the plasma lipid levels of adults. Thus, from the point of view of practical clinical nutrition, nonfat dairy products may be utilized in plasma lipid-lowering diets. The main advantage of diets constructed around vegetable protein sources would appear to be concomitant reductions in saturated fat and cholesterol, and an increase in dietary fiber.

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