PROCEEDINGS OF THE SOCIETY FOR EXPERIMENTAL BIOLOGY AND MEDICINE 167, 346–353 (1981)

The Long-Term Effects of Dietary Sucrose Polyester on African Green Monkeys[1] (41177)

MICHAEL R. ADAMS,* MARY RUTH McMAHAN,† FRED H. MATTSON,‡·[2] AND THOMAS B. CLARKSON*

*Departments of *Comparative Medicine and †Pathology, Bowman Gray School of Medicine, Wake Forest University, Winston-Salem, North Carolina 27103, and ‡Procter & Gamble Company, Miami Valley Laboratories, Cincinnati, Ohio 45239*

Abstract. Sucrose polyester (SPE) is a nonabsorbable fat which has been shown to lower plasma cholesterol concentrations when incorporated into the diet of human volunteers. This study was designed to assess the long-term (15 months) effect of oral administration of SPE on plasma cholesterol concentrations, body weights, and health of African green monkeys, a species similar to man in its lipid metabolism. All animals were fed for 2 months a high-cholesterol-containing diet to induce hypercholesterolemia. To simulate therapeutic intervention, dietary cholesterol was then decreased substantially and the effects of high or low (40 or 25%) fat content and presence or absence of SPE in the diet (as about 10% of diet) were assessed. There were four groups of animals: Group I (low fat–no SPE), Group II (high fat–no SPE), Group III (low fat–SPE), and Group IV (high fat–SPE). SPE administration resulted in 36% (high fat–SPE) and 40% (low fat–SPE) reductions in mean plasma cholesterol concentrations compared to 23% (high fat–no SPE) and 19% (low fat–no SPE) mean reductions in groups not fed SPE. The effect of SPE was statistically significant ($P < 0.003$). The effect of SPE was maximal in those animals with a high or intermediate plasma cholesterol response to dietary cholesterol and minimal or nonexistent in animals with a low plasma cholesterol response to dietary cholesterol. No significant differences between groups could be detected in body weight gain or in animal health as determined by the frequency of clinical illness and serial clinicopathologic observations.

The term sucrose polyester (SPE) is used to designate a mixture of the hexa-, hepta-, and octaesters of sucrose prepared by the esterification of sucrose with long-chain fatty acid esters (1). These esters are neither digested by pancreatic lipolytic enzymes (2), nor absorbed by the intestinal tract (1, 3, 4).

Since SPE possesses physical properties similar to those of triglycerides, the consumption of SPE results in the presence of an oil phase in the intestinal tract comparable to that present after ingestion of triglycerides. Within the intestine, dietary cholesterol distributes itself between the oil phase and the micellar phase (5). Since the oil phase of SPE is not digested, cholesterol dissolved within this phase is excreted with feces because it is not transferred to the micellar phase and absorbed (1).

The short-term effects of SPE on human volunteers have been assessed (6–8). Addition or substitution of SPE for dietary fat in a typical American diet fed to 13 normocholesterolemic human volunteers for 10 days resulted in a mean decrease of plasma cholesterol concentration of 14%. Several familial hypercholesterolemic patients did not experience reductions in plasma cholesterol concentrations under the same dietary manipulation. Urinalyses and other selected clinicopathologic determinations remained normal for the duration of the study (6).

SPE supplementation in the diet of normolipidemic, overweight subjects maintained on a weight reducing, low-cholesterol diet for 6 weeks resulted in a 6.8% decrease in plasma cholesterol concentration, decreased mean cholesterol absorp-

[1] This study was supported by grants from the NHLBI (SCOR-HL 14164) and from Procter & Gamble Company, Cincinnati, Ohio.

[2] Present address: Lipid Research Clinic, University of California—San Diego, La Jolla, Calif. 92093.

0037-9727/81/070346-08$01.00/0

tion, increased mean neutral sterol excretion, and increased bile acid excretion (7).

The addition of liquid SPE to diets containing less than 50, 300, and 800 mg of cholesterol fed to healthy, nonobese, normolipidemic male subjects for 10-day periods resulted in significant mean decreases in plasma total and low-density lipoprotein cholesterol. Urinalyses and other selected clinicopathologic determinations remained normal (8).

In this report we will describe the effects of consumption of SPE for 15 months on plasma cholesterol concentrations of African green monkeys. Additionally, we report some observations on the health of monkeys consuming SPE.

Materials and Methods. *Sucrose polyester.* The sucrose polyester (SPE) used in this study was prepared using the methods described in great detail previously (2–4, 9).

Animals. Thirty young adult male Kenyan vervets (*Cercopithecus aethiops pygerythrus*) were obtained from Primate Imports, Inc., Port Washington, New York. At the initiation of the study the monkeys ranged in age from 3 to 6 years, as estimated by dentition. Body weights ranged from 1.99 to 4.49 kg. For the duration of the study, they were housed individually in stainless-steel cages equipped with automatic water dispensers. The cages were in windowless rooms with fluorescent lighting on a 10-hr-light:14-hr-dark cycle.

African green monkeys were chosen for this study because they have been shown to be similar to man in the distribution of their plasma lipoproteins and total plasma cholesterol concentration when fed a diet similar to that of the average American (10). Also, percentage absorption of dietary cholesterol in this species has been shown to be similar to that of man (30–45%) (11). Diet-induced coronary artery atherosclerosis in this species closely resembles atherosclerosis of human beings (12).

General design of the experiment. The experimental design is summarized in Table I. After an appropriate quarantine and conditioning period, all animals were fed for 2 months (Control I Period) the Control Diet (Table II) which contained 0.7 mg/cal

TABLE I. EXPERIMENTAL DESIGN

	Control I Period	Experimental Period				Control II Period
Length of time	2 months Control Diet	15 months Four variations of Control Diet Cholesterol content reduced				3 months Control Diet
Diets, groups	All four groups	I (low fat–no SPE)	II (high fat–no SPE)	III (low fat–SPE)	IV (high fat–SPE)	All four Groups
Fat content (%)	40	25	40	25	40	40
Cholesterol content (mg/cal)	0.7	0.3	0.3	0.3	0.3	0.3
SPE content (%)	0	0	0	10.8	9.8	0

TABLE II. COMPOSITION OF THE CONTROL DIET

Ingredient	grams per 100 g	Protein (g)	Fat (g)	Carbohydrate (g)	Calories per 100 g	Cholesterol (mg)
Nonfat dry milk solids	15.0	5.3	0.2	7.8	54	0
Lactalbumin	7.0	7.0	0	0	28	0
Casein, USP	7.0	7.0	0	0	28	0
Wheat flour	25.0	2.6	0.3	19.0	89	0
Sucrose	14.0	0	0	14.6	56	0
Applesauce	4.2	0.1	0.1	0.9	5	0
Hegsted salt mixture	4.0	0	0	0	0	0
Complete vitamin mixture[a]	2.5	0	0	2.5	10	0
Crisco	12.3	0	12.3	0	111	0
Lard	4.7	0	4.7	0	36	4
Butter	4.0	0	4.0	0	42	12
Crystalline cholesterol[b]	0.3	0	0	0	0	300
Total	100.0	22.0	21.6	44.8	459	316

[a] Equivalent to ICN Nutritional Biochemicals Vitamin Diet Fortification Mixture.
[b] Equivalent to 0.7 mg. cholesterol/Cal.

cholesterol. The combination of partially hydrogenated vegetable oil,[3] lard, and butter was used to simulate the dietary fat intake of the average North American. On the basis of mean plasma cholesterol concentrations for Control I Period, four groups were established so that there would be similar mean plasma cholesterol concentrations for each of the groups (Table III).

To mimic the usual clinical situation in which a patient would be counseled to reduce dietary cholesterol along with other appropriate therapies, we reduced the cholesterol concentration of the diet from 0.7 to 0.3 mg/cal of cholesterol following the Control I Period. Group I was fed the Control Diet with half of the calories from fat replaced with fiber (low fat–no SPE). Group II continued to consume the Control Diet (high fat–no SPE). Group III was fed the Control Diet with half the fat replaced by SPE (low fat–SPE). Group IV was fed the Control Diet, to which had been added the same amount of SPE as that for Group

TABLE III. TOTAL PLASMA CHOLESTEROL (TPC) CONCENTRATIONS FOR EACH GROUP DURING THE CONTROL I AND EXPERIMENTAL PERIODS AND VALUES FOR ABSOLUTE AND PERCENTAGE CHANGE BETWEEN THE TWO PERIODS

		TPC		Absolute change (mg/dl)	Percentage change
	N	Control I Period (mg/dl)	Experimental Period (mg/dl)		
Group I (low fat–no SPE)	8	310 ± 47.9[a]	246 ± 29.1	−65 ± 21.5	−19 ± 3.7
Group II (high fat–no SPE)	8	274 ± 29.5	207 ± 20.4	−67 ± 13.1	−23 ± 3.4
Group III (low fat–SPE)	7	328 ± 37.7	183 ± 7.1	−145 ± 30.9	−40 ± 6.2
Group IV (high fat–SPE)	7	323 ± 24.0	207 ± 15.3	−117 ± 14.1	−36 ± 3.0
$P \leq$		N.S.	N.S.	0.03	0.003

[a] Mean ± SEM.

[3] Crisco, Procter & Gamble Company.

III (high fat–SPE). These dietary regimens continued for a 15-month period designated as the Experimental Period. The animals were fed once per day a quantity of diet calculated to provide 150 cal/kg body wt. In this way, each animal was fed the same number of calories, despite each diet having a different caloric density, and cholesterol and SPE were dosed on a body weight basis. Group III animals received 3.2 g of SPE and 105 mg of cholesterol per kilogram body weight. Group IV animals received 3.5 g of SPE and 105 mg of cholesterol per kilogram body weight. After the Experimental Period, the four dietary regimens continued for 14 months. All animals were then fed for 3 months (Control II Period) the Control Diet (Table II) with the cholesterol concentration remaining 0.3 mg/cal.

Clinical protocol. Determinations were made of total plasma cholesterol concentration and body weight at Weeks 4, 6, and 8 of Control I Period, at 2-week intervals for the first 6 months of the Experimental Period and at monthly intervals for the remaining 9 months, and at 2-week intervals during the 3 months of the Control II Period. The determinations of total plasma cholesterol concentration were made by the Auto-Analyzer II method of Rush *et al.* (13). The Lipid Analytic Laboratory at this institution is in full quality control with the Lipid Standardization Program of the Center for Disease Control, Atlanta, Georgia.

Each animal was examined daily by a member of the veterinary staff. Records were kept of the occurrence of any illness or treatment that was required.

Selected clinicopathologic observations were made on each animal at 28 and 42 days after initiation of feeding the Control Diet and at 60, 120, 240, and 300 days after initiation of the Experimental Period. The observations made were: hematocrit, hemoglobin, blood urea nitrogen, serum creatinine, fasting blood glucose, total serum protein, total serum albumin:globulin ratio, total and differential leukocyte counts, total erythrocyte count.

Statistical analyses. Data analyses providing means, standard error of the mean, analysis of variance, regression, and correlation analyses were calculated using the standard statistical methods available through the Biomedical Computer Programs, BMDP package (14). P values less than or equal to 0.05 were considered significant.

Results. During the Control I Period, there were no differences in body weights among the four groups. All animals gained weight during the Experimental Period, and no differences existed among the groups in body weight or absolute or percentage increase in body weight (Table IV). No differences in food consumption were noted among groups.

The values in Table III for Control I Period are mean values of the three observations made during Weeks 4, 6, and 8 of the Control I Period. Plasma cholesterol concentrations during the Control I Period were not statistically significantly different among the four groups (Table III). The introduction of the dietary treatments caused plasma concentrations of cholesterol to decrease rapidly from Control I values in all four groups (Fig. 1). Since the decline in plasma cholesterol concentration was relatively slow after the first 30 days of the Experimental Period, all values after that point were averaged across time for each group in order to obtain an Experimental mean plasma cholesterol concentration. The result of this was to derive a mean value for long-term absolute change and percentage change from the Control I values.

As can be seen from the data in Table III, there were no statistically significant differences among the groups for the Experimental mean plasma cholesterol concentration. In contrast, when we examined the absolute plasma cholesterol concentration change, a significant effect ($P \leq 0.03$) of SPE was found. Similarly, when the decreases in plasma cholesterol concentration were expressed as percentage change, there was also a significant effect ($P \leq 0.003$) of SPE. No significant differences were found attributable to the level of fat consumed (25 vs 40% fat), i.e., no differences existed between the two SPE-fed groups nor between the two groups not fed SPE.

As shown in Fig. 2, relatively strong negative correlations exist for absolute change in plasma cholesterol concentra-

TABLE IV. BODY WEIGHTS FOR EACH GROUP DURING THE CONTROL I AND EXPERIMENTAL PERIODS AND VALUES FOR ABSOLUTE AND PERCENTAGE CHANGE BETWEEN THE TWO PERIODS

	N	Control I Period (kg body wt)	Experimental Period (kg body wt)	Absolute change per animal (kg)	Percentage change
Group I (low fat–no SPE)	8	2.823 ± 0.205[a]	3.423 ± 0.186	0.600 ± 0.171	17.2 ± 4.9
Group II (high fat–no SPE)	8	3.226 ± 0.184	3.525 ± 0.100	0.299 ± 0.141	8.6 ± 4.0
Group III (low fat–SPE)	7	2.991 ± 0.244	3.320 ± 0.204	0.329 ± 0.202	9.5 ± 6.0
Group IV (high fat–SPE)	7	3.149 ± 0.308	3.556 ± 0.223	0.407 ± 0.168	12.1 ± 5.4
$P \leq$		N.S.	N.S.	N.S.	N.S.

[a] Mean ± SEM.

tions vs Control I plasma cholesterol concentrations for both the SPE-fed ($r = -0.92$) and control ($r = -0.88$) animals. Thus, animals with initially high plasma cholesterol concentrations during the Control I Period had greater decreases during the Experimental Period than did those animals with low Control I values. The additional effect of SPE over that of lowering dietary cholesterol intake alone, is shown by the significant difference ($P \leq 0.01$) between the slopes of the lines for the animals fed SPE and those not fed SPE.

Similarly, as shown in Fig. 3, a statistically significant ($P \leq .001$) negative correlation between the percentage change vs Control I plasma cholesterol concentrations for the animals fed SPE ($r = 0.77$). A weak negative correlation was determined for the animals fed the diet devoid of SPE ($r = 0.44$), but the relationship was not statistically significant. Again, the greater percentage changes in plasma cholesterol concentration occurred in those animals with the higher Control I values, with SPE consumption having an enhancing effect. This observation is supported by the finding of a

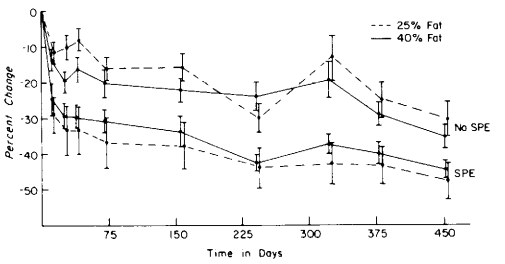

FIG. 1. Percentage change from baseline for total plasma cholesterol concentrations of each group during the experimental period.

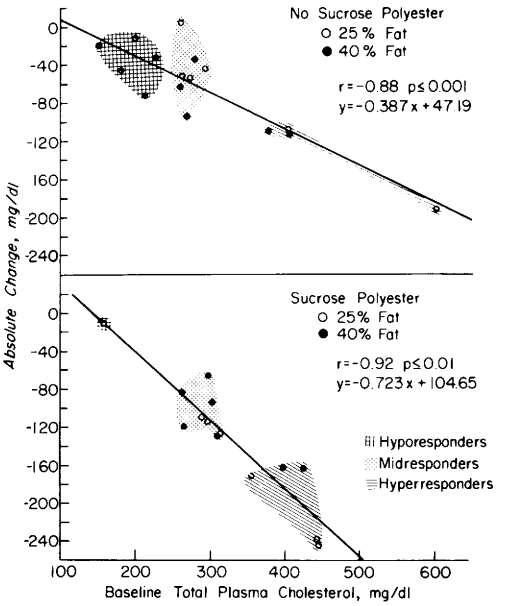

FIG. 2. Absolute change as a result of dietary treatment from baseline in total plasma cholesterol concentrations vs baseline total plasma cholesterol concentrations. Each point is the value for an individual monkey. Shaded areas represent the somewhat arbitrary classification of animals as hypo-, mid-, or hyperresponders to dietary cholesterol. Groups I (low fat–no SPE) and II (high fat–no SPE) are combined (top) and Groups III (low fat–SPE) and IV (high fat–SPE) are combined (bottom).

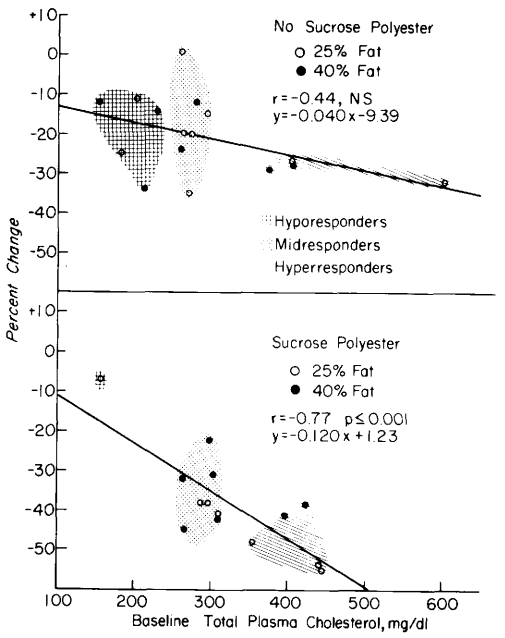

FIG. 3. Percentage change from baseline in total plasma cholesterol concentrations vs baseline total plasma cholesterol concentrations. Shaded areas represent the somewhat arbitrary classification of animals as hypo-, mid-, or hyperresponders to dietary cholesterol. Groups I (low fat–no SPE) and II (high fat–no SPE) are combined (top) and Groups III (low fat–SPE) and IV (high fat–SPE) are combined (bottom).

significant difference between the slopes of the lines ($P \leq 0.01$) for the groups fed the SPE diet and the groups not fed SPE.

African green monkeys, like other nonhuman primates, are quite variable in their response to dietary cholesterol. It was of interest to us to determine whether the declines in plasma cholesterol concentration with and without added SPE were related to the animal's response to dietary cholesterol. In Figs. 2 and 3, we have arbitrarily divided the animals into groups based upon their response to the Control I Diet. The animals with the highest plasma cholesterol concentrations were designated as hyperresponders, those with median concentrations as midresponders, and those with the lowest concentrations as hyporesponders. It was of particular interest to note that the three response groups formed very discrete clusters. In the groups in which the only treatment was lowering cholesterol intake, the hyperresponsive animals had slightly larger absolute and percentage decreases in plasma cholesterol concentration when compared with the hyporesponsive animals. However, in the two groups fed the SPE diet, the absolute and percentage decreases in the hyperresponders were strikingly larger than those in the midresponders and hyporesponders.

During Control II Period the animals were fed the Control Diet with 0.3 mg/cal cholesterol. Total plasma cholesterol concentrations during the Control II Period were not different among the four groups (Table V). The total decreases in plasma cholesterol concentration (Control I – Control II) were larger in the groups fed SPE, but they were not significantly differ-

TABLE V. TOTAL PLASMA CHOLESTEROL (TPC) CONCENTRATIONS FOR EACH GROUP DURING THE CONTROL I PERIOD AND CONTROL II PERIOD AND VALUES FOR ABSOLUTE AND PERCENTAGE CHANGE BETWEEN THE TWO PERIODS

		TPC		Absolute change (mg/dl)	Percentage change
	N	Control I Period (mg/dl)	Control II Period (mg/dl)		
Group I (low fat–no SPE)	8	310 ± 47.9[a]	204 ± 20.0	113 ± 38.2	31 ± 5.4
Group II (high fat–no SPE)	8	274 ± 29.5	170 ± 14.1	104 ± 17.4	36 ± 3.0
Group III (low fat–SPE)	7	328 ± 37.7	177 ± 8.5	151 ± 30.9	43 ± 5.0
Group IV (high fat–SPE)	7	323 ± 24.0	190 ± 10.2	134 ± 18.2	41 ± 2.9
$P \leq$		N.S.	N.S.	N.S.	N.S.

[a] Mean ± SEM.

TABLE VI. TOTAL PLASMA CHOLESTEROL (TPC) CONCENTRATIONS FOR EACH GROUP DURING THE EXPERIMENTAL AND CONTROL II PERIODS AND VALUES FOR ABSOLUTE AND PERCENTAGE CHANGE BETWEEN THE TWO PERIODS

	N	TPC		Absolute change (mg/dl)	Percentage change
		Experimental Period (mg/dl)	Control II Period (mg/dl)		
Group I (low fat–no SPE)	8	246 ± 29.1[a]	204 ± 20.0	−39 ± 16.3	−13 ± 4.1
Group II (high fat–no SPE)	8	207 ± 20.4	170 ± 14.1	−37 ± 9.0	−16 ± 3.5
Group III (low fat–SPE)	7	183 ± 7.1	177 ± 8.5	−6 ± 3.2	−3 ± 2.0
Group IV (high fat–SPE)	7	207 ± 15.3	190 ± 10.2	−17 ± 9.7	−7 ± 5.0
$P \leq$		N.S.	N.S.	N.S.	N.S.

[a] Mean ± SEM.

ent from the groups not fed SPE. There were also no significant differences among the groups for absolute change or percentage change (Experimental − Control II) (Table VI).

The health of all animals remained excellent for the duration of the study. Clinical incidents were uncommon and were confined to the following: loose stools with mucous and blood, rectal prolapses, and one case of an abcessed canine tooth (Table VII). The frequency of these findings was low and similar to that seen in other groups of African green monkeys within this colony. The differences among groups were small and not statistically significant. There were no differences among groups in stool consistency. The one case of abcessed canine tooth was in a Group III (low fat–SPE) animal. Animal No. 1400 from Group I (low fat–no SPE) died 4 months after the conclusion of the study as a result of bronchopneumonia.

The results of the clinicopathologic determinations were within normal limits and there were no differences between the groups.

Discussion. This study represents the first report of a long-term trial in humans or animals of the effectiveness of sucrose polyester as a hypocholesterolemic agent. The reductions achieved in plasma cholesterol concentration in this study were comparable to those reported in short-term studies of human patients and volunteers (6–8) and in addition persisted for 15 months.

No significant clinical side effects were noted among the animals in this study. Similarly, among human patients and volunteers fed SPE for short periods of time, no significant side effects were reported (6–8). Possible effects of SPE on gastrointestinal morphology or function have not been assessed and remain an area of future investigation.

Necropsy evaluations were not made at the conclusion of this study, as it was decided to proceed with further studies of SPE effects on lipid metabolism. In these

TABLE VII. NUMBER OF CLINICAL INCIDENTS DURING THE 15-MONTH EXPERIMENTAL PERIOD AMONG MONKEYS FED SPE-CONTAINING DIETS AND CONTROL DIETS

	Loose stools with mucous and blood	Rectal prolapse	Abcessed canine tooth
Group I (low fat–no SPE)	3	3	0
Group II (high fat–no SPE)	5	0	0
Group III (low fat–SPE)	2	0	1
Group IV (high fat–SPE)	3	1	0

later studies, all the animals were fed SPE for varying lengths of time, after which they were killed and necropsied. Therefore, conclusions could not be made regarding effects of SPE feeding on necropsy findings.

The finding that there were no differences between groups in body weight is difficult to interpret since we did not quantitate food intake. Subjectively, there were no differences among groups in food intake. All animals gained weight. The animals were fed on a calories per kilogram of body weight basis, and therefore the SPE-fed animals were fed a greater absolute quantity of diet (due to dilution of calories by SPE). It is probable that the SPE-fed animals consumed slightly more diet to compensate for the caloric dilution of the SPE, and therefore mean body weights remained similar among the four groups.

The tendency for a greater SPE effect on plasma cholesterol concentration in those animals with highest baseline concentrations (hyperresponders), as evidenced by the strong negative correlations between baseline and absolute and percentage decrease in plasma cholesterol concentration, is of particular relevance to the potential clinical usefulness of SPE in human beings since those individuals with elevated plasma cholesterol concentrations in response to dietary cholesterol might be the most likely to benefit from the use of SPE.

It was unexpected to find that removal of SPE from the diet (Control II Period) of Groups III and IV did not result in increased plasma cholesterol concentrations for those groups, while the concentrations for Groups I and II actually decreased to account for the four groups being equal in plasma cholesterol concentrations and absolute and percentage decrease from the Control I values. A possible explanation of this finding is that a period of 15 months or more was required for plasma cholesterol concentrations to reach final steady state in Groups I (low fat–no SPE) and II (high fat–no SPE) after decreasing the amount of dietary cholesterol from 0.7 and to 0.3 mg/cal. In Groups III (low fat–SPE) and IV (high fat–SPE), SPE feeding may have resulted in a more rapidly attained and initially lower steady state.

The diets used in this experiment were formulated to simulate the quantity and fatty acid composition of fat and quantity of cholesterol in the diet of the average American person. The reduction in plasma cholesterol concentration achieved by the addition of dietary SPE combined with a reduction in dietary cholesterol has been shown to be greater than that achieved by reduction of dietary cholesterol alone in a species that absorbs and metabolizes dietary cholesterol and fat in a manner similar to that of human beings.

1. Rizzi, G. P., and Taylor, H. M., J. Amer. Oil Chem. Soc. **55**, 398 (1978).
2. Mattson, F. H., and Volpenhein, R. A., J. Lipid Res. **13**, 325 (1972).
3. Mattson, F. H., and Nolen, G. A., J. Nutr. **102**, 1171 (1972).
4. Mattson, F. H., and Volpenhein, R. A., J. Nutr. **102**, 1177 (1972).
5. Surpuriya, V., and Higuchi, W. I., Biochim. Biophys. Acta **290**, 375 (1972).
6. Fallat, R. W., Glueck, C. J., Lutmer, R., and Mattson, F. H., Amer. J. Clin. Nutr. **29**, 1204 (1976).
7. Crouse, J. R., and Grundy, S. M., Metabolism **28**, 994 (1979).
8. Glueck, C. J., Mattson, F. H., and Jandacek, R. J., Amer. J. Clin. Nutr. **32**, 1636 (1979).
9. Mattson, F. H., and Volpenhein, R. A., J. Lipid Res. **3**, 281 (1962).
10. Bullock, B. C., Lehner, N. D. M., Clarkson, T. B., Feldner, M. A., Wagner, W. D., and Lofland, H. B, Exp. Mol. Pathol. **22**, 151 (1975).
11. Rudel, L. L., and Lofland, H. B, *in* "Primates in Medicine" (E. I. Goldsmith and J. S. Moor-Jankowski, eds.), Vol. 9, p. 224. Karger, Basel (1976).
12. Parks, J. S., Lehner, N. D. M., St. Clair, R. W., and Lofland, H. B, J. Lab. Clin. Med. **90**, 1021 (1977).
13. Rush, R. L., Leon, L., and Turrell, J., *in* "Advances in Automated Analysis—Technicon International Congress" (E. C. Barton *et al.*, eds.), p. 503. Thurman Associates, Miami (1971).
14. Dixon, W. J. (ed.), *in* "Biomedical Computer Programs, BMDP." Univ. of California Press, Berkeley (1975).

Received May 23, 1980. P.S.E.B.M. 1981, Vol. 167.