Differential Effect of Dietary Fat and Weight Reduction on Serum Levels of Beta-Lipoproteins

By Weldon J. Walker, M.D., Norman Weiner, M.D., and Lawrence J. Milch, Ph.D.

Twenty-five patients sustained an average weight loss of 21.7 pounds on a diet in which 73 per cent of total calories consisted of animal fat. Their “new” weight was maintained on this high-fat diet and subsequently on a low-fat diet. Standard Sf 0-12 lipoproteins were highly influenced by dietary fat intake independent of weight change. In contrast the Sf 20-400 fraction was lowered by negative caloric balance and weight reduction despite the ingestion of large amounts of animal fat. These changes were statistically highly significant. Divergent responses of different classes of beta-lipoproteins may be missed if only total beta-lipoprotein measurements are made.

IT IS generally agreed that in man there is at least a rough correlation between the incidence of atherosclerosis and high levels of serum cholesterol and various classes of lipoproteins, particularly the beta-lipoproteins.1,2 Insurance studies demonstrate that obesity is associated with human atherosclerosis, since insured overweight individuals have an increased death rate from coronary artery disease. This increased mortality fails to occur if obese individuals reduce their weight.3 Greatest longevity is encountered in individuals approximately 15 per cent underweight.4 Love and Walker5 found that in 1,000 individuals between 30 and 60 years of age there was a significant increase in both serum cholesterol and Sf 12-20 lipoprotein levels with increasing weight. A significant lowering of various classes of lipoproteins with weight reduction has been reported in 39 patients with coronary artery disease who ingested a high-cholesterol, low-fat diet.6 An association between caloric balance and serum lipoproteins was suggested by the observation that forced feeding of a low-fat, low-cholesterol diet resulted in increased lipoprotein concentrations in volunteer subjects.6 However, Keys contended that the quantity of dietary fat is the most important factor associated with elevation of serum cholesterol levels and the development of atherosclerosis in the human. He stated that obesity is a relatively unimportant factor in human atherosclerosis.7

With such divergent views it seemed desirable to study the effect of weight reduction on the serum lipoprotein levels in a group of patients ingesting a high-fat diet. It appeared advantageous to conduct such a study on a group of individuals many of whom had manifested atherosclerosis relatively early in life, since this disease process may in some measure represent an alteration in the homeostatic mechanisms controlling cholesterol metabolism. Such individuals might be more responsive to factors tending to elevate or depress serum lipoprotein levels.

METHODS AND MATERIAL

Twenty-five patients were studied. Eighteen had proved atherosclerosis, 17 having sustained 1 or more myocardial infarctions, while the eighteenth had thrombosis of the left common iliac artery. Twenty-three were males, 2 were females. Their ages varied from 33 to 66 years and the average age was 46 years. All patients were studied in the Cardiovascular Service, Brooke Army Hospital. The majority were studied as outpatients. No one with an acute myocardial infarction was included in the study. All blood samples were taken in the fasting state. Patients had 2 control determinations at intervals of at least 1 week while maintaining their weight constant and ingesting their accustomed diets. Six patients had been on a low-fat diet prior to the study; the remainder were eating what was considered an average American diet.

Following the second control determination patients were started on a regimen of weight reduction consisting of a high-fat, high-meat diet as described by Pennington.8 At each meal the subjects received a 6- to 8-ounce serving of meat (1 part of fat to 3 parts of lean by weight). In addition,
patients were allowed 1 small serving of fruit or vegetable at each meal. They were allowed coffee or tea ad lib., without added sugar or cream. If the patient was still hungry at the end of the meal he was allowed additional meat but no additional fruit or vegetable. On such a diet the daily fat intake was estimated to be at least 200 Gm. and constituted approximately 73 per cent of the total caloric intake; protein approximately 17 per cent of total calories; and carbohydrate about 10 per cent of total calories. Patients received a daily multivitamin capsule. No one complained of ill effects other than developing a distaste for meat. The minimum weight loss was 12 lb.; the maximum 48 lb. There was an average weight loss of 21.7 lb. The average rate of weight loss was 1.6 lb. per week.

After the period of weight reduction, total calories were increased on the same high-fat diet so as to maintain a constant weight. This regimen was continued for a minimum of 1 month and in the majority of cases for 2 months.

Finally the diet was changed to one of less than 50 Gm. of fat per day. This diet contained at least 1 Gm. of protein per Kg. body weight and the calories were adjusted so as to maintain a constant weight. Most subjects were continued at least 2 months on this diet—all for at least 1 month.

Lipoprotein determinations were ordinarily made at 2-week intervals during the entire period of the study. Lipoprotein determinations were done at the School of Aviation Medicine, Randolph Air Force Base, Tex. Standard Sf 0-12, 12-20, and 20-400 classes of β-lipoproteins were determined on each specimen.9 10 Serum cholesterol determinations were done in the clinical laboratory at Brooke Army Hospital, Fort Sam Houston, Tex. A change in the method of determining serum cholesterol occurred during the period of the study, and these results are therefore not reported. The data were analyzed by M. Bryan Danford, Ph.D., Analytical Statistician, School of Aviation Medicine, Randolph Air Force Base, Tex.*

* An analysis of variance was performed on the data, by standard F-ratio tests for assessing statistical significance of various main effects (subjects, diets, types of patients). Further testing was performed by using Student's t. (See Cochran, William G., and Cox, Gertrude, M. Experimental Designs. John Wiley & Sons, Inc., New York, 1950).

During the various diet periods, control, high fat-weight loss, high fat-weight maintenance, and low fat-weight maintenance, from 2 to 8 measurements were made on each individual. In tables 1 and 2, the standard errors of the means represent measures of variability of the means as taken over people as well as over the several observations made on each person. Thus if N persons are measured k times, the standard error of the mean is σ/√kN, when σ² is the mean square for persons or σ²/k is the variance among the means for the N persons.

### Results

In preliminary analysis the 18 patients with manifest atherosclerosis were separated from the 7 who did not have proven atherosclerosis. The average ages of the 2 groups were 47 and 44 years respectively. As indicated in table 1 the initial levels of all classes of lipoproteins appeared significantly higher in the group with manifest atherosclerosis (p < .05). Both groups showed the same general response to the dietary regimens and are combined in subsequent analyses. However, patients with manifest atherosclerosis tended to show a greater response to the changing dietary schedules than those without proven coronary

<table>
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<th>Table 1.—Comparison of Mean Control Serum Lipoprotein Levels in Subjects with and without Atherosclerosis</th>
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<td>$S_f$ 0-12 (mg.%)</td>
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<td>$S_f$ 20-400 (mg.%)</td>
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From 1 to 2 measurements were made on each subject.

There was a significant difference between mean control values of all classes of lipoproteins in the patients with manifest atherosclerosis as compared with those without evident atherosclerosis, p < .01 for $S_f$ 0-12 and p < .05 for $S_f$ 12-20 and $S_f$ 20-400.

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<th>Table 2.—Mean Values of Serum Lipoproteins as Influenced by Dietary Fat Intake and Weight Reduction</th>
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<td>Class of lipoproteins</td>
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<td>During period of weight loss on high-fat diet</td>
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Number of subjects measured was 25. From 2 to 8 measurements were made on each subject for each diet condition, standard errors indicated.

Changes in the $S_f$ 0-12 and $S_f$ 20-400 classes of lipoproteins were highly significant, p < .01. Whereas the $S_f$ 0-12 class was well correlated with dietary fat intake, the $S_f$ 20-400 lipoproteins were more responsive to weight reduction.
disease. Previous studies have suggested that either positive or negative caloric balance may influence serum lipoprotein levels. Hence, determinations made during the period when patients were losing weight on a high-fat diet were analyzed separately from data obtained when patients were ingesting a high-fat diet and maintaining their weight constant at the "new" reduced level. As shown in table 2, when patients consumed a high-fat diet, there was a highly significant (p < .01) elevation of the S1 0-12 class of lipoproteins as compared with control levels, in spite of the fact they were losing weight. This increase was maintained as long as they remained on a high-fat diet. When the diet was changed to one of low fat, the serum concentrations of S1 0-12 lipoproteins decreased significantly to below control levels.

The S1 12-20 lipoprotein class showed changes that were significant at the 5 per cent level (p < .05). However, the mean values on the dietary regimens were so closely grouped as to require that any interpretation be viewed with caution.

The response of the lipoprotein S1 20-400 fraction was in marked contrast to that observed for the higher density lipoproteins. There was a highly significant (p < .01) reduction in the S1 20-400 fraction soon after patients were in negative caloric balance, regardless of the amount of fat in the diet. The depression of this lipoprotein class persisted when the diet was changed from high fat to low fat as long as the "new" low weight level was maintained.

**DISCUSSION**

A significant body of data has been accumulated that indicates a high correlation between elevated serum β-lipoprotein concentrations and the development of coronary artery disease. Our data indicate that weight reduction and dietary fat content produce different effects on at least 2 of the β-lipoprotein classes. Thus, significant changes may be obscured or entirely missed if an investigator measures only total β-lipoprotein or total serum cholesterol levels.

The relative importance of the various classes of lipoproteins in the genesis of atherosclerosis is not definitely established. In our study, whereas the S1 0-12 lipoprotein class was well correlated with dietary fat content, the S1 20-400 class was more responsive to weight reduction. Such correlations, however, do not assess the relative importance of obesity versus dietary fat intake as causal factors in the genesis of human atherosclerosis. It is probable that both factors are important and the data presented lend support to this view.

**SUMMARY**

The effect of dietary fat intake and weight reduction on levels of the various classes of serum lipoproteins was determined in 25 human subjects. The majority of patients had proven coronary artery disease. During the first period of the study, the patients sustained an average weight loss of 21.7 pounds while on a diet in which approximately 73 per cent of total caloric intake consisted of animal fat. Following this period of weight loss the patients’ weights were maintained constant while they continued to ingest this high-fat diet in increased quantities. Finally, subjects were maintained at a constant weight on a diet containing less than 50 Gm. of fat per day. Standard S1 0-12 and S1 20-400 classes of β-lipoproteins showed a completely dissimilar response. The serum levels of the S1 0-12 fraction were highly influenced by dietary fat intake rising on a high-fat diet and falling on a low-fat diet, apparently independent of weight change. In contrast the S1 20-400 fraction was significantly lowered by negative caloric balance and weight reduction, despite the ingestion of large amounts of animal fat. These changes were statistically highly significant (p < .01). The S1 12-20 class of lipoproteins showed less striking responses to weight reduction and dietary fat intake. These data lend support to the concept that body leanness and restriction of dietary fat may both be important in preventing human atherosclerosis. In addition, divergent responses of different classes of β-lipoproteins to various dietary and nutritional regimens may be entirely missed if only total β-lipoprotein or total cholesterol measurements are made.
Differential Effects on Beta-Lipoprotein Serum Levels

SUMMARIO IN INTERLINGUA

Esseva determinate in 25 subjectos human le effecto del ingestion dietari de grassia e del reduction de peso super le nivello del varie classes de lipoproteina serial. Le majoritate del subjectos esseva patentes con demonstrate morbo de arteria coronari. Durante le prime periodo del studio, le patientes experienciava un perdita medie de peso de 21.7 lbs. A iste tempore lor dieta includeva grassia animal amontante a circa 73 pro cento del total ingestion caloric. Post iste periodo de perdita de peso, le pesos del patientes esseva mantenite a nivello constante durante que le dieta con le mentionate alte procentage de grassia esseva ingerite in augmentate quantitates. Finalmente, le subjectos esseva mantenite a nivello constante de peso con un dieta continent minus que 50 g de grassia per die. Le classes standard $S_1$ 0-12 e $S_1$ 20-400 de lipoproteina beta monstравa responsas completamente dissimile. Le nivello serial del fraction $S_1$ 0-12 esseva grandemente influenitate per le ingestion dietari de grassia. Illos montava con un dieta ric in grassia e descendeva con un dieta povre in grassia, apparentemente sin dependientia del alterationes de peso. Del altere latere, le fraction $S_1$ 20-400 esseva significativamente reducute per un negative balancia caloric e reduction de peso, in despecto del ingestion de grande quantitates de grassia animal. Iste alterationes esseva de grande signification statistic ($p < 0.01$). Le classes $S_1$ 12-20 de lipoproteina monstравa minus frappante responsas al reduction de peso e al ingestion dietari de grassia. Iste datos supporta le conception que magritate del corpore e restriction del grassia dietari pote ambes addicte de importancia in prevenir atherosclerosis human. In plus, divergente responsas de differente classes de lipoproteina beta a varie regimes nutritional e dietari pote escappar completemente al observation si solmente mesurationes total de lipoproteina beta o de cholesterol es executate.

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The scientist does not study nature because it is useful. He studies it because he delights in it, and he delights in it because it is beautiful.—Henri Poincaré, 1854–1912.
Differential Effect of Dietary Fat and Weight Reduction on Serum Levels of Beta-Lipoproteins
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Circulation. 1957;15:31-34
doi: 10.1161/01.CIR.15.1.31

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