Physical Activity, Serum Cholesterol and Other Lipids in Man.* (23230)

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Anderson, Lawler and Keys(1) have proposed the hypothesis that, other things being equal, the serum cholesterol concentration in man is determined by the fat transport load imposed on the blood per unit of circulation. The transport of fat from intestines to liver and from liver to fat depots is thought to be primarily involved. The transport of fat from the fat depots to the point of metabolism appears to be less directly concerned because the serum cholesterol concentration falls during negative calorie balance in spite of the fact that a great deal of fat is mobilized from the fat depots in this situation(2,3). The hypothesis explains: 1) The increase in serum cholesterol concentration observed on high fat diets and in overnutrition with a positive calorie balance; 2) The stability of serum cholesterol during calorie equilibrium and a constant fat intake and 3) The decrease in serum cholesterol on low fat diets and in negative calorie balance. The role of physical activity in this scheme needs clarification. The acute effects of physical activity have been studied in connection with dietary cholesterol loading(4) and it has been shown that when calories and activity are increased to the same extent so that calorie equilibrium is maintained, no increase in serum cholesterol concentration results(5). However, in the latter work only 3 subjects were studied, the quantity of fat in the diet was held constant while the physical activity was increased so that the proportion of calories represented by fat metabolism decreased sharply, and calorie equilibrium was not exact. It is of interest to discover whether increasing the fat content of the diet in proportion to the calories consumed by physical activity will affect the serum cholesterol concentration. This paper presents data bearing on this point.

Subjects, conditions and methods. The subjects were 9 clinically healthy university students who volunteered to participate in the experiment. The mean age was 23.3 years with a range of 21 to 28 and the mean relative weight was 108.3 with a range of 93 to 128. None of the men was excessively fat or thin. Two of the 9 played in intramural basketball but the others did not take part in organized sports.

All meals were prepared and measured in the laboratory and 2 meals a day were served in the laboratory dining room. Box lunches consisting of sandwiches, fruit and milk were carried by the subjects and eaten outside of the laboratory. All food items were served as weighed portions and the rejections were tabulated and used in calculating the composition of the diet. The diet was designed to approximate the current American practice of using liberal quantities of meat, milk, butter and eggs. It was fully adequate in vitamins and minerals. The calorie, fat and protein content are presented in Table I.

During the period of increased physical activity, the men walked for 2 hours a day on the motor driven treadmill at 3.5 miles per hour on a 10% grade in an air conditioned room in which the temperature was held constant at 78°F with a relative humidity of 50 to 60% saturation. Body weights were measured each morning before breakfast without shoes and coat. *Oxygen consumption* during work was determined by collecting expired air in a spirometer and analyzing an aliquot sample for CO_2 and O_2 concentrations in a Haldane gas analysis apparatus. *Blood* was drawn in the morning before breakfast. The total serum cholesterol was determined by a modification(6) of the method of Abell *et al.* (7). The cholesterol associated with the α and β lipoprotein was determined by cold ethanol fractionation with a modification of the procedure of Russ, Eder and Barr(8). For the determination of *lipid phosphorus*, serum samples were extracted with Bloor's

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TABLE I. Composition of Diets employed in the 2 sedentary periods and the physically active period.

Diet		Cal./day	Protein g/day	Protein % of cal./day	Fat g/day	Fat % of cal./day
Sedentary	Mean	3257	105	13.0	155	42.7
	St. dev.	78	4.6		3.6	
Physically active	Mean	4189	135	12.9	201	43.2
	St. dev.	79	8.3		5.1	

mixture and the dried extract was further purified by a second extraction with chloroform. The phosphorus was then determined following the procedure outlined by Brandt (9). Dole's method(10) was used to determine the concentration of non-esterified fatty acids.

Results. The general plan of the experiment was to have the men eat the standard sedentary diet for 2 weeks (S1 and S2, designated period I). This was followed by a transition period of 2 weeks in which the men increased their time spent walking on the motor driven treadmill from one-half to 2 hours a day (A3 and A4). Treadmill walking of 2 hours daily was then maintained for 2 weeks (A5 to A6, designated period II) and this was followed in turn by a week on the original diet (S7, designated period III) with no treadmill walking.

The body weights for the last 3 days of each week were averaged for each man. There was no significant variation in the means. At the beginning of the experiment the mean weight was 171.0; at the end of the exercise period, 171.0; and at the end of the second sedentary period, 170.8.

The results of the analyses of the blood lipids are presented in Table II. There were no significant differences in the group means of total serum cholesterol or beta lipoprotein cholesterol in the 3 periods studied. The variability between periods I and II was small while that between periods I or II and III is noticeably larger. The lipid phosphorus sustained a significant decline at the end of the activity period which was recovered after a week of sedentary existence. The nonesterified fatty acids tended to decline continuously during the entire 3 periods and the conventional T test for paired variates showed that none of the differences in the means approached statistical significance. The diet during the activity period provided an increase of 932 calories. The mean oxygen consumption of the group while walking on the treadmill was found to be 2.240 L/min. with an R.q. of 0.83. Two hours of work at this rate accounts for 1280 calories. In planning the experiment an allowance of 300 calories was made for basal metabolism and activities that would have been pursued dur-

TABLE II. Concentration of Cholesterol, Beta Lipoprotein Cholesterol, Phospholipid and Non-Esterified Fatty Acids (NEFA) of Subjects in the Several Periods. Figures in the table are means of duplicate determinations made in serum obtained from subjects on the last 2 days of designated period. All figures are in mg/100 ml of serum except NEFA which is expressed as micro equivalents of fatty acid/l of serum and Beta lipoprotein cholesterol which is in % of total.

	Serum cholesterol I	II	III	Beta lipoprotein chol. I	II	III	Phospholipid I	II	III	NEFA I	II	III
D	160	174	181	79.4	72.4	75.1	146	132	157	419	478	242
H	203	197	212	78.8	82.2	77.3	176	143	184	406	392	473
M	192	188	193	57.2	77.7	76.7	169	144	167	783	442	471
O'	144	152	179	77.1	83.6	82.7	123	129	149	423	340	256
Ol	116	122	132	80.2	72.1	77.3	113	106	128	560	442	596
P	163	159	125	79.8	82.4	76.8	136	145	110	720	1006	460
Q	147	146	140	74.2	75.3	82.1	142	130	140	439	372	525
R	150	147	144	83.3	87.8	90.1	134	118	137	475	342	394
S	150	154	148	77.3	74.7	77.0	131	121	127	345	344	320
Mean	158.3	159.8	161.5	76.3	78.7	79.5	141.1	129.7	144.3	507.7	462.0	415.2

ing the 2 hours which were occupied by treadmill work. The weight stability of the subjects during 7 weeks of the experiment suggests that this estimate was not far from correct.

Discussion. Since the oxygen intake required by the work task employed here is approximately 60% of the maximal oxygen intake found in young men of similar age and background(11), the work was entirely aerobic. The data presented by Asmussen and Nielsen(12) suggest that the cardiac output in treadmill walking of this intensity lies between 16 and 20 liters per minute or 3 to 5 times the basal rate. Circulation to the muscles is certainly increased by a larger factor since circulation thru the muscle at rest is probably only 20% of the resting cardiac output. Circulation to the muscles in the work conditions employed here is adequate to compensate for any increased fat transport to muscles that the lipoprotein cholesterol complex might take part in.

The work presented here is in agreement with the initial hypothesis that serum cholesterol concentrations are determined by the fat transport load from the intestine to the liver and to the fat depots which in turn is influenced by the circulation rate. In spite of the fact that the amount of fat eaten by the subjects increased by 46 g a day no increase in the level of serum cholesterol was observed, presumably because the circulation was increased in proportion to the additional fat load.

Mann *et al.*(5) studied 3 men who increased their calorie intake by roughly 3000 calories or 50%. The fat content of the diet was held constant so the proportion of calories provided by fat fell from 50 to 51% of the total to 24.7 to 25.2%, a reduction which might be expected to reduce serum cholesterol levels by as much as 20 mg per 100 ml of serum if activity and calories were constant (13). Heroic efforts were made by the subjects in this experiment to increase their energy expenditure to the level of roughly 6000 cal. a day. In spite of this increase in activity all men gained from 3 to 5 lb of weight suggesting that the positive calorie balance might be as high as 12,000 to 14,000 calories. The serum cholesterol levels either showed a downward trend or no change. The interpretation of these results is confused by the increase in body weight which, by itself, would tend to increase serum cholesterol levels(1). In the first 5 weeks of overnutrition, the subjects studied by Anderson *et al.*(1) gained 1.6 kilos of weight while their serum cholesterol concentrations increased by 20.3 mg per 100 ml of serum. The results reported by Mann *et al.*(5) might well be summation of two opposing factors.

Summary and conclusions. The effect of increasing the level of daily physical activity on the serum cholesterol concentrtaion was studied in 9 clinically healthy University students. The physical activity was increased by walking on the motor-driven treadmill at a rate which required 1280 cal. for 2 hours. The caloric intake was increased by 900 cal. but the proportion of calories derived from fat was held constant. There was no change in the serum cholesterol concentration. It is concluded that the results are consistent with the hypothesis that the serum cholesterol concentration is related to the proportion of total calories derived from fat.

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Strontium Metabolism and Strontium-Calcium Discrimination in Man. (23231)

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The need for a better understanding of the behavior of strontium in man has arisen because of development of nuclear weapons and potential applications of atomic energy. Radioactive strontium, disseminated worldwide, eventually finds its way into accessible calcium reservoirs of the biosphere (of which the human skeleton is one) and tends to attain steady state movement between such reservoirs. Information is needed to permit prediction of levels to be attained in the human population in terms of the amount falling out upon the earth or becoming incorporated in the diet. Since on a long-term basis the human burden will result from strontium contamination of dietary calcium, considerable advantage is gained by studying the comparative behavior of these two elements. Knowledge of the manner in which various physiological processes affect retention of strontium and calcium in the body may lead to ways in which the comparative retention can be modified at will. It is of practical importance to determine the extent to which the urine or blood levels can be used to estimate the body burden or over-all intake of radioactive strontium.

The world-wide distribution of strontium 90 has been reviewed by Libby(1) and Kulp *et al.*(2). The metabolism of strontium in laboratory and domestic animals has been extensively studied(3-6), and the behavior of intravenously injected strontium 85 in human subjects has been reported by Spencer *et al.*(7). Harrison *et al.*(8) have followed, in normal man, the course of stable strontium given in amounts (20 to 250 mg) that allowed analysis by radioactivation. These findings have been reviewed and compared with animal data by Comar and Wasserman(3).

The long-term problem is concerned with the behavior of essentially carrier-free radiostrontium ingested over an extended period with each meal. Therefore, in the present work, emphasis has been given to experiments that simulate this situation, rather than to the usual single parenteral dose-type experiment often employed in metabolic studies. Data are presented on the behavior of strontium 85 in man after single and daily feeding, and on the strontium-calcium discrimination as shown by daily feeding of strontium 85 and calcium 45 in double tracer studies.

Methods. These studies were done with chronically ill patients having leukemia or widespread malignant neoplasms. Carrier-free strontium 85 (cyclotron produced from rubidium; 65 day half life; no beta rays; 0.013 Mev X ray, 0.513 γ ray) and high specific activity calcium 45 were used. The levels of Sr 85 employed ranged from 5 to 20 microcuries for single dosage studies and from 1 to 3 microcuries per meal for the daily feeding experiments. In the double tracer studies, Ca 45 was given at about twice the microcurie amounts of Sr 85. The usual procedures for handling of samples and radioassay were employed(9) except as noted. The Sr 85 was counted with a well-scintillation crystal. Double counting was accomplished by scintillation measurement of the sample itself or of an aliquot of ash solution for Sr 85, and

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