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Metabolic Effects of Exercise
II. Residual Metabolic Effects of Exercise in Rats[1,2] (38601)

JOHN A. HEBERT AND ALFREDO LOPEZ-S

Department of Medicine, Nutrition and Metabolism Laboratory, Louisiana State University School of Medicine, 1542 Tulane Avenue, New Orleans, Louisiana 70112

There is today increasing interest in the relationship between physical activity and Coronary Heart Disease (CHD). At the present time, conclusive information is not available concerning the protective effect of exercise on CHD. The contradictory reports appearing in the literature may be due to differences in the amount, intensity and duration of exercise. It has been suggested that time-intensity interactions are important in the role played by the risk factors in the development of CHD (1). The same time-intensity interactions may be at play with the factors assumed to have a protective effect on the development of this disease.

We have reported (see paper I, this journal) that rats subjected to voluntary exercise in rodent activity cages showed the following changes when compared to sedentary rats: Gained less weight, had lower serum cholesterol, had lower serum triglycerides, larger adrenal glands and lower hepatic glucose-6-phosphate dehydrogenase (G-6-PD) activity. These effects were found to be related to the level of intensity of the exercise.

There has been very little information reported concerning both man and animals as to the duration of these changes induced by exercise after the exercise has been terminated. Some information is available on the residual effect of acute, strenuous exercise in such parameters as lactic acid, oxygen uptake and certain enzymes (2–4). However, there is a surprising lack of information on the residual effect of chronic exercise on CHD risk factors. Interest and controversy in this area has been increased by several reports in the literature concerning the lower death rate of former athletes (5–7). More information is needed about the relationships between intensity and duration of physical training and effect on the prevention of CHD.

We have initiated studies in animals and men in order to evaluate the effect of chronic exercise on serum lipids and other parameters related to lipid metabolism. The main objective of these experiments was to determine how long the effects of exercise last after the exercise is terminated. This paper reports on the results obtained with rats.

Methods. Male Fischer rats weighing 250 g were used in these experiments. The rats were paired by weight and the pairs were randomly assigned to sedentary or exercise groups. The sedentary group was housed in shoe-box type cages. The exercised group was housed in individual rodent activity cages which allowed voluntary activity in a revolving drum. Both control and exercise groups were fed Purina Rat Chow *ad-libitum*. Water was also supplied *ad-libitum*. Body weight and food consumption was measured weekly. Exercise was terminated after 10 wk.

At the termination of the study, three rats from the exercise group and three rats from the sedentary group were sacrificed by decapitation. This group was termed zero residual time. Three weeks later another group of six rats were sacrificed and termed 3-wk residual. Five weeks after termination of the exercise the remaining group of eight rats were sacrificed and termed 5-wk residual.

Blood was collected immediately after decapitation. The liver and adrenals were removed, blotted, weighed and processed for further assay or immediately frozen. Serum lipids were extracted with isopropanol and total cholesterol and triglycerides were measured by techniques developed in our laboratory (8). The enzymatic activity of

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TABLE I. RESIDUAL EFFECT OF EXERCISE ON BODY WEIGHT ADRENAL GLAND WEIGHT AND G-6-PD ACTIVITY.

Residual time	Body weight gain (g)			
	Control	Exercise	% Change	Probability
(weeks)				
0	83.8 ± 4.9[a]	77.3 ± 6.8	−7.8	$P < 0.05$
3	88.0 ± 4.0	82.3 ± 4.5	−6.5	$P < 0.20$
5	80.5 ± 3.1	78.5 ± 4.8	−2.5	$P < 0.50$
	Adrenal gland weight (mg)			
0	37.6 ± 4.1	43.4 ± 1.9	+15.4	$P < 0.20$
3	44.7 ± 0.5	41.7 ± 2.3	−6.7	$P < 0.20$
5	43.8 ± 2.2	43.3 ± 4.0	−1.4	$P < 0.90$
	Glucose-6-phosphate dehydrogenase[b] OD/min/mg protein)			
0	43 ± 6	33 ± 3	−21	$P < 0.10$
3	38 ± 22	39 ± 20	+2	$P < 0.90$
5	41 ± 19	39 ± 17	−5	$P < 0.90$

[a] Mean ± SD.
[b] Hepatic G-6-PD.

G-6-PD was measured in the 16,000 *g* supernatant fraction of liver homogenate (20% in 0.26 *M* sucrose) according to the procedure of Rudack *et al.* (9), using a Gilford Model 240 spectrophotometer with a recorder attached. Protein was measured by the biuret reaction and enzyme activity expressed as change in optical density per minute per milligram of protein.

Statistical analyses were performed by the Student's *t* test between the control and exercise group at each time period. The percent change of the exercise values compared to the control values of each parameter are given as well as the probability level for each time period.

Results. The lower body weight gain of the exercise group −7.8% ($P < 0.05$) was statistically significant after ten weeks of exercise as shown in Table I. By the 3-wk residual time, the body weights of the exercise and sedentary groups were not statistically different ($P < 0.20$). This finding was substantiated at the 5-wk residual period ($P < 0.50$).

The adrenal glands of the rats were dissected immediately after sacrifice. The wet weight of both glands were measured on a torsion balance. After 10 wk exercised rats had larger adrenal glands +15.4% ($P < 0.20$) than the sedentary group (Table I). In previous experiments we have consistently observed that exercised rats had larger adrenal glands, usually of the order of 10–20%. The difference quickly disappeared after termination of the exercise.

We have previously observed a lowered activity of G-6-PD with exercise in rat liver. Table I shows that exercised rats had a lower G-6-PD activity of 21%. The changes due to exercise were quickly abolished after termination of the exercise program as shown by the 3-wk and 5-wk residual data. As in the case of the adrenal gland, G-6-PD values seemed to approach control values rather quickly under the circumstances of our experiment.

The residual effect of exercise on serum lipids is shown in Table II. After ten weeks of exercise, the exercising group had lower serum cholesterol −10.4% ($P < 0.05$) than the sedentary group. The statistical difference between the exercise and sedentary groups disappeared within 3 wk and definitely by 5 wk. Previous experiments have shown that exercise exerts a large decrease in the serum triglycerides of fasted rats. A decrease of 39% ($P < 0.10$) was obtained in the exercise rats when compared to the sedentary rats after ten weeks of exercise. The magnitude of change indicates that exercise exerts

TABLE II. RESIDUAL EFFECT OF EXERCISE ON SERUM LIPIDS[a] OF RATS.

Residual time	Control	Exercise	% Change	Probability
	Serum cholesterol			
(weeks)				
0	77 ± 4[b]	69 ± 3	−10.4	$P < 0.05$
3	67 ± 11	57 ± 7	−15.0	$P < 0.30$
5	61 ± 5	59 ± 1	−3.3	$P < 0.50$
	Serum triglycerides			
0	82 ± 21	50 ± 9	−39.0	$P < 0.10$
3	107 ± 3	72 ± 8	−32.0	$P < 0.01$
5	108 ± 20	88 ± 20	−18.5	$P < 0.30$

[a] Values are in mg/100 ml.
[b] Mean ± SD.

the largest effect on lowering serum triglycerides. The decrease in serum triglyceride persisted at the 3-wk residual time −32% ($P < 0.01$). However, the decrease of 18.5% at 5 wk was not statistically significant ($P < 0.30$) and we thus had to conclude that serum triglyceride returned to control values between the third and fifth wk after termination of the exercise.

Discussion. The rats on exercise had a lower body weight gain than the sedentary rats. This difference quickly disappeared after termination of the exercise. In preliminary studies we have observed that exercised rats have a lower rate of weight gain than sedentary rats even though the exercise rats exhibit a greater food intake than the sedentary rats. Thus it becomes evident that the lower weight gain of the exercise rats cannot be explained by reduced caloric intake, since their food consumption was increased. However, we did not measure the energy required for the amount of exercise that the rats performed. Under the conditions of our experiment, it was not possible to separate the energy required for maintenance, weight gain and exercise.

The lower serum cholesterol of the exercise rats represents an area of controversy in the literature (10). Rat serum contains a very high concentration of α-lipoproteins which contains less cholesterol than the β- and pre-β-lipoproteins. A decrease in β-lipoprotein and pre-β-lipoprotein levels accompanied by an increase in α-lipoprotein levels, as seen in exercise (11) could explain the marked decrease in serum triglycerides and the smaller decrease in serum cholesterol.

The lower serum triglyceride levels of exercised rats was highly significant and remained lower for over three weeks after the exercise was terminated. Of the parameters tested, the lower serum triglycerides had the longest residual effect.

If the decreased weight gain with exercise was due to a decrease in adipose deposition, then this effect of exercise along with the lowered serum lipid levels indicates that exercise must be exerting some metabolic control over lipid metabolism. The exact mechanism by which exercise influences lipid metabolism is unknown. The activity of G-6-PD was lowered by exercise. In this experiment G-6-PD levels quickly returned to normal levels upon termination of the exercise. Exercise may reduce lipid synthesis by reducing the level of G-6-PD which in turn reduces the production of NADPH which is required for fatty acid and cholesterol synthesis. We have reported that certain steroid compounds affected by exercise inhibit the activity of G-6-PD (12). The lowering of G-6-PD activity with exercise could be due to the increased production of certain steroids by the enlarged adrenal gland. This report shows that the adrenal gland enlargement quickly returned to normal size upon termination of exercise. The finding that adrenal gland size and G-6-PD activity returned to sedentary values faster than did the serum lipids, further suggests a possible mechanism whereby exercise may control lipid metabolism by in-

fluencing the production of certain steroid compounds from the adrenal gland.

Extrapolation from rat experiments to humans always should be taken with reservations. With this in mind we should note that these studies suggest that exercise has some residual effect, although a transitory one, on certain parameters potentially related to CHD. More studies both in men and experimental animals are needed in order to establish whether or not short periodic exercising sessions with interim resting periods do render the same effect on CHD risk factors and eventually on mortality from CHD as do continual uninterrupted training programs. It has been suggested (13) that a changing pattern of activity with periodic peaks of activity could be the most meaningful way to study the effect of exercise on CHD. Therefore data on as to how long the effects of exercise persist after exercise is terminated become very useful.

Summary. This report describes the duration of changes in serum lipids, adrenal weight and hepatic G-6-PD activity in rats following the termination of 10 weeks of voluntary activity in a revolving drum. Exercised rats had lower weight gain, larger adrenal glands, lower serum cholesterol, lower serum triglycerides and lower liver glucose-6-phosphate dehydrogenase (G-6-PD) activity than the sedentary controls. The differences between exercise and control rats in adrenal gland weight, body weight and G-6-PD tend to disappear within 3 wk after termination of the exercise. These experiments provide evidence that exercise can affect lipid metabolism and have a beneficial effect on the lowering of serum lipids. It also shows that this effect will persist for up to 3 wk after the exercise is terminated, under the experimental conditions of this study.

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