Acta Radiol., 1930, Suppl. 10, 1.

12. Furth, J., Furth, O. B., Am. J. Cancer, 1936, v28, 54.

13. Kaplan, H. S. Brown, M. B., J. Nat. Cancer Inst., 1952, v13, 185.

14. Pollard, M., see Prog. Med. Virology, Karger Press, Basel, 1965, v4.

15. Kaplan, H. S., Brown, M. B., J. Nat. Cancer Inst., 1951, v12, 427.

16. Lorenz, E., Congdon, C. C., Uphoff, D., ibid., 1953, v14, 291.

17. Westphal, O., Luderitz, O., Bister, F., Z. Naturforsch., 1952, v7, 148.

18. Cosgrove, G. E., Upton, A. C., Congdon, C. C., Doherty, D. G., Christenberry, K. W., Gosslee, D. G., Radiation Res., 1964, v21, 550.

19. Upton, A. C., Doherty, D. G., Melville, G. S., Jr., Acta Radiol., 1959, v51, 379.

Received February 28, 1966. P.S.E.B.M., 1966, v122.

Alterations in Enzyme Activities as a Consequence of Exercise (Swimming) in the Rat.* (31185)

J. F. SANGSTER AND J. R. BEATON†

Department of Physiology, University of Western Ontario, London, Ontario, Canada

Enzymatic changes in blood and tissues in response to both acute and chronic exercise in trained and untrained individuals and animals have been studied most intensively. However, there appears to be little unanimity in this field. Nikkila *et al*(1) found that the greatest increment in enzyme increase was observed in untrained subjects and the least in trained athletes. As total work output increased, mean serum enzyme levels were correspondingly raised. Malic dehydrogenase activity (MDH) increased moderately, while 2 transaminases manifested very significant rises after all forms of exercise. Gardner *et al* (2) studied the effect of exercise on serum enzyme levels in trained subjects and observed a relationship between degree of exercise (treadmill) and serum enzyme levels; a relationship to duration of exercise was evident also. There was no significant difference in pre-exercise serum enzyme values between trained and untrained subjects. The mean increases in glutamic-oxaloacetic transaminase (GOT), glutamic-pyruvic transaminase (GPT), lactic dehydrogenase (LDH) and MDH activities after exercises were observed to be significantly less in trained subjects. Harding, Rosen, and Nichol(3) found that changes in liver GPT activity in rats appeared to reflect changes in metabolism that accompanied an enhanced rate of gluconeogenesis. Critz(4) has recently reported on the effect of swimming exercise on serum glutamic-oxaloacetic transaminase (SGOT). He found that SGOT activity was decreased by a brief swim (1 minute), but was elevated after swimming 5 minutes. An exercise period of 10 or 15 minutes produced no significant change in the SGOT activity but swimming for 30, 60 or 120 minutes caused a progressive rise in activity. It is apparent that conditions and duration of exercise are major factors in determining alterations of enzyme activities.

Several other enzymes in animals and man have been studied using various forms of exercise without any uniform pattern being established. Perhaps the major reason for this lack of unanimity is variation in the duration, type, and environment of exercise. Certain standard conditions were established for the experiments described here and changes in liver and plasma MDH and GPT activities with exposure to acute and repeated exercise (swimming) in the rat were then measured.

Materials and methods. In 2 separate experiments, male Wistar rats weighing 240-270 g were divided randomly into 4 groups: (A) control, (B) acute exercise, (C) trained + exercise, and (D) trained. Prior to experimentation rats were maintained in individual wire cages at an environmental temperature

* This investigation was supported in part by a grant from Defence Research Board of Canada.

† Medical Research Associate of Medical Research Council of Canada.

TABLE I. Effect of Exercise (Swimming 2 Hours) on Liver and Plasma Malic Dehydrogenase Activity (MDH) in the Rat.

Group	No. of determinations	Liver MDH, /mg wet tissue	No. of determinations	Plasma MDH, units/ml plasma
A Control	11	183 ± 11.15	11	102 ± 7.61
B Acute exercise	13	236 ± 12.67	13	185 ± 27.92
C Trained + exercise	11	228 ± 11.66	7	117 ± 17.77
D Trained	10	238 ± 14.19	8	122 ± 15.23
Probability, P		A *vs* B <.01 A *vs* C <.01 A *vs* D <.01		A *vs* B <.001

of 23-24°C and were fed with laboratory chow and water *ad libitum*. Temperature of the water tanks for swimming was maintained at 28-30°C. Two groups of animals were exposed to a training period consisting of a 1-hour swim 3 times per week over a period of 27 days. On the day following completion of the training period, Group C was exposed to an episode of 2 hours swimming (comparable to controls) prior to killing. The other trained group was sacrificed on the day following completion of training program, *i.e.*, without further exercise. Food was removed from control and trained animals 2 hours before killing in order to be comparable to the other 2 groups which would be without food for the duration of their 2-hour swimming period prior to sacrificing. Following intraperitoneal injection of sodium pentabarbital, blood was removed by cardiac puncture, heparinized, and plasma was separated. A liver sample was taken and for MDH, a 0.2% homogenate in phosphate buffer (pH 7.4) and for GPT, a 1% homogenate in phosphate buffer (pH 7.4) was used. MDH activities were determined by adaptation of the ultraviolet spectrophotometric method of Siegel and Bing(5). Liver and plasma GPT activities were measured by a modification of the procedure of Wroblewski and LaDue(6).

Results. As shown in Table I, acute exercise for 2 hours resulted in a significant increase in liver and plasma MDH activities as compared with non-exercised control animals. Results from both trained groups showed a liver MDH activity comparable to animals exposed to acute exercise. Of special note was the failure of trained animals exposed to an additional 2 hours of swimming to show any further elevation of liver MDH activity above that of trained animals not exercised after completion of the training period. It appears that training results in an increase in basal liver MDH activity such that the enzyme does not respond with an increased activity to a subsequent 2-hour exercise period. Plasma MDH activities were similar in trained animals and in non-exercised control animals. Acute exercise in untrained animals, however, did cause an elevation in plasma MDH activity.

The effects of exercise on GPT activity are shown in Table II. Exercise, whether acute or repeated (training), failed to have any significant effect on liver or plasma GPT activities. Similar results were obtained in repeated experiments.

Discussion. It is known that measured activity of an enzyme in serum or plasma is a result of the balance between a number of factors. The rise in plasma MDH following acute exercise could be due to both tissue damage and to altered enzyme synthesis. Halonen and Konttinen(7) postulated that enhancement in enzyme activity could be due to increased permeability of the cell membrane for which physical activity could be responsible. Hypoxia is thought to be one

TABLE II. Effect of Exercise (Swimming 2 Hours) on Liver and Plasma Glutamic-Pyruvic Transaminase Activity (GPT) in the Rat.

Group	No. of determinations	Liver GPT, units/mg wet tissue	Plasma GPT, units/ml plasma
A Control	3	42 ± .51	89 ± 5.07
B Acute exercise	4	41 ± 1.52	91 ± 2.54
C Trained + exercise	4	35 ± 6.08	74 ± 7.61
D Trained	4	36 ± 2.54	84 ± 2.54

of the major factors involved in release of enzymes. On the basis of the observed increase of liver MDH activity, an increased liver enzyme synthesis with larger quantities of enzyme diffusing out of the cell seems likely; increased cell membrane permeability would aid in this mechanism. It is of interest that although training elevated liver MDH activity, plasma MDH activity was unchanged. Gardner *et al*(2) observed no effect of training on serum enzyme activities in human subjects. Our observation of an increased plasma MDH activity with acute exercise in untrained rats is in agreement with the finding of Nikkila *et al*(1) in untrained human subjects.

The failure to observe an increase of GPT activity in plasma after exercise is in disagreement with the results obtained by Nikkila *et al*(1) and Gardner *et al*(2) with human subjects. Harding, Rosen, and Nichol (3) found that changes in the activity of GPT appeared to reflect the changes in metabolism that accompanied an enhanced rate of gluconeogenesis. It is unlikely that such a state occurred in the present conditions of exercise. Further, availability of plasma free fatty acids as a readily available fuel supply in exercise has been shown by Cohn(8), Basu and Passmore(9) and Rodahl *et al*(10). In view of the observations of Critz(4) on SGOT activities with exercise periods of varying duration, it is possible that under conditions of our experiment (2 hours swimming), a previously elevated GPT activity had returned to normal.

Summary. Liver and plasma activities of malic dehydrogenase (MDH) and glutamic-pyruvic transaminase (GPT) have been measured in adult, male rats made to swim for 2 hours either as a single, acute exercise or after repeated daily exercises (training). Acute exercise caused a significant increase of both liver and plasma MDH activity. Repeated exercise (training) caused an increased basal MDH activity in liver but not plasma; in the trained rat, a 2-hour swimming exercise did not elicit a further elevation of MDH activity in liver nor did it elicit an elevation in plasma. Neither acute nor repeated exercise caused any alteration in liver or plasma GPT activities. The possibility of using alterations in plasma MDH activity as a criterion of training is suggested.

The authors express their appreciation to Miss R. Childs and Miss M. J. Gooley for their technical assistance.

1. Nikkila, E. A., Torsti, P., Penttila, O., Metabolism, 1963, v12, 863.

2. Gardner, G. W., Bratton, R., Chowdhury, S. R., Fowler, W. M., Pearson, C. M., J. Sports Med. Phys. Fit., 1964, v4, 103.

3. Harding, H. R., Rosen, F., Nichol, C. A., Am. J. Physiol., 1961, v201, 271.

4. Critz, J. B., Proc. Soc. Exp. Biol. and Med., 1966, v121, 101.

5. Siegel, A., Bing, R. J., ibid., 1956, v91, 604.

6. Wroblewski, F., LaDue, J. S., ibid., 1956, v91, 569.

7. Halonen, P. O., Konttinen, A., Nature, 1962, v193, 942.

8. Cohn, C., Nutr. Rev., 1962, v20, 331.

9. Basu, A., Strong, J. A., Passmore, R., J. Exp. Physiol., 1960, v45, 312.

10. Rodahl, K., Miller, H. I., Issekutz, B., J. App. Physiol., 1964, v19, 489.

Received March 1, 1966. P.S.E.B.M., 1966, v122.