# Effect of Training and Exercise on Serum Ceruloplasmin in Rats[1] (36170)

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Since the original description of the copper-containing serum protein (1), questions have persisted concerning the physiological significance and function of ceruloplasmin (CP)[2]. CP has been measured in a wide variety of experimental and clinical conditions and has been observed to vary in concentration under many of these conditions. Serum CP is highly sensitive to stress conditions (3–5). Rice (6) has presented evidence which indicated that CP may behave as an acute-phase reactant, although there are factors other than inflammation which may affect serum CP activity. A nonspecific stressor such as formaldehyde markedly increased serum CP in chickens (7). Swimming rats for 7 min in 21° water nearly doubled CP (8). Haralambie (9) reported that serum CP was not affected by 1 hr of physical exercise but was increased in trained, high-performance athletes. Subsequently, it was reported (10) that 2 hr of physical exercise did significantly increase serum CP and copper concentrations. The present report contains data from a study designed to determine the effect of training and acute exercise on serum CP in rats.

*Materials and Methods.* Male rats of the Carworth (Carworth Farms, Portage, MI) CFN strain, weighing approximately 110 g at the start of the experiment, were housed in individual cages and were given water and Wayne Lab Blox (Allied Mills, Inc., Chicago, IL) *ad libitum*. Throughout the training period, room temperature was maintained at approximately 20° and the lighting was regulated to provide 12 hr of light and 12 hr of darkness.

The rats were grouped into either an untrained or a trained group. The untrained rats remained sedentary in their cages. The trained group was subjected to treadmill running on a commercial rodent treadmill (Quinton Instrument Co., Seattle, WA) which had been modified so that the individual cages measured 3 × 13 in., each containing an electrical shocker plate at the rear of the cage. The trained rats were maintained on the training schedule described by Holloszy (11) for 12 weeks.

During weeks 1, 4, 9, and 12 of the experiment, trained and untrained rats were exercised by running on the treadmill at 0.5 mph on an 8% grade. Untrained rats were run to exhaustion, and trained rats were run for the same length of time as the untrained exhausted rats. In addition, at 12 weeks, some of the trained rats were run to exhaustion at 1.25 mph. Exercised animals were decapitated immediately after they were taken from the treadmill while the control groups were sacrificed at rest. Blood was collected at sacrifice and serum CP concentrations were determined by the method of Houchin (12) as modified by Rice (13). Statistical treatment of the data was accomplished by the Student-Newman-Keuls' method of multiple comparisons of means.

*Results and Discussion.* The results of this study are summarized in Table I. There were no significant differences among the var-

[1] In conducting the research described in this report, the investigators adhered to the "Guide for Laboratory Animal Facilities and Care," as promulgated by the Committee on the Guide for Laboratory Animal Resources, National Academy of Sciences–National Research Council.

[2] The name ferro:$O_2$ oxidoreductase (EC 1.12.3.1) has been proposed based upon the principal, naturally occurring substrate (2).

TABLE I. Serum Ceruloplasmin Activities from Trained and Untrained Rats.[a]

| Group | Weeks of training | | | |
|---|---|---|---|---|
| | 1 | 4 | 9 | 12 |
| Untrained, rested | 39 ± 3.4 (6)[b] | 41 ± 3.4 (6) | 44 ± 3.6 (6) | 45 ± 3.3 (6) |
| Trained, rested | | 48 ± 2.6 (6) | 56 ± 3.6 (6)[c] | 59 ± 2.9 (5)[c] |
| Untrained, exhausted | 43 ± 3.5 (6) | 48 ± 6.0 (5) | 67 ± 6.2 (5)[c] | 70 ± 5.2 (6)[c] |
| Trained, pair-run | | 58 ± 4.3 (6) | 59 ± 3.4 (6)[c] | 66 ± 2.5 (5)[c] |
| Trained, exhausted | | | | 78 ± 2.4 (5)[c,d] |

[a] Values expressed as IU ± SEM.

[b] Number of animals in parentheses.

[c] Significantly different ($p < .05$) from untrained, rested group in the same time period.

[d] Significantly different ($p < .05$) from the trained, rested group in the same time period.

ious groups at either 1 or 4 weeks. However, at 9 and 12 weeks, all other groups had significantly higher ($p < .05$) CP activities than the untrained rested group. Further, at the 12-week period, the trained exhausted group had significantly higher ($p < .05$) serum CP than the trained rested group. Thus, these data from rats would seem to support the observations in humans (9) that serum CP is increased with training. Similarly, the stressor effect on CP was confirmed in this study at the 9- and 12-week periods wherein the exhausted rats, trained and untrained, showed greater CP than their rested counterparts. It would appear that a physical stress would have to be rather severe to alter serum CP concentrations since the trained pair-run group did not differ significantly from the trained rested control group. Two possible explanations are readily apparent for this latter observation of nonsignificance. First, the duration of the pair-run may not have been long enough to tax the trained rats. Alternately, the trained rat may be adapted to withstand stress conditions. Concerning the first possibility, at 12 weeks the trained pair-run rats ran approximately 1.25 miles; whereas the trained exhausted pair-run rats ran approximately 6 miles under a more severe work load 1.25 vs 0.5 mph). Only the trained exhausted rats differed significantly in serum CP from the trained rested control group. The possibility of adaptation (possibly by humoral control) to withstand stress occurring with training is a more difficult problem to describe due to conflicting literature data. It has been reported (14) that ACTH, administered to intact rats, and corticosterone, given to adrenalectomized rats, significantly reduced serum CP. Conversely, it was reported (15) that treatment at birth with cortisone acetate significantly increased plasma CP in mature rats. Starcher and Hill (7) reported that hydrocortisone significantly increased CP in chickens. If one accepts the premise that CP may be elevated as a result of corticosteroid increases, a plausible explanation becomes evident for the nonsignificant CP difference between trained pair-run and trained rested rats. Frenkl *et al.* (16) showed that the rise in circulating corticoid levels following exercise was less in trained than untrained human subjects and suggested that this difference seemed to be due to a less severe stress reaction in the trained subjects. Thus, since the stress in the trained pair-run rats reported here was not overly severe, and since the plasma corticoid levels may not have been markedly elevated due to the exercise, it is not unreasonable to expect no difference in serum CP levels between this group and the trained rested control rats.

In order to determine that the observed effect of training on serum CP was real and not simply a residual effect from the previous days' training exercise, an additional study was performed using 20 adult, untrained rats. Five rats were sacrificed at rest and 15 were exhausted on the treadmill. Of the rats exhausted, 5 were sacrificed immediately after exhaustion, 5 were sacrificed 24 hr postexhaustion, and 5 were sacrificed 48 hr postexhaustion. Blood was collected and CP deter-

TABLE II. Serum Ceruloplasmin Activities at Various Time Intervals Following Exhaustive Exercise in Untrained Rats.

| Time following exercise | Ceruloplasmin activity[a] |
|---|---|
| Rested controls | 52 ± 1.9 |
| Immediately following exhaustion | 69 ± 3.7[b] |
| 24 hr following exhaustion | 54 ± 4.6 |
| 48 hr following exhaustion | 54 ± 1.7 |

[a] IU ± SEM of five rats.

[b] Significantly different ($p < .05$) from all other groups.

minations made as previously indicated. The results are summarized in Table II. Exhaustive exercise significantly increased CP, but this increase returned to control values within 24 hr. These data demonstrate that there is a definite effect of training on CP, an effect not attributable to the previous days' exercise period.

Perhaps a salient feature of this study, in view of the elevation of serum CP levels in trained rats (compared with untrained rats), is the possible usefulness of ceruloplasmin concentrations as an indicator of the degree of training which has occurred as a result of a particular training regimen.

*Summary.* Serum ceruloplasmin activity was significantly increased in trained rats compared with untrained control rats. Exhaustive exercise significantly elevated ceruloplasmin in both trained and untrained rats. It is suggested that serum ceruloplasmin levels may be useful as an indicator for quantitating training.

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