Effect of Exercise on Rats Fed a Diet Deficient in Potassium.

RICHARD H. FOLLIS, JR. (Introduced by Arnold R. Rich.)

From the Department of Pathology, The Johns Hopkins Medical School, Baltimore, Md.

The production of myocardial necroses and changes in the renal tubular epithelium have been reported in several species when animals are placed on a diet deficient in potassium (K).[1,2,3,4] In our experience[4] lesions first appear in the heart and kidneys of rats after the animals have been on the K-low diet for 8 days. No changes have been encountered in the voluntary muscles of any of the rats we have studied. In K-deficient mice calcification of striated muscle fibers has been described when K is added to the diet.[3] The present experiments were designed to determine whether or not severe exercise might produce more extensive cardiac lesions and to find out whether or not changes could be made to appear in the skeletal musculature by this means. Since Heppel[5] has shown that there is a loss of K when muscle is electrically stimulated, it was thought that the store of this cation might be depleted in the muscle fibers and lesions, similar to those found in the heart, might possibly be produced.

The diet used has been described in detail elsewhere.[6] * Fifteen rats 4 to 5 weeks of age were divided into 3 groups, 2 of which were placed on the K low regimen while the third group was used as controls, K being added to the diet. After a preliminary period of 2 weeks on the respective diets, one of the deficient groups and all the controls were made to exercise 6 days a week. They were placed in a large tank of water kept at approximately body temperature. Ten g weights were fastened to their trunks and they then were forced to swim vigorously for an hour the first week and from 90 to 120 min during the 3 ensuing weeks. They were removed from the tank when exhausted. The animals were sacrificed after being on the diet for 6 weeks. Autopsies were performed and 3-4 blocks of the heart and voluntary muscles were studied in each animal. The kidneys also were studied histologically.

The growth of the rats was similar to that which has already been described when such animals are placed on this diet.[6] No significant differences in growth were noted between the exercised and non-exercised deficient animals. The former gained on an average 30 g during the 6 weeks, while the latter increased 32 g in weight; the controls gained 55 g.

Following exercise during the latter half of the experiment the behavior of the deficient animals was interesting. They seemed more exhausted than the controls. When removed from the water, however, they did not stay relatively still in the cage as did the controls, but exhibited spontaneous tetanic contractures of the muscles of the extremities. That is, when they were placed on the floor, after being removed from the tank, they jumped into the air to a height of about a foot. These spasmodic contractures were repeated 10 to 12 times after which the animals lay exhausted. The sudden cessation of movement following removal from the tank seemed to be the inciting factor in bringing on these muscular spasms.

When the voluntary muscles of the deficient animals were examined no lesions were found. In the myocardium, however, there

1 Schrader, G. A., Prickett, C. O., and Salmon, W. D., *J. Nutrition*, 1937, **14**, 85.

2 Thomas, R. M., Mylon, E., and Winternitz, M. C., *Yale J. Biol. and Med.*, 1940, **12**, 345.

3 Liebow, A. A., McFarland, W. J., and Tennant, R., *Yale J. Biol. and Med.*, 1941, **13**, 523.

4 Follis, R. H., Jr., Orent-Keiles, E., and McCollum, E. V., *Am. J. Path.*, 1942, **18**, 29.

5 Heppel, L. A., *Am. J. Physiol.*, 1940, **128**, 440.

6 Orent-Keiles, E., and McCollum, E. V., *J. Biol. Chem.*, 1941, **140**, 337.

* The liver concentrate was kindly supplied by Dr. Guy W. Clark of the Lederle Laboratories. Alpha tocopherol was kindly supplied by Dr. D. F. Robertson of Merck and Company.

were characteristic changes which have been described elsewhere.[4] The lesions were definitely more extensive in the exercised than the unexercised group. The controls showed no lesions. Changes of the same degree were found in the kidneys of the 2 deficient groups while no renal changes were found in the controls.

Since the K content of the muscles of K deficient animals is lowered,[6] it had been hoped that exercise, by causing a further reduction of this cation, might lead to anatomical changes in the skeletal muscle fibers. While this study was in progress a report appeared by Miller and Darrow[7] which showed that voluntary exercise similar to that we had employed did not significantly lower the K content of muscle (per unit of fat-free tissue) of rats, even on a diet deficient in this cation. It thus appears that our negative histological findings are in keeping with the chemical studies of the above investigators.[7]

It should also be pointed out that Carnes *et al.*[8] found no changes in the voluntary muscles of rats which had received large amounts of desoxycorticosterone acetate. These authors also pointed out a difference between the response of the rat and the dog to this hormone. In the latter animal a syndrome resembling familial periodic paralysis has been produced following large amounts of adrenal cortical hormone.[9] Studies of the muscles of other such animals on low K diets are thus needed.

The peculiar physiological response that our animals showed following a cessation of exercise is difficult to explain. It consisted of a series of spasmodic, violent contractures that individually did not last abnormally long. Thus it is not myotonia. It does illustrate again the important relationship that K bears to muscular contraction.

The added burden of exercise on the hearts of these deficient animals led to more extensive changes than in the unexercised deficient groups. Chemical studies on the myocardium such as carried out by Miller and Darrow[7] on voluntary muscle would be of interest in this connection to determine whether or not the heart muscle fibers lost K following severe exertion and if their K content could be correlated with the extent of the lesions. A decrease in the concentration of K in the myocardium of rats on a low K diet has been reported by Orent-Keiles and McCollum.[6]

Summary. A study of the effect of excessive voluntary exercise was made in animals maintained on a low K diet. No changes were encountered in the voluntary muscles; the myocardium of the exercised group showed more extensive lesions than that of the controls. Peculiar tetanic contractures of the extremities were observed in the K-deficient animals following severe exercise.

[7] Miller, H. C., and Darrow, D. C., *Am. J. Physiol.*, 1941, **132**, 801.

[8] Carnes, W. H., Ragan, C., Ferrebee, J. W., and O'Neill, J., *Endocrinol.*, 1941, **29**, 144.

[9] Ragan, C., Ferrebee, J. W., Phyfe, P., Atchley, D. W., and Loeb, R. F., *Am. J. Physiol.*, 1940, **131**, 73.