The Effect of Exercise on the Growth of a Mouse Tumor*

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There is considerable evidence to indicate that an inhibition of tumor growth is observed in animals maintained on a nutritionally adequate diet but limited in caloric intake (1, 5, 11, 12). This effect appears to be due entirely to the caloric restriction rather than to the lack of some specific growth factor. The result is especially significant since the animals maintained on the curtailed rations are generally in better health and outlive those allowed food ad libitum (5, 11). This caloric effect is not limited to laboratory animals but may pertain to human beings as well, since a review of insurance statistics concerned with the relationship of body weight to cancer incidence has shown that persons of average weight or less are not so likely to develop cancer as those who are overweight (10). It follows that the avoidance of overweight through restriction of food intake may aid in the prevention of human cancer or at least delay its onset. These observations indicate that neoplastic cells are not so likely to develop or to become established if little or no excess energy remains after the bodily requirements have been met. If this assumption is correct, it might be possible to inhibit tumor growth by subjecting animals to forced exercise and thus utilizing the excess energy. To test this possibility the influence of forced exercise on the rate of tumor growth was studied on a series of mice bearing transplantable tumors.

PROCEDURE

Young adult ABC male mice were divided into two groups, one of which was subjected to forced exercise and another kept as a control. The diet was composed of the following constituents: cerelose 71, casein 20, salts 4, corn oil 2, cod liver oil 1 and rice bran concentrate “Vitab” 2. The amount of food was limited to the amount consumed by the group that ate the least, thus assuring the same caloric intake for each group even though the food consumption varied slightly from time to time. The control groups were kept on shavings in a metal box cage while the exercised groups were placed in cylindrical wire-mesh cages 10 inches in diameter and 11 inches long each holding 25 mice. These cages were mounted in such a manner that they could be rotated by an electric motor at 2 revolutions per minute. The motor was turned on and off automatically with a special electric timing clock at any desired interval. Food and water were given when the cage was stationary. After a preliminary period of exercise of 1 or 2 weeks all mice were inoculated subcutaneously in the abdominal region with a transplantable fibrosarcoma originally obtained from the ear of a mouse which had received continued ultraviolet irradiation. The mice were weighed regularly and the size of the tumors was estimated at weekly intervals and expressed as the product of the length X depth X width in centimeters.

The experiment was conducted with two series of mice. In the first series, 100 mice were divided into two groups of 50 each; one group was subjected to exercise and the other kept as a control. Exercise was induced by rotating the cages for 16 hours continuously and was followed by a rest period for the remaining 8 hours of the day. This exercise was started 1 week before the mice were inoculated with the sarcoma. In the second series, composed of 40 mice in each group, the exercising group was rotated for 2 hours at a time with an alternate 1 hour rest period throughout the 24 hour period. The exercise was started 2 weeks before tumor inoculation and continued for the duration of the experiment.

RESULTS

It had been expected that the exercised mice would have better appetites than the control group, and although this was generally true for the first series it did not hold for the groups given the shorter rest periods. Several days after the experiment was started, it was obvious that the mice were too tired or sleepy to recover sufficiently within 1 hour to consume enough food. It was necessary therefore, to include one 4 hour period during the day to allow adequate recovery of the mice and enable them to increase their dietary consumption. Even on this schedule, however, it was
usually necessary to restrict the intake of the controls to that of the exercised groups, the reverse of the expected procedure.

While the rate of rotation was not so rapid as to exhaust the mice completely, they did become very tired, and attempted to lie on the bottom of the cage until they were carried half way up to the top before it became imperative for them to return to the bottom to avoid falling. The more frequent rest periods in the second series were introduced to reduce fatigue, but as has already been said, these mice appeared too tired to be greatly interested in their food. It is probable that lack of sleep was at least as important a factor in reducing the caloric consumption as physical fatigue itself.

However, in spite of this treatment, the mice in both series remained in good health throughout the experiment, but those receiving the exercise did not gain as much as the controls on the same caloric intake. In series I the controls gained 3.8 gm. while those in the rotating cage gained only 1.9 gm. In the second series the weight gain was 3.3 gm. and 0.9 gm. respectively. This lack of a gain in weight did not appear to interfere with the general health of the exercised mice.

The percentage of tumor takes varied from 60 per cent to 77 per cent in both groups but was not correlated with exercise. The subsequent growth of tumors, however, was affected by exercise and is summarized in Table I. In series I the average tumor size of the controls at 4 weeks was 3.21 units (range 0.43 to 6.50 units) while that of the exercised groups was 2.42 units (range 0.20 to 6.20 units). In the second series there was likewise a slower growth rate in the rotated group at the 4th week: 2.33 units (range 0.03 to 3.74 units). The range of tumor size is presented to show that there was overlapping of results in each group, but it should be stressed that this was true only in a relatively few cases. Such overlapping of results might be explained by differences in food intake by individual mice within a group. It would be desirable, although impractical, to conduct an experiment of this type in individual cages in order to avoid differences in caloric intake among the mice. Nevertheless, the general trend of retardation in the rate of tumor growth is quite definite in the exercised groups and is in harmony with results that demonstrate tumor inhibition in mice on calorie restricted diets.

This report is further proof of the caloric effect on tumor growth, but in addition it indicates that the influence can also be demonstrated by changing the caloric requirements of the mice while maintaining a constant dietary intake. The effect of altering the basal metabolic rate of animals, and its influence on tumor growth, have been studied by various investigators. Gilroy (2) reported that the administration of thyroxine to mice retarded cancer growth. Bischoff, Long, and Maxwell (1) did not confirm this finding but the caloric intake of the mice receiving the thyroxine was 120 per cent that of the controls. Kreyberg (4) has observed a general tendency to earlier tumor formation in mice given dinitrocresol or dried thyroid, while others have reported a decrease in the growth of neoplasms in animals following thyroidectomy (7, 8). Several investigators (3, 4, 6, 9) have also noted that tumors grew more slowly in hypophysectomized animals, but the general consensus of opinion indicates that the effect on tumors was directly comparable to the general body growth. Most of this work was done without attempting to control the caloric intake so direct comparisons of various experiments cannot be made, and a repetition of some of these investigations with controlled caloric feedings is definitely indicated. Nevertheless, it appears probable that all procedures that have a considerable effect on the energy requirements of the animals also influence the growth of tumors.

**SUMMARY**

Albino mice were placed in a motor-driven rotating cage and subjected to certain periods of forced exercise for a period preceding and following inoculation with a transplantable fibrosarcoma. The rate of growth of the tumors was then compared to a control series with a transplantable fibrosarcoma. The rate of growth of tumors was affected by exercise and is summarized in Table I. The subsequent growth of tumors, however, was affected by exercise and is summarized in Table I. In series I the average tumor size of the controls at 4 weeks was 3.21 units (range 0.43 to 6.50 units) while that of the exercised groups was 2.42 units (range 0.20 to 6.20 units). In the second series there was likewise a slower growth rate in the rotated group at the 4th week: 2.33 units (range 0.09 to 6.81 units) for the controls as compared to the exercised group with an average of 1.53 units (range 0.03 to 3.74 units). The range of tumor size is presented to show that there was overlapping of results in each group, but it should be stressed that this was true only in a relatively few cases. Such overlapping of results might be explained by differences in food intake by individual mice within a group. It would be desirable, although impractical, to conduct an experiment of this type in individual cages in order to avoid differences in caloric intake among the mice. Nevertheless, the general trend of retardation in the rate of tumor growth is quite definite in the exercised groups and is in harmony with results that demonstrate tumor inhibition in mice on calorie restricted diets. This report is further proof of the caloric effect on tumor growth, but in addition it indicates that the influence can also be demonstrated by changing the caloric requirements of the mice while maintaining a constant dietary intake. The effect of altering the basal metabolic rate of animals, and its influence on tumor growth, have been studied by various investigators. Gilroy (2) reported that the administration of thyroxine to mice retarded cancer growth. Bischoff, Long, and Maxwell (1) did not confirm this finding but the caloric intake of the mice receiving the thyroxine was 120 per cent that of the controls. Kreyberg (4) has observed a general tendency to earlier tumor formation in mice given dinitrocresol or dried thyroid, while others have reported a decrease in the growth of neoplasms in animals following thyroidectomy (7, 8). Several investigators (3, 4, 6, 9) have also noted that tumors grew more slowly in hypophysectomized animals, but the general consensus of opinion indicates that the effect on tumors was directly comparable to the general body growth. Most of this work was done without attempting to control the caloric intake so direct comparisons of various experiments cannot be made, and a repetition of some of these investigations with controlled caloric feedings is definitely indicated. Nevertheless, it appears probable that all procedures that have a considerable effect on the energy requirements of the animals also influence the growth of tumors.
but not subjected to forced exercise. The exercised mice gained less weight and the rate of tumor growth was also less than that observed in the control series.

REFERENCES
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