EFFECT OF SUBCUTANEOUS INJECTION OF NORADRENALIN ON OXYGEN CONSUMPTION OF MUSCLES ADAPTED TO COLD AND PHYSICAL EXERTION

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Subcutaneous injection of noradrenalin into mice adapted to cold (− 15°) and to physical exertion caused a more marked increase in oxygen consumption than in control animals.

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Noradrenalin is formed in the body by rats acclimatized to cold in amounts 3-4 times greater than in control animals [9]. Depocas found that intravenous injection of noradrenalin stimulates the respiration of cold-acclimatized rats.

In control animals no reaction was found to noradrenalin [5, 6].

The object of the present investigation was to study the effect of subcutaneous injection of various doses of noradrenalin on the oxygen consumption in albino mice adapted to life under different conditions.

EXPERIMENTAL METHOD

Experiments were performed on 79 male albino mice. The mice of group 1 were adapted to a low temperature (− 15°) [1]. The animals of group 2 were subjected to physical training. The mice were placed in groups on the walls of a wire cage which was lowered into water. The water did not permit the mice to leave the vertical wire mesh, so that they moved along it or hung from it in a stationary position. Each period of training lasted 1.5 h and was repeated daily for 45-50 days. The mice of group 3 underwent neither acclimatization nor physical training and were used as controls.

The oxygen consumption of the animals per unit of body weight was measured [3]. Readings were taken every 10 min for 30 min. The mean oxygen consumption per gram body weight per hour was taken as 100. The animals were then injected with noradrenalin in doses of 0.5, 1.5, 5, and 10 μg/g body weight and the oxygen consumption was again determined until the animal's respiration had returned to normal.

The changes in oxygen consumption after injection of noradrenalin were measured every 10 min and expressed as percentages of the initial level. A mean graph was plotted for each group of experimental animals. The results for each experimental group were compared by measuring the areas outlined by the graph of the mean change in oxygen consumption with time until respiration returned to normal.

EXPERIMENTAL RESULTS AND DISCUSSION

In the control mice the oxygen consumption increased parallel to the increase in dose of noradrenalin. The reaction to the smallest dose was only 10 conventional units. Physiological saline caused the same reaction of respiration as the small dose of noradrenalin. With an increase in dose of noradrenalin, the intensity of oxygen consumption also increased. The largest dose of noradrenalin injected (10 μg/g) caused marked inhibition of respiration in 70% of the mice of this group. In the first 10 min after injection, the oxygen consumption fell by nearly half its normal value and remained at this level for about 1.5 h. The effect of this dose was 87 conventional units for most mice. In the other 30% of control mice, the oxygen

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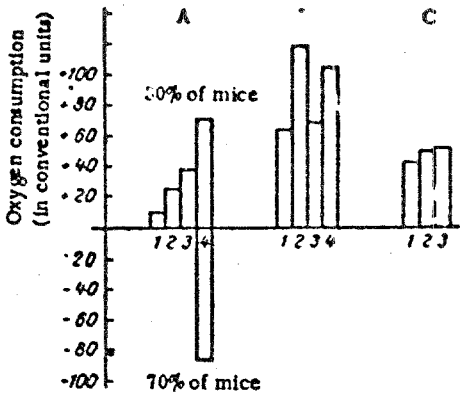

Fig. 1. Change in oxygen consumption in control (a), cold-acclimatized (b), and physically trained (c) albino mice after subcutaneous injection of noradrenalin in doses of 0.5 (1), 1.5 (2), 5 (3), and 10 (4) μg/kg. Horizontal line represents initial level of oxygen absorption.

consumption increased after injection of this dose of noradrenalin by 40-45% compared with normal. The increased oxygen consumption persisted in these animals for more than 1.5 h.

In cold-acclimatized mice the oxygen consumption after injection of all these doses of noradrenalin was much higher than in the control animals (see Fig. 1).

A dose of 10 μg/g sometimes caused death of both control and acclimatized mice. However, the control mice always died with a sharply reduced oxygen consumption, while the acclimatized mice died with a very high oxygen consumption.

During laboratory acclimatization of the mice to cold, 25-30% of the mice were able to tolerate a temperature of −15° for 10 h during the first stay in the refrigerator. The results of our experiments with noradrenalin show that approximately 30% of the control mice reacted to injection of noradrenalin just like the acclimatized mice. An additional series of experiments showed that the control mice with the greatest positive reaction of respiration to noradrenalin gave the highest survival rate at the low temperature. The extent of the increase in oxygen consumption after injection of noradrenalin was thus related to tolerance to cold. This conclusion was confirmed by our experiments on hamsters, in which the reaction of respiration to noradrenalin is very great and which are able to tolerate a temperature of −15° without special training.

Cooling and acclimatization to cold are associated with increased noradrenalin production by the body in warm-blooded animals [4, 7, 8, 9]. Noradrenalin stimulates glycogen breakdown, activates deamination and keto-acid formation, and increases the concentration of fatty acids in the blood [10]. The excess of fatty acids is oxidized by free oxidation. The decrease in the P/O ratio in the mitochondria of acclimatized pigeons [2] suggests that adaptation of warm-blooded animals to a low temperature is associated with an increased role of free oxidation. Apparently two parallel processes take place in the body during acclimatization: an increase in the amount of oxidation substrates entering the cell under the influence of noradrenalin and intensification of free oxidation, as measured by the amount of substrate oxidized or by the oxygen consumed in unit time. Adaptation of warm-blooded animals to cold (acclimatization), from the point of view of tissue respiration, may possibly be equivalent to an increase in the power of free oxidation in the mitochondria.

The reaction of respiration of the physically trained mice to the minimal dose of noradenalin tested was more than four times greater than the respiration reaction of the control mice and came closer to that of cold-acclimatized mice (Fig. 1). The reactions of the acclimatized and trained mice to medium doses of noradrenalin also were similar.

The work of V. P. Skulachev [2] demonstrated that survival of animals exposed to cold is dependent on their ability to dissociate oxidation and phosphorylation. In our experiments adaptation to severe cooling was accompanied by an increase in intensity of oxygen consumption under the influence of noradrenalin. In animals capable of tolerating severe cooling at once, without preliminary training, the reaction of respiration to noradrenalin was found to be increased. Comparison of these findings suggests that the increase of dissociation of oxidation and phosphorylation in Skulachev's experiments reflects an increase in the power of free oxidation, and that the response of the body to injection of noradrenalin may be used as a test of changes in this power. This method has the advantage that it can be used to determine changes in the power of the free oxidation system without the need for blocking phosphorylating oxidation.

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