"EXERCISE PYROGENS"

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UDC 612.532

Blood plasma taken from subjects either at rest or during muscular exercise was injected intravenously into rabbits. The rectal temperature of the animals changed differently: After injection of "exercise" plasma the temperature was at a higher level. This effect can be explained by the presence of "exercise pyrogens" in the plasma.

KEY WORDS: exercise hyperthermia; "exercise pyrogens."

Elevation of the body temperature during muscular work can be explained either by insufficiency of the mechanisms of heat loss or resetting of the centers to a higher level of temperature regulation. With regard to work of moderate intensity the second explanation is generally accepted. The level of exercise hyperthermia has been shown to be independent (within wide limits) of fluctuations in air temperature [6, 10-12, 14] and of the quantity of endogenous heat formed [7-9, 15], but it correlates with the relative intensity of oxygen consumption by the working subject [1, 13]. According to Nielsen [7-9], the trigger factor in the development of exercise hyperthermia is the appearance of certain pyrogen-like substances that are liberated into the blood stream proportionally to the intensity of aerobic processes taking place in the muscles. Similar suggestions have been made by other workers also [2, 4, 5]. However, no factual evidence has been adduced in support of the existence of such "exercise pyrogens."

The object of this investigation was to test this hypothesis experimentally. Blood plasma obtained from a person engaged in muscular work was injected into a rabbit and an attempt was made to discover the hyperthermic effect of such an injection.

EXPERIMENTAL METHODS

The subjects (healthy men aged 20-39 years) worked on a "Monarch" bicycle ergometer for 30 min. The intensity of exercise was chosen for each subject so that at the end of the test the heart rate was about 170 beats/min. During the last minute of work blood was taken by puncture from the cubital vein. Tubes containing blood (to which a drop of heparin had previously been added) were centrifuged and 10 ml of the resulting plasma was injected into the marginal vein of a rabbit's ear. The time from taking the blood to injecting the plasma was about 10 min.

The subjects' internal temperature was recorded three times: before the beginning of exercise, at its end (at the time of taking the blood), and in the recovery period (at the time of injection of the plasma). The rabbits' temperature was measured every minute: for 20 min before injection of the plasma and 40 min thereafter. A battery of copper–constantan thermocouples, housed in a flexible plastic catheter, was introduced into the subject through the nose and pharynx into the lower third of the esophagus. A similar catheter was introduced into the rectum of the rabbit to a depth of 8 cm. The sensitivity of thermometry was 0.01°C.

Altogether nine experiments were carried out in which the "exercise" plasma was injected into the rabbits and nine experiments in which plasma obtained from resting subjects (control) was injected. Since there are indications that the repeated injection of normal human plasma may cause the internal temperature of a rabbit to rise [3], each animal was used in only one experiment. The weight of the Chinchilla rabbits was about 3 kg.

The test tubes, needles, and syringes were sterilized before the experiment for several hours at 200°C.

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(Presented by Academician of the Academy of Medical Sciences of the USSR V. A. Negovskii.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 88, No. 8, pp. 144-145, August, 1979. Original article submitted July 5, 1978.

TABLE 1. Characteristics of Exertion and Temperature Changes in Subject (means ± SE)

Parameter	Value
Work load, $W \cdot kg^{-1}$	2.5 ± 0.3
Heart rate at end of work, beats/min	172 ± 3
Initial esophageal temperature, °C	37.21 ± 0.11
Deviation of esophageal temperature from initial level at end of work, °C	+1.25 ± 0.12
Deviation of esophageal temperature from initial level at time of injection of plasma into rabbit, °C	+0.51 ± 0.18

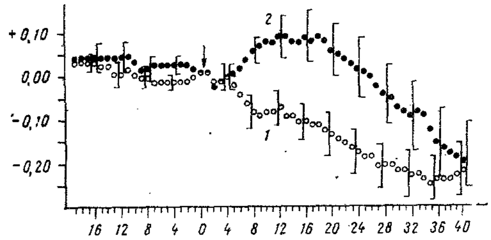

Fig. 1. Deviation of rectal temperature from initial level in rabbits after intravenous injection of blood plasma obtained from subject at rest (1) and during exertion (2). Abscissa, time before and after injection (in min); ordinate, deviation of rectal temperature (in °C) (means ± SE).

EXPERIMENTAL RESULTS

The concentration of hypothetical "exercise pyrogens" in the blood of the recipient rabbit must have been many times smaller than their concentration in the blood of the working subject. This will be clear from the following arguments. Table 1 shows that exercise for 30 min led to elevation of the subjects' esophageal temperature on average by 1.2°C. However, after the end of exercise it fell rapidly: After 10 min (at the time of injection of the plasma in the rabbits) the subjects' temperature was only 0.5°C higher than initially. The concentration of "exercise pyrogens" in the subjects' blood evidently should have changed to correspond to the temperature changes described above (although the level of "exercise pyrogens" in vitro would not necessarily decrease at the same rate as in vivo). Another, no less important fact was that the plasma injected (10 ml) was diluted about 20-fold in the blood of a rabbit weighing 3 kg. There were therefore no grounds for expecting a large increase in the internal temperature after injection of "exercise" plasma into the rabbits.

In fact, as Fig. 1 shows, the maximal rise of rectal temperature recorded 12-18 min after injection averaged only 0.08°C (this increase was not statistically significant compared with the initial level). The rectal temperature later began to fall, and by the 40th minute it was 0.20°C below the preinjection level ($P = 0.05$).

Meanwhile the rectal temperature began to fall in the control experiments during the first few minutes after injection of plasma obtained from resting subjects. After 30 min it was established at a level 0.22-0.25°C below the preinjection value ($P < 0.01$). The explanation of this hypothermic effect is unknown. It may be recalled that in Cooper's experiments [3], a similar effect was observed after intravenous injection of 2 ml normal human plasma into rabbits: The animals' rectal temperature fell on average by 0.2°C in the course of 40 min.

On the whole, as Fig. 1 shows, the character of the temperature curves differed in the groups compared. Between 8 and 30 min after injection the temperature of the rabbits receiving the "exercise" plasma was on average 0.15-0.20°C higher than the temperature of the control animals (the difference between 8 and 20 min was statistically significant; $P < 0.05$).

Although no definite hyperthermic effect was observed after injection of "exercise" plasma into the recipient animals, the result can hardly be interpreted as negative. The temperature curve of these animals was statistically significantly higher than that of the controls. The following alternative explanation can be suggested: Either during exercise, certain pyrogen-like substances appear in the blood plasma or exercise leads to disappearance from the plasma of a certain factor causing the temperature to fall in the control experiments. The second explanation, however, seems less likely because after injection of the "exercise" plasma and a 20-min delay the temperature curve fell and by the 40th minute it was at approximately the same level as in the control experiments. The results can therefore more easily be explained on the grounds that "exercise pyrogens" exist. Their chemical nature and mechanism of action require further study.

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INHIBITION OF CORTICOSTEROID PRODUCTION BY PINEAL FACTOR

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UDC 612.826.33.018.2: 612.453.018

The effect of a factor isolated from the bovine pineal gland on the blood corticosteroid level and on the ability of isolated adrenal tissue to synthesize these compounds was investigated in experiments on male Wistar rats. The method of obtaining the pineal fraction is described. Its injection in a dose of 2 mg/100 g body weight lowered the blood corticosteroid level by 74, 69, 40, 64, and 63% after 4, 5, 7, 9, and 12 days respectively. The ability of the adrenal tissue to synthesize corticosteroids was depressed. The results are evidence that the pineal gland participates in the regulation of adrenal function.

KEY WORDS: adrenal glands; steroid production; pineal factor.

Much attention has recently been paid to relations between the pineal gland and other endocrine structures. In particular, research aimed at discovering the role of the pineal gland in the regulation of adrenal function is very interesting. One of the first pieces of indirect evidence that these two glands may be closely inter-

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Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 88, No. 8, pp. 146-147, August, 1979. Original article submitted March 14, 1978.

0007-4888/79/8808-0834$07.50