

EXTRAADRENAL ACTION OF PITUITARY ADRENOCORTICOTROPIC HORMONE ON SKELETAL MUSCLE

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Intramuscular injection of ACTH (10 units/kg body weight) into normal and adrenalectomized rabbits lowers the body temperature and the oxygen tension and blood flow in the gastrocnemius muscle. Similar changes are observed also when ACTH is injected after hydrocortisone. These changes are attributed to the extraadrenal action of pituitary adrenocorticotrophic hormone.

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Most workers consider that the specific effect of ACTH is to stimulate adrenal cortical activity. However, some investigations have shown that ACTH depresses thyroid function [7], and manifests adipokinetic activity and other effects [1, 5, 9] in normal and adrenalectomized animals. Extraadrenal effects of this hormone, such as those producing ketosis, adipokinesis, hyperglycemia, and also an insulintropic action and stimulation of melanocytes have been demonstrated experimentally [2]. Other extraadrenal effects of this hormone on metabolism in the organs and tissues are also possible [2]. The object of the present investigation was to study the body temperature and the oxygen tension (pO_2) and blood flow in a skeletal muscle of normal and adrenalectomized rats after administration of ACTH. Skeletal muscle accounts for the greater part of the body mass and actively influences energy metabolism of the body as a whole. Nevertheless, the effect of ACTH on it has been studied extremely inadequately.

The temperature of organs and tissues can be used along with other indices to estimate the intensity and direction of metabolic processes [6].

EXPERIMENTAL METHOD

Experiments were carried out on rabbits. The temperature, pO_2 , and blood flow were measured in the gastrocnemius muscle of the animals [3, 4]. The temperature was measured by means of a copper-constantan thermocouple. The sensitivity of the apparatus was 0.02 deg./mm scale. The velocity of the blood flow was recorded by means of a Hensel's thermoprobe [8], and its changes were expressed in millimeters of the instrument scale. The value of pO_2 was determined polarographically, using a platinum cathode; changes in pO_2 were expressed as percentages of the initial level, subtracting the residual flow.

Three series of experiments were performed on 23 rabbits. In series I intact animals received an intramuscular injection of ACTH in a dose of 10 units/kg body weight. In series II the same dose of hormone was given 40 min after intramuscular injection of a hydrocortisone suspension in a dose of 15 mg/kg. In series III, ACTH was injected into adrenalectomized animals. Adrenalectomy was performed under ether anesthesia, bilaterally in one stage. The rabbits were used in the experiments on the 5th day after the operation.

EXPERIMENTAL RESULTS

For control purposes the rabbits received an intramuscular injection of 1 ml physiological saline at a temperature of 35-36°. This produced no definite changes in temperature, pO_2 , or blood flow of the muscle and of the rectal temperature.

Injection of ACTH into intact animals initially reduced the temperature, pO_2 , and velocity of blood flow in the muscle and the rectal temperature (Fig. 1). This change persisted for 3-4 h. In some experiments the decrease in these indices was followed by an increase. The maximal decrease in muscle temperature

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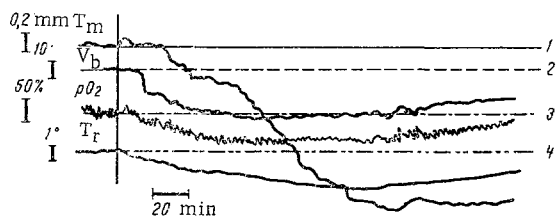


Fig. 1. Changes in temperature (T_m), oxygen tension (pO_2), and velocity of blood flow (V_b) in skeletal muscle and rectal temperature (T_r) of an intact rabbit after injection of ACTH. Vertical line denotes moment of injection of hormone; horizontal lines show initial temperature (1), initial blood flow velocity (2), pO_2 (3), and initial rectal temperature (4). Calibration scales: 0.2° for muscle temperature, 1° for rectal temperature, 50% for pO_2 , 10 mm for blood flow velocity (in mm of instrument scale); below: time marker 20 min.

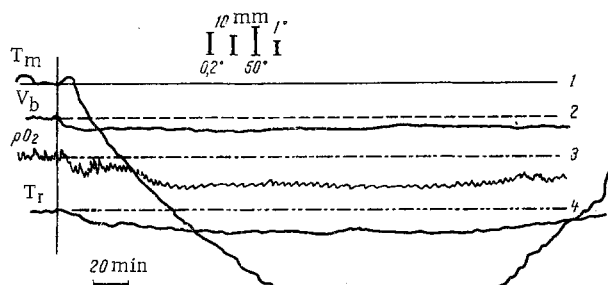


Fig. 2. Temperature, pO_2 , and velocity of blood flow in muscle and rectal temperature of an adrenalectomized rabbit after ACTH injection. Legend as in Fig. 1.

In the experiments of series III (on adrenalectomized rabbits, Fig. 2) the muscle temperature fell in 10 of the 11 animals after injection of ACTH by $2.56 \pm 0.36^\circ$ ($P < 0.001$) and the rectal temperature fell by $1 \pm 0.34^\circ$ ($P < 0.05$). The blood flow fell in nearly all experiments, and increased in only one experiment. The value of pO_2 fell by 52 ± 6.5 ($P < 0.001$). These results show that the muscle temperature in adrenalectomized rabbits fell after ACTH injection by $1.36 \pm 0.47^\circ$ more than in intact rabbits ($P < 0.05$).

It can be concluded from these investigations that ACTH, in a dose of 10 units/kg, lowers the temperature, pO_2 , and blood flow of the muscles and the rectal temperature in normal and adrenalectomized rabbits. The changes described can be attributed to the extraadrenal action of ACTH on skeletal muscle.

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was $1.2 \pm 0.2^\circ$ ($P < 0.001$), and in pO_2 , $41 \pm 8\%$ ($P < 0.001$). In some experiments the blood flow increased after injection of ACTH. It can be concluded from these results that ACTH, in a dose of 10 units/kg, lowers the temperature, pO_2 , and blood flow in the muscle of intact rabbits, and lowers the rectal temperature. These changes can be attributed, on the one hand, to the effect of ACTH on the adrenals and, hence, on the synthesis of glucocorticoids and to the effect of these substances on the muscle directly or via the central nervous system; on the other hand, it may be that the changes in the muscle are unconnected with adrenocortical activity. Extraadrenal effects of ACTH on other organs and tissues are unknown [1, 2, 7-9]. A study of the effect of this hormone on the circulation of internal organs has shown [9] that the blood flow in the ovaries of normal and adrenalectomized dogs and cats is increased after its administration.

A series of experiments was carried out in which ACTH was injected after hydrocortisone. The muscle temperature of the animals was increased by 0.2-0.4% 40 min after injection of hydrocortisone. The values of pO_2 , the blood flow in the muscle, and the rectal temperature changed variously: in some experiments they were increased, in others they were decreased. ACTH injected in a dose of 10 units/kg body weight after hydrocortisone lowered the muscle temperature by $1.1 \pm 0.125^\circ$ ($P < 0.001$), pO_2 by $61 \pm 8.8\%$ ($P < 0.001$), and the rectal temperature by $0.8 \pm 0.22^\circ$ ($P < 0.05$). These indices remained low for up to 4 h. In 2 experiments the blood flow was reduced for 40 min, and then increased.

The results of this series of experiments confirmed the extraadrenal action of ACTH on skeletal muscle.

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