CONTENT OF FREE NUCLEOTIDES IN MUSCLES OF ADRENALECTOMIZED RATS WITH COLD STRESS

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Energy metabolism was investigated in striated muscles of adrenalectomized rats exposed to cold (3°C) for 4 h. Cold stress was shown not to change the ATP level, but it led to a decrease in the creatine phosphate, glycogen, and inorganic phosphorus concentrations in the muscles. The decrease in inorganic phosphate could be evidence of increased phosphorylation in the glycolytic chain.

KEY WORDS: adrenalectomy; muscles; cold; adenine nucleotides.

The central role of the pituitary–adrenocortical system in adaptive reactions is not in dispute, for it ultimately determines the degree of adaptation of the living organism to the conditions of its existence. The pituitary and adrenal cortex also play an essential role in processes of heat metabolism. For instance, in Addison's disease or after adrenalectomy in animals, one symptom is a fall of the body temperature. Bilateral adrenalectomy lowers the resistance of animals to the action of high temperatures, whereas administration of glucocorticoids enhances it in intact and adrenalectomized animals [1].

Previous investigations by the present writer showed that ACTH administration causes phasic changes in the temperature of the muscles in both intact and adrenalectomized rabbits: An initial fall is followed by a rise, and in adrenalectomized animals the amount of the fall is twice as great as in control animals [3]. Although glucocorticoids have no thermogenic action in the classical meaning of the word, their action is clearly manifested under conditions requiring mobilization of adaptive processes. For instance, daily administration of hydrocortisone to adrenalectomized dogs increases maximal heat formation induced by exposure to cold by 20-28% [10].

In the investigation described below the effect of cold was studied on energy metabolism in striated muscles in adrenal insufficiency.

EXPERIMENTAL METHOD

Experiments were carried out on rats undergoing mock adrenalectomy and on adrenalectomized rats. Adrenalectomy was performed in one stage bilaterally under ether anesthesia. In the animals undergoing mock adrenalectomy the operation was the same except for removal of the adrenals. On the 8th day after the operation one control and one experimental animal simultaneously were placed in a refrigerator at 3°C for 4 h [9], after which they were decapitated, and the concentration of adenine nucleotides (ATP, ADP, AMP) in the gastrocnemius muscles, frozen in liquid nitrogen, was determined by electrophoresis on paper; creatine phosphate was determined as creatinine, inorganic phosphate by Delory's method, and glycogen by the anthrone method [4, 5]. The experimental results were subjected to statistical analysis.

EXPERIMENTAL RESULTS

The experiments showed the onset of muscle tremor in both the control and the adrenalectomized rats exposed to cold. Meanwhile in adrenalectomized animals the concentrations of adenine nucleotides (ATP, ADP, AMP, and total) were a little higher than in animals undergoing mock adrenalectomy – by 10.4, 40, 5, and 12% respectively (Table 1). However, only the

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TABLE 1. Concentration of Adenine Nucleotides (in μmoles/g tissue), Creatine Phosphate (in mg % creatinine), Inorganic Phosphate (in mg %), and Glycogen (in mg %) in Muscles of Adrenalectomized Rats Exposed to Cold Stress (M±m, n = 9)

Index	Control	Experiment
ATP	4,40±0,32	4,86±0,42
ADP	0,82±0,04	1,14±0,13*
AMP	0,59±0,06	0,62±0,06
ATP + ADP + AMP	5,83±0,37	6,62±0,46
Creatine phosphate	151,0±9,3	119,5±7,4*
Inorganic phosphate	58,8±4,5	48,2±1,4*
Glycogen	565,7±44,5	334,9±20,0*

*P<0.05.

ADP concentration was increased significantly. Meanwhile the creatine phosphate concentration was lowered by 20.8%, glycogen by 42.4%, and inorganic phosphate by 18% (Table 1).

Previous investigations at room temperature showed that the concentrations of the above-mentioned compounds changed differently in adrenalectomized rabbits. For instance, besides a very small increase in the concentrations of adenine nucleotides, the creatine phosphate and inorganic phosphate levels remained unchanged, and glycogen increased significantly [5]. Consequently, a combination of adrenalectomy with exposure to cold caused more substantial and detrimental changes in energy metabolism in the striated muscles: a decrease in the creatine phsophate, glycogen, and inorganic phosphate concentrations. Adrenalectomy can in fact lead to exhaustion of the carbohydrate depots during cooling [2].

It might be supposed that this tendency toward an increase in the levels of adenine nucleotides in the muscles of adrenalectomized rats was the result of increased ACTH production by the pituitary, attention to which has been drawn by many investigators [8]. After adrenalectomy combined with cold, the ACTH level in the body is even higher [9] and, consequently, the glycogen concentration in the muscles of such animals ought to be higher, for the high glycogen concentration in the muscles of adrenalectomized rabbits and rats is attributed to elevation of the ACTH level in the body [5]. However, the opposite picture was in fact observed in these investigations: a significant decrease in the concentrations of glycogen, creatine phosphate, and inorganic phosphate. The fall in these indices can be explained by the presence of cold shivering, the degree of muscular contraction during which can be compared to some degree with moderate muscular activity, a primary feature of which is a fall in the creatine phosphate and glycogen concentrations, so that there is no change in the ATP level. The fall in the inorganic phosphate concentration, with simultaneous decrease in the glycogen concentration and a tendency for the level of adenine nucleotides to rise are indeed evidence of increased phosphorylation during glycolysis. It may be that phosphorylation in the glycolytic chain is stimulated by the raised ACTH level. The basis for such a hypothesis could be previous investigations which showed that injection of ACTH into an animal 30 min before work, while not changing activity of the enzymes of the respiratory chain, increased the contractility of the muscles and reduced the breakdown of creatine phosphate and glycogen per unit work. The ATP level did not change under these circumstances [4]. These facts are also confirmed by microcalorimetric studies on the isolated frog sartorius muscle [6].

Meanwhile the lower level of glycogen and creatine phosphate in the muscles of adrenalectomized rats with cold stress may be connected with a decrease in the efficiency of utilization of high-energy compounds by the muscles during tremor, more especially because under the influence of cold, uncoupling of oxidation and phosphorylation takes place [7], and the principal supplier of ATP is evidently glycolytic phosphorylation. For instance, the writer's previous investigations showed that in adrenal insufficiency more creatine phosphate and glycogen is utilized and more heat is produced per unit work of the muscle than in animals undergoing mock adrenalectomy [5]. At the same time, these investigations show that adrenalectomy reduces the efficiency of adaptive reactions to cold. For instance, during cooling of animals unadapted to cold, with their adrenals intact, the content of high-energy phos-

phates in their muscles is significantly higher than normal [7]. In the present experiments no significant difference was found between the levels of ATP and other free nucleotides in the muscles of adrenalectomized animals kept at room temperature [5] and exposed to cold for 4 h. On the contrary, the creatine phosphate concentration was significantly reduced.

The results described above thus point to the active participation of the adrenals in the regulation of energy metabolism during adaptation to cold.

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CHANGES IN GLYCOGENOLYSIS IN THE ZONE OF ISCHEMIA IN EXPERIMENTAL MYOCARDIAL INFARCTION

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During the first minutes after occlusion of the coronary artery in dogs, increased glycogenolysis was detected, for which activation of phosphorylase, phosphofructokinase, triose phosphate isomerase, and lactate dehydrogenase was responsible; aldolase and glyceraldehyde-3-phosphate dehydrogenase reactions became the stages limiting the rate of glycogenolysis. Activation of glycogenolysis was evidently due to the combined action of hypoxia and catecholamines.

KEY WORDS: experimental myocardial infarction; glycogenolysis.

During the study of early changes in glycogenolysis in the heart in experimental myocardial infarction as a rule activity of enzymes isolated from the tissue under optimal conditions has been studied [6], although this could not reveal changes taking place *in vivo*. In some investigations [2, 8, 13] a more adequate method based on measurement of the concentration of metabolites present in the tissue *in vivo* has been used, although even in these studies cardiac arrest has been produced by the use of a cardioplegic solution [8], the aorta has been detached [2], or anoxia has been present [13].

The object of this investigation was to study the dynamics of changes in the concentration of all metabolites of glycogenolysis in the zone of ischemia in experimental myocardial infarction and to evaluate changes in the activity of the corresponding enzymes from the ratio between the acting masses [11], in the zone of ischemia in experimental myocardial infarction.

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