EFFECT OF COCARBOXYLASE ON SOME INDICES OF LYMPHOCYTE METABOLISM IN NEWBORN RATS WITH EXPERIMENTAL ASPHYXIA

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Subcutaneous injection of cocarboxylase (6-50 mg/kg) into newborn rats during the first six days of life increases the tolerance of the animal to subsequent asphyxia and prevents the increase in acid phosphatase and α-glycerophosphate dehydrogenase activity in the blood lymphocytes.

One of the causes of the lowered resistance of the body to infection in acute hypoxia is the suppression of antibody formation in the lymphoid tissue [3].

The object of the investigation described below was to study lymphocyte metabolism in rats exposed to hypoxia and the possibility of restoring it to normal by injections of cocarboxylase.

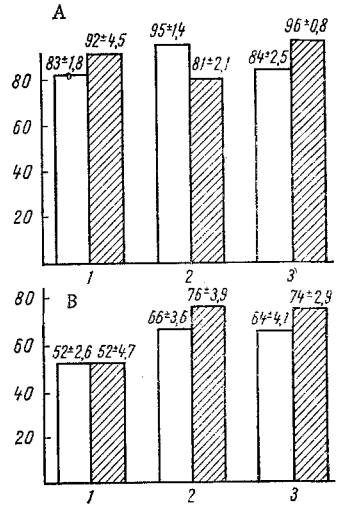

Fig. 1. Content of phosphatase-positive cells (in %) in impressions from paratracheal lymph glands (A) and spleen (B) in young rats not receiving (1) and receiving cocarboxylase in a dose of 2 (2) or 6-12 mg/kg (3). Unshaded columns represent rats not exposed to asphyxia; shaded columns represent rats exposed to asphyxia for 2.5 min.

EXPERIMENTAL METHOD

The activity of enzymes with different intracellular localization and type of action in the lymphocytes was investigated. As marker of the lysosomes and of catabolism, the hydrolytic enzyme acid phosphatase (AP) was chosen and its activity was determined in the blood lymphocytes and in impressions taken from the spleen and paratracheal lymph glands by the method of Goldberg and Barka. The intensity of anabolic processes in the lymphocytes was estimated by determining the index of activity of mitochondrial α-glycerophosphatase dehydrogenase (α-GPD) by Nartsissov's method [5]. At the same time the number of lymphocytes in 1 mm^3 blood was counted.

In experiments on 56 newborn albino rats the survival rate was studied during exposure to asphyxia for 10 min when cocarboxylase was injected subcutaneously for six days in doses of 2, 6, and 50 mg/kg daily. Animals receiving injections of 0.5 ml physiological saline acted as the controls. Asphyxia was induced by immersing the rat's head in water at 37°C.

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TABLE 1. Effect of Injection of Cocarboxylase on Number and Metabolism of Lymphocytes in Newborn Rats Exposed to Asphyxia

Group of animals	Number of lymphocytes (in thousands/mm³ blood)				Activity of								
					acid phosphatase (in thousands of phosphatase-positive lymphocytes/mm³ blood)				α-glycerophosphate dehydrogenase (in conventional units)				
	n	M	± m	P	n	M	± m	P	n	M	± m	P
Intact	13	4,9	0,25		13	3,2	0,3	—	10	152	12,3	—
Asphyxia												
2,5 min	19	7,5	0,6	<0,001	15	6,0	1,1	<0,025	19	231	7,4	<0,001
12,5 »	15	4,8	0,4	>0,05	15	3,2	0,4	>0,05	15	116	8,7	
Asphyxia 2,5 min + cocarboxylase (in mg/kg)												
2	11	6,1	0,4	<0,025	11	3,0	0,3	>0,05	11	91	11,7	<0,002
» 6	13	5,6	0,2	<<0,05	13	2,9	0,2	>>0,05	13	75	5,0	<<0,001
» 12	11	5,7	0,3	>0,05	12	3,3	0,2	>>0,05	9	95	8,8	<<0,002
» 50	10	5,2	0,4	>0,05	10	2,9	0,3	>>0,05	13	75	5,3	<<0,001
Intact + cocarboxylase (in mg/kg)												
2	7	8,4	0,9	<0,002	7	4,9	0,6	<0,025	7	91	6,0	<0,001
» 6—50	18	5,2	0,3	>0,05	18	2,5	0,2	<0,1	24	101	6,2	<<0,001

Legend: n) Number of tests; P) significance of difference compared with index in intact rats.

EXPERIMENTAL RESULTS

The young rats tolerated asphyxia lasting 2.5 min relatively easily. All animals not receiving cocarboxylase or receiving the compound in small doses (2 mg/kg) died from asphyxia lasting 10 min. An increase in the daily dose by three times (to 6 mg/kg) led to the survival of all the young rats exposed to the action of hypoxia. A large increase in the dose of the compound (up to 50 mg/kg) gave a smaller effect: only six of the 14 rats (43%) survived.

Injection of cocarboxylase into healthy young rats caused definite changes in the metabolism of the lymphocytes, and these persisted during subsequent brief asphyxia. These changes consisted of a decrease in α-GPD and AP activity, while severe asphyxia led to a decrease in the α-GPD level and to absence of the rise in AP activity (Table 1).

Simultaneous activation of the enzymes of catabolism (AP) and anabolism (α-GPD) in mild asphyxia as well as the lymphocytosis in the blood and the increase in mitotic activity in the lymph glands (an increase in the number of phosphatase-positive cells in them) were evidence of increased functional activity of the lymphocytes and of the lymphoid tissue. High activity of acid hydrolases (AP) and oxido-reductases has been observed during processes accompanied by a definite increase in the intensity of structural processes in the lymphoid tissue; during immunogenesis in vivo and during the blast-transformation reaction in vitro [4, 6-9].

The increase in functional activity of the lymphocytes during mild asphyxia is probably due not only to an increase in the number of immature lymphocytes in the blood, but also to the presence of hormonal stress, accompanied, in particular, by an increase in the noradrenalin concentration in the blood and tissues. Catecholamines, however, can be direct activators of cell metabolism; for example, they can stimulate activity of the mitochondrial enzyme succinate dehydrogenase [1, 2].

Injection of cocarboxylase probably intensifies the lymphocytopoiesis even more, as is shown during mild asphyxia by, not only the lymphocytosis in the blood, but also an increase in the total number of lymphoid cells in the spleen (compared with rats in the number of phosphate-positive cells (Fig. 1). Meanwhile, cocarboxylase, even in small doses, probably has a stabilizing action on the lysosome membranes, which could account for the absence of an increase in AP activity during asphyxia.

Inhibition of α-GPD activity following injection of cocarboxylase indicates inhibition of glycolysis, which is coupled with respiration by this enzyme. Under the influence of cocarboxylase, the system of

oxidative phosphorylation, which is more productive of energy, is intensified in the mitochondria, as a result of which the energy potential of the cell is increased and, consequently, so also is the survival rate of the animals in asphyxia.

In severe asphyxia the decrease in the α-GPD level is probably due, not to inhibition of glycolysis, but to its uncoupling from respiratory phosphorylation in the mitochondria, and the products of glycolysis in the hyaloplasm cannot be oxidized by the mitochondrial enzymes, even if their activity is high.

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