

# METABOLIC CHANGES IN THE LYMPHOCYTES OF NEWBORN RATS IN ASPHYXIA

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Hydrocortisone and cocarboxylase injected into newborn rats increased their chances of survival after asphyxia. Asphyxia was accompanied by increased succinate and dihydroorotate dehydrogenase activity in the lymphocytes, by lymphocytosis, and by an increase in the number of monocytes with hyperbasophilia of their cytoplasm in the blood and tissues. Hydrocortisone and cocarboxylase had a normalizing effect on these changes.

KEY WORDS: asphyxia neonatorum; lymphocytes.

Ways of increasing the resistance of cells of the newborn organism to hypoxia are a problem of urgent importance.

## EXPERIMENTAL

The survival rate of 103 young rats aged 6 days after asphyxia for 10 min, either untreated or receiving injections of cocarboxylase (2, 6, and 50  $\mu\text{g/kg}$  daily for 5 days) or hydrocortisone (5 mg/kg once or daily for 5 days) was investigated. The body weight and weight of the adrenals also were determined in these animals.

In other experiments the state of the energy metabolism in the blood lymphocytes was assessed from the succinate dehydrogenase (SD) activity. Changes in protein metabolism and immunologic processes were estimated from the numbers of monocytes with hyperbasophilia of their cytoplasm (indicating increased RNA synthesis [2]) in the blood and organs, from the lymphocyte count in the spleen, and the dihydroorotate dehydrogenase (DD) activity in the blood lymphocytes. DD and SD activity in the lymphocytes was investigated by a quantitative cytochemical method [1]; cytological analysis was carried out on squash preparations from lung and spleen tissue and on peripheral blood films.

All these tests were carried out on young rats aged 1 week and, sometimes, 2 weeks, subdivided into the following groups: 1) intact; 2) rats receiving cocarboxylase (12 mg/kg daily) for 5 days before testing; 3) exposed to asphyxia for 2.5 and 12.5 min on the day of testing; 4) the same, but after a 5-day course of cocarboxylase; 5) exposed to asphyxia (8 min) neonatally; 6) the same, after injection of 2.5 mg hydrocortisone. Asphyxia was produced by immersing the animal's head in water at 37°C.

## RESULTS

A single injection of hydrocortisone led to increased survival of the rats after asphyxia; a 5-day course of injections of the hormone gave a similar effect (Fig. 1), accompanied by marked slowing of the gain in body weight and weight of the adrenals ( $P < 0.001$ ). The survival rate after asphyxia in animals receiving preliminary injections of cocarboxylase depended on the dose of the substance. Increased survival ( $P < 0.05$ ) was observed after administration of 6 mg/kg. Doses of 2 and 50 mg/kg had no effect. A course of cocarboxylase injections did not affect the gain in weight of the rats, whether intact or exposed to asphyxia.

In the intact rats (Table 1) SD activity in the lymphocytes was unchanged between the first and second weeks of life, but DD activity increased ( $P < 0.05$ ). Injections of cocarboxylase increased the SD activity ( $P < 0.05$ ) but did not affect the DD activity in these cells.

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TABLE 1. Succinate and Dihydroorotate Dehydrogenase Activity in Lymphocytes of Young Rats

Group of animals	Enzyme activity (in formazan granules per 50 lymphocytes)			
	succinate dehydrogenase		dihydroorotate dehydrogenase	
	n	M±m	n	M±m
Intact aged:				
1 week	28	99,1±15,8	22	22,0±1,9
2 weeks	17	93,0±28,0	15	34,9±5,5
Intact aged 1 week, receiving preliminary cocarboxylase	17	187,0±45,4	13	21,9±2,7
Exposed to asphyxia at the age of one week for:				
2.5 min	14	161,1±9,9	14	46,0±8,2
12.5 min	15	264,5±39,6	12	27,0±3,1
The same, but receiving cocarboxylase:				
2.5 min	19	104,6±13,0	14	29,0±1,9
12.5 min	15	142,5±3,2	11	30,0±4,1
Exposed to asphyxia neonatally (8 min), investigated at the age of:				
1 week	11	207,5±4,1	12	38,7±7,7
2 weeks	5	150,0±45,1	5	62,2±14,1
Ditto, after injection of hydrocortisone, investigated at the age of 1 week	9	74,0±18,6	7	64,1±14,5

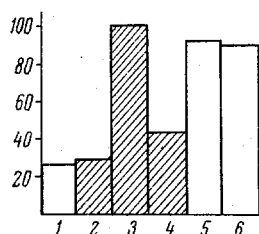


Fig. 1. Survival rate of rats aged 1 week after asphyxia for 10 min: 1) control; 2, 3, 4) preliminary injection of cocarboxylase in doses of 2, 6, and 50 mg/kg body weight daily for 6 days; 5) a single injection of hydrocortisone (5 mg/kg); 6) the same daily for 6 days. Ordinate, survival rate of animals (in %).

Asphyxia led to increased SD activity ( $P < 0.001$ ) and the effect increased with an increase in the duration of asphyxia. The DD level, on the other hand, rose only during brief asphyxia ( $P < 0.01$ ) simultaneously with an increase in the number of lymphocytes in  $1 \text{ mm}^3$  blood. During brief asphyxia the number of immunocompetent monocytes with hyperbasophilia of their cytoplasm in the blood and organs also increased appreciably. The relative number of small lymphocytes in the spleen fell sharply only during prolonged asphyxia and was not restored even 5 days later, when the blood showed lymphocytopenia and increased activity of the two enzymes in the lymphocytes. Asphyxia after a course of injections of cocarboxylase (12 mg/kg per injection) did not induce lymphocytosis in the blood and it prevented or considerably lessened the increase in the enzyme activity in the lymphocytes. Injection of hydrocortisone into newborn rats before prolonged (8 min) asphyxia also prevented the increase in SD activity in the cells usually taking place after one week. Meanwhile the DD activity in the lymphocytes remained high.

In stress, reduction of the lymphoid tissue is observed and may be reflected in the state of the immunological mechanisms of the body. The results of these experiments show that reparative processes in the cells of the lymphoid tissue are stimulated only by brief asphyxia, whereas in prolonged asphyxia these processes are delayed in surviving animals. This may evidently account for the prolonged hypoproduction of small lymphocytes — cells responsible for immunogenesis.

The lympholytic action of corticosteroids, responsible for the mobilization of protein products in stress, could be one cause of the activation of certain processes in protein and energy metabolism in intact lymphocytes. Characteristically, the chances of survival of animals after asphyxia were increased by preliminary injection of hydrocortisone. "Pharmacological adrenalectomy" by means of a massive dose of hydrocortisone, on the other hand, prevented the increase in SD activity usually taking place in the lymphocytes even a week after asphyxia.

An increase in SD activity in the lymphocytes was observed after injection of cocarboxylase into intact rats. Presumably the cocarboxylase, by ensuring a more economical energy metabolism of the cells during subsequent asphyxia, thereby contributes to the increased survival rate of the animal.

#### LITERATURE CITED

1. R. P. Nartsissov, Arkh. Anat., No. 5, 85 (1969).
2. H. Czitober, M. Gollerkeri, and W. Dameshek, in: Proceedings of the 8th Congress of the European Society of Haematology, New York (1962).