CHARACTERISTICS OF GROWTH AND HEMATOPOIESIS IN EARLY POSTNATAL DEVELOPMENT OF RATS EXPOSED PERIODICALLY TO COLD

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Erythropoiesis was observed to develop earlier in month-old rats which had developed during periodic exposure to cold than in control animals. This was reflected in a shorter period of physiological anemia. The circulating blood volume of the experimental animals was greater at all times of the investigation. As a result of the improvement to the blood supply of the organs and tissues, growth and development of the experimental rats were accelerated and the resting energy expenditure was more economic than in control rats of the same age.
KEY WORDS: *postnatal development; exposure to cold; growth; hematopoiesis; acceleration.*

In early postnatal development before antigravity reflexes take effect, the skeletal muscles are responsible for temperature regulation; during this period, the most adequate form of stimulation of the skeletal muscles is therefore an ambient temperature lower than that of the indifferent zone [1, 2, 5, 8]. It was therefore decided to study growth and hematopoiesis in early postnatal development of young rats exposed periodically to optimal degrees of cold.

EXPERIMENTAL METHOD

Experiments were carried out on 275 noninbred young albino rats (175 in the control and 100 in the experimental groups). Eight rats were left in each litter after the first day of life. The control animals were taken from the same litters as the experimental. From the 5th through the 30th days of life the experimental rats were exposed daily to short periods of cold, increasing in intensity and duration with age. The rats were placed in a cold chamber with an air temperature of 10-13°C on the 1st day and between − 4 and − 5°C starting with the 25th day of the experiment. In the course of cooling the body temperature was recorded and cooling was stopped if the temperature fell by 0.5-1°C. The first exposures lasted 30-60 sec and subsequent exposures 15-20 min. The erythrocyte and reticulocyte counts in 1 mm^3 blood, hemoglobin concentration, and hematocrite index were determined and the myelogram counted by the usual methods in rats aged 1-3 h and 1, 5, 7, 14, 21, and 30 days. The circulating blood volume (CBV) and its components were determined by the hemoglobin extraction method [7, 10] as used for the investigation of small objects. The body weight and the weight of some internal organs, the pulse rate (PR), and the oxygen consumption at rest were determined.

TABLE 1. Weight of Organs and Muscle Mass (in % of body weight) of Experimental and Control Rats Aged 30 Days (M ± m)

Organ studied	Experimental animals	Control animals	P
Total muscle mass	35,0±1,7	29,8±1,6	<0,05
Heart	0,67±0,012	0,53±0,021	<0,05
Adrenals	0,061±0,005	0,037±0,0031	<0,001
Thymus	0,66±0,032	0,36±0,04	<0,01
Spleen	0,79±0,11	0,34±0,07	<0,01

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TABLE 2. Body Weight, Resting Oxygen Consumption, Pulse Rate, and Red Blood Indices in Experimental (E) and Control (C) Rats

Experimental (E) or control (C) groups	Age (in days)	Weight (in g)	Resting oxygen consumption (in ml/kg/min)	PR	Red blood cells (in millions/mm³)	Hemoglobin (in g %)	Hematocrit index	Reticulocyte count (in ‰)	Total hemoglobin (in g/100 g body weight)	CBV: in ml/100 mg body weight	CBV: in ml
C	1—3 h	5,78±0,12	—	—	3,205±0,11	12,2±0,1	35±1,8	875±14	1,627±0,03	10,47±0,11	0,616±0,012
E	1	6,03±0,21	—	—	3,14±0,26	12,35±0,17	37±1,6	803,6±16,2	1,55±0,05	10,07±0,15	0,607±0,014
C	5	10,64±0,23	—	—	2,695±0,18	8,79±0,08	28,44±1,45	380,9±13,8	1,04±0,02	9,418±0,10	1,011±0,022
E	5	15,04±0,28	—	—	2,43±0,12	8,6±0,09	26,26±1,4	260,3±7,2	0,97±0,02	9,08±0,073	1,365±0,014
C	9	16,42±0,43*	—	—	2,85±0,10*	8,7±0,12*	26,8±0,78*	320,3±11,7	1,006±0,06*	9,886±0,13	1,52±0,037*
E	14	22,48±0,45	85,9±2,4	—	2,365±0,12	8,74±0,07	25,82±0,85	126,7±3,8	0,86±0,01	7,895±0,08	1,799±0,032
C		29,71±0,67	60,3±2,0	—	3,53±0,20	9,38±0,10	27,2±0,5*	157,8±5,4	1,01±0,02	8,58±0,09	2,559±0,057
E	21	32,83±0,68	63,5±1,5	463,7±2,8	3,59±0,1	7,9±0,13	25,88±0,6	87,8±2,7	0,69±0,02	7,06±0,06	2,318±0,071
C		36,4±0,40	49,2±2,5	427,3±3,7	4,98±0,07	9,98±0,07	30,6±0,7	86,1±3,1*	0,98±0,03	7,83±0,11	3,007±0,087
E	30	51,5±0,35	52,2±1,3	453,1±2,5	4,95±0,15	9,15±0,07	32,75±0,6	60,3±2,5	0,717±0,05	6,44±0,061	3,31±0,03
C		67,6±0,61	41,8±0,95	414,6±3,8	6,51±0,10	13,05±0,14	38,91±0,6	43,2±4,3	1,13±0,05	6,95±0,044	4,698±0,09

Legend. Difference between values for control and experimental groups given are significant in all cases ($P < 0.05$) except where marked by an asterisk, when $P > 0.05$.

EXPERIMENTAL RESULTS AND DISCUSSION

The experimental results are given in Tables 1 and 2. The young rats responded to a fall of ambient temperature by adaptive thermoregulatory reflex movements, by means of which they were able to maintain homoiothermia. This motor response, which lengthened with age, determined the duration of exposures to cold. After three exposures to cold, the number of lymphocytes in the bone marrow of the experimental rats was increased and the number of granulocytes reduced as the result of discharge of mature forms into the blood stream. On the 9th day of the experiment marked activation of erythropoiesis was observed, and subsequently the composition of the bone marrow returned to normal. A similar dynamic of the changes was recorded in the bone marrow of rats exposed to various types of stress [6]. Evidence of the stress character of exposure to cold was given by an increase of the relative weight of the adrenals of the experimental animals compared with the controls (Table 1).

However, the stress did not go beyond the physiologically adaptive level for that age, as manifested in particular by the increase in weight of the thymus. The explanation of this phenomenon could be the growth-stimulating role of the thymus in the early stages of development [11]. Observations in the writer's laboratory show that the response of physiological stress in the developing organism is characterized by excessive anabolic processes and not by exhaustion [2, 3]. The weight of the experimental animals toward the age of 30 days was much greater than that of the controls (Table 1). The growth constant as defined by Shmal'gauzen was 0.75 in the experimental animals from the 1st to the 30th day of life, but only 0.64 in the controls. This increase in weight was due to an increase in the total muscle mass. Accelerated development led to the earlier appearance of economy of energy expenditure of the experimental animals in the resting state, as reflected in lower specific values of oxygen consumption and pulse rate than in the controls. The lower pulse rate in the experimental rats was associated with a higher relative weight of the heart. These distinguishing features of the physiology of the developing experimental rats correlated with the features of development of the erythron. Rats are born with a low red cell count (Table 2). During the next 2 weeks their red cell count fell still lower, but starting with the 3rd week it rose, to reach a maximum by the 6th week (7.15 ± 0.10 millions). The dynamics of the changes in the hemoglobin concentration and hematocrit index were basically the same as for the erythrocytes. The reticulocyte count fell from 87.51% in the newborn rats to 6.03% in rats aged 4 weeks. The state of "anemia" in the early postnatal period is a physiological phenomenon. A full analysis of this problem is given in a paper by Arshavskii [4]. The dynamics of changes in the red blood indices of the experimental rats indicate activation and acceleration of erythropoiesis under the

influence of exposures to cold (Table 2). The duration of the period of physiological anemia in these animals was shortened and the increase in the red cell count, hemoglobin concentration, and hematocrit index took place considerably faster. Changes in the reticulocyte count in the blood were rather different in character. Activation of hematopoiesis led to the discharge of reticulocytes from the bone marrow into the blood stream and, for that reason, their number in the blood of the experimental animals before the 14th day was greater than in the controls. However, it then began to fall, so that on the 30th day the blood reticulocyte count was 4.32%, the same as in the adult. The system of regulation in the experimental rats also developed earlier than in the controls. For instance, by the age of 30 days the relative weight of the spleen in the experimental rats was more than twice as high as in the controls, suggesting the existence of a depot function of the organ and inhibition of erythropoietin [9]. The CBV per 100 g body weight was maximal in newborn rats and it fell steadily after birth. Changes in CBV at this time were proportional to age and body weight. In the experimental animals CBV was significantly greater than in the controls at all times of the investigation; the difference remained fairly constant, namely 0.5-0.8 ml/100 g body weight. All these changes in the red blood are aimed at improving oxygen transport to the tissues.

It can be concluded from these results that in early postnatal development adequate exposures to cold, by increasing skeletal muscular activity, lead to stimulation of growth and development of the experimental animals compared with the controls and, in particular, they bring about a substantial change in hematopoietic function.

LITERATURE CITED

1. I. A. Arshavskii, Outlines of Age Physiology [in Russian], Moscow (1967).
2. I. A. Arshavskii, Uspekhi Fiziol. Nauk, No. 4, 100 (1971).
3. I. A. Arshavskii, in: Leading Factors in Ontogeny [in Russian], Kiev (1972), p. 232.
4. I. A. Arshavskii, in: Biophysics, Physiology, and Pathology of the Erythron [in Russian], Krasnoyarsk (1974), p. 16.
5. T. A. Bal'magiya and É. Z. Rabinovich, in: Evolution of Functions in Ontogeny [in Russian], Leningrad (1972), p. 93.
6. Yu. I. Zimin, Byull. Éksperim. Biol. i Med., No. 7, 19 (1969).
7. L. I. Irzhak, The Respiratory Function of the Blood in Individual Development of Mammals [in Russian], Moscow–Leningrad (1964).
8. V. P. Prazdnikov, Fiziol. Zh. SSSR, No. 7, 858 (1968).
9. V. I. Filimonov, "Investigation of the mechanism of humoral regulation of erythropoiesis in ontogeny and the role of the spleen in this process," Author's Abstract of Doctoral Dissertation, Novosibirsk (1974).
10. H. A. Salhanick, L. M. Neal, and J. P. Mahoney, J. Clin. Endocrinol., 16, 1120 (1956).
11. I. Toro, Folia Biol. (Prague), 6, 154 (1960).