DYNAMICS OF SOME PARAMETERS OF THE ENDOCRINE AND LYMPHATIC SYSTEMS IN RATS DURING COLD ADAPTATION

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The response of the organism to strong stress is accompanied by involution of lymphoid tissue [6]. These hormonally dependent changes are the result of activation of lymphocyte migration from organs of the lymphatic system and circulation into the peripheral tissues [2]. It has been suggested that the physiological significance of mobilization of lymphoid cells in stress is activation not so much of their immune as of their trophic function, increasing the nonspecific resistance of the organism. These views, incidentally, are based on results obtained during the study of the acute period of stress or its immediate sequelae.

The aim of this investigation was to study combined behavior of the endocrine and lymphatic systems in rats at stages of long-term adaptation of the animals to moderate cold.

EXPERIMENTAL METHOD

Experiments were carried out in the winter and spring on mature male Wistar rats. During the experiments the animals were kept in single cages at a temperature of 4-5°C for 1-50 days. Control animals were kept in the animal house at a temperature of 20-22°C. The animals were decapitated at 10-11 a.m. The corticosterone concentration in the blood plasma was determined by saturation analysis [1] and serum levels of thyroxine (T_4) and triiodothyronine (T_3) were determined by radioimmunoassay, using IMMOPHASE TM T_4 and IMMOPHASE TM T_3 kits (from Corning, USA). The thymus was weighed on torsion scales. The structure of the popliteal lymph nodes (LN) was studied in histological sections stained with hematoxylin and eosin and with azure II-eosin. Morphometry of the structural components of LN was undertaken and the numbers of the various cell forms per 1000 cells were counted in different zones of LN.

EXPERIMENTAL RESULTS

The investigation showed a significant increase in resistance of rats of the experimental group to cold, detectable after the animals had been kept for 5-7 weeks at 4-5°C: the survival rate at −15°C was 4.9 ± 0.5 h in the control and 12.2 ± 1.3 h in the experiment ($P < 0.001$).

Keeping the animals in the cold caused fluctuating changes in adrenal function. In the first 2 days the plasma corticosterone concentration was significantly raised (Table 1). On the 3rd-4th day, despite continued exposure to cold, the hormone concentrations returned to their initial levels. A new and brief rise was recorded on the 7th day of the experiment. After 16 days the plasma corticosterone level was still high and remained so until the end of observation.

Activation of thyroid function is an essential component of the temperature regulating reaction [7]. In the present experiments a significant increase in the T_4 and T_3 concentrations was found in the early stage of adaptation (Table 1). The rise in the T_3 level was greater. Toward the end of the first week, signs of hypersecretion of thyroid hormones were disappearing. The T_4 level fell significantly below its initial value, but the T_3/T_4 ratio increased, evidence of an increase in deiodination of T_4 in peripheral tissues, increased formation of the biologically more active hormone T_3, and a corresponding increase in the specific action of the thyroid hormones [5].

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TABLE 1. Blood Hormone Concentrations of Animals During Exposure to Cold (M ± m)

Experimental conditions	Corticosterone, μg/100 ml	T_4, mg/ml	T_3, mg/ml	T_3/T_4
1. Control	8,8±0,7 (37)	65,2±2,7 (64)	1,05±0,02 (60)	0,016
2. Cold 1 day	23,2±0,8 (42)	70,2±5,6 (32)	1,65±0,09 (33)	0,024
3. » 2 days	16,4±1,7 (3)	78,0±4,1 (3)	1,54±0,22 (3)	0,020
4. » 3 "	13,6±4,8 (4)	69,0±13,7 (3)	1,20±0,20 (3)	0,017
5. » 4 "	10,5±3,4 (3)	67,3±11,0 (3)	1,39±0,12 (3)	0,021
6. « 7 "	19,4±3,7 (9)	46,4±4,1 (6)	1,17±0,05 (6)	0,025
7. « 10-14 "	13,8±1,7 (8)	54,0±6,8 (4)	1,03±0,05 (3)	0,019
8. « 16 "	20,2±4,1 (4)	49,6±9,3 (3)	0,97±0,34 (3)	0,020
9. « 33 "	22,8±5,2 (4)	56,3±5,8 (4)	1,12±0,18 (4)	0,020
10. « 50 "	18,4±0,4 (76)	43,8±4,7 (35)	1,00±0,07 (30)	0,023
	$P_{1-6,7,8,9}<0,05$	$P_{1-3}<0,05$	$P_{1-3,5}<0,05$	
	$P_{1-3}<0,01$	$P_{1-6}<0,01$	$P_{1-2}<0,001$	
	$P_{2-3}<0,05$			
	$P_{1-2,10}<0,001$	$P_{1-10}<0,001$		

Legend. Number of measurements given in parentheses.

The reaction of organs of the lymphatic system to cold also was phasic in character. The relative weight of the thymus characteristically fell in the early phase of adaptation: on the 7th day of the experiment its relative weight was 81.9 ± 5.1 mg/100 g body weight (102.0 ± 1.6 mg/100 g in the control; $P < 0.01$), and on the 16th day it was 73.7 ± 7.3 mg/100 g ($P < 0.01$). On the 33rd and 49th days of the experiment the relative weight of the thymus was becoming restored, at 113.3 ± 12.2 and 97.6 ± 2.8 mg/100 g, respectively.

In the popliteal LN in the first 4 days destructive changes were observed in the lymphoid tissue, corresponding to the classical picture of acute stress [3]. In the cortical tissue lymphocytolysis, destruction of lymphoid tissue, an increase in the number of macrophages with Flemming's bodies, and a decrease in the number of mitoses were observed.

During the 2nd and 3rd weeks of the experiment distinct signs of compensation of the destructive changes in the lymphoid tissue appeared. Compensation took place on account of proliferation of cells with different specializations. The most characteristic feature of this phase was an increase in the number of mitotically dividing cells and of blast forms. These changes took place in all functional zones of LN, but they were most distinct in follicles with pale centers and medullary cords. In the pale centers on the 16th day of the experiment the percentage of blast cells was 25.7 ± 0.95 (11.96 ± 0.85 in the control; $P < 0.01$), and the percentage of mitoses was 5.55 ± 0.53 (2.17 ± 0.32 in the control; $P < 0.01$). In the medullary cords on the 16th day of the experiment the percentage of blast cells was 7.5 ± 1.96 (4.1 ± 0.68 in the control) and the percentage of mitoses was 1.98 ± 0.14 (0.37 ± 0.06 in the control; $P < 0.001$).

During the 4th-5th weeks morphological and functional restoration of LN was complete. The lymph nodes became more compact and a tendency for the area of the paracortical zone to enlarge appeared. In all zones of LN a shift was observed toward mature cell forms. In the pale centers the percentage of blast cells was close to the control level, but the percentage of medium-sized lymphocytes was significantly increased (23.25 ± 0.14 compared with 19.03 ± 1.12 in the control; $P < 0.01$). In the medullary cords the percentage of mature plasma cells was increased to 44.75 ± 6.44 compared with the control (27.17 ± 5.06; $P < 0.05$); the proportion of small lymphocytes also was increased (34.33 ± 3.72% compared with 16.6 ± 3.09% in the control; $P < 0.05$). In the paracortical zone the percentage of blast forms was a little higher than initially, and there was a marked macrophagal reaction (3.0 ± 1.12% of macrophages compared with 0.3 ± 0.08% in the control; $P < 0.05$).

During the 7th week of the experiment the structural and functional parameters of LN were established at close to their initial levels or a little higher. Just as at the previous time of observation, differentiated cells predominated in all zones of LN. In the paracortical zone the percentage of blast cells remained higher than initially (2.5 ± 0.04 compared with 1.37 ± 0.08 in the control; $P < 0.01$). The percentage of macrophages in the medullary cords (4.15 ± 0.69) also was significantly higher than in the control (0.3 ± 0.06; $P < 0.001$).

If the trends of the parameters of the control systems are assessed as a whole, it will be noted that in the acute phase of the reaction hormonally dependent inhibition of activity of the lymphoid tissue was recorded. During the 4th-5th week, despite the continued action of stress and the high corticosterone level, the character of the reaction changed. The mechanism of this "escape" of the lymphoid tissue is not yet clear. It can be tentatively suggested that one cause of it is an increase, in the total lymphocyte population, of the fraction of cells insensitive to the cytotoxic action of adrenal steroids. The increase in activity of the lymphoid tissue in the phase of adaptation may also be connected with intensification of the peripheral action of thyroid hormones, for we know that thyroid hormones stimulate function of the lymphoid organs [4], and that hypothyroidism inhibits activity of the immune system [8].

During long-term adaptation, in the phase of consistently increased specific resistance, a new type of endocrine-lymphoid relation is thus formed, and it differs significantly from that both in the original state and in the acute phase of stress.

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CHANGES IN BLOOD MICROCIRCULATION IN THE ORAL MUCOSA IN EXPERIMENTAL STOMATITIS

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The view that aphthous lesions of the oral mucosa (OM) are neurodystrophic in nature [7] has subsequently undergone further development [1, 5, 8, 10, 11]. During the creation of an experimental model of the pathological process trophic disturbances were discovered in the course of its development, which enable the pathogenesis of the disease to be examined from the neurotrophic standpoint and which provide a theoretical basis for the inclusion of neurotrophic drugs in the therapeutic arsenal available in aphthous stomatitis. From this point of view the study of corrective influences of sympathetic inhibitors is particularly interesting, for changes in functional status of the sympathicoadrenal system and of concentrations of catecholamines and vasoactive substances in the tissues of OM can be claearly noted during the development of the disease [2-4, 9, 12-15]. These observations make it necessary to study the state of the vascular system, as one of the most sensitive functional targets of adrenergic regulation: intravital analysis of the histophysiological parameters of the microcirculation of the oral mucosa under different experimental conditions could help to clarify the pathogenesis of the disease and provide an objective assessment of the effectiveness of the appropriate treatment.

This paper describes the study of the effect of ligation of the common bile duct on the state of the microcirculatory system of OM in dogs accompanied or not by treatment with the β-adrenoblocker propranolol.

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