2. A. G. Babaeva, in: Mechanism of Regulation in the Blood System, Part 1 [in Russian], Krasnoyarsk (1978), pp. 68-70.
3. A. F. Blyuger and Kh. M. Veksler, in: Australian Antigen (Scientific Review) [in Russian], Moscow (1973), pp. 110-121.
4. L. M. Gol'ber, Outlines of Physiology and Pathophysiology of the Hepatolienal System [in Russian], Moscow (1977).
5. I. F. Kolpashchikova, Byull. Éksp. Biol. Med., No. 4, 410 (1978).
6. R. V. Petrov, Immunology and Immunogenetics [in Russian], Moscow (1976).
7. R. V. Petrov and Yu. M. Saretskaya, Transplantation Immunity and Radiation Chimeras [in Russian], Moscow (1965).
8. H. H. Fudenberg, in: Immunobiology, edited by R. A. Good, Stamford, Conn. (1971), pp. 175-183.
9. H. Popper and I. Mackay, Lancet, 1, 1161 (1972).

MITOTIC ACTIVITY OF LYMPHOCYTES IN THE THYMUS CORTEX DURING HYPOKINESIA AND READAPTATION

G. V. Kharlova and S. E. Li

UDC 612.438-06:612.766.2

Changes in the weight and mitotic index in the thymus cortex of Wistar rats were studied during hypokinesia for 10 days followed by recovery for the same period. The mitotic index was reduced by half, 24 h after immobilization of the animals. During readaptation a stage of secondary stress (when the mitotic index was reduced by 71%) was followed by a stage of true readaptation after 10 days.

KEY WORDS: hypokinesia; mitotic activity; thymocytes; readaptation.

Exposure to stressors leads to involution of lymphoid organs [3, 4, 7]. Atropic changes have been observed in the lymphoid organs of mice [6] and rats [5] during immobilization. The object of the present investigation was to study stress changes during hypokinesia and recovery of the thymus after immobilization of the animals ended.

Attention was concentrated on the cellular mechanisms of stress, as reflected in the mitotic activity of cortical lymphocytes.

EXPERIMENTAL METHOD

Wistar rats weighing 130-160 g were used. Hypokinesia was induced by placing the animal in a closely fitting transparent plastic mold, the lid and one wall of which were movable. The mold was so designed that all movements of the animal except of its head were prevented. Immobilization continued for 12 h and 2, 8, and 10 days. After immobilization for 10 days the animals were allowed out into a general cage. The animals were tested 6, 12, and 18 h and 2, 8, and 10 days after the beginning of recovery. They were killed in the mornings, 5 to 8 rats at each time. In histological section cells and mitoses were counted in the cortex of the thymus (the zone located 2-3 fields of vision away from the capsule). The mitotic index (MI) was expressed in promille.

EXPERIMENTAL RESULTS

After the animals had been secured in the molds, the weight of the thymus fell very quickly (Fig. 1), by 60% of its initial value on the 10th day.

A statistically significant increase in MI of the cortical lymphocytes (19.1‰), control (13.1‰) was observed. However, comparison of the phases of mitosis in the experimental and control groups showed that the increase

Institute of Human Morphology, Academy of Medical Sciences of the USSR, Moscow. Institute of Marine Biology, Vladivostok. (Presented by Academician of the Academy of Medical Sciences of the USSR A. P. Avtsyn.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 88, No. 10, pp. 480-482, October, 1979. Original article submitted March 5, 1979.

 0007-4888/79/8810-1208 $07.50

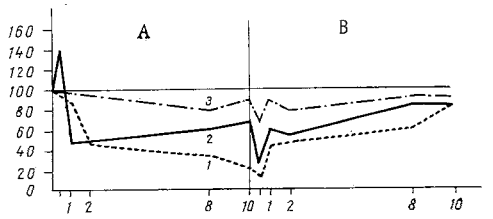

Fig. 1. Changes (in % of control) in weight of thymus and mitotic activity of rats during hypokinesia (A) and readaptation (B). Abscissa, time from beginning of experiment (in days). 1) Weight of thymus; 2) MI; 3) number of cells in field of vision.

TABLE 1. Changes in Thymus Cortex during Hypokinesia and Readaptation

Period	Duration	Weight of thymus, % of control	Number of cells per field of vision, % of control	MI ‰		
				experiment	control	P
Hypokinesia	12 h	96,5	95	19,1	13,4	0,0037
	1 day	82,1	98,9	6,1	13,4	0,001
	8 »	31,0*	83,3	8,1	13,2	0,002
	10 »	38,9*	89,8	7,9	12,6	0,002
Readaptation	6 h	21,6*	76*	8,5	12,4	0,155
	12 »	16,4*	57,9*	3,46	12,4	0,005
	18 »	37,4*	90	8,6	12,4	0,223
	2 days	50,0*	77*	7,1	12,4	0,058
	8 days	62,0	92	12,5	14,7	0,562
	10 »	93,1	93	13,0	14,7	0,450

* Difference from control significant.

in the mean MI in the experimental groups cannot be regarded as stimulation of mitotic activity, for there was no increase in the number of prophases. If the number of early and late prophases and also of metaphases in the control group is taken as 100%, in the experimental group the values were 63.5 and 120% respectively.

The increase in MI was evidently due to an increase in the duration of mitosis and, in particular, of metaphase because the percentage of metaphases was increased. There was no change in the number of anaphases and telophases. Adrenalin, which is secreted during immobilization, is a stressor factor. It has been shown [2] that adrenalin can influence the increase in the duration of mitosis in the cornea of mouse embryos; in the present experiments an increase in MI was observed but did not reflect a true increase in proliferation.

After 24 h MI in the cortical thymocytes fell very sharply – to 6.1‰ compared with 13‰ in the control (Fig. 1). In individual animals MI fell to 2.8‰. This sharp decrease in MI in the thymus suggests that hypokinesia for 24 h corresponds to the alarm phase of chronic stress. On the 8th-10th day of immobilization of the animals, slight stimulation of proliferation was observed in the thymus. The incomplete recovery of the weight of the thymus and the very small increase in MI are evidence that partial atrophy of the organ persisted in the animals after immobilization for 10 days (Table 1).

Repair processes in the thymus did not begin immediately after the end of immobilization of the animals and their return to the common cage. To begin with, there was a period of marked secondary stress, the duration of which varied from 18 to 48 h in different animals.

During secondary stress, the weight of the thymus again fell sharply (to 16.4% of its weight in control animals). Death of the thymocytes and immature T-cells takes place more frequently at this time [10]. Many dying Hassall's corpuscles were seen, with reversal of the layers and a decrease in the number of cells per field of vision, evidence of a disturbance of migration. Proliferation in the organ was depressed after 6 h and

MI for the group was 8.5‰, although in some cases it fell lower still – to 4.7‰ (control 12.42‰). A particularly sharp decline in MI was observed 12 h after the end of immobilization. The mean value of MI for the group was 3.46‰, although in some animals it did not reach 1‰. The overall value of MI for the group rose considerably 18 h after the end of immobilization, to 8.6‰. In most rats, the thymus was restored after 2 days, when MI was 7.1‰. In two rats, however, MI still remained low, at 1.5 and 4.5‰.

Consequently, recovery after the end of immobilization can be deemed to have started only after 18-48 h, but even then, only in individual animals. In preparations of the thymus at these times large pyroninophilic cells (of the blast cell type), with nucleoli displaced to the side of the nuclear membrane, could be seen at these times. Sometimes mitoses were visible in these cells. The weight of the thymus after 2 days of regeneration was increased, up to 50% of the weight in the control animals.

The weight of the thymus 8 and 10 days after the end of immobilization of the animals was increased considerably, and now reached 93% of the control (i.e., it did not differ statistically significantly from the weight of the thymus in the control rats). MI 8-10 days after the end of immobilization was indistinguishable from the control. However, the regenerating thymus glands differed a little from the control in their structure: the cortex was thicker and some of the thymocytes were larger.

The general syndrome of hypokinesia in these experiments was thus aggravated by stress changes, arising in response to injury. The alarm stage of primary stress was characterized by depression of proliferation in the thymus cortex by 50%. A considerable decrease in MI in this alarm stage also was observed in the liver and adrenals by Kirillov [5], who immobilized rats in molds. In the resistance stage proliferation increased a little in the thymus cortex, but adaptation was incomplete after immobilization for 10 days. The secondary stress which was found immediately after the animals had been returned to the general cage thus had a different background initially: MI was 7.9‰ compared with 13.4‰ initially. The alarm stage of secondary stress was much more marked (3.4‰ compared with 6.1‰). The development of acute stress was described [3] in the rat thymus 9-11 h after landing of the artificial earth satellite Kosmos-782. During both primary and secondary stress in the present experiments proliferation and differentiation of the thymocytes were disturbed. The stroma of the organ was undamaged and preserved its powers of proliferation, on account of which the thymus was able to recover. During the recovery period the stage of secondary stress must be distinguished from the stage of true regeneration (readaptation).

The repair processes observed after hyopkinesia are similar to those found after cortisone-induced involution of the thymus, and also after syngeneic or semisyngeneic transplantation, and they differ from processes induced by trauma [8].

LITERATURE CITED

1. P. D. Gorizontov and T. N. Protasova, The Role of ACTH and Corticosteroids in Pathology [in Russian], Moscow (1968).
2. V. N. Dobrokhotov and V. S. Valvas, Byull. Éksp. Biol. Med., No. 4, 102 (1974).
3. G. N. Durnova, A. S. Kaplanskii, and V. V. Portugalov, Arkh. Anat., No. 5, 14 (1977).
4. Yu. I. Zimin and N. V. Ermolaeva, Probl. Éndokrinol., No. 1, 96 (1970).
5. O. I. Kirillov, Processes of cell renewal and Growth Under Conditions of Stress [in Russian], Moscow (1977).
6. V. V. Portugalov, A. S. Kaplanskii, and G. N. Durnova, Vestn. Akad. Med. Nauk SSSR, No. 10, 29 (1971).
7. H. Selye, Essays on the Adaptation Syndrome [Russian translation], Moscow (1970).
8. G. V. Kharlova, Regeneration of Lymphoid Organs in Mammals [in Russian], Moscow (1975).
9. J. B. Peter, J. Levy, and E. V. Baunett, J. Clin, Invest., 53, 565 (1974).