EFFECT OF HYPOPHYSECTOMY ON NEUTROPHILOPOIESIS

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The role of the pituitary for the regulation of erythropoiesis has now been proved, but its role in the regulation of neutrophilopoiesis is not yet clearly defined. For instance, removal of the pituitary from sexually mature dogs and rats had virtually no effect on neutrophilopoiesis [4, 7-11], whereas in young rats weighing 90-100 g, it led to inhibition of granulocytopoiesis [1]. In a previous investigation [3] the writer found no significant changes in the number of neutrophils in the bone marrow and circulating blood of sexually mature hypophysectomized rats. On the basis of hypophysectomy alone, the role of the pituitary in the regulation of neutrophilopoiesis could not be defined in the majority of cases. To reveal more clearly the character of response of the blood system, it was decided to carry out an investigation on hypophysectomized animals exposed to various stimuli.

This paper gives the results of a study of neutrophilopoiesis with particular reference to the state of the bone marrow and peripheral blood in hypophysectomized rats exposed to the action of ionizing radiation or to immobilization for 6 h, leading to additional changes in the blood system.

EXPERIMENTAL METHOD

Experiments were carried out on 144 hypophysectomized female Wistar rats weighing 160-190 g and on 141 similar animals undergoing a mock operation. The pituitary was removed by the transauricular method [6]. The completeness of the hypophysectomy was verified by the absence of gain in body weight after the operation and by a study of the pituitary region of the animals after sacrifice. The hypophysectomized rats and rats undergoing the mock operation were used in the experiments on the 15th day after the operation. Total single irradiation of the rats in a dose of 400 R was carried out on the ÉGO-2 apparatus with a dose rate of 153 R/min. To reproduce the stress reaction the rats were immobilized (on the operating table in the supine position) for 6 h.

The investigations were carried out on the 2nd, 5th, 7th, 10th, 15th, 20th, 25th, and 30th days after irradiation and 6, 9, 12, 24, 48, and 72 h after the beginning of immobilization. The total number of cells was determined in the femoral marrow. The myelogram was counted, and the absolute number of cells of the different generations calculated. The morphological indices of the peripheral blood were studied by the usual methods. The numerical results were subjected to statistical analysis.

EXPERIMENTAL RESULTS

A study of post-irradiational regeneration of hematopoiesis showed that recovery of the neutrophil series in the bone marrow (Fig. 1A, B) and of the number of neutrophils in the peripheral blood (Fig. 1C) of the hypophysectomized rats was considerably delayed compared with animals undergoing the mock operation.

Liberation of mature neutrophils into the peripheral blood followed by activation of neutrophilopoiesis are among the characteristic changes observed in the bone marrow in the early period of the stress reaction [2]. In the present experiments immobilization for 6 h gave rise to a sharp decrease in the number of mature neutrophils in the bone marrow of both the hypophysectomized rats and rats undergoing the mock operation, down to a minimum 9 h after the beginning of immobilization. Later, whereas the number of neutrophils in the control animals returned to normal, in the hypophysectomized rats the number of mature neutrophils in the bone marrow remained low (Table 1). Activation of granulocytopoiesis in the bone marrow was observed 24-48 h after the beginning of immobilization for 6 h in the rats undergoing the mock operation, and this was

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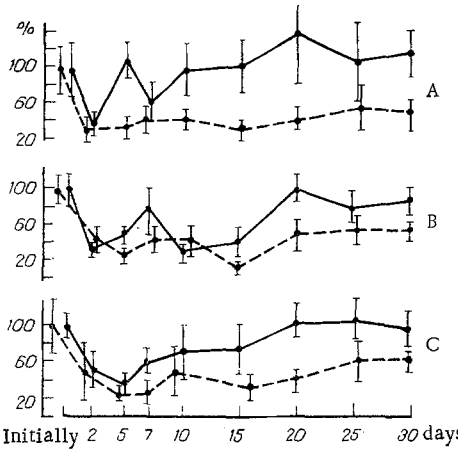

Fig. 1. Changes in number of young cells (myeloblasts + promyelocytes + myelocytes) of neutrophil series (A), of mature (stab cells + polymorphs) neutrophils (B) in bone marrow, and neutrophilic granulocytes in circulating blood (C) after irradiation in a dose of 400 R. Abscissa, time after irradiation (in days); ordinate, number of cells (in % of initial). Continuous line – rats undergoing mock operation; broken line – hypophysectomized rats.

TABLE 1. Change in Number of Cells (in millions) in Femoral Marrow after Immobilization for 6 h (M ± m)

Cell population	Group of animals	Initial value	Time after beginning of immobilization, h					
			6	9	12	24	48	72
Stab cells and polymorphs	Undergoing mock operation	59,8±8,9 (7)	49,3±5,9 (7)	38,4±3,8* (7)	53,5±7,5 (6)	44,1±4,4 (7)	44,1±6,1 (6)	52,3±5,7 (6)
	Undergoing hypophysectomy	70,4±4,4 (10)	50,5±6,3* (10)	41,9±8,6* (8)	54,1±9,4 (7)	44,7±6,4* (6)	46,5±13,1 (5)	42,2±4,3* (6)
Myeloblasts and myelocytes	Undergoing mock operation	3,6±0,3	3,1±0,7	4,2±0,8	3,9±0,2	4,7±0,3*	4,9±0,4*	4,2±0,3
	Undergoing hypophysectomy	3,9±0,4	2,6±0,4*	2,0±0,4*	3,4±0,5	0,8±0,07*	2,6±0,6	1,2±0,2*

Legend. *) Values differing significantly ($P < 0.05$) from initial values. Number of animals given in parentheses.

reflected in an increase in the number of young cell forms of the neutrophil series. This phenomenon was not observed in the hypophysectomized animals (Table 1).

The experimental results showed that whereas hypophysectomy itself did not significantly affect the level of neutrophilopoiesis, if additional loads were thrown on an animal with its pituitary removed, functional insufficiency was revealed, manifested during investigation of the bone marrow as inhibition of post-irradiational regeneration of neutrophilopoiesis and absence of transient activation of granulocytopoiesis in the period from 24 to 48 h after the beginning of immobilization for 6 h.

One possible explanation of the inhibition of neutrophilopoiesis after hypophysectomy may be the influence of the thymus on the direction of differentiation of hematopoietic stem cells. It was shown in [5] that in adult thymectomized mice differentiation of stem cells in the direction of granulocytopoiesis is inhibited. In a previous investigation [3] the present writer found marked inhibition of lymphocytopoiesis in the thymus and spleen in hypophysectomized rats. The deficiency of T lymphocytes in hypophysectomized animals, when additional demands are made on the blood system, may perhaps lead to a reduction in the differentiation of hematopoietic stem cells toward neutrophilopoiesis.

The results of the present experiments thus show conclusively that the pituitary plays a role in the regulation not only of erythropoiesis, but also of neutrophilopoiesis.

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MITOTIC ACTIVITY AND CELL COMPOSITION OF ACINI IN REGENERATING EXTRAORBITAL LACRIMAL AND SUBMANDIBULAR SALIVARY GLANDS

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After partial injury to the salivary and lacrimal glands proliferative processes spread to all the residual parts of the glands [1, 3, 5] and, according to the concept of regeneration hypertrophy [4], they ought to lead to a definite increase in its weight. It has, however, been shown that the terminal portions in the remnant of the glands do not increase in size [1]. The question thus arises: how can new cell formation be interpreted in this case. It has been suggested that before proliferation begins, cells throughout the remnant of the gland die at a more rapid rate, and that the wave of mitosis is intended to make good this loss. To shed light on this phenomenon, it seemed logical to study the composition of the terminal portions, where a decrease in the number of cells could indicate the scale of cell death, whereas an increase could indicate the completeness of regeneration.

The object of this investigation was to compare mitotic activity in remnants of the extraorbital lacrimal and submandibular salivary glands with data on the cell composition of their acini at successive periods of regeneration.

EXPERIMENTAL METHOD

Experiments were carried out on 59 noninbred male albino rats weighing 250-300 g. In the experiments of series I about one-third of the extraorbital lacrimal gland was destroyed by burning in 21 rats. In series II the submandibular salivary gland was subjected to the same injury in 23 rats. The glands of five (series I) and ten (series II) animals, not subjected to any form of procedure, served as the control. The material was processed by the usual histological methods. Cells found in the acinus (total secretory cells, mono- and binuclear cells separately) were counted in sections 7-10 μ thick in regions remote from the site of trauma in 100 terminal portions from each animal. Mitoses were counted in 10,000 cells in the same zone. The numerical results were analyzed by Student's t-test and the Wilcoxon–Mann–Whitney U-test [2].

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