

# GRANULOPOIESIS IN THE BONE MARROW OF HYPOPHYSECTOMIZED RATS

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Experiments on rats showed that 2-3 months after total hypophysectomy the blood leukocyte count is raised on account of eosinophils and lymphocytes. The number of neutrophils is reduced. The relative indices (percentage of granulocytes in the bone marrow) do not reflect actual changes in granulopoiesis. The decrease in concentration and absolute content of granulocytes in the bone marrow is evidence of reduction in the functioning mass of granulocytes. Inhibition of proliferative activity of the granulocytes, determined from the decrease in mitotic activity, begins in the early stages of granulopoiesis.

The principal effect of deprivation of pituitary function on hematopoiesis is anemia of hypoplastic type [5, 2, 9, 16-19]. The possibility of a simultaneous defect of granulopoiesis has also been reported [5, 7]. Cases of severe Simmonds' disease with marked granulocytopenia or granulocytosis have been described [6, 8, 11, 12, 15, 20].

The study of granulopoiesis in hypophysectomized animals has usually been confined to the circulating blood and to the relative content of granulocytes in the bone marrow. In most investigations the development of leukocytosis, eosinophilia, and lymphocytosis has been observed a short time after hypophysectomy [3, 4, 10, 17]. In some cases examination of the sternal marrow has revealed an increase [5, 18] and in others a decrease [13, 14, 17] in the number of myeloid cells against the background of hypoplasia.

The object of the investigation described below was to study the dynamics of changes in the number and composition of the blood leukocytes during the 3 months after hypophysectomy and to compare them with changes in the indices of granulopoiesis in the bone marrow.

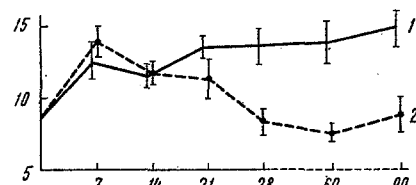


Fig. 1. Changes in leukocyte count in hypophysectomized rats (1) and rats undergoing mock hypophysectomy (2) at different times after operation. Abscissa, day of investigation; ordinate, leukocyte count (in thousands).

## EXPERIMENTAL METHOD

The number and composition of the leukocytes were studied in male Wistar rats initially weighing 90-100 g, in three groups: 1) 35 intact animals; 2) 47 undergoing mock hypophysectomy; and 3) 87 hypophysectomized rats. The indices of granulopoiesis were studied by method described previously [1, 2].

## EXPERIMENTAL RESULTS

In the immediate post-operative period both the control (mock operation) and the hypophysectomized animals developed neutrophilic

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TABLE 1. Relative and Absolute Bone Marrow Indices of Hypophysectomized Rats (experiment) and Rats Undergoing Mock Hypophysectomy (control) at Different Times after Operation

Time of investigation in days	Content of granulocytes, in percent				Concentration of granulocytes (number per mm <sup>3</sup> bone marrow, in thousands)				Absolute number of granulocytes in total volume of femoral marrow (in millions)				Frequency of mitoses among granulocytes capable of division (in percent)			
	control		experiment		control		experiment		control		experiment		control		experiment	
	M±m		M±m		M±m		M±m		M±m		M±m		M±m		M±m	
	n	n	n	n	n	n	n	n	n	n	n	n	n	n	n	n
Before operation	35	43,4±3	6													
7-	6	47,9±3,3	6	60,3±5,2	<0,01	913,9±93			48,3±7,5				0,9	44	1,3±0,07	
14-	6	53,2±4,0	9	54,3±2,4	>0,5	1059,5±45,0	1124,3±45,0	>0,2	53,1±4,4	35,1±3,4	<0,01	1,51,611	1,11±0,2	7	2,12±0,3	<0,05
21-	10	42,9±2,6	11	55,7±2,4	<0,01	1119,7±98,4	543,2±48,0	<0,001	44,2±3,4	23,7±2,3	<0,001	1,10,6	1,4±0,1	27	1,35±0,1	>0,5
28-	10	48,1±1,9	24	48,4±1,4	>,05	1035,6±41,7	874,7±35,3	<0,001	52,4±2,3	33,8±2,3	<0,001	1,81,1	1,8±0,4	13	1,3±0,2	<0,01
60-	7	57,7±4,2	7	65,8±4,2	>0,05	1021,6±32,9	937,9±25,9	<0,5	57,4±3,2	36,0±1,7	<0,001	2,11,210	1,7±0,15	22	0,68±0,09	<0,01
90-	8	60,0±3,1	13	56,0±2,2	>0,2	1341,0±89,0	953,0±64,0	<0,01	85,0±5,3	39,2±1,6	<0,001	3,01,2	2,3±0,18	10	1,2±0,007	<0,01
						1493,7±61,8	1149,7±67,7	<0,001	123,1±3,9	36,7±1,8	<0,001	1,81,6	1,7±0,09	8	1,0±0,05	<0,05

leukocytosis, evidently because of the blood loss. In the control animals the leukocyte count returned to its initial level 21-28 days after the operation. In the hypophysectomized rats, on the other hand, the leukocytosis continued to increase (Fig. 1). This increase took place on account of an increase in the mass of eosinophils and lymphocytes. The number of neutrophils decreased.

Calculation of the myelograms (Table 1) showed that the percentage of granulocytes increased in the post-operative period in both groups of animals. In addition, this index in the control rats continued to rise as the animals grew and gained in weight. Hypophysectomy produced a greater increase in the proportion of granulocytes among the other cells in the bone marrow 7 days after the operation than in the control group. This was due not only to blood loss, but also to a decrease in the mass of erythroblasts in this period [1, 2]. The concentration of granulocytes per mm<sup>3</sup> bone marrow, reflecting the density of granulocytes in the hematopoietic tissue, was considerably reduced in the hypophysectomized animals 2 weeks after the operation, returned gradually to its initial level by the 28th day of observation, but still remained below its value in the control animals during this period of the investigation (Table 1). In the course of the 2nd and 3rd months the concentration of myeloid cells in the bone marrow of the hypophysectomized animals was 70% of its level in the control animals of the corresponding age.

A more direct index of the state of myelopoiesis is the number of granulocytes in the total volume of femoral bone marrow, which evidently reflects changes in the total mass of granulocytes in the bone marrow.

In the animals undergoing the mock operation the absolute number of granulocytes increased with an increase in their age and weight, and was relatively independent of factors such as blood loss. For instance, the mass of granulocytes in the total volume of femoral marrow of the control animals was increased by 2-2.5 times 2-3 months after the operation (Table 1). Hypophysectomy caused a sharp decrease in the absolute content of granulocytes 2 weeks after the operation. During the next 2 weeks it increased only very slightly, and remained at this level until the end of the experiment. After 60-90 days the mass of granulocytes of the hypophysectomized rats was reduced by 1.3 times compared with its initial level and by 2.2-3.3 times compared with its level in animals of the same age undergoing the mock operation. These changes were independent of the decrease in body weight, because the ratio between the mass of granulocytes and the relative weight of bone marrow in the hypophysectomized rats was less, starting from the 2nd week, than the corresponding index in the animals undergoing the mock operation (Table 1).

The sharp decrease in functioning mass of myeloid cells in the bone marrow was accompanied by a decrease in the frequency of mitosis among granulocytes capable of division (Table 1). Inhibition of proliferation began with the early precursors of the myeloid series.

Hypophysectomy thus reduces the content of both the erythroid and myeloid tissue of the bone marrow in the late stages after the operation. This is revealed only by investigation of the absolute, and not of the relative, indices.

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