CHANGES IN THE BLOOD OF RATS AT VARIOUS STAGES OF THE ADAPTATION SYNDROME

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Many workers have reported that a series of nonspecific compensatory or adaptive reactions, known as the general adaptation syndrome (Selye), may develop in the organism in response to harmful influences. The development of the adaptation syndrome is accompanied by changes in the nonspecific reactivity of the organism, and these are reflected in the names given to the various stages of the syndrome (the phases of mobilization, of resistance, and of exhaustion). Meanwhile, the mechanism of the increase or decrease of the resistance of the organism in stress has not yet been adequately explained.

The blood system is known to be one of the more important systems taking part in adaptive processes. However, few investigations of the state of the bone marrow in stress have been made; no detailed analysis of the state of the blood system in the various stages of the adaptation syndrome has been undertaken. This formed the subject of the present investigation.

METHOD

Experiments were conducted on 59 male albino rats of the Wistar line, weighing 190-210 g. The state of stress, manifested as the adaptation syndrome, was produced by electrical stimulation. This took the form of repeated interrupted stimuli, in the course of which an alternating current was passed through the iron bars of the cages in which the animals were kept. The conditions of stimulation were as follows: duration of each impulse 2 sec, interval between impulses 1 min, strength of current 2 mA, frequency 2000 cps. With each stimulus the animals gave a powerful motor reaction but did not develop a state of shock.

The state of the animals at the end of the first hour of electrical stimulation could be described as the initial period of the mobilization stage (the alarm reaction), which, according to Selye, lasts for 6-48 h. If the rats were subjected to this type of stimulation for 3 h daily for 1 week, they developed the stage of resistance. The animals became to some extent accustomed to daily stimulation, and tolerated it with less disturbance than on the first days, so that they grew and gained weight just like the intact rats. The experimental rats were found to possess increased radioresistance at this period.

The stage of exhaustion appeared on approximately the 14th day of electrical stimulation given for 6-8 h daily. The rats were untidy, hemorrhages developed in the skin and mucous membranes, they were apathetic and they lost their appetite. They began to lose weight, with increasing rapidity from day to day, and they died after 3-5 days with continued stimulation. The radioresistance of the rats at this period was obviously depressed. In our experiments hematological investigations were conducted only at the initial period of the stage of exhaustion, before the changes enumerated above became severe.

Blood for analysis was taken from the caudal vein of the animals before the experiment and after reproduction of the required phase of the adaptation syndrome. The bone marrow was investigated once after decapitation of the animals; the results were compared with the indices obtained in the healthy, intact rats.

The investigation of the marrow utilized the technique of counting the total number of myelokaryocytes [7], and to study the mitotic activity of the marrow cells a special staining method was used [6]. With these methods,

Absolute Number of Myelokaryocytes (millions) in Marrow of a Whole Femur of Rats at Different Stages of the Adaptation Syndrome

Index	Control	Stage of mobilization	t	Stage of resistance	t	Stage of exhaustion	t
Total no. of cells	60,6 ±1,38	57,9 ±7,51	n/s	74,6 ±3,41	>3	49,25±3,17	>3
Including:							
reticulo-endothelial	2,81±0,15	2,8 ±0,66	n/s	4,02±0,81	n/s	5,21±0,82	>2
erythroblasts-							
pronormoblasts	1,1 ±0,06	0,66±0,11	n/s	1,29±0,12	n/s	0,63±0,17	n/s
normoblasts	16,1 ±0,57	16,3 ±3,26	n/s	22,17±1,13	>4	14,7 ±1,92	n/s
All erythroblasts	17,2 ±0,59	16,96±3,43	n/s	23,46±1,05	>5	15,33±1,97	n/s
myeloblasts-myelocytes	3,4 ±0,15	3,28±0,36	n/s	5,15±0,52	>3	2,22±0,17	>5
metamyelocytes-segmented							
neutrophils	22,4 ±0,72	22,7 ±3,03	n/s	27,17±1,91	>2	14,31±1,7	>4
eosinophils	5,6 ±0,26	4,14±0,36	>3	4,11±0,37	>3	1,46±0,33	>9
All cells of myeloblastic series	31,5 ±0,7	30,34±3,56	n/s	36,43±1,94	n/s	18,96±2,17	>5
Lymphocytes	8,2 ±0,5	5,6 ±1,39	n/s	9,24±1,59	n/s	7,68±0,36	n/s

Note. n/s—Difference between control and experimental values not statistically significant.

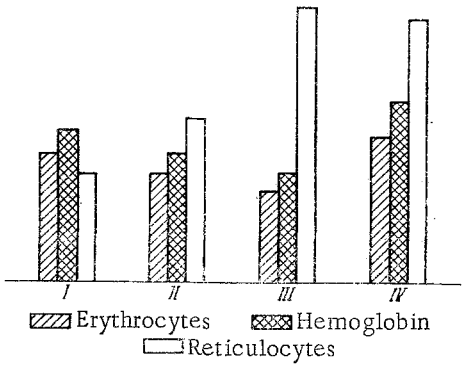

Fig. 1. Some indices of the red blood of the intact rats and rats in different phases of the adaptation syndrome; in stage of mobilization (initial period—II), of resistance (III), and of exhaustion (IV); I) control.

in conjunction with analysis of the myelograms, the absolute numbers of individual marrow cells and the total number of dividing cells (mitoses) in the femoral marrow of the rats could be calculated. The experimental and control animals were almost equal in weight, so that the degree of scatter of the quantitative marrow indices was slight.

RESULTS

Control animals. The table shows that the number of myelokaryocytes in the whole femoral marrow of the intact rats averaged 60,600,000±380,000. The number of mitoses per 1000 myelokaryocytes was 7.1±0.34, and the total number of dividing cells in the femoral marrow was 424,000±18,200. The peripheral blood indices of the control and experimental animals before stimulation were indistinguishable from the mean data described in the literature.

Stage of mobilization (initial period). In the peripheral blood (Fig. 1) there was a small decrease in the number of erythrocytes and in the hemoglobin concentration, a slight reticulocytosis, and a slight leukopenia on account of a lymphocytopenia and eosinopenia. No significant changes were observed in the marrow, apart from a small decrease in the number of eosinophils. The mitotic activity of the marrow at this stage was lowered, as shown by a decrease in the mitotic index and in the absolute number of dividing cells (Fig. 2). The percentage of reticuloendothelial cells and granulocytes in the spleen rose as a result of a fall in the number of lymphocytes.

Stage of resistance. The number of erythrocytes in the blood showed a slight fall and a reticulocytosis was present; the total and differential leukocyte counts were the same as initially. In the marrow the number of myelokaryocytes was raised to 74,600,000±3,410,000 on account of an increase in the number of all types of cells, except lymphocytes and eosinophils. The mitotic activity of the marrow was intensified: the mitotic index was raised, and the absolute number of dividing cells was increased. The relative proportions of the cells in the spleen showed little change.

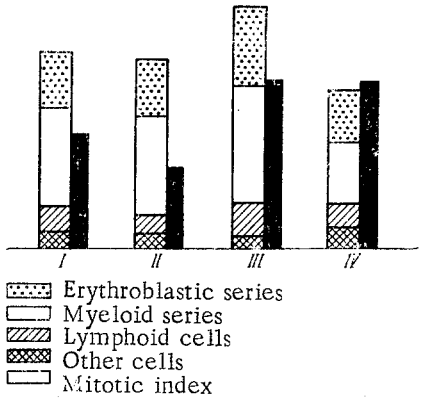

Fig. 2. Numbers of individual types of myelokaryocytes and mitotic index in bone marrow of rats in different phases of the adaptation syndrome. Legend as in Fig. 1.

Stage of exhaustion (initial period). The main distinguishing feature of the hemopoiesis in the stage of exhaustion was the hypoplastic state of the marrow, as revealed by a reduction in the numbers of all types of cells (except reticulo-endothelial cells). The total number of myelokaryocytes fell to 49,200,000±3,170,000. It is possible that the transformation of the reticulo-endothelial cells into more mature hemopoietic cells was disturbed. The shift in the morphological composition of the blood resembled the hematological changes in the stage of mobilization: a lymphocytopenia, eosinopenia, neutrophilia (to 20,000-30,000 per mm^3), and reticulo-cytosis were observed.

When harmful agents act on the body, many well defined changes are known to take place in the circulating blood. The results obtained in these experiments indicate that the development of the adaptation syndrome is accompanied by marked functional and morphological changes in the hemopoietic organs.

In the opinion of most workers, the hematological changes in the adaptation syndrome are largely dependent on the functional state of the endocrine system. For example, the development of a lymphocytopenia is attributed to the direct destructive action of corticosteroids [3-5].

Many workers have found that cell division is inhibited in various animal tissues during the action of harmful agents, and also after administration of adrenalin or cortisone. It is possible that the depression of mitotic activity of the bone marrow in the initial period of the stage of mobilization also has an hormonal mechanism and is the result of the action of corticosteroids, the secretion of which is increased at this period.

The reduction in the number of erythrocytes in the stages of mobilization and resistance may also, perhaps, be associated with hormonal influences (mineralocorticoids) and may be dependent on dilution of the blood with fluid entering the blood stream from the tissues.

The results of this investigation suggest that the strengthening of the nonspecific resistance of the organism in the stage of resistance [1, 2, 8] is to some extent brought about by an intensification of hemopoiesis. Since the blood plays a large part in the processes of metabolism, humoral and cellular defense, and so on, it may be postulated that the stimulation of hemopoiesis during this period is one of the protective, adaptive reactions leading to an increase in the resistance of the organism to the action of the harmful agents. On the other hand, the depression of hemopoiesis in the stage of exhaustion is evidence of profound disturbances in the organism and, in particular, of a disturbance of the neuro-humoral regulation of hemopoiesis.

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