EFFECT OF THE FACTORS OF SPACE FLIGHT ON ERYTHROPOIESIS

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After orbital flight for 19-22 days on the satellites "Kosmos-605" and "Kosmos-782" erythropoiesis of rats was inhibited and the morphology of their megakaryocytes was modified. These changes disappeared by the 25th-27th day after the flight.

KEY WORDS: *cosmic space*; *erythropoiesis*; *megakaryocytes*.

The decrease in the erythrocyte volume observed in the crews of space ships may be based on several mechanisms including hemolysis, shortening of the life cycle of the erythrocytes, and inhibition of medullary hematopoiesis [8]. The role of inhibition of hematopoiesis in the reduction in the erythrocyte volume under conditions of weightlessness is demonstrated, in particular, by the results of histological analysis of the bone marrow of mice exposed on the space ship "Apollo-17" [10], where hyperoxia was present. A distinguishing feature of manned satellites of the "Kosmos" type is the normoxic medium, on account of which the state of medullary hematopoiesis can be estimated under conditions of pure weightlessness.

The object of this investigation was to study the bone marrow of rats after orbiting on the manned satellites "Kosmos-605" and "Kosmos-782."

EXPERIMENTAL METHOD

Male Wistar rats (Kosmos-605) and a colony of Wistar SPF rats (Kosmos-782) weighing initially 200-230 g were used. The duration of flight of the animals on the first satellite was 22.5 days and on the second 19.5 days. The composition of the atmosphere of the manned satellite Kosmos-605 was not kept constant during the flight: From the 12th through the 22nd day hyperoxia was present [3], whereas the composition of the atmosphere of the satellite Kosmos-782 was stable; no hyperoxia was recorded at any time during the experiment. Three groups of animals were studied. Group 1 consisted of rats exposed on the satellite and killed 8-11 h (Kosmos-782) and 48 h (Kosmos-605) and also 25 and 27 days after touchdown. Group 2 consisted of rats used in model experiments on the ground in which all the factors of cosmic flight except weightlessness were simulated. Group 3 consisted of animals kept in the animal house.

In all the animals the cell composition of the femoral marrow was determined histologically. Material was fixed in Bouin's fluid, decalcified in 5-7% HNO_3, and embedded in paraffin wax. Sections 5-7 μ thick were obtained with hematoxylin and eosin. The state of erythropoiesis was estimated from histological sections in 10 fields of vision (objective 90, ocular 7) with a total of 2000 cells. In some series of 10 fields of vision 100 megakaryocytes were counted and the number of those with pathological changes was determined.

EXPERIMENTAL RESULTS AND DISCUSSION

Erythropoiesis was inhibited in the animals orbiting for 3 weeks on both satellites (Table 1). In the rats exposed to cosmic flight the erythroid series was represented by a few widely scattered small groups of cells. The number of morphologically identified erythroid cells in the section of the bone marrow reached 14-15% of the total number of nucleated cells (26-32% in the control).

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TABLE 1. Number of Cells of Erythroid Series and Number of Altered Megakaryocytes in Femoral Marrow

Index studied	Time after experiment, days	Nature of experiment					
		Kosmos-605	model experiment	control	Kosmos-782	model experiment	control
Cells of erythroid series (% of total number of all nucleated cells)	0,3—0,5	—	—	—	15±3 (5)	26±2 (5)	32±2 (10)
	2	14±3 (4)	25±3 (4)	30±3 (9)	—	—	—
	25	—	—	—	23±2 (5)	28±2 (5)	30±3 (10)
	27	25±3 (4)	27±3 (6)	28±2 (11)	—	—	—
Altered megakaryocytes (% of total number of megakaryocytes)	0,3—0,5	—	—	—	27±3	6±2	2±1
	2	19±3	2±1	0	—	—	—
	25	—	—	—	0,2±0,2	2±1	2±1
	27	0,1±0,1	0,2±0,2	0	—	—	—

Note. Number of animals investigated in parentheses.

In the period after flight erythropoiesis was restored and by the 25th-27th day the number of erythroid cells had regained the control level. In rats from the ground model experiments no changes in erythropoiesis compared with the control rats (group 3) were observed at any time of the investigation. The inhibition of medullary erythropoiesis in the rats exposed to cosmic flight was thus reversible.

Although hyperoxia was present on the satellite Kosmos-605 and absent on Kosmos-782, the changes in erythropoiesis were the same in the animals orbiting on both of them. This suggests that the main cause of inhibition of erythropoiesis was exposure of the rats to weightlessness. During a deficiency of muscular exertion the body's oxygen requirement is reduced substantially; this leads to a decrease in the erythrocyte production in the bone marrow. In other words, inhibition of erythropoiesis during weightlessness is determined by a decrease in the volume of the functional requirements of the locomotor apparatus.

Atrophy of the thymico-lymphatic apparatus [2], lymphocytopenia [7], and an increase in the weight of the adrenals [6] have been found in rats after space flight. Elevation of the cortisol level in the urine and blood plasma of astronauts has been described both during and after flight. These observations may reflect a stress response arising as a result of exposure to a combination of factors. The action of stressors such as acceleration, vibration, noise, etc., such as exist in the initial stage of the flight, can be supported by weightlessness. During long-term flight adaptation evidently develops to weightlessness and is accompanied by corresponding upsets in the cell composition of certain organs (the lymphoid system, bone marrow, etc.). Finally, the last stage of flight, culminating in landing, takes place under conditions of the transition from weightlessness to the earth's gravitational field, and this may cause the development of a "new stage" of a stressor state or simply of new stress. Animals returned to earth may thus "bear the traces" of changes arising in the different stages of the flight.

Adrenocortical hormones are known to activate the process of differentiation of young forms of cells of the erythroid series [5]. During the investigation of bone marrow films of rats from the satellite Kosmos-605 on the first and second day after flight (data of M.P. Kalandarova) no significant decrease was found in the number of young forms of cells of the erythroid series but the number of lymphocytes was reduced. Meanwhile a characteristic feature of the stress response is an increase in the number of lymphocytes in the bone marrow [1, 11] and in the number of early forms of cells of the erythroid series [5]. Kalandarova's observations thus indicate that the changes in hematopoietic activity of the bone marrow of the rats after the end of the flight of 19-22 days were not due to a stress reaction but to other mechanisms, possibly connected with inhibition of growth of the long bones. Depression of bone formation was observed in rats exposed on the satellite Kosmos-605 [9], and it is in harmony to some extent with the concept of Korzhuev [4] according to which the absence of the force of gravity must lead to reconstruction of the bone of the skeleton and, consequently, to the depression of hematopoiesis.

The decrease in the erythrocyte volume observed during cosmic flight is due, it is tentatively suggested, to increased destruction of erythrocytes. Considerable deposition of products of erythrocyte destruction, in the form of granules of hemosiderin, was in fact found in the spleen of rats orbiting on Kosmos-605 [2]. Erythrocyte breakdown products are known to stimulate the system of erythropoiesis by the feedback principle [8]. However, under on-

flight experimental conditions inhibition of erythropoiesis was observed. All these findings are evidence that the state of erythropoiesis, especially during long-term space flights, is determined by the volume of the function performed by the locomotor apparatus rather than by the action of stressor factors of cosmic flight or changes in hemolytic activity.

Two groups of megakaryocytes were found in the bone marrow of the rats: those of normal appearance with a juicy, properly constructed nucleus and granular cytoplasm, and megakaryocytes with a pycnotic nucleus and a strongly eosinophilic, structureless cytoplasm. The number of altered megakaryocytes in the rats exposed to cosmic flight rose to 19-27% of the total number of those cells, whereas in the bone marrow of the animals of the other group the number of the altered megakaryocytes did not exceed 6%. On the 25th-27th day after the end of the flight the number of altered megakaryocytes was restored to normal.

These destructive changes in megakaryocytes were thus completely reversible in character. Similar results were obtained by the present writers when they studied megakaryocyte populations in rats kept under conditions of restricted mobility. These observations rule out any connection between degenerative changes in megakaryocytes and the effects of the overloading and weightlessness which existed during the flight.

LITERATURE CITED

1. P. D. Gorizontov, Arkh. Pat., No. 3, 3 (1973).
2. G. N. Durnova, A. S. Kaplanskii, and V. V. Portugalov, Aviat. Space Environ. Med., 6, 47 (1976).
3. E. A. Il'in, L. V. Serova, and A. D. Noskin, Kosmich. Biol., No. 3, 9 (1976).
4. P. A. Korzhuev, Zh. Obshch. Biol., 29, No. 5, 587 (1968).
5. S. I. Ryabov, Usp. Sovrem. Biol., 79, No. 3, 387 (1975).
6. E. A. Savina, V. V. Portugalov, et al., in: Aviation and Space Medicine (5th All-Russian Conference), Vol. 1 [in Russian], Moscow–Kaluga (1975), pp. 34-36.
7. L. V. Serova, in: Aviation and Space Medicine (5th All-Russian Conference), Vol. 1 [in Russian], Moscow–Kaluga (1975), pp. 36-38.
8. Ya. G. Uzhanskii, The Physiological Mechanisms of Regeneration of the Blood [in Russian], Moscow (1968), p. 86.
9. V. S. Yagodovskii, L. A. Triftanidi, and G. P. Gorokhova, Aviat. Space Environ. Med., 47, No. 7, 681 (1976).
10. J. T. Ellis, L. M. Kraft, C. C. Lushbaugh, et al., Aviat. Space Environ. Med., 46, 641 (1975).
11. A. S. Fauci, Immunology, 28, 669 (1975).