EXPERIMENTAL BIOLOGY

Monotonic and Undulating Circadian Variations in the Rat Myelogram

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Key Words: *bone marrow; regulation of hemopoiesis; biorhythms*

Regular circadian changes in the distribution of proliferating cells of the bone marrow dependent on the phases of the cell cycle [1,2,7] and a circaseptan (weekly) rhythm in the level of peripheral blood lymphocytes [6] may cause analogous changes in the contribution of different cell subpopulations in the myelogram. The present study was undertaken to elucidate this problem.

MATERIALS AND METHODS

The experiments were performed on nonpedigree albino rats weighing 180-250 g with access to food and water ad libitum that were changed every morning. The working day in the vivarium began at 09:00 h. The electric light was switched on during the daytime and switched off in the evening and at night. Eight groups of rats (5 males and 5 females in each) were investigated at 3-h intervals starting at 12:00 h. on February 2, 1990. Sunrise and sunset were at 08:30 h. and 17:00 h., respectively. Bone marrow smears were obtained from the femur by a routine method. In every case 100 cells were analyzed and the mean percentage (y, %) and standard error ($m(y)$) were determined. The total share of myeloblasts, promyelocytes, myelocytes, proerythroblasts, and basophilic and polychromatophilic erythroblasts was taken as the value of the proliferative pool (P_c) of the bone marrow. Parameters a and b in the linear regression equation and their standard errors were determined by the method of least squares from the following equations: $y = ax + b$ and $m(y) = m(a)x + m(b)$, where x is the time in hours.

RESULTS

The regression analysis revealed reliable monotonic changes in all myelogram parameters and P_c during the course of 24 h. A monotonic decrease in the case of the granulocyte subpopulation (Fig. 1, *a*) and an increase in the case of the erythroid cells (Fig. 1, *b*, Table 1) was not influenced by elimination of lymphocytes from the myelograms. These changes were superimposed by rhythmic changes with a period of less than 24 h. Thus, coexistence of a circadian rhythm with a rhythm of higher periodicity [4] is also valid for myelogram parameters in rats. The monotonic changes may be due to a monotonic anti-phase correction of the production of committed precursors for granulocytopoiesis and erythropoiesis. The changes

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TABLE 1. Average Fractions of Granulocytic and Erythroid Subpopulations in Rat Bone Marrow at Different Times of Day and Parameters of Linear Regression Equation

Subpopulation of bone marrow cells	Mean value and standard error of share of different cells (%) for indicated time of day								Linear regression equation	
	12	15	18	21	0	3	6	9	a, %/h	b, %
Myeloblasts, promyelocytes, and myelocytes	21.3	21.0	18.9	19.8	20.3	19.5	17.1	17.7	−0.168	21.2
	2.2	2.3	3.0	2.7	1.7	2.7	1.5	2.0	0.029	2.6
Metamyelocytes	11.4	11.2	8.6	7.4	12.3	9.9	7.7	9.1	−0.098	10.7
	2.5	1.4	1.5	1.0	1.6	1.2	0.9	1.4	0.042	1.9
Rod−nuclear and segment−nuclear granulocytes	44.5	50.7	47.0	45.9	37.5	37.8	44.6	45.6	−0.233	46.7
	5.2	3.8	3.5	2.7	3.0	5.9	2.4	4.0	0.031	4.1
Proerythro− and erythroblasts (baso− and polychromatophils)	11.2	10.9	11.9	14.2	16.7	13.0	16.2	15.7	0.253	11.1
	2.7	2.7	1.5	1.6	2.3	2.2	1.8	2.5	0.012	2.3
Oxyphilic erythroblasts	11.5	5.0	8.2	12.8	10.4	13.3	10.4	11.1	0.147	8.8
	3.6	1.3	1.4	2.0	2.9	4.1	2.6	2.6	0.034	2.2
Proliferating cells of bone marrow	32.5	31.9	31.0	33.6	37.1	32.8	34.3	35.6	0.169	31.8
	3.9	3.2	3.4	3.5	2.6	3.5	2.0	3.4	0.018	3.3
Proliferating cells of granulocytic subpopulation	27.7	25.3	24.6	26.9	29.0	27.1	24.6	25.0	0.051	26.8
	2.8	2.8	2.9	3.4	1.6	3.6	1.9	3.0	0.012	2.9
Proliferating cells of erythroid subpopulation	51.3	67.1	59.5	53.3	6.4.6	54.4	63.8	59.9	0.158	57.6
	6.8	6.3	5.2	4.1	5.2	5.9	6.5	3.8	0.067	6.2

Note. Standard errors of the mean for each subpopulation are presented in the lower row.

in the P_c value reflect the changes in the production of mature cells due to the existence of the circadian rhythm of proliferative activity [1,5]. The anti-phase character of the changes in P_c for the granulocyte and erythroid cell subpopulations (curves *4* and *7*) provides the basis for assuming that inhibitors and stimulators of bone marrow cell proliferation [3,4,8] produce an opposite effect on these cell populations at one and the same time of the day (for instance, within the transition from the G1 to the S phase [1,3,4]). Circadian changes in the share of rod-nuclear and segment-nuclear granulocytes (curve *3*) are most expressed and antiphasic vis-a-vis the other subpopulations. The reason for these changes may be regulation of the flow of mature granulocytes from the bone marrow to the peripheral blood.

Regular changes in rat myelograms revealed in this study confirm the relativity of the notion "homeostasis" and the need to substitute the term

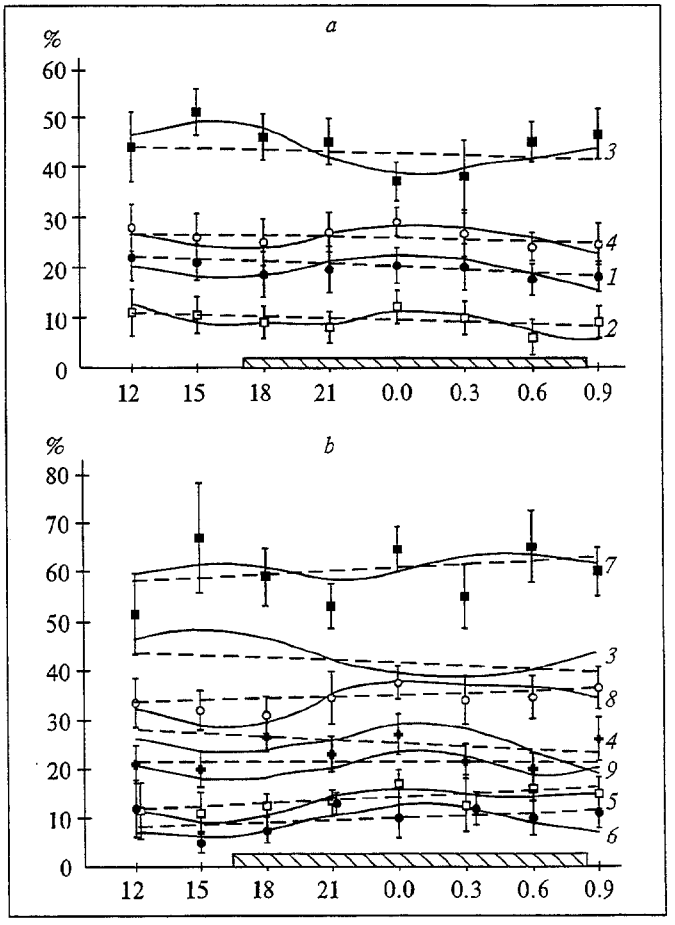

Fig. 1. Circadian changes in the fraction of bone marrow cell subpopulations in rats. *a*) granulocyte subpopulation; *b*) erythroid subpopulation and lymphocytes. *1*) myeloblasts, promyelocytes and myelocytes; *2*) metamyelocytes; *3*) rod nuclear and segmentated granulocytes; *4*) proerythroblasts; basophilic and polychromatophilic erythroblasts; *5*) oxyphilic erythroblasts; *6*) proliferating cells (proliferative pool); *7*) lymphocytes. Linear regression equations are presented by straight lines. Abscissa: time of day, h (region corresponding to dark period is shaded); ordinate: fraction of cells, %.

"homeokinesis". The results obtained are in good agreement with Halberg's ideas about the chronome [5] as a genetically determined system of rhythmic changes of different frequency manifested at all levels of cognition of living matter.

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MORPHOLOGY AND PATHOMORPHOLOGY

Effect of Weightlessness on the Early Posttraumatic Regeneration of the Soleus Muscle in Rats

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Gaining information on how reparative processes proceed under conditions of weightlessness is an important objective of research in space biology and medicine, and such information is of both theoretical and practical interest. In skeletal muscles, regeneration in weightlessness occurs in the presence of atrophic and degenerative changes [3,5,6,8,9], as well as of local and general metabolic disturbances, and it is therefore likely that the regenerative process is modified by weightlessness.

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In this ultrastructural study, we examined the course of posttraumatic regeneration in muscles of rats that had been exposed to weightlessness.

MATERIAL AND METHODS

For the ultrastructural study we used soleus muscles from 5 male Wistar rats that had spent 14 days on board the Kosmos-2044 biosatellite and from 5 rats each of three control groups: a vivarium control group (control group 1), one for which all flight conditions except weightlessness had been simulated (control group 2), and one in which the rats had been suspended by the tail in an antiorthostatic position (control group 3). Two

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