SEASONAL DIFFERENCES IN CIRCADIAN RHYTHMS OF PERIPHERAL BLOOD LEUKOCYTE COUNT IN WISTAR RATS

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The existence of circadian and circannual rhythms of the total number of leukocytes and neutrophils, and also of lymphocytes and their subpopulations in the peripheral blood of healthy individuals has now been conclusively proved [5, 6, 14]. Seasonal changes in hematologic parameters have been described in squirrels [3] and circadian rhythms of the peripheral blood cell composition in mice of different phenotypes [4]. Data on the biorhythmologic structure of the hematologic parameters of laboratory rats, however, are contradictory [11, 15].

The aim of this investigation was to study seasonal differences in the circadian rhythm of the peripheral blood leukocyte count in intact Wistar rats.

EXPERIMENTAL METHOD

Blood from the caudal vein of male Wistar rats, kept under conditions of natural daylight and darkness, was studied in 1985-1990, in the fall (October), winter (January), spring (April), and summer (July) at 3-hourly intervals for 3 days. Values of the total leukocyte count and the relative percentages and absolute numbers of different types of leukocytes were subjected to statistical analysis with calculation of significance by Student's t test and by the "Cosinor" program, with calculation of the length of the period, the mean diurnal level, amplitude, and acrophase.

EXPERIMENTAL RESULTS

Analysis of the circadian rhythm of the total leukocyte count in different seasons of the year revealed the highest mean daily level in the spring and the lowest in summer. For all periods of the year circadian rhythms for the total leukocyte count were statistically significant. The clearest seasonal differences in the position of the acrophases were: In the fall, winter, and summer – at night, and in spring – in the morning. The greatest values of the amplitude of the rhythm were regularly found in spring and the least in summer (Table 1). Statistically significant circadian rhythms of the relative percentage of neutrophils were found throughout the year. The rhythmometric parameters exhibited seasonal variability. The highest mean-daily percentage of neutrophils was found in winter, the lowest in spring. The acrophase in the fall and spring corresponded to night, in the winter and summer to the afternoon. Differences between the amplitudes were significant: in winter it was maximal, in spring and summer it was minimal.

Rhythmometric analysis of the absolute neutrophil count revealed seasonal differences in the mean daily level: the largest number of cells was a feature of winter, the smallest of summer. Statistically significant circadian rhythms were found in the fall and winter. In winter the acrophase regularly occurs in the evening, in the fall – at night. In spring and summer statistically significant rhythms of the absolute neutrophil count were not found. The greatest amplitude of the circadian fluctuations was found in winter, the least in spring (Fig. 1).

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TABLE 1. Rhythmometric Parameters of Peripheral Blood Leukocyte Count ($\cdot 10^{12}$/liter) in Wistar Rats at Different Times of Year (M ± m)

Parameter	Time of year	Period	Mesor	Amplitude	Acrophase
Total leukocyte count	F	24,5±0,7	13,10±1,20	1,97±0,60	00,42/23,24:02,04/
	W	24,2±0,9	14,53±1,02	2,01±0,70	22,06/21,06:23,32/
	Sp	24,0±0,2	15,69±1,76	2,52±0,60	10,48/09,44:12,20/
	Su	23,9±1,4	10,85±3,90	1,77±0,60	03,42/02,12:05,12/
Absolute neutrophil count	F	24,2±1,0	3,19±0,74	0,77±0,30	01,00/23,24:03,40/
	W	24,2±1,1	3,69±0,58	1,20±0,50	21,36/20,04:23,44/
	Sp		2,76±0,20		нет ритма
	Su		2,05±0,27		нет ритма
Absolute lymphocyte count	F	23,8±0,9	8,82±1,47	1,39±0,70	01,00/23,16:02,44/
	W	23,5±0,6	10,63±0,86	2,69±0,70	01,24/00,28:02,40/
	Sp	26,0±2,7	12,81±1,53	2,14±0,60	10,30/09,28:12,12/
	Su	24,3±1,5	6,25±1,30	1,56±0,30	03,36/02,04:05,04/
Absolute monocyte count	F		0,55±0,04		нет ритма
	W	24,0±2,0	1,62±0,16	0,66±0,20	07,48/05,44:09,52/
	Sp	24,1±1,1	0,51±0,06	0,19±0,06	04,12/03,08:10,04/
	Su	24,0±1,5	0,21±0,06	0,17±0,05	10,42/09,08:13,04/

Legend. F) Fall, W) winter, Sp) spring, Su) summer.

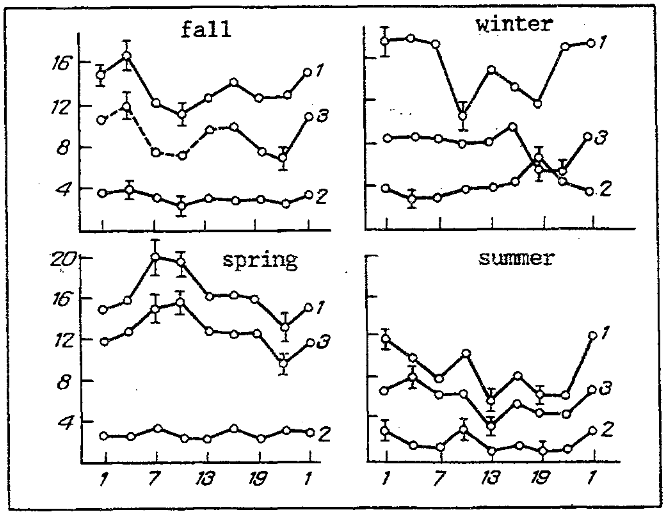

Fig. 1. Circadian rhythm of peripheral blood leukocyte count in Wistar rats: abscissa, clock time; ordinate, number of cells ($\cdot 10^{12}$/liter). 1) Total leukocyte count; 2) absolute neutrophil count; 3) absolute lymphocyte count.

A regular rhythm of the relative and absolute eosinophil counts could not be found, but seasonal fluctuations of the mean daily number of cells were observed. The maximum of the relative and absolute eosinophil counts occurred in the fall, the minimum of the relative count in winter, and of the absolute count in summer.

Analysis of the circadian rhythm of the relative and absolute lymphocyte counts revealed statistically significant circadian rhythms for these parameters also. In the spring the greatest values of the mesors of the relative and absolute lymphocyte counts were recorded. The maximal lymphocyte count was found in winter, the minimal absolute lymphocyte count in summer. The acrophase of the relative lymphocyte count in the fall and in spring occurred during the daytime, in winter and summer at night. In different seasons of the year, different values of the amplitude of the relative lymphocyte count were obtained: its highest value was found in summer, its lowest in spring.

Seasonal changes in the amplitudes and acrophases of the circadian rhythms of the absolute lymphocyte count were most significant. In the fall, and in winter and summer the maximum occurred at night, in spring – in the morning. Thus in winter, spring, and summer the circadian rhythms of the relative and absolute lymphocyte counts were synchronized.

When data on the relative monocyte count at different times of the day and year were compared, no statistically significant rhythmic fluctuations could be found. However, the highest mean daily count was discovered in winter, the lowest in summer. The essential point is that the profiles of the circadian rhythm coincide in winter and summer: a rise of the relative monocyte count is a regular feature of the daylight hours, a fall is a feature of night. In spring and the fall, the amplitudes of the fluctuations were minimal.

Rhythmologic analysis of the absolute monocyte count revealed statistically significant circadian rhythms in the winter, spring, and summer, and also revealed seasonal differences in the mean daily level: the highest monocyte count was recorded in winter, the lowest in summer. Seasonal variability of the position of the acrophases was noted: in winter and spring the profiles of the circadian rhythms coincided, with a maximum in the period of darkness. In summer the highest monocyte count occurred during daylight. The amplitude of the rhythms exhibited seasonal variation: its value was highest in winter and lowest in summer. In the fall rhythmic fluctuations of the absolute monocyte count exhibited a 12-hourly rhythm, with highest values in the morning and evening and lowest in the night and day.

The question of the basic mechanisms of formation of biological rhythms of physiological systems [8] and of hemopoiesis, in particular, is still a matter for debate. It has been found that the circadian rhythm of the number of lymphocytes and their subpopulations is largely determined by fluctuations of glucocorticoids [6, 10]. We also know that the number of neutrophilic granulocytes depends on the glucocorticoid level [7, 12]. There is no doubt that seasonal changes in heliogeographic factors, by modulating activity of the sympathicoadrenal system, determine the regular response of hematopoiesis and of the hematologic parameters [1, 2, 5]. It is perfectly probable that in rats, the anabolic effect of the sex hormones, the level of which is highest in spring and in early summer, must be regarded as one of the factors stimulating leukopoiesis during the spring [9, 13].

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