DIURNAL PERIODICITY OF MITOTIC CELL DIVISION IN THE INTERALVEOLAR SEPTA OF RAT LUNGS

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Knowledge concerning the diurnal periodicity of mitotic cell division in various mammalian organs enables the biologist to possess a clearer picture of the organ's capacity for physiological regeneration and to evaluate the way in which the organ will react to a variety of experimental stimuli more accurately [1, 3].

In a recent publication dealing with the characteristics of histological structures in the mammalian lung, Bertalanffy [8] has described the site of physiological regeneration in this organ as inferred from the results of previous workers.

By using colchicine to inhibit mitosis, it has been demonstrated [4, 6, 7] that in adult rats the mean number of metaphases in the cells of the interalveolar septa may vary within limits of 3.15-13.8% throughout the day. In these particular experiments, the rats were killed at 4 definite times in the 24 h period, but this number was obviously insufficient to detect the full range of variation in mitotic activity for this organ in the course of the day. Without the use of colchicine injections, the mitotic activity of rat lung cells have been studied at only one time of the day - 11 h. It was established that the mitotic coefficient underwent individual variation from 0.4 to 1.81% and possessed a mean value of 1.1%.

The present research aimed at establishing the nature of any diurnal rhythm in the cells of the interalveolar septa of the rat lung.

EXPERIMENTAL METHODS

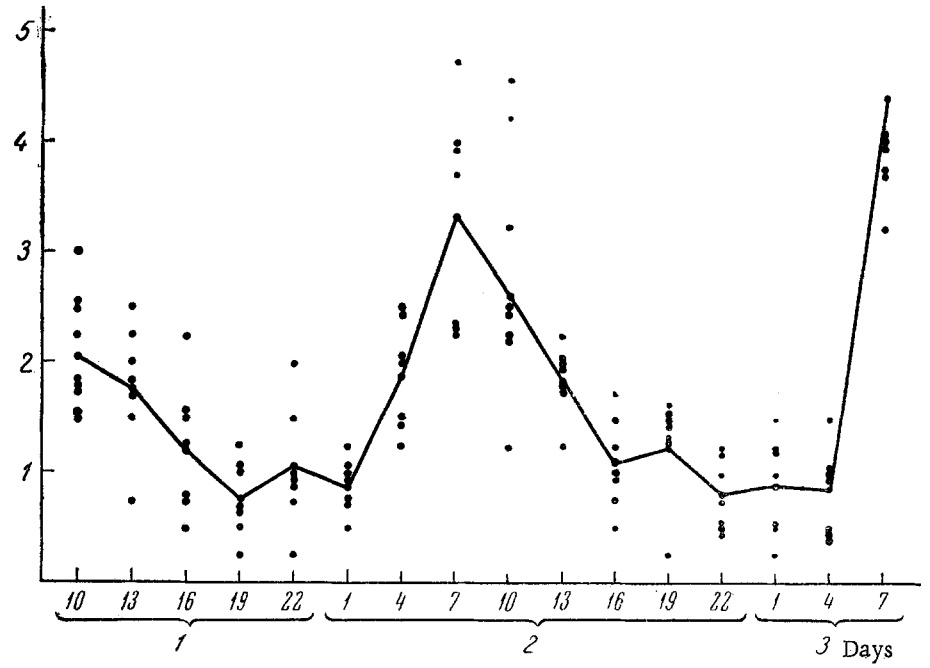
Our experiments were carried out on adult male white rats, weighing 160-180 g. For two weeks prior to the experiments the rats were kept 10 to a cage. They were subjected to the natural pattern of light and darkness for June. Food (rat pellets) was given once a day between 10 and 11 o'clock in such amounts that some food was still present in the cage the following morning.

The first group of rats to be killed (by decapitation) were taken at 10 h and had received no food that morning. Animals of the 15 subsequent groups were killed at 3 hourly intervals over a period of 2 days. Each group killed at one time consisted of 7-9 animals.

The lungs were fixed in Zenker's fluid and embedded in paraffin wax. Mitoses were counted in 4000 cells of the interalveolar septum (excluding blood cells) from sections 7 microns thick. The mitotic coefficient (MC) was expressed as a percentage. The data obtained was subjected to the Fisher-Student test of statistical significance.

EXPERIMENTAL RESULTS

It is evident from both the figures and the table that the greatest mitotic activity among cells of the interalveolar septa in the rat lung occurs between 7-10 h. From 10 h until 19 h there is a gradual reduction of mitotic activity and between 19 h and 1 h of the following day the number of mitoses is very low. From 1 h onwards there is a definite increase in the number of mitoses.



Curve showing changes in mitotic activity among cells of the interalveolar septa of the rat lung during a period of 2 days. Abscissa axis - hours of day; ordinate axis - value of mitotic coefficient (MC) as a percentage.

Changes in Mitotic Activity among Cells of the Interalveolar Septa of the Rat Lung over a 2 Day Period

Time of fixation (hour of day)	1st day				2nd day			
	total mitosis	(MC) (as %)	*P*	K	total mitosis	(MC) (as %)	*P*	K
10	74	2,05	0,334	9,0	84	2,62	0,046	8,3
13	50	1,78	0,082	7,3	52	1,85	0,003	5,5
16	34	1,21	0,115	4,7	31	1,10	0,497	9,1
19	22	0,78	0,253	21,4	35	1,25	0,069	7,7
22	30	1,06	0,497	4,0	23	0,82	0,769	7,1
1	25	0,89	0,001	11,7	25	0,89	0,922	24,4
4	53	1,89	0,004	9,6	24	0,85	0,0001	5,0
7	93	3,32		22,3	124	4,42		29,8

Note. K = phase coefficient: relationship between early phases of mitoses (prophase-metaphase) to later (anaphase-telophase).

The changes in mitotic activity, observable during the second day, agree almost exactly with those characteristic of the first day and in consequence it can be stated that the variation in number of mitoses is a constant and regular phenomenon from one day to another.

It can therefore be said that the cells of the interalveolar septa of the rat lung, like those of certain other tissues (cornea, esophageal epithelium, ventricle, cortical layer of kidney, etc), exhibit a definite diurnal rhythm [1, 3, 5]. This rhythm in the lung cells is characterized as a curve with a single peak, with the maximum number of mitoses in the morning (7-10 h) and the minimum number in the evening and early night (19-1 h). The mean (MC) for the first day was 1.62% and for the second 1.73%.

The ratio of early phases of mitosis to later phases varied insignificantly over the 24 h period, except for 19 and 7 h of the first day (21.4 and 22.3 respectively) and 1 and 7 h of the second day (24.4 and 29.8 respectively). The considerable excess of early phases of mitosis over later at 7 h of each day is indicative of an increase in the number of new cells entering mitosis i.e., initiation of increased mitotic activity. The high values for the early-to-

late phase coefficient, associated with 19 h and 1 h, do not appear to be of any great significance, for at these times of the day mitotic activity is very low (MC = 0.78 and 0.89%) and the values for the phase coefficient do not reflect any definite onset of mitotic activity among the cells.

If we use available information [8], which suggests that the duration of mitosis in cells of the interalveolar septa of the rat lung is 50 min, then at a mean MC of 1.6% the duration of interkinesis in parenchymatous tissue of rat lungs is equal to 520 h and complete renewal of these cells occur every 21.6 days. A more precise and exact estimate of the period of renewal of this type of cell would necessitate special investigations to determine the exact duration of mitosis for this kind of cell [9].

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