DIURNAL RHYTHM OF MITOTIC ACTIVITY IN CELLS OF THE INTERALVEOLAR SEPTA OF THE RAT LUNG AND ITS VARIATION WITH AGE

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The diurnal rhythm of mitotic activity in cells of the interalveolar septa of the lungs of 20-day rat fetuses corresponds to the rhythm in the adult. In rats aged 1, 3, and 10 days the curve of diurnal fluctuations of mitotic activity has a maximum in the evening and a minimum in the morning. After the 17th day of postnatal development the definitive diurnal rhythm with a maximum of the number of mitoses in the morning and the minimum in the evening is established in the lung tissue. The mean diurnal mitotic activity, although very high in the fetus, falls sharply immediately after birth. It rises again on the third day, but falls on the seventh day and later.

KEY WORDS: age changes; diurnal rhythm of mitosis; cells of interalveolar septa; lungs.

Investigations of the dynamics of changes in mitotic activity of the lung cells during the 24-h period have recently been published [4, 6]. The diurnal rhythm of cell division in the interalveolar septa of the lungs has been shown to follow a unimodal curve with a maximum of the number of mitoses in the morning and a minimum in the evening. Investigations carried out in the Department of General Biology of the Second Moscow Medical Institute have shown that the level of mitotic activity and the character of the diurnal rhythm of cell division depend on the age of the animal [1-3].

The rapid morphogenetic processes taking place in the lungs during the first days and weeks after birth [5, 7, 9] must evidently be reflected in the proliferative activity of the lung cells.

However, the problem of how the rates of proliferation vary with the animal's age, and the age at which the definitive diurnal rhythm of mitotic activity is established in the lung tissues remain unexplained. The present investigation was carried out in an attempt to shed light on these problems.

EXPERIMENTAL METHOD

The lungs of 400 albino rats aged 1, 3, 7, 10, 17, 28, and 45 days and the lungs of 20-day fetuses were used. The animals were decapitated at intervals of 4 h during the 24-h period, six or seven animals at each time.

The number of mitoses in 5000 cells of the interalveolar septa of the lungs was counted in paraffin sections, 6 μ in thickness and stained with hematoxylin and eosin. The larger proportion of mitoses was found in the alveolar cells, and mitoses were extremely rare in cells of the endothelium and the surface epithelium of the lung [6]. The mitotic index was expressed per 1000 cells.

EXPERIMENTAL RESULTS

The results are given in Figs. 1 and 2. Changes in mitotic activity of the cells of the interalveolar septa during the 24-h period were found in the lungs of rats of all age groups. The most distinct diurnal

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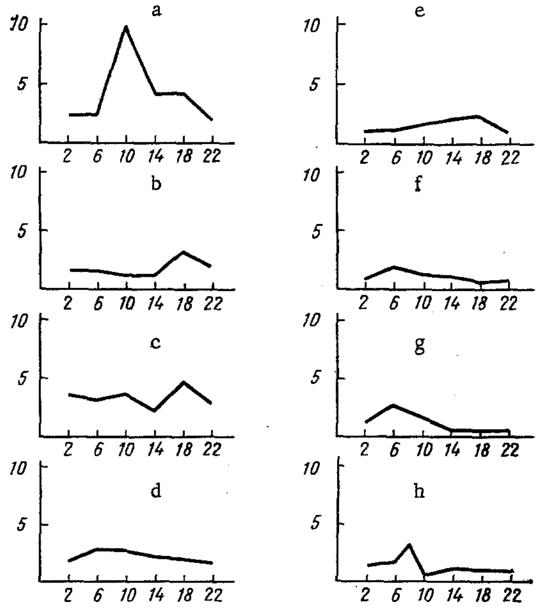

Fig. 1. Curves of changes in mitotic activity of cells of interalveolar septa from rats of different ages during the 24-h period: a) 20-day fetuses; b) young rats aged 1 day, c) 3 days, d) 7 days, e) 10 days, f) 17 days, g) 28 days, and h) 45 days. Abscissa, time of day; ordinate, mitotic index (in $^0/_{00}$).

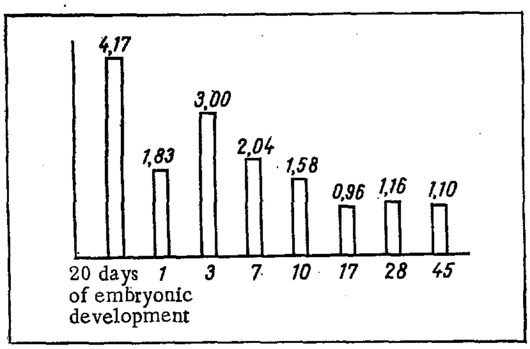

Fig. 2. Changes in mean diurnal mitotic activity of cells of interalveolar septa of the lungs in rats of different ages. Abscissa, age of animals (in days); numbers above columns show mitotic index (in $^0/_{00}$).

rhythm of cell division was observed in fetuses (Fig. 1a) and in sexually mature animals (Fig. 1h). The maximum of the number of mitoses in the fetuses was observed during the morning (10 a.m.) and the minimum at 10 p.m. ($P = 0.000$). The mean diurnal mitotic activity was high ($4.17^0/_{00}$). The fact was noted that the character of the diurnal rhythm in the lungs of the fetuses corresponds to the character of the rhythm in the lungs of adult animals. The dynamics of proliferative processes in the tissues of the fetuses probably depends on hormonal regulation by the mother for similar results have been obtained with other organs [1].

Curves of the diurnal rhythm of mitotic activity in the lungs of rats aged 1, 3, and 10 days were similar in the time of their maximum, which ocurred during the evening.

In rats aged 7 days the diurnal fluctuations of mitotic activity were slight.

In rats aged 17 and 28 days the maximum of the number of mitoses was shifted to the morning. Differences between the maximal and minimal values of mitotic activity were statistically significant ($P = 0.001$). It is at this age that the hormonal status of the rats is formed, and this is evidently reflected in the character of the diurnal rhythm of mitotic activity in cells of different organs and, in particular, of the lungs.

The diurnal rhythm of mitosis in the lungs of animals aged 45 days is definitively established and it corresponds to that in the adult.

The mean diurnal values of mitotic activity of cells of the interalveolar septa of the lungs also vary with age (Fig. 2). In the fetus these indices are very high ($4.17^0/_{00}$), and they fall sharply immediately after birth ($1.83^0/_{00}$). The process of birth itself evidently has an inhibitory action on cell proliferation, for the same fact was observed during the study of the diurnal rhythm of mitosis in the liver of fetal and neonatal rats [1].

On the third day of postnatal development the mean diurnal index of mitotic activity rose ($3.00^0/_{00}$), but on the seventh day and later it fell. These results agree with those obtained in experiments on the lungs of golden hamsters and mice [8], although the authors cited did not take into account diurnal variations in mitotic cell division.

During postnatal development of lung tissue there is thus a gradual decrease in the mean diurnal mitotic activity of the cells of the interalveolar septa of the lungs and a change in the character of the diurnal rhythm of mitosis. In the first 2 weeks after birth the dynamics of changes in mitotic activity in the course of the 24-h period is described by a curve rising to a maximum of the number of mitoses during the evening. After the 17th day the definitive diurnal rhythm is established, with a maximum of the number of mitoses in the morning and a minimum in the evening. It is interesting to note that, just as in the lung tissue, the diurnal rhythm of mitosis in the early stages of postnatal development of the liver, esophagus, and epidermis was the reverse of the diurnal rhythm of mitosis in the tissues of adult animals, and during growth of the animal the maximum of mitotic activity shifted to the morning.

The similarity between the changes in the rhythm of mitotic activity in the lungs and other tissues evidently indicates that cell division is regulated by common factors.

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