EFFECT OF BURNS OF THE SKIN ON THE DIURNAL RHYTHM OF MITOTIC ACTIVITY IN THE RAT CORNEAL EPITHELIUM

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Experiments on rats showed that thermal burns of the skin disturb the diurnal rhythm of mitotic activity in the corneal epithelium. Compared with normal animals, an additional peak of the number of mitoses appears during the period of minimal mitotic activity (evening). It was also shown that the duration of mitosis in burned rats varies from 0.8 h (maximum of mitotic activity) to 4.4 h (minimum of mitotic activity).

Under certain experimental conditions the diurnal rhythm of mitotic activity can be shifted or even disturbed without a change in the mean diurnal index [8]. The study of cell division in the corneal epithelium after thermal burns has shown that on the second day after burning the number of mitoses increases in the morning but decreases in the evening compared with the control. No information on the effect of burns on the diurnal rhythm of cell division could be found in the accessible literature.

The object of this investigation was to study the diurnal rhythm of mitotic activity in the corneal epithelium and the duration of mitosis after thermal burns of the skin.

EXPERIMENTAL METHOD

The corneas (90) from 45 noninbred rats weighing 80-100 g were used for the investigation. The hair was shaved from the back of the control animals. A burn was inflicted on the shaved surface of the back of the experimental animals by application of a lighted spirit swab (about 20% of the body surface, exposure 30 sec). The animals were sacrificed starting 32 h after burning. The control animals were sacrificed every 2 h and the experimental every 4 h for 24 h. An injection of 5 mg/kg colchicine was given to the experimental animals 4 h before sacrifice. The mitotic index (MI) was calculated for 100 fields of vision after counting mitoses in total preparations of the cornea [4]. To calculate the duration of mitosis, the mean value of MI was determined for the control animals for each of the periods of action of colchicine on the corresponding group of experimental animals. The duration of mitosis was calculated by the equation in [6, 7]. The significance of differences was assessed by means of the nonparametric criterion of inversion (V). The null hypothesis was not true when $P \leq 0.01$.

EXPERIMENTAL RESULTS

Calculation of MI in the corneas of the control rats showed that there is a definite diurnal rhythm in the number of mitoses. The character of the diurnal changes was similar to that described in the literature [1, 3, 5]. Two maxima of mitotic activity (at noon and midnight) and 2 minima (at 4 p.m. and 4 a.m.) were observed. The differences between the values of MI at the maximum and minimum of mitotic activity were statistically significant ($P < 0.01$). Histological investigation of the corneas of the experimental animals showed no anaphases or telophases, indicating that the correct dose of colchicine had been chosen. The graph (Fig. 1) clearly showed the diurnal character of accumulation of colchichine metaphases (C-metha-

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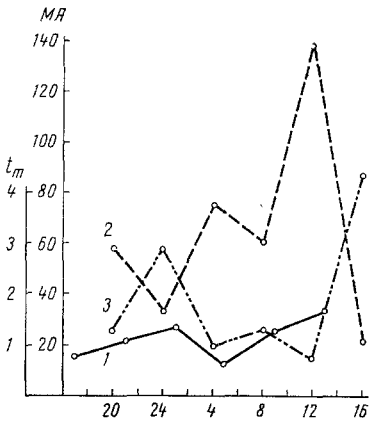

Fig. 1. Change in diurnal rhythm of proliferation in corneal epithelium 32 h after burning of the skin: 1) control; 2) experiment; 3) rate of mitosis. Abscissa, time of day; ordinate: MA) mitotic activity (mitotic index for control, number of C-metaphases for experiment) per 100 fields of vision, t_m) duration of mitosis (in h).

phases). The dynamics of the accumulation of C-metaphases differed in character from the diurnal rhythm in the control. Three peaks of mitotic activity of cell division were observed – at 8 p.m., 4 a.m., and noon. Whereas in the control MI increased from 4 p.m. to midnight (first peak), in the experimental series the number of C-metaphases fell until midnight. During the period of minimum mitotic activity in the control animals (2-6 h) a fresh increase in the number of C-metaphases was observed in the cornea of the experimental rats. The third maximum of mitotic activity in the experimental series coincided with the morning maximum of MI in the control. In the burned animals the diurnal rhythm of mitotic activity in the cornea at night (10 p.m.-2 a.m.) and in the early morning (4-6 a.m.) was thus changed by comparison with the control animals. The duration of mitosis in the burned rats varied from 0.8 h (at 10 a.m.-2 p.m.) to 4.4 h (at 2-6 p.m.). The longest duration of mitosis was observed in the evening: 2.9 h from 10 p.m. to 2 a.m. and 4.4 h from 2 to 6 p.m. At these times the number of C-metaphases was similar to MI in the control. Consequently, the rate of mitosis was in fact slowed.

Similar changes in the duration of mitosis in the cornea of normal mice were demonstrated by Mamontov and Ivanova [6]. Irradiation does not affect the diurnal rhythm of mitotic activity in the normal or regenerating liver [2].

No data on the diurnal variations in the rate of mitosis in the normal rat retina could be found, and the question of whether burns affect the rate of mitosis must therefore remain open.

After thermal burns of the skin changes thus take place in the diurnal rhythm of cell division in rats in the morning (maximum of mitotic activity in the corneal epithelium): an additional peak of proliferative activity appears in the period of minimum mitotic activity (the evening). Diurnal changes also take place in the duration of mitosis in burned rats: from 0.8 h (maximum of mitotic activity) to 4.4 h (minimum of mitotic activity).

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