CIRCADIAN RHYTHM OF MITOSIS IN CERTAIN ORGANS OF 10-WEEK HUMAN FETUSES*

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Fluctuations in the number of mitoses during the 24-hour period were found in the adrenal cortex of 10-week human fetuses: the number of cell divisions reached a maximum at night (3-4 a.m.) and a minimum during the morning (7-8 a.m.). The level of mitotic activity in the corneal epithelium and endothelium and in the kidney was the same at different times of day or night. It is postulated that the rhythm of mitosis in the embryonic adrenal is connected with the early beginning of its functional activity.

The circadian rhythm of cell division still remains an inadequately investigated aspect of the general problem of biological rhythm. The establishment of the circadian rhythm of mitosis during the embryonic and early postembryonic periods of development has been studied least of all. The only investigations concerned with this problem have been undertaken on albino mice and rats [2,5,6,11] and on chick embryos [3]. So far as man is concerned, few investigators have examined this problem [8,9]. These workers removed the prepuce from male infants at the age of 8 days at different times of day and investigated its epidermis. They showed that the mitotic activity is much higher during the late evening and night than in the morning. Whether a circadian rhythm of mitosis exists at earlier stages of human individual development remained unknown.

In the present investigation, the rhythm of mitotic activity was studied in certain organs of 10-week human fetuses.

EXPERIMENTAL METHOD

Material was obtained after abortions for medical reasons on women aged 20-35 years. The operations were carried out at different times of day (Table 1) in the course of August, 1962. Some of the fetuses were fixed actually during operation. Age was established from the history, the size of the uterus, and the size of the fetuses. From 7 to 10 embryos were examined at each time. Mitotic activity was determined in total preparations of the cornea and in sections (10 μ) of the kidney and adrenal cortex (outer zone). The mitotic activity was judged from the number of dividing cells in a constant area of the specimen (1.65 mm^2). The results obtained were subjected to statistical analysis by the Fisher–Student method.

EXPERIMENTAL RESULTS

The mitotic activity in the corneal epithelium and endothelium and in the kidney was uniformly high at different times of day or night (Table 1).

The small increase in the number of cell divisions in the corneal endothelium at 3-4 a.m. was not statistically significant ($P = 0.09$). No circadian rhythm of mitosis could thus be found in these organs. However, in the adrenals the mitotic activity showed regular changes throughout the 24-hour period (Table 1). The number of cell divisions reached a maximum at night (3-4 a.m.) and a minimum in the morning (7-8 a.m.). The differences between the maximal and minimal values of mitotic activity were significant ($P < 0.001$). During the afternoon (2-3 p.m.) the number of cell divisions increased ($P = 0.03$), but later (by 11 p.m. to midnight) the mitotic activity fell slightly.

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TABLE 1. Changes in Mitotic Activity in Certain Organs of 10-Week Human Fetuses in the 24-hour Period

Organ	Number of mitoses					
	7-8 a.m.	11 a.m. to noon	2-3 p.m.	7-8 p.m.	11 p.m. - midnight	3-4 a.m.
Corneal epithelium	53,6	52,5	53,5	49,4	52,3	50,0
Corneal endothelium	56,4	62,6	60,7	57,3	61,5	69,1
Adrenal cortex	55,1	—	76,0	—	66,1	94,2
Kidney	117,7	—	114,4	—	115,1	118,3

The results obtained indicate that the circadian rhythm of mitosis in some human organs exists at the early stages of embryonic development. It is also evident that the circadian rhythm of cell division arises at different times in different organs. In 10-week fetuses, for instance, it is not found in the cornea or kidney, while in the adrenals it is seen distinctly.

These differences may perhaps be connected with the character and level of physiological activity of these organs. The work rhythm of an organ is one of the main factors responsible for the pattern of circadian rhythm of mitosis in adult animals, [1,4]. It may be postulated that in the embryonic period this dependence plays an important role. The embryonic cornea and kidney at the 10th week of intrauterine life can hardly be said to form a specific function. At the same time, no circadian rhythm of mitosis is observed in these organs. The adrenal cortex is characterized by an early beginning of its functional activity [7,10]. This is perhaps connected with the well-defined rhythm of mitosis in this organ.

Correlation between physiological and mitotic rhythms in the embryonic adrenals requires further investigation. High mitotic activity and a circadian rhythm of cell division are found in the outer zone of the adrenals of 10-week fetuses (in the germinative zone hardly any mitoses are found), while the existence of physiological activity at this stage of development can be assumed for the inner (germinative) zone. On the assumption that these periodic processes in the intact organism are interconnected, it is natural to conclude that the physiological rhythm of the germinative zone will be responsible for the synchronization of cell divisions in the outer zone of the cortex.

The impression is thus gained that during embryonic development one of the factors responsible for the appearance of a mitotic rhythm is the presence of specific physiological activity in the organ concerned.

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