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Mitotic Rhythm in Human Epidermis.

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Studies of mitotic rhythm, *per se,* have been few, although the number of mitoses found in various tissues has been used as an index of functional activity of these organs when subjected to various experimental conditions. The work of Loeb and his students[1, 2] on the thyroid gland, using the mitotic index as a basis for the measurement of the effect of various chemicals and hormones upon this organ is most significant. All the work that has been done on plants,[3–6] mice and cats,[7, 8] indicates the existence of a rhythm in cell division, which must obviously be taken into consideration in experimental studies; but, to the best of our knowledge, no observations have been reported on rhythmic periodicity of mitotic division in human tissues.

The relatively small number of mitoses that can usually be found in sections of human epidermis is striking, especially since the epidermis is known to be constantly renewed at a rather rapid rate, but as a general rule the sections of skin in which mitosis has been studied have been secured (by biopsy or by operation) during the day time. Consequently, the question arises whether more mitoses might not be observed in skin obtained during the night when, perhaps, cell division is occurring at a different rate than during the day.

The skin covering the prepuce of infants, which is removed at circumcision, was selected as a convenient tissue for experimentation. The babies were all of approximately the same age (8 days) and had been kept from birth under practically identical environmental

1 Friedman, H., and Loeb, L., *Anatom. Rec.,* 1934, **59**, 5.

2 Margolin, E. S., PROC. SOC. EXP. BIOL. AND MED., 1933, **30**, 495.

3 Karsten, G., *Z. f. Bot.,* 1915, **7**, and 1918, **10** (quoted by Carleton).

4 Stålfelt, M. G., *Kunst. Svenska Vetensk. Hand.,* 1921 **62**, 1 (quoted by Carleton).

5 Kellicott, W., *Bull. Torrey Bot. Club,* 1904, **31** (quoted by Carleton).

6 Friesner, R. C., *Am. J. Bot.,* 1920, **7**, 380.

7 Fortunyn-Van Leyden, Droogleever (Mrs.), *Proc. Soc. of Sciences,* Amsterdam, 1916, **19**, 38, and 1926, **29**, 979 (quoted by Carleton).

8 Carleton, A., *J. Anat.,* 1933, **68**, 251.

conditions, at the St. Louis Maternity Hospital. The specimens were obtained at various hours throughout the day and night, through the courtesy of the Director of the Hospital, Dr. Otto Schwartz. Immediately after circumcision (performed always by the same method), they were placed in a 1% solution of acetic acid and allowed to remain in this fluid for 24 hours. It was then possible to separate completely the layer of epidermis from the underlying dermis. This separated layer of epithelium was then stained *in toto* with Ehrlich's hematoxylin, dehydrated in alcohol, cleared in oil of wintergreen and xylol, and mounted. Mitoses were counted by using an oil immersion lens and focusing through the various cell layers, with less chance of missing cells in division than would be possible in serial sections. In each specimen 5000 cells were counted in successive fields and the number of cells in mitosis recorded. All counts were made by one observer in order to eliminate the element of individual variations in accuracy. Thus, the experimental error was reduced to a minimum.

In the specimens in which cell counts have been completed, a marked increase in the number of mitoses in the specimens obtained at night has been found.

TABLE I.

Time of taking specimen	No. of mitoses found	No. of cells counted
7:30 A.M.	14	5046
7:30 "	16	5034
9:00 "	10	5152
9:30 "	15	5014
10:25 "	7	5000
10:30 "	8	5068
11:40 "	28	5094
8:45 P.M.	23	5009
9:45 "	35	5124
10:45 "	31	5080
11:55 "	25	5013
11:50 "	23	5086
12:45 "	23	5016

Since the results obtained thus far seem to indicate that a rhythmical periodicity in mitotic division is present in human tissues, it is proposed to determine whether this rhythm is also present in cancer tissue, or whether it is altered or interrupted. In preparation for this study, carefully controlled biopsies are being made on tissue from patients with normal uterine cervices and from those with carcinoma of the cervix. One biopsy is obtained during the day and another at night from the same patient. The results of the mitotic counts upon this material will be reported later.