

Daily Variations in Mitotic Activity of Adrenal Cortex, Thyroid and Oral Epithelium of the Rat.* (22067)

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(Introduced by Franz Halberg.)

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Daily physiologic periodicity seems to characterize mitotic activity in the oral epithelium(1,2) as well as in a variety of other tissues from plants and animals (for review see 3 & 4). These daily changes in mitotic activity may be influenced by daily periodicity in various environmental factors which affect the organism. But intrinsic, partly hormonal mechanisms also may contribute to the 24-hour spacing of peaks in mitotic activity(2,4). In this latter connection, the following questions were explored in this study. First, whether day-night differences may be detected in the mitotic activity of certain endocrines under the standardized environmental circumstances and at those times of day at which significant day-night differences have been demonstrated in the oral epithelium(2). If day-night differences existed in the mitotic activity of the glands studied, it also was of interest to know whether the times of "high" and "low" in number of mitoses were roughly the same in endocrine and non-endocrine tissues.

Materials and methods. For 3 weeks prior to their sacrifice, 32 Sherman albino rats weighing about 135 g were kept in single cages in a room illuminated from 6:00 to 18:00, darkened from 18:00 to 6:00, and maintained at $24 \pm 1^\circ\text{C}$ and $49 \pm 2\%$ relative humidity. A commercial diet (Lab Blocks, Allied Mills, Chicago) and tap water were available to the rats *ad libitum* since weaning and throughout the period of standardization. A subgroup composed of 16 rats was decapitated between 7:00 and 7:30 ("Day-rats") and another subgroup of 16 rats between 21:30 and 22:00 ("Night-rats"). The adrenal glands, the thyroid and part of the oral epithelium were immediately fixed by means of Zenker-Formol.

Serial sections, 4μ thick, were then prepared and stained with Hematoxylin-Eosin. Mitotic activity in every section from each tissue and rat was then evaluated. In the case of the adrenal cortex, mitotic activity was related to area-units of 10 mm^2 . For the thyroid, mitoses were counted in 150 oil-immersion fields(83 ± 1 cells per field). In the oral epithelium, mitoses were counted in units of 10 mm length of basal membrane. The length of basal membrane was measured by the use of a special device which will be described elsewhere(5).

Results. A summary of results in Fig. 1 shows the considerable variability of the data for individual rats, which are given by the height of the columns graphed. More important, some considerable day-night differences in mitotic activity also become apparent from a comparison of the horizontal lines, which denote the means in mitotic activity by day and by night. For the thyroid and for the oral epithelium, there is a day "high" and a night "low" in number of mitoses. By contrast, a night "high" and a day "low" appear to characterize mitotic activity in the adrenal cortex of the nocturnally active rat.

Discussion. These data seem to demonstrate, first, a 24-hour periodicity of mitosis in the thyroid and adrenal of the rat. Second, the data also reveal that daily mitotic periodicity in the thyroid is synchronized with the 24-hour spacing of mitosis in the oral epithelium. Mitotic periodicity in the oral epithelium, in turn, has been shown to be synchronized with 24-hour periodicity of mitosis in other tissues(2) and with the 24-hour rhythms in eosinophil count and in rectal temperature (1,2). It also has been shown that the adrenals are essential for the maintenance of 24-hour rhythms in eosinophil count(4,6) and in some aspects of hepatic phospholipid metabolism(7). If, as seems likely(4), the

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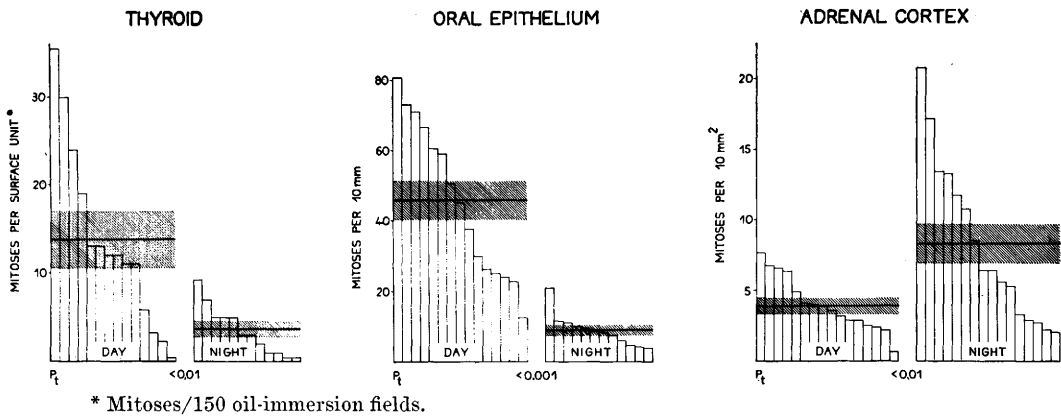


FIG. 1. Mitotic activity at two times of day in tissues investigated. (Columns show data for individual rats; horizontal lines and shaded areas denote means ± 1 S.E.; day = 7:00-7:30; night = 21:00-21:30.)

adrenal constitutes a fundamental mechanism of physiologic daily periodicity, the phase-difference noted herein between its mitotic periodicity and the 24-hour spacing of other rhythms may call for a detailed analysis of adrenal mitotic activity (with more frequent sampling during the 24-hour period).

Summary. Daily periodicity characterizes mitotic activity in the adrenal, the thyroid and the oral epithelium of male Sherman albino rats, kept under standardized environmental circumstances. The daily times of "high" and "low" in number of mitoses are roughly synchronized for the thyroid and the oral epithelium, while the 24-hour periodicity in mitotic activity of the adrenal cortex shows a

different timing.

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Oxytomic Action of Rat Hypothalamus Extracts. (22068)

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Vogt(1) confirmed the presence of vasopressor, antidiuretic and oxytomic activities in extracts of dog hypothalamus. According to her results the hypothalamus differs from the posterior pituitary in that the relative oxytomic activity of the hypothalamus is much lower than the expected value, the P/O ratio (pressor activity/oxytomic activity) being 14.6. Inasmuch as Lawler and du Vigneaud

(2) have shown that oxytocin-free vasopressin possesses an oxytomic activity corresponding to 5% of the pressor activity, Vogt(1) suggests that the oxytomic substance extracted from the hypothalamus may be pure vasopressin. This interpretation is of importance in view of the findings of Bargmann and Scharer(3) on production of hormones of the pars nervosa of the hypophysis by the neuro-