

DIURNAL CHANGES IN MITOTIC ACTIVITY AND DISTRIBUTION OF MITOSES IN THE GASTRIC MUCOSA OF ALBINO RATS

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The diurnal rhythm of mitotic activity has been demonstrated in many organs, but the data relating to the periodicity of cell division in the gastro-intestinal tract are incomplete and conflicting. Least attention has been paid to the study of the diurnal rhythm of mitosis in the mucous membrane of the stomach. A few workers [7, 12], using colchicine for their experiments and fixing their material only 3 or 4 times a day, failed to observe a diurnal periodicity in the mitoses taking place in the mucous membrane of the fundus of the stomach.

Many writers have studied the localization of mitoses in the gastric mucosa. It has been found that the site of cell proliferation in the mucous membrane of the fundus [5-8, 10-13] is the isthmus and neck of the glands. The movement of cell material from the neck to the mouth of the glands has been demonstrated [3, 4, 10, 12]. Opinions differ regarding the source from which new peptic and parietal cells are derived. Some writers [6, 10] consider that cells of both types may very rarely divide, while others [3, 8] are inclined to believe that the renewal of peptic and parietal cells takes place at the expense of the mucous cells of the neck.

In the mucous membrane of the pyloric division of the stomach, a region of intensive mitotic activity has been located at the border of the pits with the mucous glands or in the depth of the pits [6, 9, 10, 13]. Some of these workers [9, 13] also consider that there is a zone of division, formed by the glandular cells of the pyloric glands.

The object of the present investigation was to find out if a diurnal periodicity of cell division is present in the mucous membrane of the pyloric and fundal portions of the stomach, and also to clarify one or two aspects of the localization of mitoses in the glands of these divisions.

Diurnal Changes in Mitotic Activity
in the Gastric Mucosa of Albino Rats

Time of fixation (hour of day)	Mitotic coefficient (in ‰)	
	pyloric portion	fundus
10	11.5	4.8
13	10.6	3.5
16	10.3	3.9
19	14.5	5.1
22	13.3	4.3
1	11.9	3.5
4	12.4	4.6
7	13	4.8
10	14.5	4.2
13	10.3	2.4

EXPERIMENTAL METHOD

Experiments were carried out on 100 male albino rats with an average weight of 170 g. The animals were kept in natural light. Once a day, at 10:30 A.M., the rats received a natural meal in a quantity so large that they could not eat it all, but left some until next day. Rats were sacrificed (by decapitation) starting from 10 A.M., at intervals of 3 hr, 10 animals at each time. The stomachs were fixed by pouring in Carnoy's fluid through the duodenum. The material was embedded in paraffin wax, cut into sections 7 μ thick, and stained by the Dominici-Kedrovskii method. The pyloric and fundal portions of the stomach were investigated separately. Mitoses were counted in 50 glands, cut strictly longitudinally, under the binocular microscope (eye-piece 7 \times , objective 90 \times).

The pyloric glands were divided along their length into four portions: the 1st and 2nd were situated in the upper part of the gland (their cytoplasm stained pink by Kedrovskii's method), and the 3rd and 4th were in the basal part of the gland (stained blue). Staining with mucicarmine showed that the 3rd and 4th portions corresponded to the

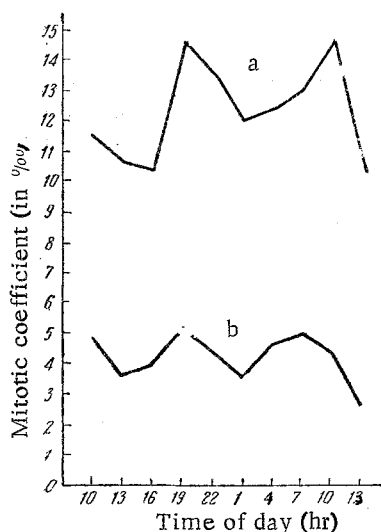


Fig. 1. Diurnal changes in the mitotic coefficient in the epithelium of the pyloric region (a) and fundus of the stomach (b).

Despite the lower coefficient at 10 A.M. on the first day, the difference between it and the coefficient at 10 A.M. on the second day was not significant ($P = 0.09$). From an analysis of these results it may be supposed that the curve of the diurnal changes in mitotic activity is approximately bimodal in character, with maxima at 10 A.M. and 7 P.M. However, the maximum of the curve at 10 A.M. on the first day was ill defined. Meanwhile, it may be noted that the amplitude of the diurnal changes in mitotic activity in the mucous membrane of the pyloric portion of the stomach was smaller than in several other organs [1, 2].

The mean daily mitotic coefficient for the epithelium of the pyloric portion of the stomach was $7.8‰$ and for the region of the neck and base of the glands $12.2‰$.

Counts of the individual phases of mitosis revealed no significant change in their relative proportions throughout the 24 hours. The mean proportion of early prophase was $5.7‰$, prophase $17.3‰$, metaphase $38‰$, anaphase $10.9‰$, telophase $15.8‰$, and reconstructions $12.3‰$. Hence, it may be concluded that the differences in the mitotic coefficients were due to changes in the absolute number of mitoses and not to changes in the duration of any particular phase of mitosis.

Mucous membrane of the fundus of the stomach. In the fundal glands, $37.2‰$ of mitoses were situated in the surface epithelial cells, $51.3‰$ in the mucous glands of the neck, $7.4‰$ in the principal cells, and $4.1‰$ in the parietal cells.

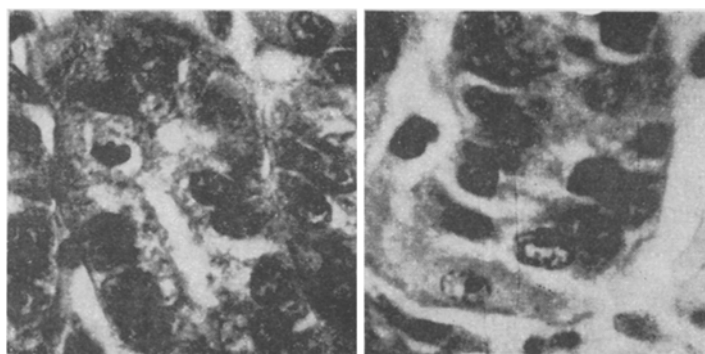


Fig. 2. Mitoses in the peptic cells of the glands in the fundus of the stomach from albino rats.

neck of the gland and to its glandular part. In each case mitoses were counted in 3,750 cells. Since we found that $99.1‰$ of mitoses were in the 3rd and 4th portions of the gland, i.e., in the cells of the neck and the glandular cells, the mitotic activity was determined in these divisions alone.

In the mucous membrane of the fundus, the mitoses were counted separately in four types of cells: surface epithelial, mucous cells of the neck, parietal, and principal cells. In 50 glands, an average of 5,400 cells in each was counted.

The mitotic coefficient (MC), i.e., the number of mitoses found in 1,000 cells, was calculated. The results were analyzed statistically by the Fisher-Student method.

EXPERIMENTAL RESULTS

Pyloric part of the gastric mucosa. The changes in mitotic activity during the 24 hr period are shown in the table and in Fig. 1, a.

From 10 A.M. until 4 P.M. on the first day the mitotic coefficient remained at roughly the same level, and at 7 P.M. it rose ($P = 0.0001$), and this was followed by a not strictly significant ($P = 0.03$) fall at 1 A.M. At 10 A.M. next day another increase was observed, followed by a fall at 1 P.M. ($P = 0.015$).

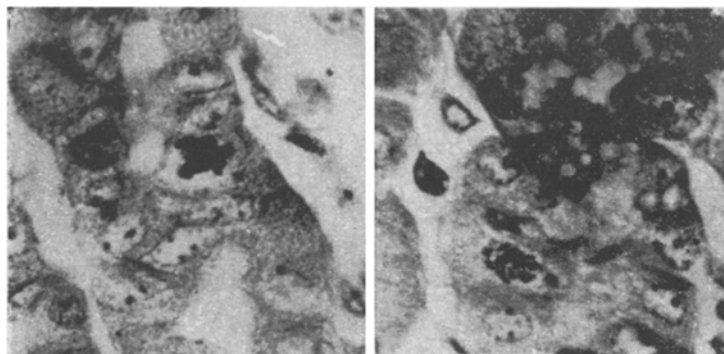


Fig. 3. Mitoses in the parietal cells of the glands of the fundus of the stomach in albino rats.

The diurnal changes in mitotic activity determined in the surface epithelial cells and the mucous cells of the neck are given in the table and in Fig. 1, b. At 10 A.M., the mitotic coefficient was 4.8‰, decreasing until 1 P.M. ($P = 0.061$) and increasing again until 7 P.M. ($P = 0.061$). The decrease until 1 A.M. was statistically insignificant, like the increase until 7 A.M., but the decrease in the number of mitoses until 1 P.M. on the next day was significant ($P = 0.001$). The difference in the number of mitoses at 1 P.M. on the first and second days was not significant ($P = 0.89$); the increase until 7 P.M. compared with the value at 1 P.M. on the first and second days was significant ($P = 0.001$).

Hence, the diurnal changes in mitoses in the mucous membrane of the fundus were less marked than in the pyloric portion of the stomach. In general, the curve of the diurnal periodicity was close to bimodal.

The mean daily mitotic coefficient of a whole gland in the fundus of the stomach was 2.04‰, and in the region of the maximal concentration of mitoses (the surface epithelial cells and the mucous cells of the neck) — 4.2‰; in the peptic cells it varied from 0.27 to 0.79‰ and in the parietal cells from 0.28 to 1.06‰. Since mitoses were observed in both parietal and principal cells (Figs. 2 and 3), we suggest that they are renewed independently, and at a much slower rate, moreover, than the surface epithelial cells and the mucous cells of the neck.

In the surface epithelial cells and the mucous cells of the neck, as in the pyloric portion, no change was observed in the percentage of the phases at different times of day. The mean percentage of early prophase in the mucous membrane of the fundus of the stomach was 11.1%, of prophase 18.8%, metaphases 39.3%, anaphases 6.4%, telophases 15.4%, and reconstructions 9%.

If it is conventionally accepted that the duration of mitosis is about 30 min, with this intensity of mitotic activity the rate of renewal of the whole gland in the fundus of the stomach will be 10.2 days, and that of the surface epithelial cells and the cells of the neck 4.95 days, which is close to the values obtained by Stevens and Leblond [12].

SUMMARY

A study was made of the daily changes of mitotic activity and of mitosis distribution in the mucosa of the pylorus and the fundus of the stomach of albino rats. In the pylorus 99.1% of mitoses occurred in the lower portion of the gland. The average daily mitotic coefficient in the glands of the pyloric portion was 7.8‰. The curve of the daily rhythm is double-peaked in shape with maximal levels at 10 A.M. and 7 P.M. In the glands of the gastric fundus 88.5% of all the mitoses occurred in the surface-epithelial and mucous cells of the cervix, 7.4% in the peptic cells, 4.1% in the parietal cells. The average daily mitotic coefficient in the glands of the fundus is 2.04‰.

In the mucous membrane of the fundus the curve of the daily periodic mitotic activity is similar to that of the pyloric portion, but it is less pronounced.

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