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# CHRONOBIOLOGICAL STUDIES OF THE INTESTINAL EPITHELIUM IN THE ACUTE PHASE OF OPISTHORCHIASIS


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KEY WORDS: experimental opisthorchiasis; intestine; biorhythm; mitotic activity.


Opisthorchiasis causes lesions of varied severity in organs of the gastrointestinal tract [3, 8-11]. In the acute phase of opisthorchiasis, a gastroenterocolitic type of course of the disease is distinguished by clinicians [1, 5, 10].

The involvement of the gastrointestinal tract as a functional system in the pathological process in opisthorchiasis may be associated with changes in the kinetics of the epithelium and with disturbances of regeneration and adaptation in it. Structural disturbances in the organs are preceded by deviations at the time level [2]. Hence, the need for a study of the diurnal rhythm of mitosis in the gastric and intestinal epithelium as an indicator of cell renewal and of the regenerative capacity of the tissues.

The object of this investigation was to analyze the diurnal rhythm of mitotic activity of the intestine of the jejunum, ileum, and cecum in the acute phase of experimental opisthorchiasis.

## EXPERIMENTAL METHOD

Experiments were carried out on 64 sexually mature golden hamsters (32 experimental and 32 control) weighing $88.35 \pm 2.16$ and $85.55 \pm 2.01$ g respectively. The acute phase of opisthorchiasis was reproduced by introducing 50 viable metacercariae, isolated from a freshly killed ide, into the pharnyx of the animals. The animals were decapitated after open ether anesthesia on the 30th day after infection at 9 a.m., 3 and 9 p.m., and 3 a.m. Pieces of jejunum, ileum, and cecum were fixed in 10% neutral formalin and embedded in paraffin wax. Sections 5-7 $\mu$ thick were stained with hematoxylin and eosin, by Van Gieson's method, and by the PAS reaction. The number of mitoses was counted in 1000 cells in the region of the intestinal crypts – the zones where cambial cells which are the sources of regeneration are situated [6, 7, 12]. The characteristics of mitotic activity studied included the following: mitotic index (MI), mean diurnal value of MI ($M \pm m$), the coefficient of diurnal rhythm (CDR) as described by Krotov and Lugovoi [4], the index of diurnal adaptation (IDA), and the coefficient of functional synchronization (CFS) [2].


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TABLE 1. Changes in Mitotic Activity (MI, ‰) of Intestinal Epithelium of Golden Hamsters Infected with Opisthorchis felineus in the Course of the 24-Hour Period (M ± m)

| Part of gastro-intestinal tract | Experimental conditions | Time of day | | | | Mean diurnal index of mitotic activity | Amplitude of diurnal fluctuations of mitotic activity |
|---|---|---|---|---|---|---|---|
| | | 9 a.m. (n=16) | 3 p.m. (n=16) | 9 p.m. (n=16) | 3 a.m. (n=16) | | |
| Jejunum | Normal | 13,36±0,44 | 9,00±0,33 | 13,81±0,38 | 17,07±0,37 | 12,88±0,41 | —3,88±0,08<br>4,19±0,04 |
| | Infected animals | 9,31±0,32 | 10,88±0,47 | 12,69±0,47 | 11,56±0,56 | 11,11±0,27 | —1,80±0,05<br>1,58±0,20 |
| Ileum | Normal | 15,50±0,40 | 10,38±0,24 | 15,69±0,60 | 20,43±0,62 | 15,39±0,50 | —5,01±0,26<br>5,04±0,12 |
| | Infected animals | 16,06±0,63 | 13,56±0,62 | 17,88±0,57 | 17,25±0,72 | 15,86±0,36 | —2,30±0,26<br>2,02±0,21 |
| Cecum | Normal | 13,50±0,39 | 8,94±0,36 | 14,25±0,25 | 16,56±0,39 | 13,31±0,39 | —4,37±0,03<br>3,25±0,00 |
| | Infected animals | 13,14±0,47 | 11,06±0,85 | 11,69±0,54 | 13,81±0,38 | 12,40±0,32 | —1,34±0,53<br>1,41±0,06 |

Legend. Number of animals in parentheses.

## EXPERIMENTAL RESULTS

Morphological changes in the jejunum, ileum, and cecum of the golden hamsters in the acute phase of opisthorchiasis consisted mainly of circulatory disorders in the form of congestion and stasis in the capillaries and edema in the subepithelial layer.

Histological variants of lesions of the jejunum, ileum, and cecum of the golden hamsters in the acute phase of opisthorchiasis were studied in the following numbers of cases: 1) normal structure and functional disturbances of the jejunum 24, of the ileum 25, and of the cecum 24; 2) superficial jejunitis 7; 3) diffuse jejunitis 1; 4) superficial ileitis 6; 5) diffuse ileitis 1; 6) eosinophilic infiltration of the cecum 4; 7) typhlitis 4.

Despite different forms of intestinal lesion, the mitotic regime was comparable in all groups, so that the data could be pooled. Indices of mitotic activity in the epithelium of the jejunum, ileum, and cecum of healthy animals showed a maximum at 3 a.m. and a minimum at 3 p.m. In the acute phase of opisthorchiasis, changes in the mucous membrane of the cecum were similar in character, but in the jejunum and ileum the peak of mitotic activity was shifted to 9 p.m. The amplitude of the diurnal fluctuation of mitotic activity in the infected animals was significantly lower than in the control ($P < 0.01$). Numerical values for mitotic activity of the intestinal epithelium are given in Table 1.

The mean diurnal mitotic activity in all parts of the intestine of the infected animals studied remained higher than normal ($P > 0.01$). However, figures reflecting the rate of cell renewal and the lability of this process during the 24-h period in the acute phase of experimental opisthorchiasis showed considerable changes. CDR in the jejunum was reduced from 1.38 to 1.20, in the ileum from 1.39 to 1.18, and in the cecum from 1.37 to 1.05. IDA was increased in the jejunum from 3.37 to 36.31%, in the ileum from 1.22 to 11.33%, and in the cecum from 5.56 to 11.03%. In the healthy golden hamsters significant negative correlation was found between the time of day and mitotic activity of the epithelium in different parts of the intestine (in the jejunum CFS was $-0.55$, $P < 0.01$; in the ileum CFS was $-0.62$, $P < 0.01$; in the cecum CFS was $-0.46$, $P < 0.01$). Infestation caused desynchronization of mitosis (in the jejunum CFS was $-0.17$, $P > 0.05$; in the ileum CFS was $-0.04$, $P > 0.05$; in the cecum CFS was $-0.14$, $P > 0.05$).

In the acute phase of experimental opisthorchiasis, mobilization of the vital resources thus takes place in the epithelium of the jejunum, ileum, and cecum (a high mean diurnal index of mitotic activity, a rise in IDA). On the other hand, the diurnal regime of mitotic activity is disturbed (a fall in CDR and CFS). On the whole this leads to smoothing of the diurnal biorhythm of mitotic activity of the intestinal epithelium in the acute phase of opisthorchiasis. These changes correspond to the stage of functional stress, which passes into the stage of functional overstrain of the general adaptation syndrome [2]. The decrease in amplitude of the diurnal fluctuations of mitotic activity in the acute phase of opisthorchiasis impairs the power of adaptation of the intestinal epithelium and lowers its functional and structural reserves.

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# EFFECT OF ADRENORECEPTOR FUNCTION ON MITOTIC ACTIVITY OF THE REGENERATING RAT LIVER


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KEY WORDS: liver; mitotic activity; adrenoreceptors.


Analysis of the recent literature [2-6] shows that the regenerative activity of the liver depends to a definite extent on the original functional state of the adrenoreceptors. The present writer showed previously in rats [1] that administration of two doses (1 h before and 24 h after resection of the liver) of the $\alpha$-adrenoblocker phentolamine considerably reduced the mitotic index, whereas administration of the $\beta$-adrenoblocker propranolol at the same times increased the mitotic index in the regenerating liver. Neither adrenoblocker had any marked effect on the ratio between early and late phases of mitosis. The aim of the present investigation was to discover the effect of administration of a single dose of the adrenoblockers at different times after partial hepatectomy.

## EXPERIMENTAL METHOD

Noninbred male albino rats weighing 200-250 g were used. About 70% of the liver by weight was removed from the animals. Some animals were given a single intraperitoneal injection of phentolamine, others a single dose of propranolol, 20 mg/kg in both cases. The drugs were given 1 h before, or 30 min, 8, and 24 h after resection of the liver. Control rats received physiological saline in the same volume at the same times. The animals were decapitated 30 h after the operation, in all cases at 3-4 p.m. Histological sections were prepared from the liver (fixation in Carnoy's fluid, embedding in paraffin wax, staining with hematoxylin).

The regenerative activity of the liver was estimated from the mitotic index (in promille), the phase coefficient (the ratio of early and late phases of mitosis, in %), and the number of binuclear cells (in %). At least 100 fields of vision of the microscope under a magnification of 40 × 16 were examined in each section. The glycogen content in the liver also was determined by the method of Vertar and Wenner.


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