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# EXPERIMENTAL BIOLOGY

# Stimulation of Hepatocyte Proliferation in the Normal and Pathologically Altered Liver under a Pulsed Magnetic Field

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**Key Words**: *stimulation; proliferation; pulsed magnetic field; hepatitis; cirrhosis*

One of the currently studied aspects of liver regeneration is stimulation of the proliferative processes by means of various physical agents. Commonly used for this purpose are direct and pulsed currents of rectangular and exponential form and a low-frequency varying magnetic field. However, not all of these agents are sufficiently effective [6-9].

In this investigation we studied the effect of a pulsed magnetic field (PMF) with induction of 100 mT and exponential pulses lasting 1.2-3.5 msec, with a frequency of 1-10 Hz, on hepatocyte proliferation in the normal and pathologically altered liver as well as the mechanisms of cell division stimulation. In light of the fact that sympathetic nervous system transmitters play a significant role in the regulation of proliferative processes [1-5,12,14] experiments were performed to switch off the autonomic impulses by means of chemical desympathization using guanethidine and treatment with the α- and β-adrenoblockers phentolamine and anapryline.

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## MATERIALS AND METHODS

Proliferative activity of hepatocytes was assessed by the value of the mitotic index (MI) in parts per 1000. The following models were used: regenerating liver of normal rats (179), of rats with toxic hepatitis (128), and of rats with cirrhosis (28) induced by 70% oil solution of $CCl_4$ in a dose of 0.3 ml s.c. 4 times a week for 3 and 5 months.

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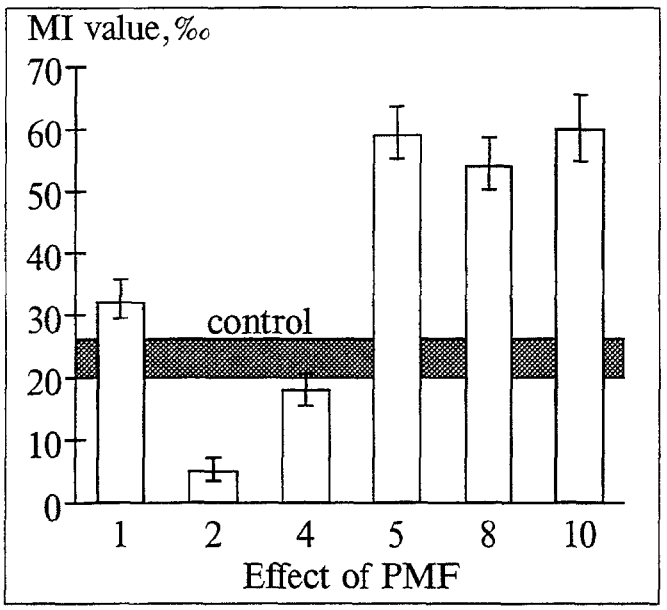


**Fig. 1.** Mitotic index of hepatocytes 24 hours after liver resection and PMF of different frequencies. Abscissa: effect of PMF (columns); ordinate: MI value (in ‰).

Guanethidine was injected in a dose of 50 mg/kg daily for 14 days, since the maximum concentration in the neurons is reached after two weeks of administration [10,11,13]. After 30% liver resection, the animals were treated with a PMF with a frequency of 10 Hz during 30 min. The animals were killed 28 hours after partial hepatoectomy. The number of visibly normal neurons was calculated on 10 random sections from different parts of the plexus coeliacus ganglion (periphery, intermediate zone, center) on a test area of a measuring grid. Ten visual fields occupying the whole slide were measured at magnification 40×10×1.5. On the basis of the findings the volume share of neurons on the test area of the slide was calculated in conventional units. Mitotic activity of hepatocytes was studied simultaneously.

Catecholamines act on hepatocytes largely via the membrane receptors. Excitation of α-adrenoreceptors or blocking of β- adrenoreceptors has a stimulatory effect on proliferative activity in the regenerating liver [2]. Phentolamine and anapryline were injected twice a day in a dose of 20 mg/kg 10 times. After liver resection, PMF with a frequency of 10 Hz was performed for 30 min. The animals were killed 28 and 48 hours after treatment.

Peters' formula was used to estimate the arithmetic means and significance of the differences [8].

## RESULTS

The study of the mitotic activity of hepatocytes of regenerating normal liver under different PMF frequency showed that the maximal increase of the number of mitoses corresponded to the frequencies 5.8 and 10 Hz (Fig. 1). To achieve an increase in the number of the mitoses, it is best to apply a PMF during the early stage of liver regeneration : on the day of resection, the next day, and one day later. The MI value of the hepatocytes was 77±6.16‰ after 24 hours, 55.0±4.30‰ after 48 hours,and 69.41±6.50‰ after 72 hours (in the control 21.77±3.07‰, 26.5±3.18‰, and 14.73±1.50‰, respectively).

Stimulation of hepatocyte proliferative activity is also noted in the regeneration of altered liver. Animals with toxic hepatitis and cirrhosis subjected to PMF after liver resection had a three-times elevated MI value compared to the control animals. Twenty-eight hours after treatment MI was 49.70±5.21‰ (in the control 16.00±2.50‰), while in the group with cirrhosis it was 30.87±1.16‰ (in the control 11.45±0.20‰). After 48 hours MI decreased in both groups: in the first group 16.70±2.90‰ (in the control 10.50±0.50‰) and in the cirrhosis group 16.80±2.70‰ (in the control 7.87±1.70‰).

A study of the mitotic activity of normal regenerated liver hepatocytes under the conditions of nearly total desympathization (the number of neurons on the test area was 1.04±0.21 c.u.; Fig. 2) revealed no stimulating effect of PMF on hepatocyte proliferation. The MI was a mere 3.40±1.0‰.

Where there were more intact neurons (3.18±0.19 c.u.) the MI was 20.0±3.36‰. Under α- adrenoreceptor blocking with phentolamine a stimulating effect of PMF was observed. Twenty-eight hours after resection the MI value of normal hepatocytes was 60.00±8.70‰(in the control 14.30±0.85‰). The animals with toxic hepatitis had a 5 times higher MI value than the animals which were not subjected to PMF: 43.80±6.3‰(in the control 9.20±1.13‰).

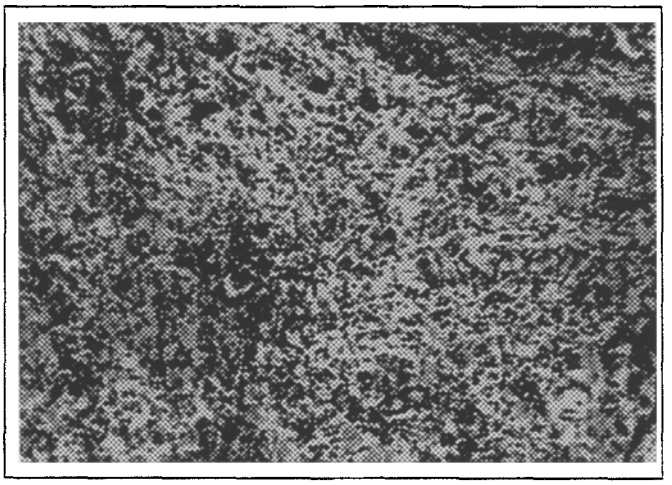

**Fig. 2.** Destruction of neuronal elements of plexus coeliacusganglion under chemical desympathization with guanethidine. Small-cell infiltration of ganglion stroma. Stained with hematoxylin – eosin. ×120.

Anapryline injection coupled with PMF showed no significant increase of mitosis number.

Thus, PMF stimulates the proliferative activity of the normal and altered liver. A significant role in the realization of this effect belongs to the sympathetic part of the autonomic nervous system.

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# Blood Pressure Monitoring according to the "Womb to Tomb" Program with Consideration of the Chronome in Humans


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**Key Words:** *chronome; arterial pressure monitoring*

The development of miniature recorders for arterial pressure (AP), respiration rate (RR), oxygen saturation ($O_2$), ECG, EEG, gastric juice acidity, body and surface temperature, motor activity, and other functions has made diagnostic medicine more effective. Many new monitoring methods are reserved for solving some special problems, those of chronobiology among them.

Chronobiology is the science of the temporal structure of life. The concepts and facts belonging to this discipline relate to the information containing time series.

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