EFFECT OF ADAPTATION TO HIGH MOUNTAIN CONDITIONS ON CIRCADIAN RHYTHMS OF MITOTIC ACTIVITY OF THE EPITHELIUM OF THE CONVOLUTED TUBULES OF THE ALBINO RAT KIDNEY

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The number of spontaneous mitoses fluctuates rhythmically during the 24-h period and depends on several external factors [2, 3, 5, 7, 9, 11]. If animals sustain wounds or fractures during the first day after being taken up into the mountains, post-traumatic regeneration processes are delayed [1, 4, 6, 10]. Meanwhile relative adaptation, arising after a stay of 15-30 days in the high mountains, improves the rate of regenerative reactions to some degree, so that it is virtually the same as in the plains [4, 6, 10]. Regeneration of tissues and organs is based on cell proliferation, and it was therefore important to discover, first, how elevation to a high altitude itself is reflected in the mitotic activity (MA) of the animal, with particular reference to the epithelium of the convoluted tubules of the albino rat kidney, and second, how routine adaptation correlates with the circadian rhythym of mitosis.

The aim of the present investigation was to study the circadian rhythm of proliferative MA of the epithelium of the convoluted tubules of the kidney during exposure to a combination of extremal factors in the high mountains (hypoxia, low atmospheric pressure, high UV radiation and ionization of the air, sharp fluctuations of temperature, etc.).

EXPERIMENTAL METHOD

Experiments were carried out at an altitude of 3379 m above sealevel (Anzob Pass) on 240 noninbred male albino rats reighing 100-120 g, kept on a standard diet. The animals were decapitated 1, 3, 5, 30, and 60 days after their arrival in the mountains, at 3-hourly intervals, from 6 a.m. to 3 a.m., five at a time. Rats kept in the plains (Dushanbe, 820 m above sealevel) served as the control. The number of mitoses and cells was counted under a binocular microscope (ocular 7, objective 90) with 8 × 8 mm diaphragm, in the cortical layer in transverse sections through the center of the kidney. Two sections 5 μ thick, taken at intervals of 5-6 sections from the right kidney of each rat were used. In each section the number of fields of vision examined, the number of mitoses found in the different phases, and the total number of cells were counted at 8 levels (the distance between the levels was equal to two fields of vision, with the same diaphragm) of the cortex on the horizontal plane. Data for two sections were added together and the mitotic coefficient (MC) was determined by calculation for 20,000-30,000 cells. The numerical results were subjected to statistical analysis by the method in [8].

EXPERIMENTAL RESULTS

A histological study of the structure of the kidney during a 2 months' stay of the animals in the mountains showed disturbance of the hemodynamics of the kidney on the 1st and 2nd days: dilatation of capillaries, phenomena of stasis perivascular edema. On the 5th day these phenomena became less pronounced and by the 15th day they had completely disappeared.

Counting the number of mitoses showed (Table 1) that ascent into the mountains led to marked inhibition of MA of the epithelium of the convoluted tubules of the kidney: the average MC for the 24-h period was $0.68 \pm 0.03‰$ in the plains, and it fell by 70-72% ($P > 0.001$) immediately after the ascent. The number of

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TABLE 1. Dynamics of Changes in MA (MC, ‰) of Epithelial Lining of Convoluted Tubules of Rat Kidney under High Mountain Conditions (M±m)

Experimental conditions	Time of experiment	Clock time								Average for 24 h period.
		6 a.m.	9 a.m.	12noon	3 p.m.	6 p.m.	9 p.m.	midnight	3 a.m.	
Plains (control)	—	0,69±0,03	0,73±0,03	0,89±0,04	0,73±0,03	0,66±0,03	0,53±0,03	0,61±0,03	0,63±0,03	0,68±0,03
Mountains	1	0,21±0,01	0,24±0,02	0,30±0,2	0,20±0,01	0,17±0,01	0,16±0,01	0,17±0,01	0,19±0,01	0,20±0,01
	3	0,22±0,02	0,26±0,02	0,32±0,02	0,21±0,01	0,17±0,01	0,17±0,01	0,18±0,01	0,20±0,01	0,22±0,01
	5	0,39±0,03	0,56±0,03	0,68±0,04	0,41±0,03	0,39±0,02	0,27±0,02	0,30±0,02	0,34±0,02	0,41±0,04
	15	0,52±0,03	0,61±0,03	0,72±0,04	0,53±0,03	0,50±0,03	0,43±0,02	0,42±0,01	0,49±0,02	0,53±0,03
	30	0,53±0,03	0,70±0,04	0,77±0,03	0,64±0,03	0,53±0,03	0,42±0,02	0,42±0,02	0,45±0,03	0,56±0,04
	60	0,61±0,03	0,71±0,03	0,81±0,04	0,70±0,04	0,58±0,03	0,44±0,02	0,45±0,02	0,47±0,03	0,60±0,04

mitoses reached a maximum at noon both in the plains (0.89±0.4‰) and in the mountains (0.30±0.02‰). The number of divisions reached a minimum in both cases at 9 p.m.: 0.53±0.03 and 0.16±0.01‰ respectively. MC was higher in the morning and afternoon than in the evening and night: In the plains it was 0.84 and 0.61‰, in the mountains 0.24 and 0.12‰ on the 1st day after the climb. On the 5th day after the rats were taken into the mountains marked activation of MA of the epithelial cells of the renal convoluted tubules took place and MC on the 3rd day had increased from 0.22 ±0.01 to 0.41 ± 0.04‰ ($P < 0.001$), although this was 1.6 times less than in the control. On the 15th day after the ascent the number of spontaneous mitoses was increased, and was even closer to the values obtained in the plains. The longer the animals remained in the mountains, the more favorable the process of normalization of MA of the epithelium of the convoluted tubules of the renal cortex: MC was 0.56 ± 0.04‰ on the 30th day and 0.60 ± 0.04‰ on the 60th day of the experiment.

The circadian rhythm of MA of the epithelium of the renal convoluted tubules, incidentally, did not differ in the control and experiment at any of the times of observation and it was monophasic in character: Its one maximum occurred at noon and its minimum at 9 p.m. Meanwhile the number of mitoses was greater in the morning and afternoon than in the evening and night, a characteristic feature of nocturnal animals. As regards the relative percentages of the individual phases of mitosis in the plains and in the mountains, the change was not significant.

It can thus be concluded from these results that a combination of extremal mountain factors has a marked inhibitory effect on mitotic cell division of the epithelium of the renal convoluted tubules on the 1st-3rd days after rats are transported from the plains into the mountains. MA begins to increase at the end of the 1st week, approaches the control level on the 30th day of adaptation, and is almost completely restored to normal by the 60th day of the animals' stay in the mountains. Meanwhile the course of the circadian rhythm of MA was undisturbed, evidently because of the genetically determined stability of this process.

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