MITOTIC ACTIVITY OF THE KIDNEY UNDERGOING COMPENSATORY HYPERTROPHY AT HIGH ALTITUDES

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Experiments on 420 male albino rats weighing 105-120 g showed that at high altitudes the maximal increase in mitotic activity of the renal cortex and medulla during compensatory hypertrophy is 2-2.5 times less than in the valley, and it is observed on the fifth, and not the second, day after unilateral nephrectomy.

Investigations at high altitudes [1-4, 7] have shown that regenerative processes in animals (dogs, rabbits, albino rats and mice) transferred there from the valley take place more slowly in their organs and tissues. The relative adaptation developed by animals during a stay of one month at high altitudes has a favorable effect on the animal and largely restores these processes to the level observed in the valley [1, 2, 7].

The object of the present investigation was to determine the effect of combined high-altitude factors (rarefaction of the atmosphere, increased solar and cosmic radiation, sharp drop of temperature from day to night, low absolute humidity of the air, strong wind, etc.) on the mitotic activity of the kidney undergoing compensatory hypertrophy at various times after the climb into the mountains, and to compare the results with the corresponding data obtained in the valley at the same external environmental temperature as in the mountains.

EXPERIMENTAL METHOD

Experiments in the mountains at an altitude of 3379 m above sea level (Anzob Pass) were carried out on 280 sexually mature male albino rats weighing 105-120 g, which were divided into four groups (70 animals in each group). Left sided nephrectomy was performed on the animals of group 1 on the 2nd-3rd day after their arrival in the mountains. The animals of group 2, with intact kidneys, served as controls. Left-sided nephrectomy was performed on the rats of group 3 on the 31st-32nd day after their arrival in the mountains. The controls for these animals were those of group 4, with intact kidneys. All animals were kept on the same diet and under identical conditions, with 10 rats sharing standard cages.

The rats were decapitated in groups of 10 at each time, always at 12 noon, and 1, 2, 5, 10, 15, 30, and 60 days after the beginning of the experiment. Similar experiments were performed on 140 rats of the same weight, divided into two groups, in Dushanbe (altitude 820 m above sea level). The left kidney was removed from 70 animals, while the other 70 acted as the control.

The methods of histological processing of the material and counting of the mitoses were described in the previous paper [6].

EXPERIMENTAL RESULTS

The results of the study of mitotic activity in the mountains and valley are shown in Table 1.

An increase in mitotic activity in both the cortex and medulla of the residual kidney was observed one day after unilateral nephrectomy in the valley. It is worth mentioning that no increase in mitotic

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TABLE 1. Mitotic Activity of Rat's Kidney

Time of investigation (in days)	MI in control kidney (in ‰)		MI in kidney undergoing compensatory hypertrophy (in ‰)	
	cortex	medulla	cortex	medulla
	In the valley			
1	0,71±0,0	0,44±0,10	1,44±0,02	0,66±0,03
2	0,72±0,04	0,46±0,09	3,38±0,19	1,89±0,04
5	0,77±0,04	0,45±0,07	1,93±0,14	1,16±0,02
10	0,73±0,03	0,45±0,05	1,67±0,06	0,99±0,02
15	0,82±0,04	0,47±0,04	1,36±0,03	0,84±0,03
30	0,74±0,03	0,47±0,04	1,08±0,02	0,62±0,01
60	0,69±0,02	0,46±0,02	0,90±0,02	0,59±0,02
	In the mountains; rats not yet adapted			
1	0,27±0,01	0,16±0,01	0,23±0,01	0,15±0,01
2	0,32±0,02	0,20±0,01	0,72±0,03	0,44±0,02
5	0,39±0,02	0,24±0,01	1,38±0,04	0,73±0,02
10	0,45±0,01	0,30±0,02	1,32±0,03	0,70±0,02
15	0,54±0,02	0,33±0,03	1,12±0,04	0,62±0,02
30	0,59±0,01	0,38±0,01	0,98±0,02	0,59±0,02
60	0,63±0,01	0,43±0,01	0,84±0,03	0,51±0,01
	In the mountains; rats adapted			
1	0,60±0,01	0,42±0,01	0,99±0,15	0,59±0,02
2	0,64±0,01	0,45±0,02	1,35±0,04	0,79±0,03
5	0,63±0,03	0,43±0,02	1,94±0,10	1,03±0,02
10	0,67±0,03	0,44±0,02	1,69±0,07	0,95±0,04
15	0,66±0,03	0,47±0,01	1,29±0,08	0,79±0,04
30	0,68±0,05	0,48±0,02	1,06±0,08	0,60±0,01
60	0,67±0,02	0,46±0,01	0,93±0,06	0,57±0,03

Note. MI denotes mitotic index.

activity in the medulla of the kidney undergoing compensatory hypertrophy was found previously in rats [8]. The mitotic index (MI) reached a maximum on the second day [5, 8], and remained high for 2 months. It was 1.5-2 times higher in the cortex than in the medulla.

The experiments carried out in the mountains on unadapted animals showed that their transfer from the valley to the mountains sharply inhibited mitotic activity in the intact kidney. Whereas in the valley, MI in the cortex of the control kidneys varied from 0.69 ± 0.02 to 0.82 ± 0.04 ‰, and the medulla from 0.44 ± 0.1 to 0.47 ± 0.04 ‰; 1 day after the arrival of the rats in the mountains the MI was reduced by more than 2.5 times, to 0.27 ± 0.01 ‰ for the cortex of the intact kidney and 0.16 ± 0.01 ‰ for the medulla. The differences are statistically significant ($P < 0.001$).

Gradual adaptation of the animal to the combination of high-altitude factors had a beneficial effect on the mitotic activity of the renal epithelium. After the rats had been 2 months in the mountains, MI was 0.63 ± 0.01 ‰ for the cortex and 0.43 ± 0.01 ‰ for the medulla. The differences from data obtained in the valley were no longer statistically significant ($P > 0.05$).

Under high altitude conditions, in the kidney of the unadapted rats undergoing compensatory hypertrophy 1 day after the operation, MI in the cortex and medulla was reduced (0.23 ± 0.01 and 0.15 ± 0.01 ‰ as against 0.27 ± 0.01 and 0.16 ± 0.01 ‰ in the intact animals), but these differences are not statistically significant ($P > 0.05$). At these last times mitotic activity showed a marked increase, reaching a maximum on the fifth day, when MI in the cortex was 3.5 times higher than in the control, and in the medulla 3 times higher ($P < 0.001$). MI still remained at almost the same level 10 days after the operation. On the 15th, 30th, and 60th days, MI was still higher than the control by a statistically significant degree ($P < 0.001$). Consequently, the mitotic activity in the kidney of unadapted animals, when undergoing compensatory hypertrophy under high altitude conditions, began to increase after the second day, reached a maximum on the fifth day, and then remained high for 2 months. The maximum increase in mitotic activity was 2.5 times smaller than in the valley.

In experiments on rats relatively adapted to high altitude conditions, MI in the kidneys of intact animals was largely back to its normal valley level, although MI in the cortex remained lower by a statisti-

cally significant degree throughout the first week. Compared with the unadapted animals, MI was significantly increased until the 30th day of the experiment in both the cortex and the medulla. In the kidney of relatively adapted rats undergoing compensatory hypertrophy 1 day after the operation, MI was significantly higher than in the intact kidney: in the cortex it was raised to $0.99 \pm 0.15‰$ compared with $0.60 \pm 0.01‰$ and in the medulla to $0.59 \pm 0.02‰$ compared with $0.42 \pm 0.01‰$; for the cortex $P < 0.05$ and for the medulla $P < 0.001$.

Two days after the operation MI was still greatly increased, being $1.35 \pm 0.04‰$ for the cortex and $0.79 \pm 0.03‰$ for the medulla in the experimental series compared with $0.64 \pm 0.01‰$ and $0.45 \pm 0.02‰$ in the control. MI reached its maximum after 5 days, namely 1.94 ± 0.1 and $1.03 \pm 0.02‰$ compared with 0.63 ± 0.03 and $0.43 \pm 0.01‰$ in the control ($P < 0.001$ in both cases), i.e., in the rats relatively adapted to high altitudes the process followed in the same course as in the unadapted animals but the mitotic activity was higher. After 5 days MI was 1.4 times higher in both the cortex and the medulla. The differences were still statistically significant ($P < 0.02$). Subsequently, on the 10th, 15th, 30th, and 60th days, the changes in mitotic activity of the adapted rats resembled those in the kidney of the unadapted animals.

Comparison with results obtained in the valley showed that mitotic activity at high altitudes in the kidney of relatively adapted rats undergoing compensatory hypertrophy was significantly reduced only during the first 2 days: MI in the mountains 1 day after arrival was $0.99 \pm 0.15‰$ for the cortex and $0.59 \pm 0.02‰$ for the medulla compared with 1.44 ± 0.02 and $0.66 \pm 0.03‰$ in the valley, ($P < 0.001$ for the cortex and $P < 0.05$ for the medulla), while 2 days after arrival MI for the cortex was $1.35 \pm 0.04‰$ and $0.79 \pm 0.03‰$ for the medulla compared with 3.38 ± 0.19 and $1.89 \pm 0.04‰$, respectively ($P < 0.001$).

The differences found at later stages of the investigation were no longer statistically significant.

Consequently, if animals are kept for 1 month at high altitudes this has a significant effect on the mitotic activity of their kidney undergoing compensatory hypertrophy; from the fifth day after the operation, their values of MI approximate to those in the valley. However, the maximum increase in mitotic activity is reduced by almost half, and it is observed not on the second day, but on the fifth day just as in rats not adapted to high altitudes.

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