

# CHANGES IN THE MITOTIC ACTIVITY OF THE RENAL EPITHELIUM IN RELATION TO THE FUNCTIONAL ACTIVITY OF THE KIDNEY

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The changes in the interrelation between the functional activity of cells and their division has attracted the attention of cytologists for a long time. This is no coincidence, as the functional activity of cells is one of the factors which determine the pattern of cell division in the animal body [1,3]. The data concerning the relation between functional activity of cells and their division are of different value. To elucidate this question the majority of authors used pharmacological methods of changing the functional activity of organs (pilocarpine, adrenaline), or the method of injecting supravital stains [2,5,6,7]. The results of these investigations must be assessed with great caution, as they do not exclude a possible direct influence of the pharmacological preparations and stains used upon the cell multiplication independently of the functional activity of the organ in question. In view of this fact, physiological methods of stimulating cellular activity or the detection of relations between the natural function of cells and their division offer better prospects [1,3,4]. Blumenfeld [3] found, using this method, a reverse proportion between the functional activity of the organs and their mitotic activity. I. A. Alov [1] had shown that distortion of the normal order of functional activity in the digestive organs leads to corresponding changes in the daily periodicity of mitotic activity in the lungs and in the gut.

In the present study we made attempts to establish a relation between the functional activity of the kidneys and the cell division in the renal epithelium, using both physiological and pharmacological methods of stimulating the activity of that organ.

## METHOD

The experiments were carried out on white mice (males aged 2-2½ months) and rats (males aged 3-5 months). The mitotic activity was assessed in kidney sections (10 μ) stained with hematoxylin-eosin. The cells in a state of division were counted in the epithelium of the chief part of the nephron in four sections. The intensity of the mitotic activity was assessed by the number of cells in a state of division found within a standard area (3.08 mm<sup>2</sup>), by the percentage proportion of the various mitotic phases and by the phase coefficient. The findings obtained were evaluated statistically by the method of Fisher and Student.

Three series of experiments were carried out on 157 animals. In the first series of experiments we studied the relation between the daily pattern of renal function in rats and the mitotic activity found in that organ. The changes in the functional activity of the kidney in the course of the day were assessed by the rate of diuresis. The animals were kept in cages with a funnel-shaped bottom. Every three hours the quantity of urine passed by the animals was recorded. The daily rhythm of diuresis was observed for eight days. After this period the animals were killed at various times corresponding to the maximum and minimum daily activity of the kidneys.

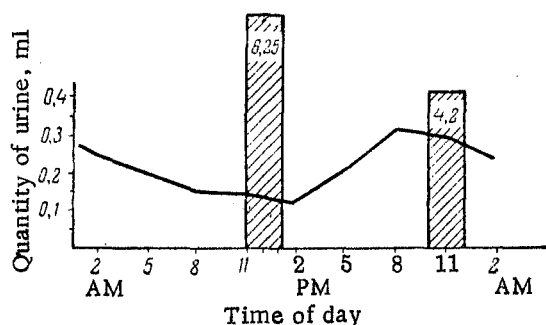
In the second series of experiments we studied the changes in the mitotic activity in the renal epithelium while the animal body was flooded with water. Normal saline was administered by subcutaneous injection. Mice (of 15-20 g weight) were given 1 ml and rats (of 80-100 g weight) 5 ml normal saline. Animals which were given only a prick with the needle without injection of normal saline served as control. The mitotic activity in the kidneys was assessed 1, 2 and 3 hours after the injection.

In the third series of experiments the animals were given diuretin (0.1% solution). White mice were given diuretin in a dose of 1 mg, rats in a dose of 5 mg per animal. The total quantity of liquid injected in this series

of experiments was the same as the amount of liquid used to flood the animals with water in the previous series of experiments.

## RESULTS

The findings obtained after continuous observation lasting for eight days showed that the renal activity of rats is governed by a well marked daily rhythm with a minimum and maximum (see figure). The minimum diuresis takes place in daytime between 8 a.m. and 2 p.m. then follows a rapid increase in the diuresis up to a maximum observed between 8 p.m. and 11 p.m. From then on the curve of diuresis shows a slow fall gradually reaching the minimum level.



Daily diuresis and mitotic activity in the kidneys of rats. On the ordinate: the quantity of urine, on the abscissa: the time (in hours) are plotted. The columns show the mitotic activity in the kidneys during the period of maximum and minimum renal activity.

In view of these findings we investigated the mitotic activity of the animals at different times which coincided with the minimum and maximum renal activity. Twelve rats were killed at the peak of diuresis (11 p.m.) and 11 rats during the minimum excretion of urine (12 noon).

The results of these experiments showed that the mitotic activity in the kidneys as well as in other organs undergoes certain changes in the course of the day. High indices of mitotic activity were found in the morning hours and low indices at night ( $P=0.005$ ). Similar to the results obtained in the experiments of Blumenfeld [3], the reverse proportion between the functional activity and the mitotic activity of that organ deserves attention. The high indices of mitotic activity coincide with the minimum activity of the kidneys, and conversely at the peak of diuresis the mitotic activity was low (see figure).

Changes in the Mitotic Activity in the Renal Epithelium of Rats and Mice after Flooding with Water

Animals	Group	No. of animals	Time after water admin., hr	No. of mitoses	Phase co-efficient*	P
Rats	Control	7	—	26,1	2,8	
	Experimental	7	2	16,1	2,1	<0,01
		6	3	17,3	2,0	<0,02
Mice	Control	9	—	5,4	2,6	
	Experimental	10	1	3,4	2,8	0,03
	Control	10	—	11,1	2,3	
	Experimental	10	2	8,3	2,2	0,2
		10	3	10,0	2,7	0,3

\* The coefficient reflects the relation between the number of prophase and metaphases, on the one hand, and the number of anaphases and telophases, on the other hand.

The above data warrant the assumption that the functional activity of the organ leads to a decrease in the intensity of cell multiplication. It would, however, be premature to draw a final conclusion, as a coincidence of two processes in time does not always imply a causative link between these processes. In view of this consideration we undertook the second series of experiments, in which we studied the changes in the mitotic activity of the kidneys in animals flooded with water.

The results of these experiments showed that the short-lasting increase of the diuretic function of the kidneys leads to a decrease in the mitotic activity in that organ (see table). The most striking data were obtained in experiments on rats. Two hours after injection of normal saline the mitotic activity in the chief parts of the kidneys decreased more than  $1\frac{1}{2}$  times. After three hours the mitotic activity was still on a very low level.

Similar results were obtained in experiments on mice. In the kidneys of the control mice the mitotic activity usually varies within a fairly wide range and consequently the experimental results are not always sufficiently consistent. In all experiments on mice a decrease of the mitotic activity could be observed 1-2 hours after administration of water which was more or less marked in different experiments. Three hours after injection of normal saline the mitotic activity usually returned to the original level. The results of these experiments thus warrant the assumption that the coincidence between the low mitotic activity and the maximum of the diuretic function was not of incidental character. A short-lasting functional exertion of the kidneys leads to a decrease in the intensity of cell multiplication.

In the third series of experiments we studied changes in the mitotic activity of the kidneys after injection of diuretin. The preparation was administered in the same volume of normal saline as in the preceding series of experiments. Although in this group of experiments two factors increasing the activity of the kidneys were used (flooding with water + a diuretic substance) the results were inconsistent and did not enable us to draw definite conclusions. In one group of experiments the injection of diuretin slightly decreased the mitotic activity; in two other groups the mitotic activity increased. The changes were insignificant and not sufficiently consistent. We gained the impression that diuretin in itself exerts an influence upon cell division independently of its diuretic effect. In our opinion the use of pharmacological preparations for the study of the relation between the cell division and functional activity represents an unreliable method for the solution of that problem.

Comparison of the daily pattern of renal function with the intensity of cell multiplication in that organ and experiments consisting of the flooding of the animal body with water thus showed that a definite relation exists between the cell division and the functional activity of the kidneys. A reverse proportion between these processes could be established. At the peak of functional activity and during short-lasting functional exertion the cell division appeared to be delayed. This conclusion is naturally valid only for the conditions of our experiments, i. e., for short-lasting intensive exertion of the kidneys. It cannot be excluded that during prolonged but moderate functional activity other interrelations between renal function and cell division in the kidneys might be found.

#### SUMMARY

Rats and mice were experimented upon to inquire into changes occurring in the mitotic activity of the kidney in various functional conditions of the organ. An inverse relationship was found to exist between the functional activity of the organ and mitosis. High level of mitotic activity was noted during hours of minimal diuresis, and a low one at the time of maximal diuresis. A brief increase of the renal function achieved by way of water loading resulted in a reduction of mitotic activity in this organ.

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All abbreviations of periodicals in the above bibliography are letter-by-letter transliterations of the abbreviations as given in the original Russian journal. *Some or all of this periodical literature may well be available in English translation.* A complete list of the cover-to-cover English translations appears at the back of this issue.

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