It can be concluded from these results that increased sensitivity of the mycocardium to the harmful action of adrenalin is present in the rats investigated, which are characterized by genetically determined hypertension provoked by stress; it is manifested only in relation to types of lesions connected with a disturbance of permeability of the cardiomyocyte sarcolemma. The molecular-genetic and physiological bases of this phenomenon will be elucidated by future investigations.

LITERATURE CITED


1. A. L. Markel', in: The Use of Models of Pathological States in the Search for Biologically Active Preparations [in Russian], Moscow (1983), pp. 70-71.
2. Yu. V. Postnov and S. N. Orlov, Kardiologiya, No. 12, 5 (1983).
3. V. S. Rukosuev, Kardiologiya, No. 9, 54 (1968).
4. L. A. Semenova and Yu. G. Tsellarius, Ultrastructure of Heart Muscle Cells in Focal Metabolic Lesions [in Russian], Novosibirsk (1978).
5. V. Yu. Urbakh, Biometric Methods [in Russian], Moscow (1964).
6. É. Sh. Khalfen, Kardiologiya, No. 1, 19 (1983).
7. Yu. G. Tsellarius and N. K. Eriskovskaya, Byull. Éksp. Biol. Med., No. 5, 71 (1970).
8. Yu. G. Tsellarius and L. A. Semenova, Histopathology of Focal Metabolic Lesions of the Myocardium [in Russian], Novosibirsk (1972).
9. Yu. G. Tsellarius, L. A. Semenova, and L. M. Nepomnyashchikh, Arkh. Patol., No. 12, 3 (1980).
10. I. Hütter, G. Rona, and R. H. More, Arch. Path., 91, 19 (1971).
11. S. P. Kent, Am. J. Path., 56, 623 (1967).
12. "Nomenclature of hypertensive rat strains," Hypertension, 3, 506 (1981).


# LIPID GRANULARITY AND TOPOGRAPHIC FEATURES OF RENOMEDULLARY INTERSTITIAL CELLS IN SPONTANEOUSLY HYPERTENSIVE RATS


B. N. Tsibel' and E. V. Nefedova



UDC 616.12-008.331.1-055.5/.7-07:616.61-008.939.15

KEY WORDS: kidneys; renomedullary interstitial cells; spontaneous hypertension.


The interstitial cells (IC) of the renal medulla have been shown [13, 14] to possess internal secretory activity and, in particular, to produce prostaglandins (PG). However, it is not clear how important is the role of renomedullary IC (RMIC) in the general system of arterial pressure regulation. Potentiation of synthesis of renal PG during arterial hypertension [2, 11] is evidence of activation of the antihypertensive function of the renal interstitial tissue.

The electron-microscopic picture of RMIC in different types of hypertension in rats has now been described in fair detail [3, 5, 10]. Nevertheless, the admitted limitation of the material which can be studied by electron microscopy prevents consideration of the topography of the renal medulla as a whole. The zonal structure of the renal papilla, for instance, is heterogeneous in both vertical and horizontal directions. Consequently, there is reason to assume that in this case a light-optical study will be sufficiently acceptable. In some cases [7, 9, 12] it has been found possible to study the morphological and functional state of IC on the basis of indirect data, namely the concentration of the lipid granules. As has been shown [6], blocking synthesis of PG and storage of their precursors (mainly triglycerides of unsaturated fatty acids) leads to accumulation of lipid granules in the cytoplasm of IC and to an increase in their volume.

The aim of this investigation was to study the concentration of lipid granules in RMIC in spontaneously hypertensive rats on the basis of structural heterogeneity of the renal papilla.


Department of Pathological Anatomy, Irkutsk Medical Institute.


(Presented by Academician of the Academy of Medical Sciences of the USSR D. S. Sarkisov.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 99, No. 3, pp. 358-360, March, 1985. Original article submitted May 18, 1984.




0007-4888/85/9903-0362$09.50

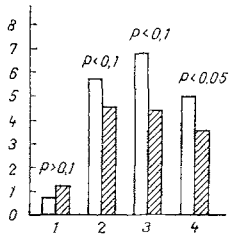


Fig. 1

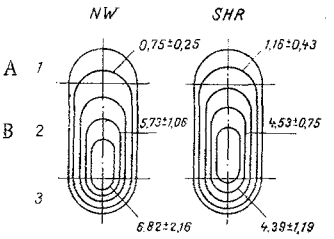


Fig. 2

Fig. 1. Number of lipid granules in IC of renal medulla in Wistar (NW) rats and in spontaneously hypertensive rats (SHR). Abscissa, zones of renal medulla; ordinate, ICI. 1) Base of papilla, 2) middle part of papilla, 3) apex of papilla, 4) renal papilla as a whole. Unshaded columns, control (NW rats); shaded columns, experiment (SHR rats).

Fig. 2. Scheme of topography of granular IC of renal medulla in normotensive control rats (NW) and spontaneously hypertensive rats (SHR). A) Outer zone of medulla, B) inner zone of medulla; 1) base, 2) middle part, 3) apex of renal papilla. Isolines connect points with similar values of ICI. Numbers are mean values of ICI in the given zones.

## EXPERIMENTAL METHOD

Inbred male SHR rats aged 4 months, with a steady arterial pressure of 160 ± 18 mm Hg, were used. Normotensive inbred male Wistar rats (NW) of the same age, with an arterial pressure of 98 ± 3 mm Hg served as the control. Each group consisted of 10 animals, kept under identical conditions.

Kidneys for light-optical investigation were fixed in 10% neutral formalin solution. The excised renal papillae were postfixed in 1% $OsO_4$ solution and embedded in paraffin wax. Longitudinal sections through the papillae, under 3 μ thick, were reblackened in 70° alcohol and counterstained with safranine.

The number of lipid granules in IC and the number of cells with granules relative to the total number of RMIC were counted under a mgnification of 630 with an immersion objective. The papillae were studied from the base to the apex by a scanning method, with random choice of sections and fields of vision. In each papilla on average 2000 IC (from 1100 to 2900 cells depending on the area of section) were investigated. In each field of vision all RMIC were studied, the number of granules was counted in the cells, and the interstitial cell index (ICI) (mean number of granules per cell) was calculated per 100 IC. The mean values of ICI for the papilla as a whole and for its individual zones, and also fluctuations in ICI within the papilla also were determined. In the course of the investigation attention was paid to the relative size of the granules and, depending on this, cells with mainly large granules also were counted.

Statistical analysis included the use of Student's test and calculation of the coefficient of correlation.

## EXPERIMENTAL RESULTS

The planimetric investigation revealed definite rules for the distribution of IC containing granules in different parts of the papilla to correspond with the zonal structure of the renal medulla. The functional organization of the kidneys is responsible for the existence of two zones in the medulla: outer and inner, corresponding to the convoluted and straight portions of the tubular system. The outer zone of the medulla lies at the base of the renal papilla whereas the inner zone of the medulla forms the renal papilla directly and is divided conventionally into a middle part and an apex. Within these zones different levels of organization of the renal medulla can be distinguished. The principle of the laminar

structure of the renal medulla presupposes the existence of definite structural and functional zones in it, which of course are not absolute. Considering the specific features of the renal medulla, it can be postulated that RMIC are exposed to the greatest functional load in the zone of action of the countercurrent-concentrating mechanism, namely in the renal papilla.

The results of calculation of ICI for the papilla as a whole and its different zones are given in Fig. 1. A decrease in the number of lipid granules in IC was found in SHR rats for the papilla as a whole (ICI = 3.63 ± 0.35) compared with the control (ICI = 4.99 ± 0.44, $P < 0.05$). Incidentally, a decrease in the number of granules was observed in IC of the inner medulla, and at the apex of the papilla the decrease was more marked than in its middle part, whereas in the outer zone of the medulla (at the base of the papilla) ICI was higher than in the control. Furthermore, a decrease in fluctuation of ICI (differences between the largest and smallest values of ICI) was found in SHR rats within the papilla as a whole (7.7 ± 0.4) compared with the control (10.1 ± 1.2, $P < 0.01$); this may be evidence of a decrease in reserve storage of lipids and an increase in PG utilization. A decrease in the number of granules in RMIC compared with the normotensive control was found in human patients with essential hypertension [8].

By the method of schematic fixation of fields of vision followed by marking out the corresponding value of ICI on a diagram of the papilla, the concentric character of distribution of granular IC in the renal papilla could be demonstrated. The points with similar values of ICI marked according to the zones investigated lay on concentric closed curves (Fig. 2). In the control the highest value of ICI was observed in the central part of the papilla nearer to its apex, which corresponds to the region of the limb of the loop of Henle. The number of granules in IC decreases toward the periphery of the papilla, its apex, and its base. Positive correlation was found between the number of granules and their size ($r = 0.66$, $P < 0.05$).

Unlike in the control, in SHR rats the zone of granular IC widens in the papilla as a whole, including its base. The number of granular cells as a percentage of the total number of RMIC is 43.1 ± 2.8, compared with 37.7 ± 1.7% in the control ($P < 0.1$). The highest value of ICI was observed in the middle part of the papilla, which corresponds to the region of thin segments of the loop of Henle. Some degree of concentric equalization of ICI for the papilla as a whole, including base, middle part, and apex, was observed under these circumstances. Correlation between the number of granules and their size weakened compared with the control.

The decrease in the content of lipid granules, widening of the zone of granular IC, and also the different distribution of cells containing different numbers of granules in the papilla as a whole, observed in spontaneous hypertension, are perhaps evidence of a more or less uniform increase in functional activity of IC in all zones of the renal papilla on account of an increase in the load on the organ as a whole and the "switching" of the kidney to a hypertensive work schedule [4]. The results of the present investigation suggest that the concentration of lipid granules in RMIC may to some extent reflect the state of function of the cells and may correlate with the degree of functional activity of IC, which differs in different zones of the renal papilla because of its structural and functional heterogeneity. The cause of the differences in estimates of the number of lipid granules in RMIC in rats, observed in a number of studies [1, 3, 9], in rats in similar morphological and functional states may be not only the limited volume of research material, but also the fact that only certain parts of the renal papilla were studied. It must be emphasized that statistically significant changes in ICI in SHR rats were found as a result of the study of a relatively large material, and observation of the papilla as a whole. Differences observed in the density of lipid granules in IC in individual zones of the papilla in hypertensive and normotensive animals evidently reflects differences in functional significance of the different zones of the renal papilla under both normal and pathological conditions.

The authors are grateful to Professor Yu. V. Postnov for generously providing the animals.

## LITERATURE CITED

1. E. G. Antonova, V. V. Vinogradov, G. V. Pravotorov, et al., Tsitologiya, 21, 1106 (1979).
2. A. I. Kutsenko, V. M. Shpil'kin, P. P. Boyadzhan, et al., Kardiologiya, No. 4, 41 (1980).
3. Yu. L. Perov and Yu. V. Postnov, Byull. Éksp. Biol. Med., No. 6, 755 (1976).
4. Yu. V. Postnov, Kardiologiya, No. 12, 30 (1979).

5. Yu. V. Postnov and Yu. L. Perov, Arkh. Patol., No. 6, 70 (1972).
6. R. I. Sokolova, A. A. Nekrasova, and N. P. Legon'kaya, Arkh. Patol., No. 6, 29 (1977).
7. R. I. Sokolova and A. M. Vikhert, Kardiologiya, No. 7, 55 (1981).
8. B. N. Tsibel' and L. S. Khodasevich, Kardiologiya, No. 5, 102 (1980).
9. B. Anavi and M. Dragiev, Arkh. Patol., No. 3, 20 (1981).
10. A. Hornych, Cont. Nephrol., 12, 54 (1978).
11. C. Limas, C. J. Limas, and D. Ragan, Lab. Invest., 34, 606 (1976).
12. E. E. Muirhead, G. Germain, B. E. Leach, et al., Circulat. Res., 30-31, Suppl. 2, 161 (1972).

# LOWERING THE THRESHOLD OF CARDIAC PACING BY SATURATING THE ELECTRODE WITH GLUCOCORTICOIDS

J. J. Bredikis,* I. J. Skučas, P. P. Stirbys, G. A. Marinskii, and E. R. Putelis

UDC 615.47:616.12-008.315-08+612.018

KEY WORDS: cardiac pacing; pacing threshold; electrode; glucocorticoids.

The response of the heart to implantation of an electrode is for the pacing threshold to rise, and this is especially marked on the 7th-14th day after the operation, so that sometimes the electrical pacemaker cannot impose its rhythm on the heart. To suppress this response an electrode containing porous material in the form of a separate component, filled with dexamethasone, has been used [1]. This agent, escaping gradually through the pores of the electrode, acts on neighboring tissue without any general effect on the body as a whole.

We have suggested and tested a simpler method: saturating the porous electrode with dexamethasone immediately before use.

We made the porous electrodes under laboratory conditions from chromium carbide or titanium carbide. The geometric area of the outer surface of the electrode was 8-12 mm$^2$. Before implantation the electrodes were kept for 20-30 min in a sterile solution of dexamethasone sodium phosphate. The electrode was then introduced into the right ventricle of a dog under general thiopental anesthesia (four cases). The pacing threshold was then measured for 30 days. The results were compared with those of investigation of porous electrodes (13 cases).

During pacing with the test electrode the threshold on the day of implantation was higher than in the control (Table 1) but the peak threshold value did not reach 1.5 V. On

TABLE 1. Changes in Threshold (in V) of Cardiac Pacing in Early Period after Implantation of Electrode (duration of stimulating pulse 0.5 msec)

| Time (days) | Type of electrode | |
|---|---|---|
| | saturated with dexamethasone | control |
| 0 | 1,0±0,1 | 0,41±0,05 |
| 3 | 0,6±0,07 | 0,66±0,06 |
| 7 | 1,0±0,15 | 1,62±0,17 |
| 15 | 1,15±0,12 | 1,41±0,16 |
| 30 | 0,6±0,1 | 1,14±0,12 |

*Corresponding Member of the Academy of Medical Sciences of the USSR.

First Surgical Department, Kaunas Medical Institute. Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 99, No. 3, pp. 360-361, March, 1985. Original article submitted February 22, 1984.

0007-4888/85/9903-0365$09.50  