Thus graded mechanical injury enables the intact abdominal skin surrounding the defect to be involved in the process of its repair, and also considerably speeds up the formation of the definitive focus of regeneration.

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# MORPHOLOGICAL AND FUNCTIONAL CHANGES IN THE KIDNEYS IN THE EARLY STAGE OF VENOUS STASIS AND DURING RESTORATION OF BLOOD DRAINAGE FROM THE ORGAN


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KEY WORDS: venous stasis; intrarenal veins; regional renal blood flow.


Kidney diseases associated with obstructed venous drainage from them are found comparatively frequently [4, 8]. Most investigations in this field have been devoted to the study of disturbances of kidney function [2, 3, 5, 6, 9-11]. Restorative processes in the kidneys after correction of venous stasis have not yet been adequately studied [7]. By using light-optical, electron-microscopic, and radioisotope methods we have studied changes in the intrarenal veins and structural elements of the kidney after experimental constriction of the renal vein, in the early stages, and also repair processes after restoration of the venous drainage from the kidney.

## EXPERIMENTAL METHOD

Experiments were carried out on 30 noninbred adult male and female albino rats weighing 180-210 g. Under pentobarbital anesthesia and under sterile conditions, after midline laparotomy the lumen of the left renal vein was constricted by 50%, by tying the vein over a metal tube of the required diameter distally to the point of entry of the adrenal and gonadal veins. The creation of an obstructed venous drainage was judged by the increase in volume of the kidney, and dilatation of the segment of the vein distal to the ligature. Material for light-optical and electron-microscopic investigation was collected on the 3rd day after constriction of the vein, and also on the 30th day after removal of the ligature and restoration of the venous drainage. The intrarenal veins were subjected to morphometry, with measurement of their external and internal diameter and the thickness of their wall. The regional renal blood flow was determined with the aid of the radioactive gas $^{133}Xe$ on an "Ksenon-3" apparatus [1]. The results were subjected to statistical analysis.

## EXPERIMENTAL RESULTS

The results showed that 3 days after constriction of the left renal vein, the mass of the kidney was significantly increased (1028.41 ± 51.13 compared with 745.15 ± 32.40 g in the control). Macroscopically the kidney was swollen, the fibrous capsule was stretched, and the kidney was dark violet in color. On frontal section foci of hemorrhage were found

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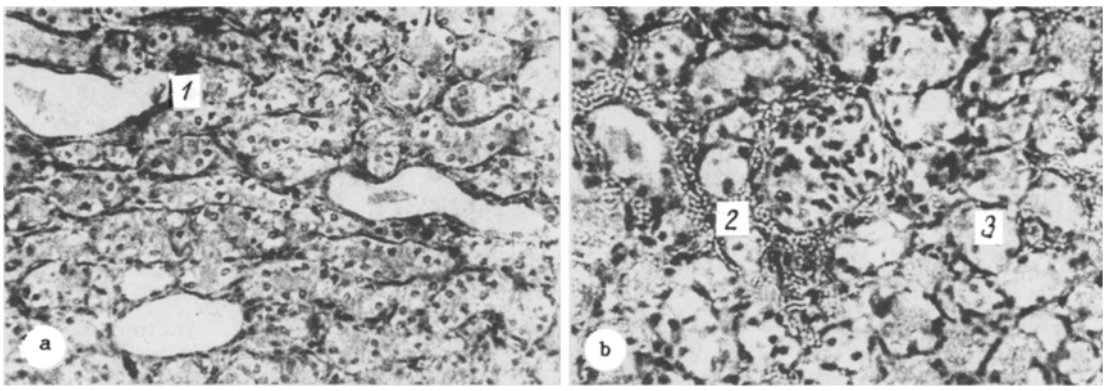


Fig. 1. Renal cortex of rat 3 days after 50% constriction of left renal vein: a) dilatation of intrarenal veins (1). 200 ×; b) peritubular capillaries are congested with blood cells (2), degenerative changes in brush-border cells of proximal and distal parts of tubules of nephrons (3). 400 ×. Hematoxylin-eosin.

TABLE 1. Morphometric Properties of the Change in Diameter of Intrarenal Veins in the Early States of Venous Stasis and during Reduction in Blood Drainage from the Kidney in Comparison with the Control (M ± m, n = 10)

| Object of study | External diameter | | | Interior diameter | | |
|---|---|---|---|---|---|---|
| | control | venous stasis | reduced drainage | control | venous statis | reduced drainage |
| Interlobar vien | 184,63±9,23 | 224,23±10,11* | 189,87±11,52 | 164,33±9,51 | 208,37±10,23* | 170,51±11,32 |
| Loop | 89,35±9,85 | 138,51±8,51* | 94,83±9,31 | 75,71±8,92 | 127,55±10,11* | 81,25±9,33 |
| Interlobar (small) | 45,71±6,55 | 62,51±7,21* | 48,29±7,02 | 35,27±5,32 | 54,02±5,01* | 39,11±4,98 |
| Straight-line venule | 27,37±4,27 | 46,51±6,37* | 30,05±4,52 | 20,31±4,02 | 41,13±5,92* | 24,21±4,73 |

Legend. *$p < 0.05$.

in the juxtamedullary zone, and the interlobular veins were distended with blood. In histologic sections stained with hematoxylin and eosin, and also with fuchselin-picrofuchsine, marked stasis of blood was observed in the glomerular and peritubular capillaries, in all the intrarenal veins, especially in the juxtamedullary zone, and in the vasa recta of the pyramid (Table 1). Veins distended with blood had the appearance of thin-walled sinusoids (Fig. 1a). In some places areas of de-endothelization were observed. The distance was increased between individual smooth-muscle cells of the interlobar veins. Morphologic changes demonstrating a disturbance of the intrarenal blood flow correlated closely with the results of radioisotope determination of the regional renal blood flow (RBF). RBF in the experimental animal was 19.82 ml/min and in the control 31.63 ml/min ($p < 0.05$). Cloudy-swelling and vacuolar degeneration were observed in nerve cells of the proximal and distal part of the tubule of the nephron, the cytoplasm was pale, and the nuclei partially pycnotic. The lumen of the distal tubules was filled with homogeneous contents (Fig. 1b).

Electron-microscopic investigation showed that the lumen of the majority of peritubular capillaries was filled with erythrocytic sludge (Fig. 2a). The luminal surface of the plasmalemma formed outgrowths. An increase in the number and diameter of the pores was observed (Fig. 2b). Profiles of the Golgi complex and of the rough endoplasmic reticulum were flattened. The number of free ribosomes and polysomes was reduced. The nuclei were enlarged, the nuclear membrane even, the chromatin condensed into discrete granules, and located mainly marginally. The mitochrondria were swollen with a translucent matrix and with reduced cristae. In the smooth myocytes the nuclei were oval in shape, the mitochondria small, and the number of cristae reduced. The distance between individual smooth-muscle cells was increased and the number of intercellular contacts reduced. The cytoplasm in the brush-border and cubical cells of the proximal and distal parts of the tubule of the nephron contained many vacuoles, distributed not only in the apical, but also in the basal part of the cells. Brush border of the endothelial cells was swollen and its villi were deformed. The nuclei were enlarged and the chromatin grouped into discrete granules. Components of the Golgi complex were dilated. The mitochondria were swollen and the cristae disorganized. The number of ribosomes attached to membranes of the rough endoplasmic reticulum was reduced.

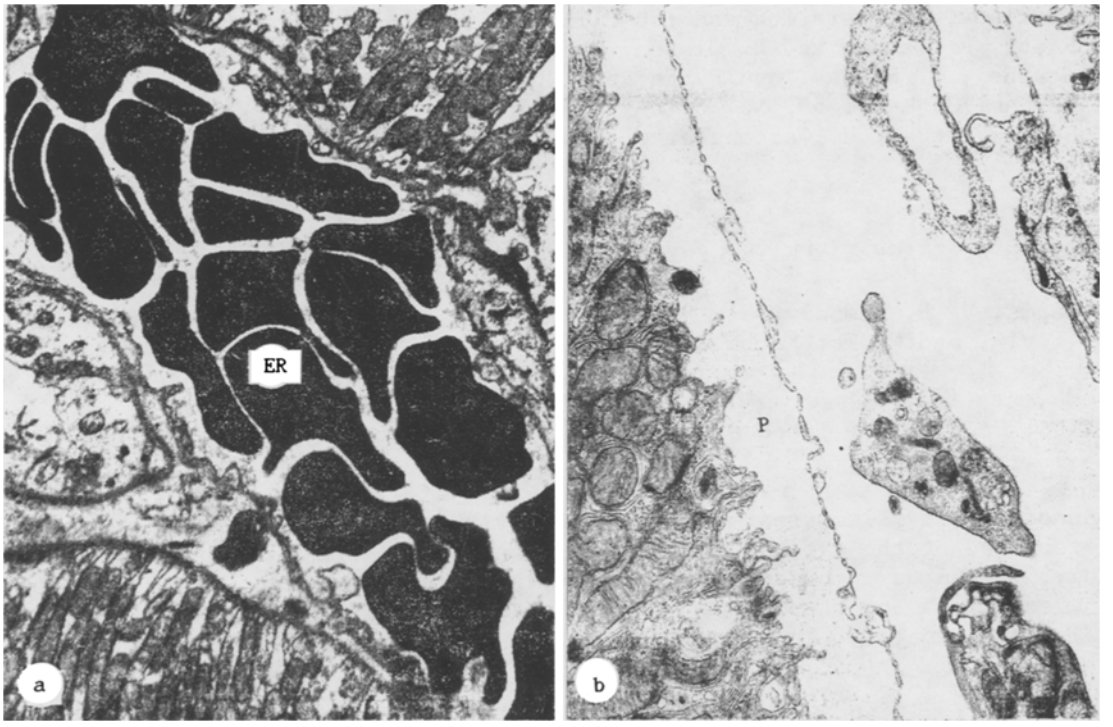


Fig. 2. Ultrastructural changes in peritubular capilaries of renal cortex of rat 3 days after 50% constriction of the left renal vein: a) erythrocytic sludge (ER) in their lumen. 6000×; b) enlargement of pores (P) and formation of outgrowths on luminal plasmalemma of endotheliocytes. 14,000×.

On the 30th day after temporary 50% constriction of the left renal vein (for 3 days) the mass of the kidney was close to that of the control animals. Restoration of the venous drainage from the left kidney in most cases led to restoration of the normal structural components of the vessels and parenchmya. Radioisotope investigation showed that RBF in the control kidney was 32.3 ± 4.51 ml/min compared with 37.22 ± 5.12 ml/min in the control ($p > 0.05$). Electron-microscopic investigation showed that in some structural components of the small veins and peritubular capillaries, and in epitheliocytes of the proximal and distal parts of the tubules of the nephrons, evidence of hyperplasia and hypertrophy of the intracellular structures was noted. The number of vesicles of the Golgi complex was increased. many cisterns and saccules were formed in the rough endoplasmic reticulum, and the number of attached ribosomes was increased. The nuclei had numerous invaginations of the nuclear membrane and there was a diffuse increase in size of the chromatin granules. The matrix of the mitochondria varied in electron density and the cristae were distinctly outlined.

Thus 50% temporary (for 3 days) constriction of the renal vein led to disturbances of the intrarenal blood flow and to the development of degenerative changes in structural elements of the veins and of the brush border and cubical cells of the proximal and distal parts of the tubules of the nephrons. After restoration of the venous blood drainage (30 days) the structures of the tubules and vessels regained their normal morphological appearance. In some areas changes of a compensatory and adaptive nature were observed.

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# CONTROL OF LYMPH DRAINAGE PATHWAYS OF THE EYE BY DALARGIN

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Methods of conservative treatment, aimed at stimulating the lymphatic component of the microcirulatory bed of the eye have not so far been used to treat pathological processes in ophthalmology, including in order to reduce the intraocular pressure (IO) in glaucoma, even though recently a new trend has developed, namely elinical lymphology, based on regulating the lymph drainage of the tissues [1-4].

The aim of this investigation was an experimental study of the effect of dalargin on the drainage channels of the eye under normal conditions and in experimental hypertension, used as a model of secondary glaucoma.

## EXPERIMENTAL METHOD

Altogether three series of experiments were carried out on 82 eyes of chinchilla and white giant rabbits. Of this number, 52 rabbits acted as the control. In series I of the investigation, the aim of which was a morphological study of the drainage channels the anterior chamber of 16 eyes and the vitreous body (VB) of four eyes were perfused with ink containing gelatin, after subconjunctival (or electrophoretic) injection of dalargin (0.1%, 0.2-0.3 ml). The ink with gelatin was injected into the anterior chamber after preliminary paracentesis of the corena with a fine needle, and into VB by puncture of the sclera with a fine needle in the zone of the ciliary body, after preliminary paracentesis and release of the aqueous humor of the anterior chamber. Control experiments consisted of injecting ink into the anterior chamber (10 eyes) and into VB (10 eyes), followed by morphologic study of the drainage channels. One type of control in this series of investigations was subconjunctival injection of physiological saline (four eyes) followed by injection of India ink into the anterior chamber and into VB. The experiments of Series II were carried out to discover the effect of dalargin on the level of ophthalmotonus, in the presence of a normal IOP and in experimental ophthalmic hypertension. Before the experiments began, IOP was measured on a Maklakov tonometer with a weight of 10 g. Next, dalargin was injected subconjunctivally (0.1%, 0.2-0.3 ml), and 20-30 min later IOP was again measured (normal IOP 20-22 mm Hg), and control experiments were carried out on four eyes (Fig. 1b). After measurement of IOP a model of "secondary glaucoma" was created as follows: under general and local anesthesia (1 ml of morphine solution injected subcutaneously, 1 ml of procaine solution injected by the retrobulbar route) with a fine needle, sulfuric acid was applied to the zone of the limbus and to the perilimbic region, at a distance of 1 mm away from it around the whole perimeter of the cornea. The IOP was again measured after 20, 30, and 45 min. After creation of the experimental model of ophthalmic hypertension or "secondary glaucoma" due to the burn, dalargin was injected subconjunctivally (0.1%, 0.2-0.3 ml) into 10 eyes and IOP was again measured at various times (from 15 min to 3 h) after injection of the preparation (Fig. 1a).

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