# DYNAMICS OF REACTIVITY OF MESENTERIC MICROVESSELS IN RATS WITH EXPERIMENTAL RENAL AND HORMONAL HYPERTENSION

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Reactivity of mesenteric arterioles 10-30 μ in diameter to application of histamine (100-500 μg), adrenalin, and noradrenalin (1-10 μg) was studied in rats with experimental renal and hormonal hypertension. The sensitivity of the microvessels to the vasoactive substances was shown to vary with the stage of development of experimental hypertension.

KEY WORDS: microcirculation; reactivity of arterioles; vasoactive substances.

Responses of microvessels to vasoactive agents during hypertension have been inadequately studied. The few experimental [15] and clinical [7-9, 11, 12] data have been obtained without consideration of the dynamics of development of the pathological state, hypertension for example, and by imperfect methods of recording responses of the microvessels.

The object of this investigation was a comparative biomicroscopic study of microvascular reactivity to vasoactive agents at various stages of development of experimental renal and hormonal hypertension in rats.

## EXPERIMENTAL METHOD

Experiments were carried out on male rats weighing 260-450 g anesthetized with urethane (1.6 g/kg). Renal hypertension was produced by applying a metal coil, 0.3-0.35 mm in internal diameter, over the left renal artery, followed after 15-20 days by removal of the opposite kidney [2]. Experimental hormonal hypertension was induced by Selye's method [14]: From the 8th-20th day after left-sided nephrectomy for 30 days the rats received a daily intramuscular injection of a 0.5% oily solution of deoxycorticosterone acetate (DOCA) in a dose of 10 mg. The animals were given 2% common salt solution to drink. The blood pressure was measured by a bloodless method without anesthesia by means of a piezoprobe of original design [4]. For biomicroscopy of the mesentery the method adopted in the writer's laboratory [5] was used.

Histamine (100-500 μg) and adrenalin and noradrenalin (1-10 μg) were applied in 0.1 ml physiological saline to the mesenteric microvessels. The internal diameter of the arterioles (10-30 μ) was recorded by the split-image method [1] under a magnification of 400, with an accuracy of 0.5 μ during the 20-24 min after application of the substances. The reactivity of the mesenteric microvessels was studied 7, 14, and 28 days after the second operation (renal hypertension) or after the beginning of DOCA injections (hormonal hypertension).

Changes in the diameters of the microvessels were assessed by determining the maximal degree of dilatation and constriction. The arithmetic mean of these maximal values was then determined and expressed in per cent.

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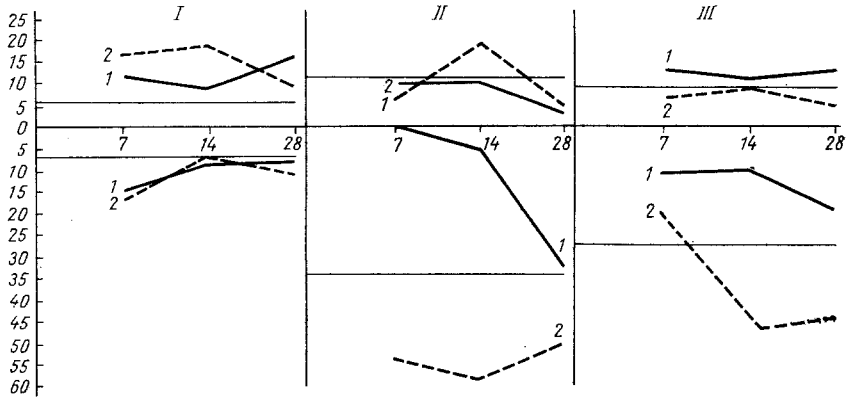


Fig. 1. Changes in diameters of arterioles (10-30 $\mu$) during application of histamine (I), noradrenalin (II), and adrenalin (III): 1) renal hypertension; 2) hormonal hypertension. Abscissa, duration of hypertension (in days); ordinate, percentage of increase (above) or decrease (below) in diameter of vessels. Continuous lines mark extent of changes in diameters of vessels in control animals (without hypertension).

## EXPERIMENTAL RESULTS AND DISCUSSION

The arterial blood pressure of the control animals was 95 ± 3.6 mm. The pressure rose by 48% 1 week after the first operation during renal hypertension (141.5 ± 3.3 mm Hg, $P < 0.001$) and by 42% during hormonal hypertension (135.0 ± 4.1 mm Hg, $P < 0.01$).

During the next 4 months, renal hypertension was accompanied by fluctuations in pressure of between 150 and 111 mm Hg. With hormonal hypertension, the pressure showed a tendency to fall during the first month of observation.

As a rule, spontaneous vasomotor changes in the diameters of the arterioles did not exceed 1.5 $\mu$, whereas changes in the nuclei of the smooth-muscle cells (2-8.5 $\mu$) did not exceed 0.7 $\mu$.

In 68% of cases, a spontaneous decrease in the lumens of the arterioles was accompanied by simultaneous thickening of the nuclei of the smooth-muscle cells, whereas an increase in their lumens was accompanied by flattening of the nuclei. Less frequently, the thickness of the nuclei changed after a change in the lumen of the arteriole. Sometimes vasoconstriction was accompanied by flattening of the nuclei and vasodilatation by thickening of the nuclei. In the first (more common) case constriction of the microvessels was evidently due to contraction of the smooth-muscle cells in their walls. The mechanisms of the other types of relationships between the lumens of the arterioles and the thickness of the nuclei of the smooth-muscle cells require special analysis.

The vasoactive agents evoked both constriction and dilatation of the microvessels (Fig. 1). A change in the sensitivity of the microvessels to the vasoactive substances was observed by the 7th day of development of hypertension. In renal hypertension sensitivity to histamine was increased but sensitivity to catecholamines was reduced; and in the early stages of hormonal hypertension, sensitivity to histamine and noradrenalin was increased and sensitivity to adrenalin was reduced. After 2 weeks renal hypertension was characterized by a normal response of the microvessels to histamine, a reduced response to adrenalin, and a reversed response to noradrenalin (less marked constriction, but more marked dilatation). By the same period of hormonal hypertension, the dilator effect of histamine and the vasoconstrictor effect of the catecholamines were sharply increased. After 1 month the sensitivity of the arterioles to histamine increased again in renal hypertension on account of the dilator response, but sensitivity to catecholamines was close to the control level. At the same time, during hormonal hypertension a tendency was observed toward restoration of normal reactivity of the microvessels.

Changes in the sensitivity of microvessels to humoral stimuli in hypertension have been described in the literature [3, 8, 10, 12, 13, 15]. These changes may be connected with fluctuations in the activities of the nervous and humoral components of the sympathetic nervous system during development of the pathological condition [6].

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