# CONSTRICTOR RESPONSES OF ISOLATED FEMORAL ARTERIES AND BRANCHES, AFTER PROLONGED EXPOSURE TO ARTERIAL HYPOTENSION, TO TRANSMURAL ELECTRICAL STIMULATION

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It was shown previously [1] that lowering the blood pressure (BP) in vessels of the posterior part of the body in rats gives rise to a definite but temporary inhibition of responses of the resistive vessels of the hind limb to impulses traveling along sympathetic nerves. Gradually the responses to stimulation of the sympathetic fibers increased, and at least 3 months (or possibly earlier) after the fall of BP, the magnitude of the vascular responses to sympathetic nerve stimulation was completely restored.

However, data obtained during limb perfusion reflected the integral response of the whole vascular bed. The aim of the present investigation was to study changes in response of the femoral artery and its principal branches, after long exposure to conditions of arterial hypotension, in response to electrical stimulation of adrenergic endings in the walls of these vessels.

## EXPERIMENTAL METHOD

Arterial hypotension was produced in vessels of the hind part of the body in noninbred rats weighing 180-220 g, by constricting the abdominal aorta distally to the site of origin of the renal arteries by means of a nichrome coil, with three turns and with an internal diameter such that the pressure in the femoral artery was 30-50% lower than that in the carotic artery of the same animal. The operation was performed under sterile conditions.

Throughout the chronic experiment the animals were kept in cages under ordinary animal house conditions with natural alternation of daylight and darkness, and on a standard diet.

The animals were used in the acute experiment 14-90 days after constriction of the aorta. On the day of the acute experiment the rats were decapitated and the femoral artery and its main branches (a. epigastrica superf., ramus muscularis, a genu descendens, a. saphena) were quickly but carefully dissected. Next, a fine cannula was introduced into the femoral artery immediately below Poupart's ligament in the peripheral direction, and the popliteral artery was ligated by a no-stretch thread, the end of which was connected to the lever of a myograph (Statham, USA). By means of the myograph contractions of the segment of the femoral artery in the longitudinal direction could be recorded. These data are not examined in this communication. Branches of the femoral artery lay freely in the perfusion chamber.

Perfusion of the vessels was carried out with Krebs' solution in an oxygenator. Carbogen (95% $O_2$ + 5% $CO_2$) was bubbled in through a ceramic filter, placed in the oxygenator, from a cylinder. The Krebs' solution was pumped from the oxygenator by means of a roller pump (Miniflow pump, type 304, Poland) along the connecting tubes into a cannula fixed in the bottom of the perfusion chamber, after which it entered the femoral artery and its branches. From the branches of the femoral artery the solution escaped into the chamber, where it mixed with the superfusate, and later, it passed into a collecting vessel through a special drain located in the top part of the chamber. The volume velocity of perfusion was set in order to obtain a perfusion pressure of 30-40 mm Hg.

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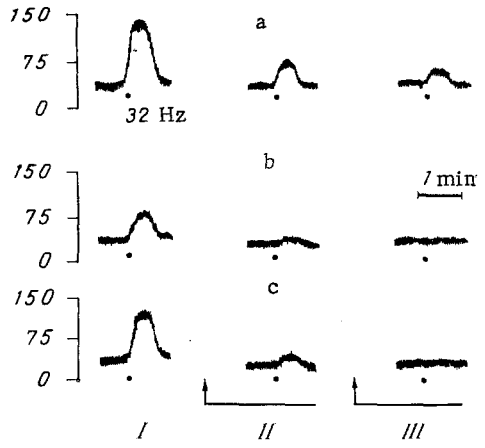


Fig. 1. Increase of perfusion pressure in response to transmural electrical stimulation (80 V, 32 Hz, 0.5 msec, 30 sec) of adrenergic endings in walls of femoral vessels of control rat (a) and of rats with arterial hypotension lasting 14 (b) and 90 (c) days. I) Initial experiments; II, III) after treatment of preparations with quanethidine ($10^{-5}$ M) and phentolamine ($3.5 \cdot 10^{-5}$ M) respectively.

Superfusion was carried out with Krebs' solution of the same composition as that used for perfusion of the vessels. From the delivery vessel, which simultaneously played the role of oxygenator, the superfusate passed along the connecting tubes, fitted with a screw clamp (so that the volume velocity of superfusion could be regulated) into the perfusion chamber, where it mixed with perfusate.

The perfusion pressure was recorded at the entry into the femoral artery by means of a P23 DB electromanometer (Statham) and recorded on a "Varioscript" automatic writer (Schwarzer).

All the vessels and tubes were enclosed in a water jacket, through which water was pumped at a temperature of 37°C by the pump of an ultrathermostat.

The femoral arteries and their branches were placed along the vertical axis of the chamber in the center of circular platinum electrodes, through which the nerve endings in the vessel wall were stimulated transmurally. Square electric pulses ("Grass" S48 stimulator) of direct current with supramaximal amplitude, frequency 4-32 Hz, and duration 0.5 msec, were used. The duration of stimulation was 30 sec.

The composition of the Krebs' solution was as follows (in mM): NaCl 118, KCl 5, $MgSO_4$ 1.2, $NaHCO_3$ 25, $CaCl_2$ 2.5, $Na_2$-EDTA 0.032, citric acid 0.55, glucose 11.0.

## EXPERIMENTAL RESULTS

In experiments on isolated vessels of control rats an increase in frequency of the stimulating pulses evoked a clear increase in magnitude of the constrictor response; treatment of the vessels with guanethidine ($10^{-5}$ M), an agent blocking neuronal uptake of the neurotransmitter, and thus exhausting its reserves in adrenergic nerve endings, sharply reduced the constrictor responses to transmural stimulation, whereas treatment with phentolamine ($3.5 \cdot 10^{-5}$ M), a powerful α-adrenoblocker, almost completely blocked these responses (Figs. 1 and 2).

It will be clear from Fig. 2 that in experiments on arteries exposed for 14 and 30 days to arterial hypotension, transmural stimulation caused much weaker constrictor responses than stimulation of the arteries of the control animals. Meanwhile, in experiments on vessels taken for investigation 90 days after constriction of the aorta, the degree of increase of perfusion pressure in response to transmural stimulation of any frequency was virtually indistinguishable from the corresponding responses of control rats.

Inhibition of responses of arteries after transmural stimulation observed on the 14th day after the lowering of BP might be connected with a temporary change in their adrenergic apparatus or reduction of the contractile response of the vascular smooth muscles as a result of prolonged hypotension.

In our opinion, the decrease in the effectiveness of neuromuscular transmission described above in vessels kept for 2 weeks under hypotensive conditions was not connected with suppression of the contractile response of their smooth muscles. Evidence in support of this view is given by the results of experiments to study responses of isolated vessels to injection of noradrenalin ($5 \cdot 10^{-7}$ g/ml) into the perfusion fluid. It follows from the data given in Fig. 3 that the magnitude of the constrictor response of vessels kept for 2

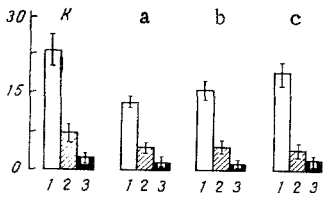


Fig. 2

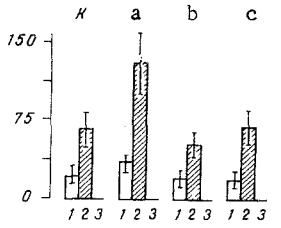


Fig. 3

Fig. 2. Magnitude of constrictor response (in mm Hg) to transmural electrical stimulation (80 V, 32 Hz, 0.5 msec, 30 sec) of adrenergic endings in walls of femoral vessels of control rats (K) and rats with arterial hypotension lasting 14 (a), 30 (b), and 90 days (c). Here and in Fig. 3: 1) initial data; 2) after guanethidine ($10^{-5}$ M); 3) after phentolamine ($3.5 \cdot 10^{-5}$ M).

Fig. 3. Magnitude of constrictor response (in mm Hg) to noradrenaline ($5 \cdot 10^{-7}$ g/liter) in control rats (K) and in rats with arterial hypotension lasting 14 (a), 30 (b), and 90 days (c).

weeks under hypotensive conditions was by no means lower than that of vessels of the control animals. As might be expected, treatment of the vessels with guanethidine potentiated the response to noradrenalin; moreover, it did so to a particularly marked degree in the case of 14-day hypotension, whereas treatment of the vessels with phentolamine completely blocked the reaction.

The character of changes in responses of hypotensive arteries to transmural stimulation of adrenergic nerve endings, observed in the present investigation, was similar in principle to the time course of the responses of hind limb vessels to electrical stimulation of sympathetic fibers running in the sciatic nerve [1]. A distinguishing feature of these changes was a temporary reduction of the efficiency of neuromuscular transmission followed by the virtually complete recovery of adrenergic influences on the vessels, despite persistent arterial hypotension.

The preliminary experiments showed that during perfusion of the isolated trunk of the femoral artery without its branches constrictor responses to transmural stimulation were very weak. It can therefore be considered that in the experiments described above the main contribution to the change in hydraulic resistance of the vascular preparation in response to transmural stimulation was made by branches of the femoral artery. The results obtained can accordingly be regarded as evidence that changes in responses to adrenergic influences in arterial hypotension involve not only resistive vessels, but also the principal branches of the femoral artery.

## LITERATURE CITED

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