ATROPHY OF THE SMOOTH-MUSCLE CELLS OF THE CAUDAL DIVISION OF THE ABDOMINAL AORTA AND ITS BRANCHES IN RATS WITH EXPERIMENTAL REGIONAL HYPOTENSION

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The lumen of the abdominal aorta was constricted by half its diameter caudally to the origin of the renal arteries in noninbred albino rats weighing 250-300 g, resulting in a fall in blood pressure in the distal portions of the abdominal aorta and its branches whereas the volume velocity of the blood flow was unchanged. Two weeks after constriction signs of atrophy of the smooth-muscle structures appeared in the wall of the abdominal aorta and its branches caudally to the point of occlusion, and they reached their most marked degree after three months. Atrophy of the smooth muscles was accompanied by a decrease in the hydraulic resistance of the resistive vessels.

In coarctation of the aorta the walls of the blood vessels become thinner distally to the site of coarctation [6, 7] although the atrophic changes which arise do so primarily through degeneration of elastic elements [7]. After occlusion of the femoral artery in dogs as the result of implantation of a thrombus-forming coil into the vessel, sclerotic changes and atrophy of the muscular coat are found caudally to the point of occlusion [5].

The object of the present investigation was to study whether atrophic changes in the smooth-muscle cells can arise in the wall of arteries of different caliber as a result of a decrease in the pressure constantly acting on them, to determine the time of appearance of the initial atrophic changes, and to study the dynamics of the process over a period of three months.

EXPERIMENTAL METHOD

By means of a metal coil [4] the aorta of noninbred albino rats of both sexes weighing 250-300 g was constricted below the origin of the renal arteries until the pressure in the femoral artery had been reduced approximately by half. At various times after constriction of the aorta the pressure in the carotid and femoral arteries was recorded by means of an electromanometer in the animals undergoing the operation and also in control animals under urethane (1 g/kg body weight) anesthesia. Immediately after this procedure, warm (37°C) x-ray contrast material as described by Arutyunov [1], was injected into both vessels simultaneously for 10 min under the pressure recorded in the carotid artery. After fixation of the rats' cadavers in 5% formalin solution, roentgenograms were taken of the vessels by the method published previously [2]. The diameter of the lumen of the thoracic aorta, the abdominal aorta caudally to the site of constriction, and both femoral arteries was measured on the roentgenograms. Sections were cut from

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TABLE 1. Thickness of Walls (in μ) and Kernohan's Index (in %) of Small Muscular Arteries Located Caudally to Point of Constriction of Aorta at Various Times after Operation (M ± m)

Diameter of arteries (in μ)	Index	Control	Time after operation (in days)		
			3—7	14—30	90
120—60	Thickness of wall	5,3±0,7	3,9±1,3	3,3±0,8	1,5±0,3
	Kernohan's index	1: (18±2,0)	1: (22±5,3)	1: (29,5±5,5)	1: (65±10,5)
60—20	Thickness of wall	3,2±0,2	2,4±0,3	2,2±0,2	2,4±0,3*
	Kernohan's index	1: (10±0,8)	1: (10±1,0)	1: (12±1,0)	1: (15±1,8)
Under 20	Thickness of wall	2,9±0,1	2,8±0,3	2,0±0,2	1,4±0,1†
	Kernohan's index	1: (3±0,2)	1: (3±0,2)	1: (4±0,4)	1: (6±0,7)

*$P < 0.05$.
†$P < 0.01$ relative to control.

TABLE 2. Volume of Nuclei (in μ^3) of Smooth-Muscle Cells in Parts of Aorta Cranially and Caudally to Point of Constriction (M ± m)

Time after constriction of aorta (in days)	No. of rats	Part of aorta			B/A
		Cranial (A)	Caudal (B)	P	
3—7	10	37,5±1,5 (200)	46,2±1,7 (200)	<0,001	1,22
14	7	42,3±1,8 (200)	63,6±2,2 (200)	<0,001	1,45
30	6	53,4±2,2 (200)	34,0±1,6 (200)	<0,001	0,64
90	4	51,3±1,1 (400)	34,5±1,1 (400)	<0,001	0,65
Control	3	45,0±2,6 (100)	48,0±3,0 (100)	=0,5	1,06

Note. Number of measurements given in parentheses.

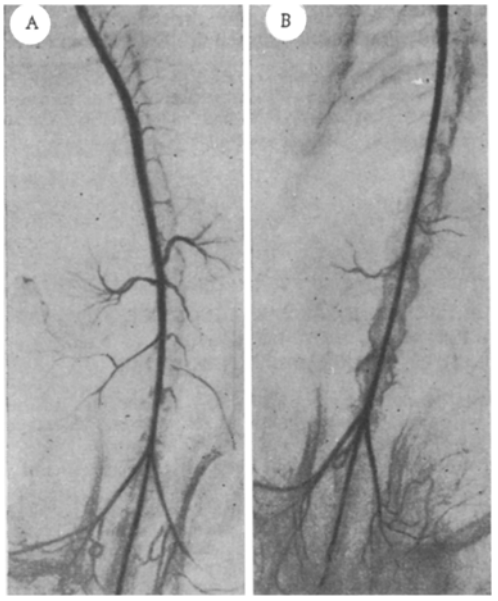

Fig. 1. Postmortem roentgenograms of aorta, iliac, and femoral arteries filled with contrast material under pressure measured during life in the carotid artery: A) intact animal; B) 3 months after construction of abdominal aorta. Three months after constriction of abdominal aorta no large collaterals are present, and by comparison with intact rats, abdominal aorta and its branches caudally to point of constriction are dilated. Films taken life-size.

parts of the wall of the aorta (transverse and tangential) caudally and cranially to the point of constriction, from the femoral arteries, and from the muscles of the fore and hind limbs.

The number of elastic membranes in the tunica media and the thickness of the membranes and the intermembranous spaces were measured in the walls of arteries of elastic type between 1.4-1.6 and 0.6 mm in diameter, and to calculate the volume of the nuclei of the smooth-muscle cells their diameter and length were also measured. The thickness of the muscular coat and the diameter of the lumen were measured in muscular arteries under 150 μ in diameter, and the ratio between these two values (Kernohan's index) also was calculated. Details of the staining and morphometric methods were described previously [3].

In five experimental animals (2 months after the operation to constrict the aorta) and in 14 control animals under urethane anesthesia the volume velocity of the blood flow into the hind limb was measured. To do this, cannulas were introduced into the central end of the right carotid artery and into the central end of the right femoral artery, and these were connected through three-way cocks with a photoelectric drop counter, which in turn was connected to the peripheral end of the left femoral artery. In this way the blood supply to the hind limb of the animals could be measured after the operation during perfusion of the limb under normal pressure and also under the pressure when reduced by constriction of the aorta.

EXPERIMENTAL RESULTS

The pressure in the carotid and femoral arteries of the control rats was virtually identical and its mean value was 102 mm Hg. In the experimental animals, the pressure in the carotid artery was equal to 111±3.2 mm Hg; in the femoral artery, it was 52±2.8 mm Hg. On roentgenograms taken even three months after constriction of the aorta, there was no sign of the formation of large collaterals (Fig. 1). Two months after the operation the volume velocity of the blood flow in the femoral artery during perfusion under reduced pressure because of constriction of the aorta was 0.64-1 ml/min (mean 0.77 ml/min), and it was indistinguishable from the velocity of the blood flow in the control animals, which was 0.63-1.09 ml/min (mean 0.76 ml/min). However, when the limb was supplied with blood from the carotid artery, i.e., when the pressure was raised to the normal value, the volume blood flow in the femoral artery increased to 1.1-2.32 ml/min (mean to 1.65 ml/min), i.e., by 2.1 times. This result shows that a prolonged local fall of 50% in the arterial pressure causes a substantial decrease in the hydraulic resistance of the resistive vessels of the hind limbs, one possible cause of which could be an increase in the elasticity of their wall.

This hypothesis was confirmed by the results of the morphological investigation. After constriction of the aorta a tendency toward a progressive increase in the diameter of the lumen of the blood vessels in the hind part of the body, filled with contrast material, was observed. In the intact rats the lumen of the femoral arteries was 40-42% of the lumen of the middle third of the thoracic aorta, while from the 14th day after the operation it rose from 50-52%. The lumen of the femoral arteries 3 months after constriction of the aorta reached a mean value of 880 ± 27 μ (compared with 720 ± 42 μ in the control), or 55.9% of the diameter of the lumen of the thoracic aorta (42.1% in the control; $P = 0.01$).

In the intact rats the thickness of the wall of the aorta above the bifurcation averaged 55 μ (76% of the thickness of the wall of the thoracic aorta). One month after the operation the thickness of the aortic wall caudally to the point of constriction had fallen to 36.4 μ (46%), and 3 months after the operation to 25 μ (29%) of the thickness of the wall of the thoracic aorta. Three months after constriction of the aorta the thickness of the wall of the femoral arteries was reduced by 2-2.5 times (from 40 to 14-20 μ). The decrease in thickness of the wall of the blood vessels was mainly due to thinning of the layers of smooth-muscle cells, for the thickness of the elastic membranes showed only very slight changes. No sclerotic changes could be found in the walls of the large and small arteries lying distally and proximally to the site of constriction.

The results given in Table 1 show that regional hypotension, starting from the second week, leads to a decrease in thickness of the muscular coat of the small arteries of the thigh and to widening of their lumen. These changes increased progressively for 3 months after constriction of the aorta. From 1 to 3 months after the creation of permanent regional hypotension the volume of the nuclei of the smooth-muscle cells in parts of the aorta lying distally to the point of constriction was considerably reduced, being only 0.64-0.65 of the volume of the nuclei measured in the smooth-muscle cells of the thoracic aorta (Table 2).

Reducing the blood pressure on the wall of arteries of elastic and muscular type by half was thus followed by atrophy of the smooth-muscle cells of the tunica media of these vessels. Atrophic changes in the smooth-muscle cells developed comparatively slowly and were visible morphologically from the 14th day after lowering of the pressure.

Atrophy of the smooth-muscle cells developing during regional hypotension was reflected functionally in a decrease in hydraulic resistance of the resistive vessels 2 months after the constriction of the aorta.

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