A SIMPLE NEW METHOD FOR THE CONTROLLED CONSTRICTION OF THE RENAL AND OTHER ARTERIES IN SMALL LABORATORY ANIMALS DURING CHRONIC EXPERIMENTS*

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In experimental pathology, the controlled constriction of arterial vessels is used: 1) for producing models of hypertension and stenosis of the aorta; 2) for the controlled ischemization of organs, etc. However, up to the present time, due to the absence of simple and, at the same time sufficiently precise methods, experiments on the controlled constriction of arteries in small laboratory animals such as rats, etc. (occupying the leading position with regard to utilization in many of the world's laboratories) present considerable difficulties. Goldblatt's well-known vascular clamp [8], suggested for the constriction of renal arteries, is hardly ever used in experiments on small animals (rats, etc.) because of the relative complexity of setting it up,and difficulty of manufacture.

The U-shaped clamps suggested by Pickering and Prinzmetal [9] are not entirely convenient because: 1) the possibility of their slipping off the artery has not been entirely excluded, especially when the degree of constriction is slight (since, after applying the clamps to the vessels, the clamps remain open); 2) the precision of constriction by U-shaped clamps can easily be disrupted, because when they are applied to the artery the ends of the clamps are first unbent and are then again squeezed together; 3) the Pickering-Prinzmetal clamps do not produce uniform constriction of vessels to various diameters. They constrict the vessels to only one diameter.

Drury's [7] method of constricting renal arteries by means of applying relatively loose silk ligatures on the arteries of young animals on the premise that they will gradually press together in the process of growth of the animal is distinguished by lack of accuracy in controlling constriction, and by the necessity for long periods of waiting for the desired results. The Menn-Collins [6,10] method of constricting arteries by means of applying wire of a given diameter to them and then tightening silk ligatures around the artery together with the wire,with the subsequent removal of the wire, is also insufficiently precise. The extent of constriction here depends not only on the diameter of the wire, but also on the force of tightening of the ligature. According to our data [1,2], which agree with the results of Zbinden's observations [11], this method is not very effective for the controlled constriction of renal arteries in rats for the purpose of obtaining renal hypertension. The method proposed by F. Z. Meerson and G. V. Kobozev [5] for the gradual controlled creation of vitium cordis by means of a cannula can be used successfully for constricting large arteries (aorta, pulmonary artery). This method makes it possible to eliminate stenosis without a secondary operation. However, it is relatively complicated for the irreversible constriction of arteries in small animals.

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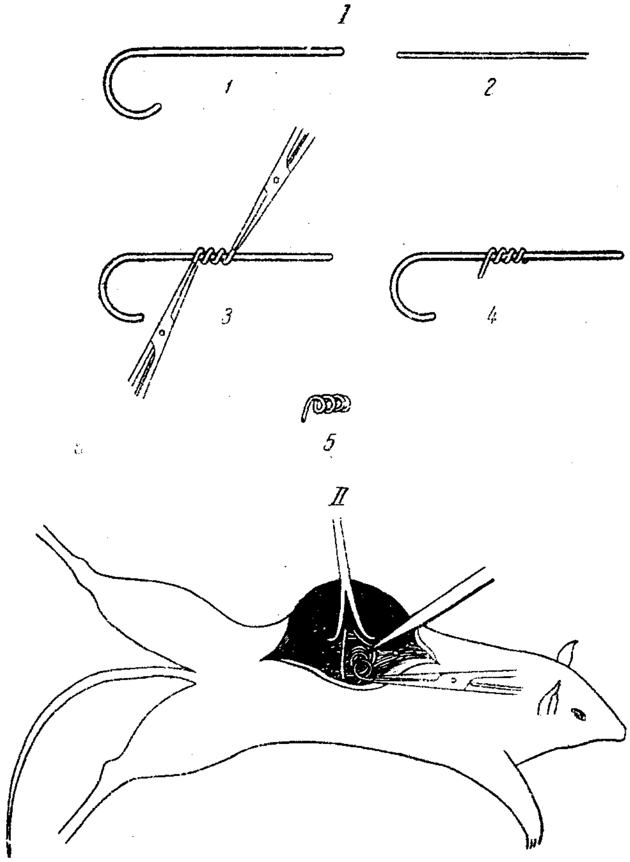

Fig. 1. I) Preparation of vessel-constricting spirals: 1) rigid steel wire (molding core); 2) wire made of tantalum or other nonrusting metal for preparation of the spiral; 3) the preparation of the spiral; 4) finished spiral (remains on the core until the operation); 5) spiral removed from the molding core. II) Application of the vessel-constricting spiral to the renal artery of a rat.

The method which we are proposing consists in the application on the vessel undergoing constriction of a spiral with a known given diameter of the loops. As the result of this, the diameter of the vessel usually decreases to the diameter of the loops of the spiral. The spiral is applied by means of twisting the dissected vessel into it. The spirals are prepared by the experimenter himself, from wire made of some nonrusting metal (tantalum, nichrome, stainless steel, etc.), by coiling it on another rigid steel wire or string (so-called molding core) of a known given diameter, accurately measured with a micrometer. The diameter of the coils of the spiral is equal to the diameter of the molding core.

The technique of preparing the spiral consists of the following (Fig. 1). The wire from which the spiral is prepared is grasped from both ends (5-8 mm at each end) by two arterial clamps. One end of the wire near the molding core is fastened securely by means of a clamp. Using the second clamp, the wire is stretched and tightly wound on the core in the form of a spiral.

The excess wire is cut off from only one end. The cut end can be additionally bent in order to make it blunt. The second, longer end of the spiral is left for convenience in holding it with the clamp at the time of application to the vessel. Finished spirals (in quantities of 15-25) are left threaded on the molding core until the time of the operation, and are sterilized in this form by means of boiling or with alcohol. We proved out the proposed method on rats (females weighing 195-260 g) in experiments on the constriction of renal and mesenteric arteries. Spirals made of tantalum and nichrome wire, and measuring 0.2-0.3 mm in diameter, were employed. The spirals had 3-4 coils measuring 0.24-0.4 mm in diameter. The length of the spirals was 2-2.5 mm. Following the application of a spiral with a loop diameter of 0.3-0.35 mm to one renal artery, the corresponding

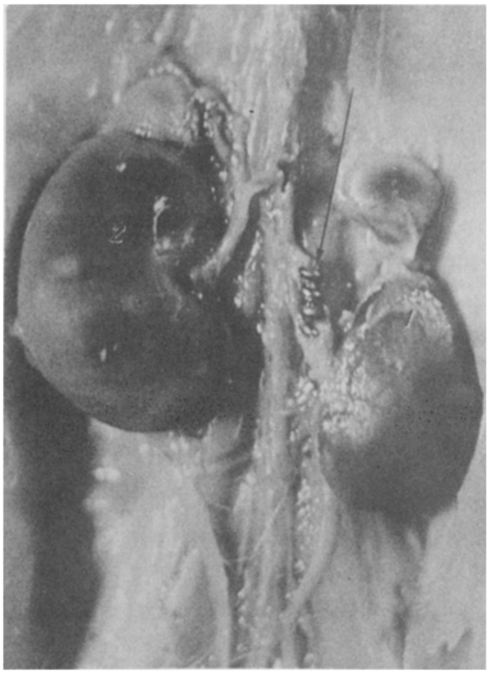

Fig. 2. Atrophy of ischemized kidney (1) and hypertrophy of the contralateral intact kidney (2) in 58 days following constriction of the renal artery (1) by a spiral with a loop diameter of 0.35 mm.

kidney underwent atrophy, while the intact kidney became hypertrophied (Fig. 2). However,if a spiral with a coil diameter of 0.3-0.35 mm was applied to the artery of one kidney with the simultaneous constriction of the artery of the second kidney by a spiral with a coil diameter of 0.26 mm, then in surviving rats,the first kidney (with arterial stenosis to 0.3-0.35 mm) underwent hypertrophy rather than atrophy, while the kidney with arterial stenosis to 0.26 mm atrophied (Fig. 3). This shows that, with the same degree of stenosis of the artery supplying the organ, the condition of its function and structure may differ sharply, depending on the level of the demands made upon it by the organism. In part of the rats (3 of 13), hypertension developed following the constriction of the arteries of one kidney – stable in one, and peaked (irregular) in two others. In rats in which hypertension did not develop or was peaked, a spiral was applied to the second renal artery after 4-10 weeks, as a result of which hypertension developed in the overwhelming majority of the animals surviving the second operation (the number of surviving animals in preliminary experiments constituted $^3/_4$ of the total number of those operated on twice – 9 of 12; hypertension developed in seven rats, peaked in three of these). In some rats, periods of stable blood pressure (for method of measurement see [3,4]), alternated with periods when it spread over a wide range (to 50-67 mm of mercury). The start of the rise in blood pressure was usually noted by the end of 1-3 weeks; in part of the rats these intervals varied.

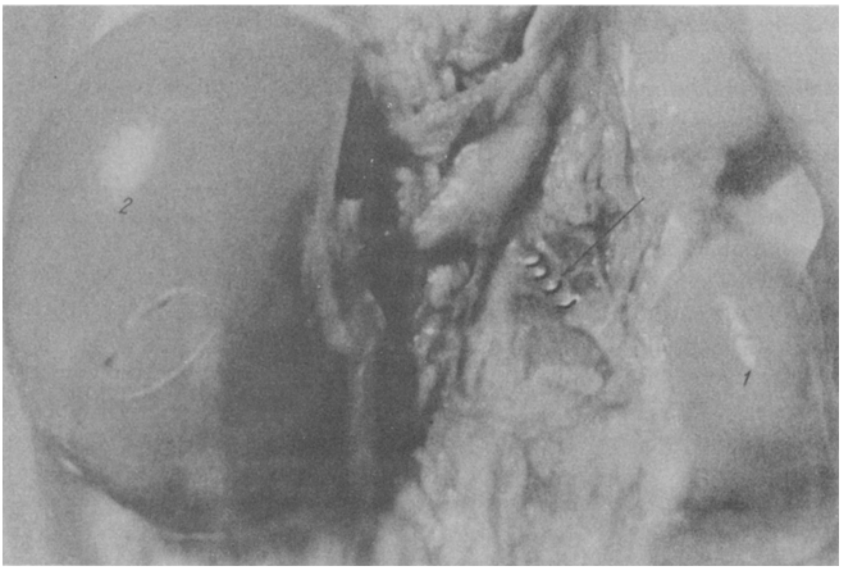

Fig. 3. Atrophy of the kidney (1) and hypertrophy of the kidney (2) in 35 days following simultaneous constriction of the arteries of both kidneys; the artery of kidney (1) was constricted by a spiral with a loop diameter of 0.26 mm, while the artery of kidney (2) was constricted by a spiral with a loop diameter of 0.3 mm.

During hypertension,the blood pressure rose by 40-120 mm of mercury. Morphologically, hypertension in rats is characterized by hypertrophy of the heart and sclerotic affectation of the vessels which is especially pronounced in the pancreas, mesentery, kidneys, and heart. We also conducted experiments in which spirals with a coil diameter of 0.3-0.4 mm were applied to the superior mesenteric artery. In this case, gangrene of the intestine developed, and the rats died. The experiments on the investigation of the effect of precisely controlled ischemization of various organs on blood pressure will be continued by us.

Thus, a method of controlled constriction of renal and other arteries is proposed which can be used for: 1) the production of models of hypertension and stenosis of the aorta; 2) for the controlled ischemization of organs. The method: 1) is distinguished by its convenience of application in experiments on small animals (rats, etc.), but can also be used in experiments on large laboratory animals; 2) ensures a sufficiently precise controlled, and, at the same time, uniform, constriction of vessels; 3) is technically simple and can be carried out in any laboratory.

SUMMARY

The author proposed a new, simple technique of controlled constriction of the renal and other arteries. This method may be used for creating a model of diseases (hypertension – renal and coarctation, stenosis of the aorta), as well as for the study of collateral circulation. The method may be conveniently used for experiments both on small and large laboratory animals. It consists in placing a spiral with a set diameter upon the vessel, which constricts and becomes equal in diameter to the spiral. The method was successfully tested on rats in experiments with induction of renal hypertension by producing stenosis of renal arteries.

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* Original Russian pagination. See C.B. translation.