NEW MODEL OF EXPERIMENTAL HYPERTENSION PRODUCED BY ISCHEMIZATION OF THE SPLEEN

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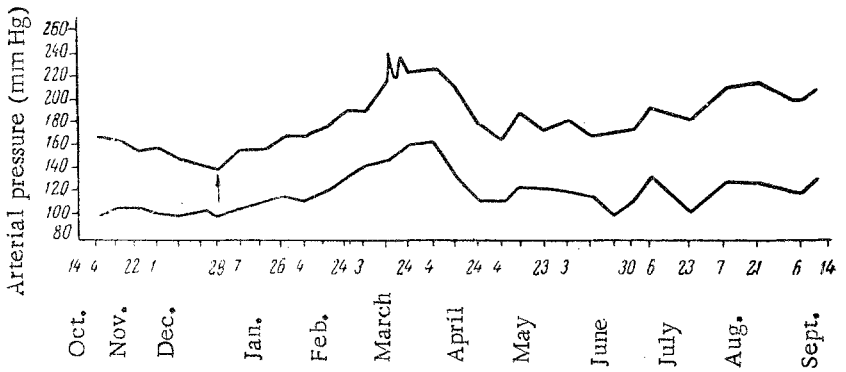
Experimentally induced hypertensive states serve as models for the study of the disturbances associated with this condition, from which conclusions may be drawn respecting the initiation and development of those physiological processes present in the diseased organism which lead to the prolonged elevation of blood pressure, so providing an approach to the elucidation of the pathogenesis of hypertensive disease. The variety of methods which have been applied for the elicitation of experimental hypertension is indicative of the common pathogenesis of the hypertensive states produced. In our opinion, this general factor is characterized by the initiation of trophic and vasopressor reflexes and by changes in metabolism and production of vasopressor substances. As has been shown by numerous researches, the latter are formed as a result of hypoxia of ischemic organs, with disturbances of their trophism.

As far back as 1870 I. O. Navalikhin, and in our times N. N. Anichkov [1] and others have shown that experimental ischemia of the brain is followed by a rise in blood pressure. Experimental hypertension following ischemization of the kidneys was shown to occur by Ya. Ya. Stolnikov [5], and later by Goldblatt [3] and numerous others. More recently fairly prolonged hypertensive states have been found to result from cardiac and uterine ischemia [2, 4]. It is not yet known, however, whether ischemia of other organs, in particular the spleen, plays any part in the pathogenesis of hypertensive disease.

The present paper deals with the production of experimental hypertension by causing ischemia of the spleen (G. V. Kasatkina took part in the experiments).

EXPERIMENTAL METHODS AND RESULTS

Our experiments were conducted on 15 dogs of different sexes and ages. One of the carotid arteries was displaced to a subcutaneous position or to a skin pedicle. The dogs were then familiarized with laboratory conditions and with those of the experiment, over a period of two months. Blood pressure was measured daily for each dog in a special room, by Korotkov's method, and the pulse and respiratory rates were recorded. After the dogs had become accustomed to this routine they were subjected to laparotomy. The abdomen was opened, under morphine-ether anesthesia, and under aseptic conditions, and a number of branches of the splenic vein and artery were ligated, after which the spleen was inserted into a subcutaneous pouch formed in the abdominal wall. In other dogs we constricted the splenic artery and one or two arterial branches, shifted the spleen to the abdominal cavity, and closed the wound.



Alterations in blood pressure observed in the dog Jack after producing splenic ischemia. Explanation of tracings (from above down): maximum arterial pressure, minimum arterial pressure, ↑ when operated.

The dogs all withstood the operation well. They showed no noticeable subsequent behavior changes. Arterial pressure began to rise gradually in all the dogs soon after the operation, from initial levels of 138-140/99-100 mm Hg to 241/100 mm Hg $1^1/_2$-2 months later, and in some cases to even higher levels. After this, arterial pressure gradually declined, probably as a result of compensation of the experimentally produced disturbances in the circulation and metabolism of the spleen.

Alterations were also observed in the pulse and respiration: the pulse rate rose by 30-40 beats per minute, and the respiratory rate by 10-12 respirations per minute.

The carotid arteries of the dog Jack were fixed in a subcutaneous position. During $2^1/_2$ months of control observation of the general condition of the animal and of its blood pressure, pulse, and respiration, we proceeded to the operation. Before the operation arterial pressure was 142/99 mm Hg, pulse rate 86, and respiration 19 per minute. We ligated two branches of the splenic artery, and shifted the spleen to the peritoneal cavity. The wound was then closed, and it healed uneventfully. As appears from the Figure, arterial pressure rose gradually after the operation, to reach a level of 243/145 mm $2^1/_2$ months later. After two weeks it began gradually to fall, but did not reach the initial level over the period of observation. It is probable that complete return to normal pressure was prevented by a skin disease which supervened (hyperemic patches on the head and body, with falling out of hair and formation of boils). The affected areas of skin were painful. Similar skin conditions were seen in three other dogs. These dogs, similarly to Jack, showed a rise in blood pressure; ischemization of the spleen had not been carried out for one of them. Together with rise in arterial pressure, we observed acceleration of the pulse, from 86 before the operation to 118 on the 3rd day after it, and to 130 after 3 months. Rise in respiratory rate was less marked.

A different variant of the operation was applied in the case of the dog Bobik. After laparotomy, two branches of the splenic artery and one splenic vein were ligated. The spleen was moved to a skin pouch in the wall of the abdomen, and the wound was closed in layers. After a number of days arterial pressure began slowly to rise, reaching a maximum of 194/132 mm after 2 months, i.e., rather sooner than for the dog Jack, and then began to fall. During the first few days after the operation the pulse rate rose from 93 to 118 beats per minute. The respiratory rate increased from 20 preoperational to 28 after the operation.

The respiratory rate reverted to the initial frequency sooner than the pulse. Development of hypertension proceeded in the same way in the other animals as for the ones described above.

DISCUSSION OF RESULTS

We think we are justified in remarking that one is not justified, in the present state of knowledge, in limiting secondary pathogenic factors of hypertensive disease only to renal ischemia. The published data, as well as our findings that experimental hypertension may be produced as a result of ischemia of the spleen, are evidence of the role played by other viscera, liable to ischemia and to anoxic metabolism, in the pathogenesis of the disease. We have no information regarding the relative importance of splenic ischemia, as compared to that of other organs, in the pathogenesis of hypertensive disease. This question, and also that of the elucidation of the actual physiological mechanism of development of hypertension in our experiments will be the subjects of our further research.

LITERATURE CITED

[1] N. N. Anichkov, Vestnik Khir. Pogran. Obl., Vols. 16-17, Nos. 48-49, pp. 105-109 (1929).

[2] M. A. Volin, E. S. Tsvilikhovskaya, T. I. Beslekoev, and V. S. Mayat. Terap. Arkh., 22, No. 6, 17-25 (1950).

[3] Goldblatt, cited from Klin. Med., 17, No. 8, 4-9 (1939).

[4] P. D. Gorizontov and D. S. Shlyapin, Arkhiv Patol., No. 3, 13-17 (1948).

[5] Ya. Ya. Stol'nikov, Archives of Clinical Internal Diseases* by S. P. Botkin, Vol. 6, pp. 306-308 (1880).

* In Russian.