circulation rises, in response to stimulation from the reflexogenic zones of the carotids and aorta. This explains the significance of the reflex from the superior vena cava under conditions of normal activity of the cardiovascular system.

Venous pressure also rises when the activity of the heart is depressed, but the organism is not able to counteract this tendency by reflex stimulation of cardiac activity. Raised pressure in the superior vena cava evokes a pressor reflex acting on the lymphatic vessels, and impeding the flow of lymph. Lymph is at first retained in the parts of the body most distant from the heart, and then, with increasing venous pressure and striction of lymphatic vessels, edema makes its appearance in other parts of the body. Hulse [3] has reported that in patients displaying progressive edema the thoracic duct and the cisterna chyli are empty, but fill up with lymph as soon as resorption of edema fluid begins. According to Hulse, the incidence of this effect is so regular that it is possible to deduce from it what stage of the edematous process is present, without clinical examination of the patient.

This reasoning applies, obviously, only to edema associated with raised venous pressure. Thus factors tending to lower venous pressure will bring about a weakening of the pressor reflex, and so favor transfer of edema fluid to the blood stream.

Rusnyak [2] has in a recently published paper drawn attention to certain inconsistencies with Starling's theory of causation of edema, such as, for example, the beneficial effect of ligating the inferior vena caca of patients with cardiac decompensation. Not only does this not aggravate the edema of the lower extremities, as would be expected from Starling's theory, but on the contrary, it lessens it.

Rusnyak does not enter into a consideration of the reasons for this effect. We would, on the basis of our experimental findings, suggest the following explanation. Ligature of the inferior vena cava involves a diminution in the flow of blood to the right auricle, at least until the establishment of an adequate collateral circulation. As a result, the pressure in the right auricle and the superior vena cava falls, and the pressor reflex becomes weaker. In addition to this, the pressure in the part of the vein below the ligature rises, causing reflex dilatation of the lymphatic channels, which will tend still further to inhibit the pressor reflex from the superior vena cava. In consequence, the patency of the lymphatic vessels is restored, and the edema of the lower extremities disappears. We would emphasize that Rusnyak also attaches significance to the lymphatic vessels in development of edema.

LITERATURE CITED

[1] V. V. Petrovsky, Fiziol. Zhur. SSSR, No. 3 (1954).

[2] I. Rusnyak, Klin. Med. No. 1, 23-35 (1954).

[3] W. Hulse, Klin. Wschr., 1923, No. 2, S. 63-65.

INFLUENCE OF SPLENIC INTEROCEPTORS ON BLOOD PRESSURE AND RESPIRATION IN ONTOGENESIS

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We know from the literature [6] that the spleen of adult animals (dogs, cats) contains receptors, which when stimulated evoke reflex changes in respiration, arterial and venous pressure, and flow of lymph.

The present paper is devoted to a study of the effects of splenic interoceptors on blood pressure and respiration in ontogenesis.

EXPERIMENTAL METHODS

We performed short experiments on the stimulation of splenic receptors of puppies aged from 1 day to 3-4 months.

We studied reflexes affecting respiration and arterial pressure, originating from splenic baroceptors and chemoceptors. The baroceptors were stimulated by blocking the venous outflow from the spleen, thus causing engorgement with arterial blood, or by raising the pressure of fluid with which the spleen was being perfused through its blood vessels. The spleen was in the latter case in a state of humoral isolation. Perfusion was performed with Ringer-Locke solution. The chemoceptors were stimulated by adding histamine and acetylcholine to the perfusion fluid.

We measured the blood pressure in the carotid artery during the experiments, using a Ludwig mercury manometer. Respiration was recorded through a tracheal cannula connected with a Marey capsule. We used 52 puppies in our experiments.

EXPERIMENTAL RESULTS

We performed 3 series of experiments with the object of elucidating the effects of splenic receptors on blood pressure and respiration at different ages. In the first 2 series we examined the origination of interoceptive effects from splenic baroceptors on blood pressure and respiration. For this purpose we raised the blood content of the spleen by blocking venous outflow (1st series of experiments).

The main trunk of the splenic vein was exposed, and a ligature was placed beneath it, in readiness for tightening. Arteries and nerves accompanying the vein were preserved intact. All other vessels were ligated and severed. The ligature under the splenic vein was then tightened, thus temporarily preventing the outflow of blood from the spleen, while retaining its arterial supply.

In this way we achieved an engorgement of the spleen with blood, as could be seen by direct observation; its volume increased, and it acquired a firmer consistency. In all the experiments of this series (28), using puppies aged up to $1^1/_2$-2 months, the systemic arterial pressure fell. The changes in blood pressure took place immediately after constricting the vein, i.e., with an extraordinarily brief latent period. Apart from this, we observed a prolonged after-effect, lasting in some cases for 1-2 minutes after release of the ligature in 1-3-day old puppies. This after-effect shortened with increasing age of the puppies. The magnitude of the hypotensive effect varied according to the age of the animals. It was inconsiderable for 2-3-day-old puppies (a fall of 3-5 mm Hg), and was greater for somewhat older puppies (up to 15 mm Hg). Puppies aged $1^1/_2$-2 months (4) did not display any increase in blood pressure after constricting the vein. No effect on respiration was evident in the great majority of our experiments. Examples of the effects on blood pressure and respiration of constriction of the splenic vein are given by the kymograph tracings of Figures 1 and 2 (1- and 7-day old puppies, respectively).

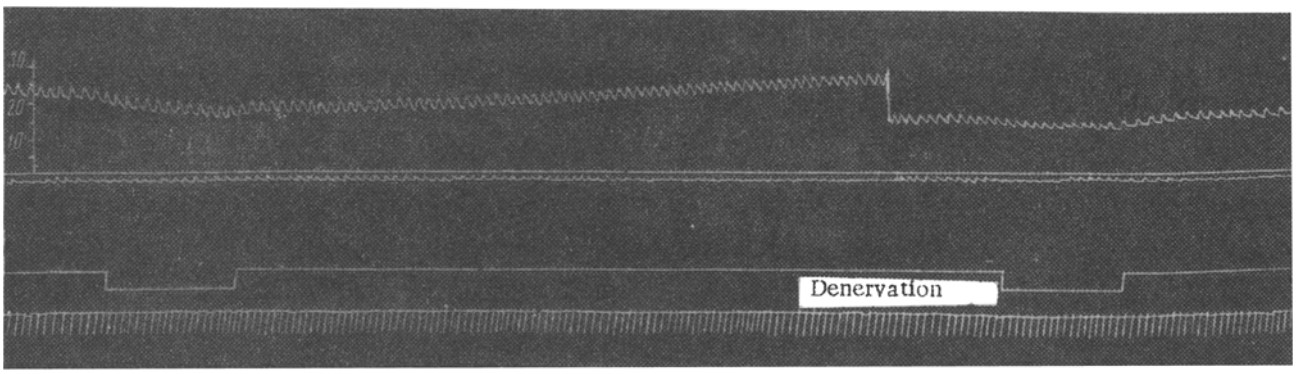

Fig. 1. Changes in blood pressure and respiration following stimulation of splenic receptors by distention of the spleen with blood. Constriction of the splenic vein of a day-old puppy. Explanation of tracings (from above down): blood pressure, base line, respiration, stimulation signals; time marker (3 seconds).

In order to elucidate the reflex nature of the effects observed we repeated the experiments after severing nervous connections with the spleen. All the visible nerve fibers accompanying the splenic artery and vein were cut, and the vessels were painted with procaine or phenol solutions. The effects on blood pressure previously observed were not abolished by denervation, ie., engorgement of the spleen following constriction of the vein, with an intact arterial supply, led to a similar lowering of blood pressure as before denervation.

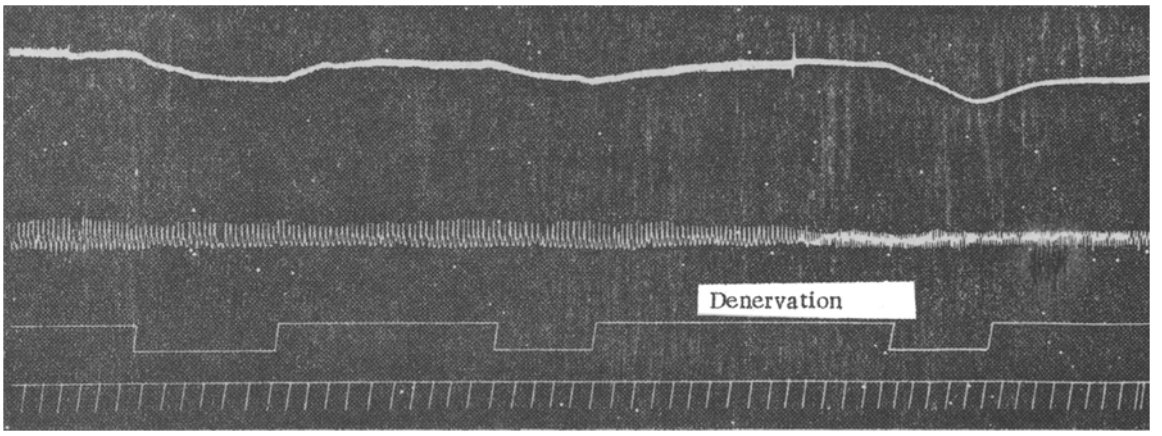

Fig. 2. Changes in blood pressure and respiration following constriction of the splenic vein of a 7-day old puppy. Explanation of tracings (from above down): as in Figure 1. Time marker (5 seconds).

Evidently the fall in arterial pressure observed after constriction of the splenic vein of very young animals is a consequence of the passive reception of blood by the spleen, which acts as a blood depot at this age, and which also releases it passively, as is evidenced by the prolonged after-effect found after release of the ligature from the vein.

In the 2nd series of experiments engorgement of the spleen was achieved by raising the pressure within the splenic vessels.

The spleen, after isolation from the systemic circulation, and hence from humoral factors, was perfused, through its main artery, with oxygenated Ringer-Locke solution at 37-38°. Pressure was raised within the limits 60-110 mm Hg by elevating the reservoir containing perfusion fluid. Higher pressures were achieved by forcing liquid in by means of a syringe. Pressure was measured by means of a mercury manometer.

In the 13 experiments of this series, on puppies aged from 17-20 days to 2 months, stimulation of the baroceptors of the splenic vessels had no effect on arterial pressure and respiration.

With puppies aged from 2 to 4 months, in half of the experiments performed raising the perfusate pressure to 80 to 110 mm Hg caused a slight rise in carotid artery pressure, but had no effect in the other half. More considerable changes in carotid pressure resulted from greater elevations of perfusate pressure, achieved by injection with a syringe.

The absence of reflex reactions from splenic baroceptors of young puppies, acting on blood pressure and respiration, may be deduced from the results of our experiments. The changes in blood pressure observed following stimulation of the baroceptors of the spleen of adult animals were seen in our experiments on 2-3-month old puppies.

These findings are in accordance with those of A. P. Polosukhin [2, 3], who found that reflex regulation of the volume of the spleen is established at the age of $2^1/_2$-3 months, up to which age the spleen takes no active part in the processes of distribution of blood in the organism.

The absence of any reflex regulation through changes in arterial pressure under conditions of splenic engorgement in young puppies may be ascribed to the functional immaturity of the nerve centers, since it is known from the literature that the terminal ramifications of the splenic nerves are capable of conducting and transmitting stimuli at birth.

The third series of experiments was on the effects on blood pressure and respiration of stimulating splenic chemoceptors.

Solutions containing 30 to 100 μg of histamine or acetylcholine were introduced into spenic vessels with intact innervation. The solutions were injected through the walls of the rubber tubing attached to the perfusion cannula. In order to avoid excessive dilution of the reagents the flow of perfusion fulid was discontinued during the injection. We performed 16 experiments in this series.

Owing to the difficult anatomical approach to the main trunks of the spenic artery and vein in very young animals we were obliged to do the perfusion experiments on puppies aged 17-20 days or more.

In the great majority of experiments introduction of histamine caused a rise in blood pressure. In 10 of the 16 experiments there was no effect on respiration. In some of the experiments we observed a diminution in the amplitude of the respiratory movements, without change in frequency, or with slight retardation. Acetylcholine also affected blood pressure, but at higher dosage levels, and the effects were less pronounced than with histamine. Respiration was unaffected.

As is evident from Figure 3, introduction of histamine or acetylcholine into the splenic vessels of a month-old puppy led to a rise in blood pressure.

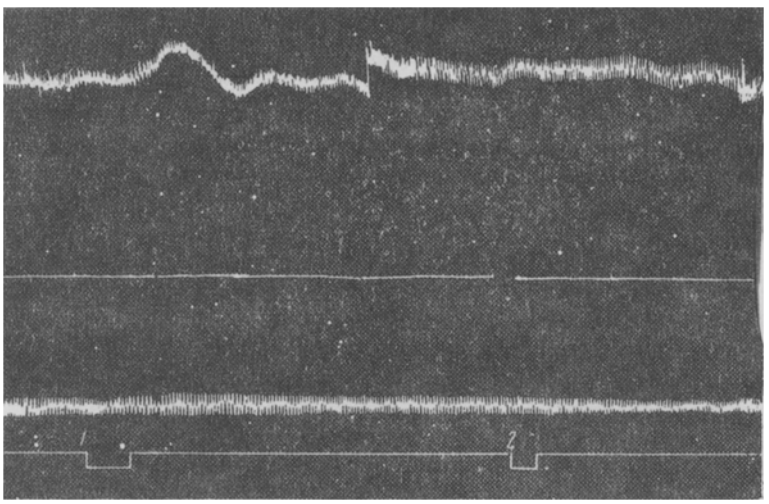

Fig. 3. Changes in blood pressure and respiration following stimulation of splenic receptors by means of introduction of histamine (1) or acetylcholine (2) into a month-old puppy.
Explanation of tracings (from above down): as in Figure 1.

Our experiments thus show that stimulation of the splenic chemoceptors of 17-20 day-old puppies causes changes in blood pressure and repiration. The development of these reflexes at an earlier age is not excluded by our experiments, since we could not perform splenic perfusion of younger puppies.

Our findings show that reflex vasomotor and respiratory reactions to stimulation of splenic baroceptors, characteristic of adult animals, are absent at birth, and first appear at the age of $2^1/_2$-3 months.

Interoceptive effects from splenic chemoceptors are demonstrable at an earlier age.

LITERATURE CITED

[1] M. I. Kokhanina, Izvest. Akad. Nauk Kazakh. SSR, Ser. Fiziol., No. 73 (2), 111-119 (1919).

[2] A. P. Polosukhin, Development of Humoral and Reflex Regulation of the Spleen, as a Blood Depot, in Ontogenesis,* Thesis, 1939.

* In Russian.

[3] Ibid., Byull. Eksptl. Biol. i Med., 6, No. 2, 216-219 (1938).

[4] E. G. Skipina, Byull. Eksptl. Biol. i Med , 39, No. 6, 14-18 (1955 .

[5] E. G. Skipina, Reflex Effects on Venous Pressure from Visceral Reactors.* Thesis, Alma-Ata (1952).

[6] V. N. Chernigovksy, Afferent Systems of the Viscera;* Kirov, 1943.

EXPERIMENTAL PITUITRIN HYPERTENSION AND CORONARY INSUFFICIENCY IN MONKEYS

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It has been shown by A. A. Belous [1, 2] that daily intravenous injection of 0.5 ml of pituitrin for 13-15 days gives rise to persistent hypertension in dogs and rabbits. This author noted that pituitrin causes changes in cardiac activity. A comparison of the electrocardiograms taken before and after pituitrin treatment of dogs showed changes in the activity of the heart typical of coronary insufficiency. In rabbits, the electrocardiograms showed disturbances indicative of myocardial dystrophic change (arrhythmia, bradycardia, change in the electrical axis of the heart, lowered potentials).

Although experimental pituitrin hypertension in dogs and rabbits is not identical with the human condition, there are nevertheless grounds for believing that changes in the functioning of the endocrine glands, in particular the neurohypophysis, are of considerable importance in the pathogenesis of human hypertensive disease.

We thought it of great importance for the elucidation of the role of pituitrin in the causation of hypertensive disease to study the possibility of inducing pituitrin hypertension, and also the effects of pituitrin on the action of the heart of monkeys.

According to the reports of the Sukhumi Medicobiological Station [6, 7], spontaneous hypertension with symptoms of coronary insufficiency, resembling the picture seen in human hypertensive disease, is not infrequently encountered among monkeys maintained under artifical conditions. We attempted to establish whether pituitrin-induced hypertension with cardiac disturbances could be produced in monkeys, in the same way as in rabbits and dogs.

EXPERIMENTAL METHODS

The experimental animals consisted of 9 rhesus monkeys aged from $3\frac{1}{2}$ to 12 years, including 3 females and 6 males. Irrespective of age and weight all the monkeys were given one intravenous injection daily of 0.5-0.6 ml of pituitrin, for 18-22 days, except in one case (the monkey Karlik) in which only 12 injections were given when persistent hypertension set in. Blood pressure was measured daily in vessels of the forelimbs by means of a Riva-Rocci instrument, for 3 days before the course of injections, during the injection period, and after the injections had been discontinued. Electrocardiograms were taken over the whole of the observation period.

EXPERIMENTAL RESULTS

The initial blood pressure varied from 130/70 to 150/100 mm for 6 monkeys (Forum, Artam, Nil, Perepel, Vilya, Vanessa), and from 160/100 to 170/100 mm for 3 monkeys (Zlatka, Slepen', Karlik). Rise in blood pressure was observed after 4-8 injections, but it was not persistent. For this reason injections were continued

*In Russian.