CHANGES IN THE BLOOD PRESSURE AND THEIR MECHANISM OF DEVELOPMENT AFTER INJECTION OF HYPERTONIC SOLUTIONS INTO THE BLOOD STREAM

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Many workers have studied the reactions after the injection of various chemical irritants into the blood stream.

Heger [10] and Pagano [11] first expressed the idea of a reflex mechanism of these reactions. G. P. Konradi [6] described the peculiarities of the changes in the blood pressure after the injection of hypertonic sodium chloride solutions into an artery and showed that peripheral mechanisms of maintenance of vascular tone were concerned in the production of these reactions.

A. G. Bukhtiyarov [2], studying thse problems at a later date, observed different reactions after the intra-arterial and intravenous injection of hypertonic solutions of sodium chloride and of other substances, and came to the conclusion that the increase in the blood pressure under these circumstances was connected with the stimulation of receptors situated in the arterial trunks.

We have shown [8] that the increase of pressure after injection of certain chemical irritants into peripheral arteries is connected with the stimulation of the peripheral vascular network, and probably with the tissue receptors. These findings were confirmed by other workers [3, 4].

More complex are the changes in the blood pressure arising after the intravenous injection of hypertonic solutions. Several workers [1, 2, 3, 4 8] have observed a fall in the blood pressure after the intravenous injection of sodium chloride and glucose.

Under these circumstances the possibilities for the deciphering of the complex reaction arising after the intravenous injection of hypertonic solutions have been widened by the establishment of the regular features of the sequence of changes in the blood pressure [8].

EXPERIMENTAL METHOD

Experiments were performed on dogs of various weights and ages (70 animals).

Chloralose, morphine-ether-oxygen and sodium amytal anesthesia were used.

Direct synchronous registration of the hemodynamic mechanisms was carried out on a Brodie-Starling electrokymograph with a multichannel water-mercury manometer, by means of catheterization of the main vessels and the chambers of the heart.

Catheterization of the cardiovascular system was also used for applying the stimuli to the various reflexogenic zones. Catheters were introduced into the pulmonary artery, the right heart and the venae cavae through the right external jugular and femoral veins, and into the arterial part of the greater circulation and the left ventricle of the heart – through the left carotid and femoral arteries. Heparin was injected intravenously (25 i. u./kg) before introduction of the catheters. The position of the catheters was determined by the level

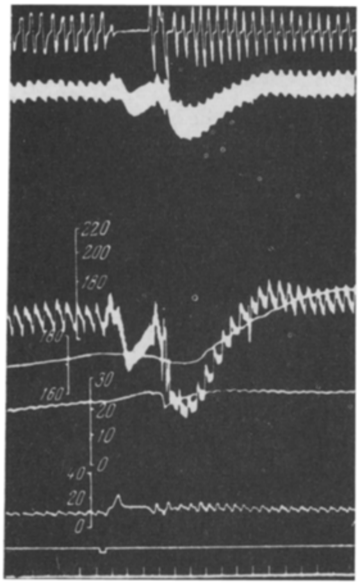

Fig. 1. Changes in the blood pressure and respiration after the intravenous injection of 20 ml of 40% glucose solution (chloralose anesthesia). Significance of the curves (from above down): respiration; blood pressure in the femoral artery (membrane manometer); blood pressure in the femoral artery in mm Hg; venous return from the limb; central venous pressure in mm of water; pressure in the pulmonary artery in mm Hg; injection marker; time marker (5 seconds).

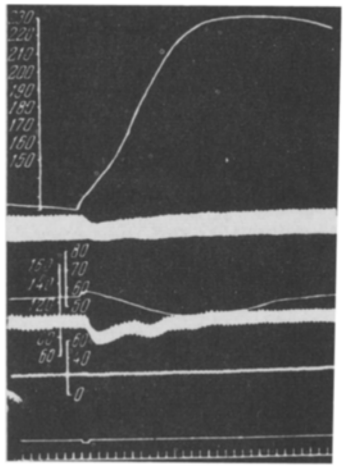

Fig. 2. Changes in the blood pressure after injection of 5 ml of 40% glucose solution into the perfusate of a lobe of the lung isolated in respect to its blood vessels. Significance of the curves (from above down): pressure of the input into the perfused circulation in mm of water; pressure in the femoral artery (membrane manometer); pressure of the outflow from the perfused circulation in mm of water; pressure in the femoral artery in mm Hg; pressure in the pulmonary artery in mm Hg; injection marker; time marker (5 seconds).

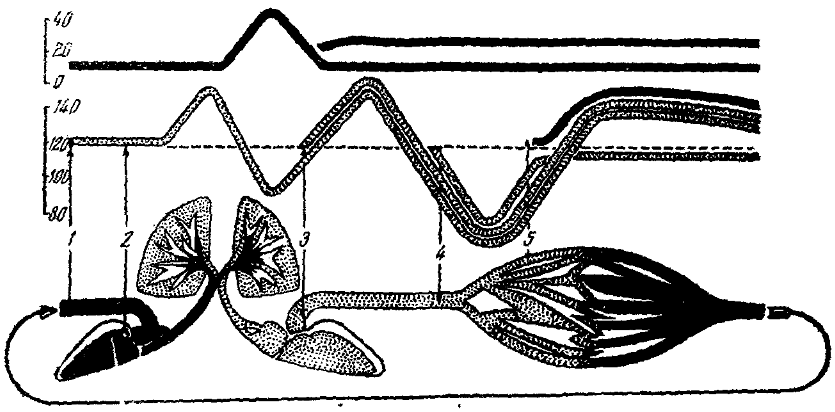

Fig. 3. Scheme of formation of the reaction. Phases of the successive changes in the arterial pressure in the systemic (lower scale) and pulmonary (upper scale) circulations after the intravenous injection of hypertonic solutions 1), injection into the right ventricle of the heart 2), into the left ventricle of the heart and aorta 3), into the arterial trunks 4), and into the peripheral vascular network 5). The circulation is shown in diagrammatic form below.

of the blood pressure, the character of the pulse and respiratory waves, and so on. At the end of the experiment the situation of the catheters was verified by postmortem examination.

Perfusion of a limb, isolated in respect to its blood vessels but retaining its nervous connections with the rest of the animal's body, was performed by V. N. Chernigovskii's method, and perfusion of a lobe of the lung, also isolated in respect to its blood vessels but retaining its nerve connections with the body, was carried out with venous blood from the peripheral end of the femoral vein. Blood from the vein of the perfused lobe of the lung flowed into the central end of the femoral vein. In another variant perfusion of the lobe of the lung was carried out with blood from the pulmonary artery of another dog, the blood then passing into the left atrium of the latter animal.

EXPERIMENTAL RESULTS

The multiphase changes in the blood pressure after intravenous injection of glucose, as was shown previously [8], follow a perfectly regular sequence.

In response to the rapid injection of 10-20 ml of 40% glucose solution or of 5-10 ml of a 12-20% sodium chloride solution into the femoral or external jugular vein, the arterial pressure at first changed in the form of a three-phase, pressor-depressor-pressor wave, then fell and again rose above its original level (Fig. 1). Clearly defined experimental conditions, rapid injection of the irritant and a satisfactory condition of the animal under even anesthesia ensured the constancy of this reaction.

The production of the first pressor wave could be explained by the increase in the inflow to the heart on account of the injection, and probably by reflex changes to the increased filling of the venae cavae. This wave was reproduced by injection of an isotonic solution of sodium chloride, although in some experiments the increase in blood pressure was usually slightly less than after injection of hypertonic solutions.

Of particular interest was the sharp and brief fall in the blood pressure following the first pressor wave (the depressor wave), arising as a result of stimulation of the receptors of the lesser circulation.

Under these circumstances respiration was arrested as a rule in expiration and the activity of the heart was greatly retarded.

The depressor peak was absent after injection of hypertonic solutions into the "shunt" of the pulmonary circulation, i.e., by injecting through the catheter in the left ventricle of the heart and the ascending aorta. In these conditions the reaction began only with the second pressor wave, and the later sequence of changes in the blood pressure was preserved.

The depressor reaction with retardation of the activity of the heart and arrest of respiration in expiration was observed not only after injection of hypertonic solutions into the vessels of the pulmonary circulation, but also after their injection through the catheter into the bronchial vascular network.

It might be assumed that the tissue receptors of the lungs were of fundamental importance in the mechanism of this reaction. The injection of hypertonic solutions into the vessels of the perfused lobe of the lung with its nervous connections intact, also led to a depressor reaction in the systemic circulation of the animal (Fig. 2).

The reflex retardation of the cardiac activity and arrest of respiration in expiration in response to stimulation of the receptors of the pulmonary circulation with hypertonic solutions were brought about by participation of the vagus nerves. After bilateral division of the vagus nerves in the neck these components of the reaction were absent, whereas in the majority of the experiments the depressor crest was merely reduced in size, but was nevertheless preserved.

In investigations by Schuwiegk [12], using other methods of stimulation of the receptors of the pulmonary circulation, two effector mechanisms of the depressor reflex were described: dilatation of the peripheral vessels and slowing of the activity of the heart.

According to our findings obtained in experiments with synchronous registration of the pressure in the pulmonary artery and of the circulation in the systemic vessels, a third effector mechanism during stimulation of the receptors of the pulmonary circulation is constriction of the pulmonary vessels. A sharp rise in the pressure in the pulmonary artery corresponded to the depressor trough (see Fig. 1).

In experiments with perfusion of a lobe of the lung isolated in respect to its blood vessels, in addition to a depressor reflex there was observed to be an increase in the resistance – an increase in the inflow pressure and a fall in the outflow pressure of the perfused circulation (see Fig. 2).

The sharp constriction of the pulmonary vessels led to a decreased inflow of blood to the left heart and to a fall in the arterialpressure in the systemic circulation. The principal feature of the third effector mechanism in response to stimulation of the receptors of the pulmonary circulation with hypertonic solutions was thus that the effect on the systemic circulation was produced by local vasomotor reactions in the pulmonary circulation.

In some experiments the increase of pressure in the pulmonary artery was very considerable, and the level of its maximum increase was 2-3 times higher than its original level. Constriction of the pulmonary vessels under the influence of hypertonic solutions in dogs with the thorax opened, unconnected with the reaction which we have described, was also observed by Binet and Burstein [9].

In response to strong stimuli, the reflexes from the pulmonary circulation acquired a dominating importance. The depressor reaction, with participation of all three effector mechanisms, under these circumstances could be very marked, thereby disturbing the whole complex of usual successive changes in the blood pressure and the character of the reaction.

The first pressor wave and depressor trough appeared after injection of the hypertonic solutions through the venous system and the right heart into the vessels of the pulmonary circulation, and the remainder of the reaction, starting with the second pressor wave, appeared after injection of the solutions into the left heart and ascending aorta. The depressor trough was not, therefore, the result of the Bezold-Jarisch reflex.

By comparison of the effects following the injection of glucose and sodium chloride into the right and left heart, into the pulmonary artery and the ascending aorta, the firm impression was gained that the passage of these irritants directly through the chambers of the undamaged heart caused no changes in the rhythm of action of the heart nor in the blood pressure in either the systemic circulation or the pulmonary artery.

Direct stimulation of the heart is probably important after the injection of much larger doses of the concentrated solutions, and when the outflow of blood is retarded.

The mechanism of the second pressor wave is still unexplained. The view was originally put forward that it arose as the result of stimulation of the receptors of the ascending aorta. This wave could also be preserved, however, after injection of the hypertonic solutions into the descending aorta.

The mechanism of the second wave of fall and subsequent increase in the blood pressure has been described previously [8]. The effector mechanism of the second wave of fall of blood pressure is dilatation of the peripheral vessels. The last phase of the reaction was the most complex, since the stimulus had left the aorta and the main arteries to enter different organs and tissues.

The causes of the increased pressure were demonstrated by experiments with perfusion of a limb, isolated from the body in respect to its blood vessels and retaining only its nervous connections, and after intra-arterial injection of the stimuli. Stimulation of the receptors of the peripheral vascular network led to an increase in the activity of the heart and, probably, to constriction of the peripheral vessels. The vessels of the heart and kidneys were, however, dilated at this period, and the blood flow through the femoral vein was increased.

It had to be assumed that the peripheral mechanisms of maintenance of vascular tone, described in the papers by G. P. Konradi [6], A. P. Kandel' [5] and others, also took part in the mechanism of this reaction.

The complex multiphase reaction appearing after injection of hypertonic solutions of glucose and sodium chloride into the blood stream was thus the result of successive stimulation of different reflexogenic zones, of different physiological function, extending over the course of the blood-flow during its first circulation around the body.

Besides the reflexogenic zones in the major vessels, the receptors of the pulmonary circulation and of the peripheral vascular network also take part in the formation of the reaction.

A significant part also belonged to the receptors of the pulmonary circulation, stimulation of which caused a powerful depressor reflex, mediated through the vagus nerves. The sharp increase of pressure in the pulmonary artery under the influence of hypertonic solutions demonstrated the great vasomotor potentialities of the vessels of the lesser circulation.

Our investigations enabled us to further develop our previously suggested scheme of formation of the reaction in response to the injection of hypertonic solutions into the blood stream.

By comparison with the diagrammatic representation of the circulation (Fig. 3) are shown the individual phases of the reaction which may be obtained in any order, in the same or in different experiments, after injection of the test stimulants into different areas of the cardiovascular system. The scheme clearly demonstrates the role of the sequence of stimulation in the formation of the multiphase reaction described.

SUMMARY

Following quick intravenous injection of hypertonic glucose and sodium chloride solution,the arterial blood pressure in dogs increases in 2 waves with a depressor wave in-between. It then drops and subsequently rises to its initial level.

The author conducted experiments with catheterization of the cardiac cavities and of the great vascular trunks, with prefusion of the isolated pulmonary lobe and extremity. It was demonstrated that the changes of the blood pressure described above are determined by a successive stimulation with hypertonic solution of reflexogenic zones of the pulmonary circulation, the great arterial trunks, the peripheral vascular network (with a possible paticipation of the peripheral mechanisms). In strong stimulation powerful depressor reflexes from the receptors of the pulmonary circulation are prevalent with constriction of the pulmonary vessels. This brings about a sharp temporary rise of the blood pressure in the pulmonary artery and a fall of the general arterial pressure. The main afferent and efferent mechanisms and scheme of the reaction are described.

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