ANALYSIS OF THE REFLEX CHANGES IN THE CARDIOVASCULAR SYSTEM FOLLOWING STIMULATION OF THE PERICARDIAL CHEMORECEPTORS. REPORT 2. THE ROLE OF THE HEART AND OF VARIOUS VASCULAR FIELDS IN THE DEVELOPMENT OF THE PRESSOR REACTION

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Stimulation of the chemoreceptors of the pericardium with solutions of nicotine under identical experimental conditions may cause the general level of the arterial pressure to be changed in different ways [4, 9]. The view is held that the character of the arterial pressure reaction arising in these circumstances is dependent on the strength of stimulation of the pericardial receptors [5].

In our previous investigations [7] we also demonstrated that different changes in the level of the arterial pressure could occur after injection of nicotine solutions into the pericardial cavity. In the same experimental conditions, the changes in the arterial pressure could take the form of depressor, pressor, or mixed depressor-pressor reactions.

We showed in the previous report that when a depressor reaction of the general arterial pressure takes place in response to stimulation of the pericardial chemoreceptors with nicotine, an important part is played by the vessels of the lungs, which act as a blood depot, and by changes in the activity of the heart (slowing of the heart rate). The strength of the cardiac contractions and the tone of the blood vessels of the other organs are less important.

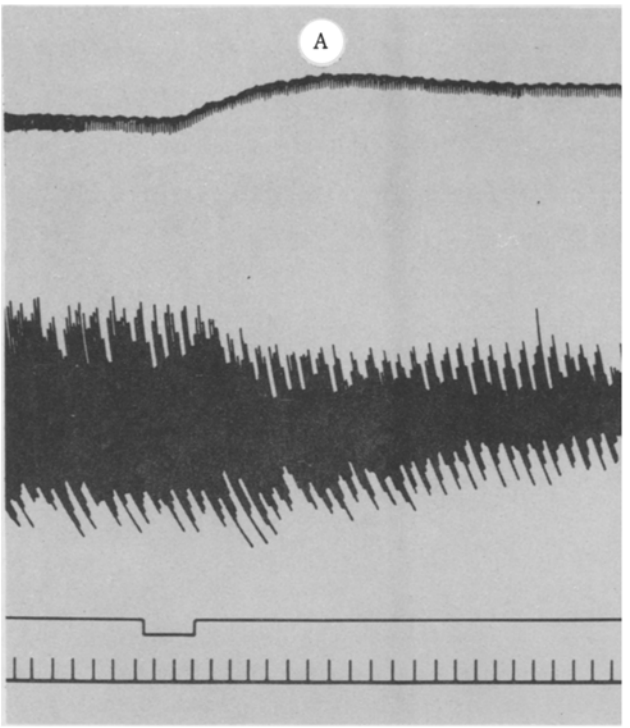
The aim of the present study was to discover the role of the heart and the peripheral vessels in the elevation of the arterial pressure following stimulation of the pericardial chemoreceptors with nicotine solutions. Acute experiments were carried out on cats. The experimental method was described in the first report.

EXPERIMENTAL RESULTS

The pressor reaction of the arterial pressure in response to stimulation of the pericardial chemoreceptors with nicotine solutions was observed immediately after a depressor response or without any preceding fall in the level of the arterial pressure. In either case the increase in arterial pressure was accompanied by a decrease in the strength of the cardiac contractions and frequently by an increase in the rate of the heart (Fig. 1, A). Comparison of the times of the changes in the arterial pressure and the strength and frequency of the cardiac activity showed that the decrease in the strength of the cardiac contractions always took place at the same time as the arterial pressure began to rise. The heart rate increased either at the beginning of the pressor reaction or when the rise in arterial pressure had actually occurred.

Considering the character of the changes in cardiac activity, the pressor reaction of the arterial pressure could not be explained by these changes. The significance of the vessels in different parts of the body in the mechanism of this reaction required elucidation.

We observed no changes in the tone of the arteries of the lungs during the pressor reaction of the arterial pressure; this corresponded to what was observed during the depressor reaction. In contrast to the depressor reaction, however, the pressor reaction was not abolished by exclusion of 3/4 of the lungs. Similar results were also obtained from experiments in which the pulmonary branches of the vagus nerves were divided (Fig. 1, B). Measurement of the volume



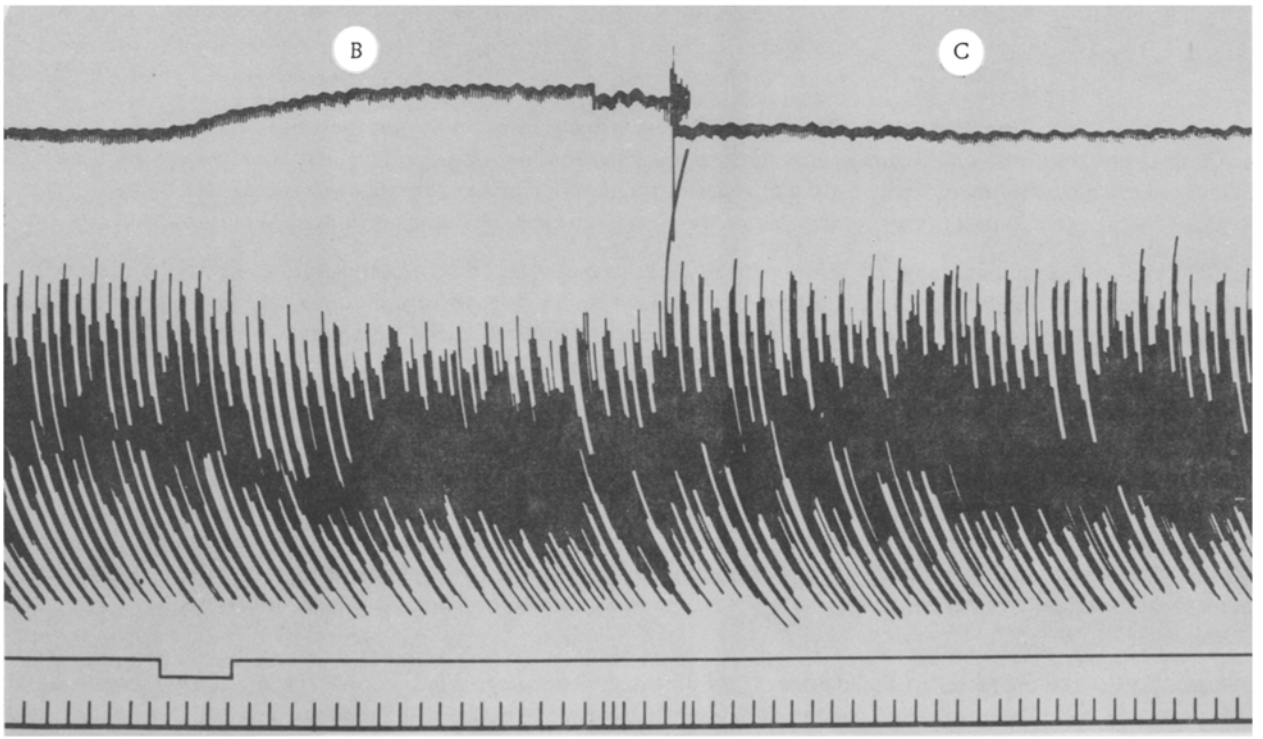


Fig. 1. Changes in the arterial pressure and strength of the cardiac contractions in response to stimulation of the pericardial chemoreceptors with 0.5 ml of a 10^{-3} solution of nicotine (A), after division of the pulmonary branches of the vagus nerves (B), and after removal of the adrenals (C). Significance of the curves (from above down): arterial pressure in the carotid artery; strength of the cardiac contractions; marker of injection of stimulus; time marker (2 sec).

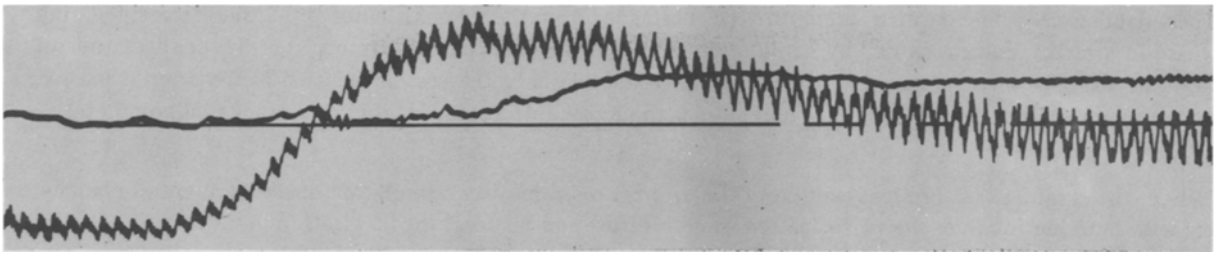


Fig. 2. Changes in the velocity of the blood flow in the pulmonary arteries and in the general arterial pressure after stimulation of the pericardial chemoreceptors with 0.5 ml of a 10^{-3} solution of nicotine. Significance of the curves (from above down): volume velocity of the blood flow with zero line; arterial pressure in the carotid artery.

velocity of the blood flow in the vessels of the lungs showed that in both arteries and veins the velocity was increased after stimulation of the chemoreceptors of the pericardium with nicotine. However, this increase took place after the arterial pressure had begun to rise (Fig. 2), and it probably resulted from the increase in pressure.

These experiments showed that the pulmonary vessels are not of decisive importance in the production of the pressor, in contrast to the depressor, reaction of the arterial pressure during stimulation of the pericardial chemoreceptors with nicotine.

The study of the functional state of the vessels in other parts of the body showed that during the increase in arterial pressure taking place in response to stimulation of the pericardial receptors with nicotine the tone of the vessels of the spleen, the small intestine, the kidneys, the pelvis, and the limbs was always increased.

The changes in the vascular tone in regions supplied with blood from the carotid, subclavian, and vertebral arteries were inconstant, and it was increased only when the pressor reaction of the arterial pressure followed a depressor reaction.

Hence, the leading part in the pressor reaction of the arterial pressure after stimulation of the pericardial chemoreceptors with nicotine was played by an increase in the tone of the peripheral vessels.

In order to discover the degree to which the various vascular fields take part in the pressor reaction, we used the method of temporary exclusion of these fields from the general circulation. We found that the principal part in the elevation of the arterial pressure in these experiments was played by the vessels of the small intestine and spleen, for if these were simultaneously excluded from the general circulation the pressor effect was considerably decreased. The successive exclusion of other vascular fields, while the circulation of the intestine and spleen remained intact, had almost no effect on the magnitude of the pressor reaction. Nevertheless, after exclusion of the spleen and intestine from the general circulation, the other vascular fields may bring about a slight increase in the arterial pressure, although this decrease is much smaller than when the vessels of the spleen and intestine take part in the reaction.

We may conclude from these findings that the increase in tone of the peripheral vessels after stimulation of the pericardial chemoreceptors with nicotine is effected through the sympathetic nervous system. This was also demonstrated by experiments in which the splanchnic nerves were divided, for after bilateral division of these nerves the pressor reaction was almost completely abolished.

Stimulation of the splanchnic nerves increases vascular tone, as a result both of direct nervous stimulation and of an increase in the secretion of adrenalin by the adrenals [1]. Various workers have demonstrated [2, 3, 6, 8] that a humoral mechanism is involved in the reflex increase in arterial pressure after stimulation of various nerves.

Since in our experiments the pressor reaction in response to stimulation of the pericardial chemoreceptors with nicotine arose as a result of an increase in the vascular tone in various parts of the body, the reflex influences on which were transmitted through the sympathetic nervous system, the possibility of reflex influences on the adrenals was not excluded. This was confirmed by experiments conducted on the frog's heart, isolated by Straub's method. Changes in the activity of the isolated frog's heart when perfused with blood taken from a cat during the pressor reaction resembled the typical adrenalin effect of an increase in the rate and strength of the cardiac contractions. The adrenalin-like substances in the cats' blood could be detected after stimulation of the pericardial chemoreceptors with nicotine solutions in different experiments for 20-60 min. The time during which they circulated in the blood of these cats was directly dependent on the degree of elevation of the arterial pressure.

These facts were evidence that adrenalin-like substances from the adrenals entered the blood stream during the increase in arterial pressure caused by stimulation of the pericardial chemoreceptors. Further confirmation of this hypothesis was given by the fact that after removal of the adrenals, the pressor reaction of the arterial pressure in response to stimulation of the pericardial receptors with nicotine decreased sharply or disappeared completely (Fig. 1, C).

Hence, the single-phase pressor reaction of the arterial pressure after stimulation of the pericardial chemoreceptors with nicotine involves the participation of both reflex and humoral mechanisms, and takes place as a result of the action of the sympathetico-adrenal system on the blood vessels.

If a depressor-pressor reaction is observed in response to stimulation of the chemoreceptors of the pericardium, the increase in arterial pressure is a reflex compensatory reaction to the preceding fall in arterial pressure. In this case the pressor reaction of the arterial pressure is dependent on reflex influences from the carotid sinus and aortic zone on the adrenals.

We have stated above that the depressor reaction of the arterial pressure during stimulation of the pericardial chemoreceptors with nicotine is dependent on retention of blood in the lung depot and on a slowing of the heart rate. If, under these circumstances, the pressure in the arteries falls, reflex influences arising from the pressure receptors of the carotid sinus and aorta act on the adrenals, causing an increase in the secretion of adrenalin. Proof of this is given by the fact that during the biphasic changes in the general arterial pressure, if the depressor reaction is abolished (by dividing the pulmonary branches of the vagus nerves or excluding 3/4 of the lungs from the general circulation), the subsequent increase in arterial pressure also fails to develop. Denervation of the aortic zone and exclusion of the carotid sinuses (by clamping the carotid arteries) also prevented manifestation of the pressor reaction after the depressor phase (Fig. 3). Denervation of the aortic zone alone, or exclusion of the carotid sinuses alone, was followed by a decrease in the pressor reaction but did not abolish it completely.

Division of the splanchnic nerves or removal of the adrenals in animals showing a depressor-pressor reaction of the general arterial pressure abolished the pressor reaction arising after the depressor phase.

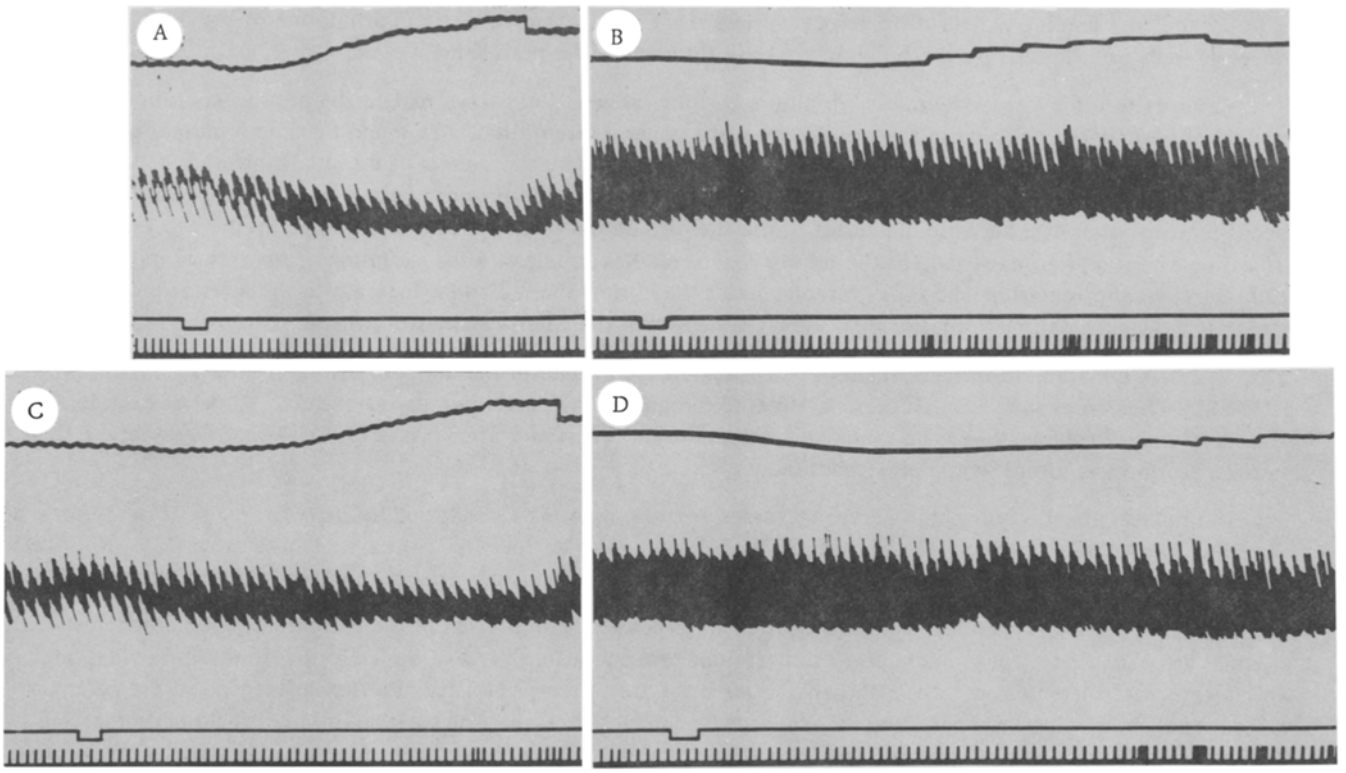


Fig. 3. Changes in the pressor phase of the depressor-pressor reaction of the general arterial pressure caused by stimulation of the pericardial chemoreceptors by 0.5 ml of a 10^{-3} solution of nicotine, after exclusion of the carotid sinus and aortic reflexogenic zones. A) Initial magnitude of the reaction; B) after clamping the carotid arteries; C) after denervation of the aortic zone; D) after denervation of the aortic zone and clamping the carotid arteries. Significance of the curves as in Fig. 1. Arterial pressure recorded in the femoral artery.

The possibility that reflex influences from the carotid sinuses may affect the secretion of adrenalin by the adrenals was demonstrated many years ago [10, 11, 12, and others].

The efferent pathways of the reflex arc responsible for the single-phase pressor reaction are the centrifugal fibers of the sympathetic nervous system to the various vascular fields, and primarily the splanchnic nerves. The increase in arterial pressure in this case is due to a reflex increase in the tone of the peripheral vessels, and also to reflex influences on the adrenals; the latter, by secreting adrenalin-like substances into the blood stream, in turn increase the peripheral vascular tone. If a pressor reaction arises immediately after a depressor, the efferent pathway of the reflex, starting from the carotid sinuses and the aortic zone, runs in the splanchnic nerves to the adrenals. The increase in arterial pressure in this case is due to an increased tone of the peripheral vessels, changes in which result from the entry of adrenalin-like substances from the adrenals into the blood stream.

The decrease in the strength of the cardiac contractions observed in our experiments during the increase in arterial pressure must evidently be regarded as a reflex compensation in response to the pressor reaction. Actually, the abolition of this reaction of the general arterial pressure (by division of the pulmonary branches of the vagus nerves in the case of depressor-pressor changes, and also by division of the splanchnic nerves or removal of the adrenals in case of pressor changes) led to the disappearance of this negative inotropic effect on the heart.

SUMMARY

Acute experiments were staged on cats under urethane anesthesia. As demonstrated, stimulation of pericardial chemoceptors by nicotine solution caused various arterial pressure changes: depressor, pressor or depressor-pressor reaction. As demonstrated in report 1, in effecting the pressor reaction the leading role was played by the vessels of the lungs, which deposited the blood as well as by decelerated cardiac rhythm. Stimulation of the pericardial chemoceptors by the nicotine pressor reaction was accompanied by reduction of the strength of cardiac conditions and often by accelerated cardiac rhythm. Pulmonary vessels did not participate in the appearance of the pressor reaction. Resistance of the vessels of the spleen, small intestine, kidneys, pelvic area and of extremities always increases. In experiments with temporary exclusion of various vascular areas from the general circulation it was shown that the main role in the rise of arterial pressure belonged to the vessels of the small intestine and of the spleen. Bilateral section of the splanchnic nerves and adrenalectomy eliminated the indicated pressor reaction. Participation of the humoral link in effecting this reaction was demonstrated in experiments on the isolated frog hearts.

A rise in arterial pressure in depressor-pressor reaction, which is a reflex compensation in response to the preceding arterial pressure reduction, is connected with the stimulation of the baroceptors of the sinocarotid and aortic zones and the effect from them on adrenal secretion.

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