CHEMOREFLEXES FROM THE RECEPTORS OF THE PULMONARY VESSELS ON THE CARDIOVASCULAR SYSTEM

D. P. Dvoretskii

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Injection of solutions of nicotine, acetylcholine, veratrine, and several other chemical substances into the pulmonary blood vessels causes a reflex lowering of the general arterial pressure and bradycardia [2, 5, 9, 10, 12]. The afferent pathways of these reflexes are the vagus nerves [5, 9, 12]. Besides this effect, if alcohol, ether, or chloroform is injected into the blood vessels of the lungs, pressor and pressor-depressor reactions of the systemic arterial pressure are observed [1, 3], although their nature has not been studied. The role of the receptors in different parts of the pulmonary vessels in the production of chemoreflexes from these areas on the circulatory system has been studied only in isolated investigations [9, 11].

The object of the present investigation was to study the character of the chemoreflex influences from different parts of the pulmonary vessels on the general arterial pressure and the cardiac activity.

EXPERIMENTAL METHOD

Experiments were carried out on cats anesthetized with urethane (1 g/kg) or a mixture of chloralose and urethane (0.05 and 0.5 g/kg respectively). The chest was opened, artificial respiration was applied, and heparin given (5000 units).

In the experiments of series I the chemoreflexes from the receptors of the main trunk of the pulmonary artery and its bifurcation were investigated. Through an incision in the right auricle, a polyethylene tube (2-2.5 cm long and 4-6 mm in diameter) was introduced into the pulmonary artery, and its end was manipulated into the left branch of this artery, where it was fixed by a ligature, the opposite end of the tube being fixed by a ligature at the point where the pulmonary artery leaves the right venticle. After division of the pedicles of all the lobes of the right lung, a humorally isolated "vascular sac" (the bifurcation and main trunk of the pulmonary artery) was obtained. Catheters were inserted into the central ends of the upper-lobe and lower-lobe arteries of the right branch, through which the isolated vascular part of the pulmonary circulation was perfused with venous blood (taken from another cat) or with Tyrode solution. The chemical substances were injected into the perfusion fluid.

In the experiments of series II the chemoreflexes from one lobe of the lung were studied. The central end of the artery of the retrocardiac lobe was connected by a catheter (30 cm long and 2 mm in diameter) with the peripheral end of the upper or lower lobe, the vein of which was joined by means of a transparent polyethylene tube (1.5-2 mm long and 4-6 mm in diameter) to the left auricle. At the same time as the chemical substance was injected into the vessels of the investigated lobe of the lung by puncturing the catheter, an air bubble was introduced into the initial part of this tube and its movement served to indicate the velocity of movement of the substance. At the point of entry into the left auricle, the blood with the chemical substance and air bubbles was switched for a period of 30-35 cardiac contractions through a 3-way tap into an open glass cylinder. An equal volume of stored blood was returned to the animal's venous system. The time taken by the substance to pass along the tube to the three-way tap was deliberately made longer than the duration of the reactions observed in the cardiovascular system, so that during these reactions blood from the vein of the investigated lobe of the lung entered the left atrium along the tube without any traces of the chemical substance. The withdrawal of the blood with the chemical substance into the cylinder and its compensation with stored blood were carried out after the reflex reactions had been recorded on the kymograph. Penetration of the substances into the general circulation was excluded by ligation of the azygos vein and, in some experiments, by isolating the investigated lobe with packs from the parietal pleura, and also by separate ventilation of the isolated bronchus of this lobe.

Laboratory of the Circulation and Respiration, K. M. Bykov Department of General Physiology, Institute of Experimental Medicine, Academy of Medical Sciences of the USSR, Leningrad (Presented by Active Member of the Academy of Medical Sciences of the USSR D. A. Biryukov). Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 63, No. 4, pp. 8-11, April, 1967. Original article submitted October 28, 1965.

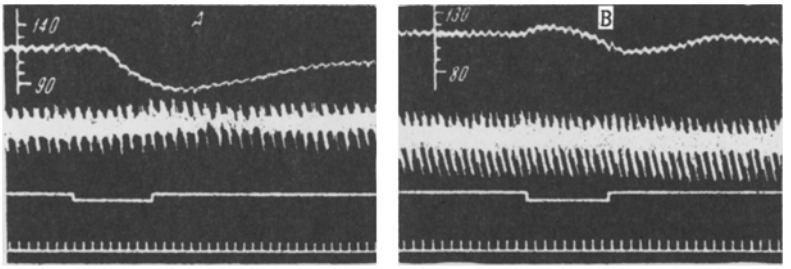

Fig. 1. Reflex changes in the general arterial pressure and cardiac activity after injection of 1 ml of $1 \cdot 10^{-5}$ serotonin (A) and 1 ml chloroform (B) into the blood vessels of the lower lobe of the right lung. From top to bottom: arterial pressure, amplitude of cardiac contractions, marker of injection of substance, time marker 2 sec. Scale graduated in mm Hg.

In the experiments of series III the chemoreflexes were studied from the arterial and venous part of the lobe of the lung only. Catheters (0.4-0.6 mm in diameter) were introduced into the artery and vein of the lobe, which was perfused as in series II, almost until they became wedged in the vessels (the position of the catheters were verified at the end of the experiment). If the blood flow along the vessels of the lobe was direct (arteries → veins), the slow injection of chemical substances through the catheter inserted into the vein caused stimulation mainly of the receptors of the veins of medium and large diameter in this lobe. If the direction of the blood flow in the lobe was reversed (veins → arteries), injection of the substances through the catheter inserted into the artery led to stimulation mainly of the receptors of the arteries of medium and large caliber.

The general arterial pressure was measured in the subclavian artery by a mercury manometer. Using and Engelmann's lever, the amplitude of the cardiac contractions was recorded. Solutions of the following substances, divided for convenience of subsequent description into two groups, were used as chemical stimuli: group I — nicotine, serotonin, acetylcholine, veratrine, adrenalin, histamine, potassium chloride, and sodium cyanide, and group II — 50% chloroform, 70° alcohol, and 50% ether.

EXPERIMENTAL RESULTS

Series I (22 experiments). After injection of 1 ml of the substances of group I in concentration of $1 \cdot 10^{-6}$ - $1 \cdot 10^{-4}$ into the humorally isolated main trunk of the pulmonary artery, no changes were observed in the cardiovascular system in any of the experiments. Administration of the same substances in higher concentration ($1 \cdot 10^{-3}$ - $1 \cdot 10^{-2}$) and of the substances of group II was accompanied in 38% of experiments by changes in the arterial pressure and cardiac activity, arising 21-36 sec from the time of injection of the stimulus. Bilateral vagotomy, stellate ganglionectomy, and procaine anesthesia of the wall of the main trunk of the pulmonary artery did not abolish these reactions, indicating that they were not reflex (but evidently resorptive) in nature.

The results obtained show that in relation to the stimuli used, the extralobular arterial portion of the pulmonary circulation is evidently not the zone of origin of chemoreflexes affecting the systemic arterial pressure and cardiac activity. This is confirmed also by morphological data [6], showing that the receptor apparatus of the media and, in particular, of the intima of the main trunk of the pulmonary artery is poorly developed. With respect to the glomera of the pulmonary artery, whose chemoreceptor function has been discussed in the literature [4, 6], all that could be concluded from the results of these experiments was that no chemoreflexes affecting the heart and general arterial pressure originated from them. There are reports in the literature that the glomera are closely connected with the respiratory function [11]. Bearing in mind that the endocardium of the right ventricle and the initial portion of the pulmonary artery share a common ontogenetic development, it is interesting to note that no chemoreflexes affecting the cardiovascular system likewise could be demonstrated from the endocardium of the right half of the heart [8].

Series II (63 experiments). Injection of the substances of group I in concentrations of $1 \cdot 10^{-6}$ - $1 \cdot 10^{-4}$ into the vessels of the investigated lobe lowered the arterial pressure on the average by 27 mm in 31 of the 36 experiments, slowed the cardiac contractions by 6-42 beats per min (in 88% of the experiments), and modified their amplitude (Fig. 1A). Injection of the stimuli of group II in 18 of 27 experiments caused pressor-depressor reactions of the systemic arterial pressure (the mean value of the pressor phase was 8 mm, and of the depressor — 6 mm) without changing the amplitude and frequency of the cardiac contractions (Fig. 1B). The latent period of all these reactions was 3-6 sec.

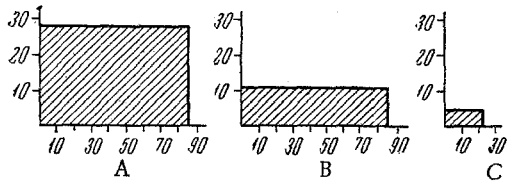

Fig. 2. Comparison of the reflex changes in the general arterial pressure following injection of chemical substances of group I into the whole vascular system of the lower lobe of the lung (A), or into its venous (B) and arterial (C) portion. Along the axis of ordinates — mean changes in pressure (in mm); along the axis of abscissas — frequency of reactions (in % of total number of experiments for each part of the vascular system).

Bilateral vagotomy abolished the depressor reactions and changes in the cardiac activity, while stellate ganglionectomy led to the almost total disappearance of the pressor phase of the arterial pressure, demonstrating the reflex nature of the changes observed in the cardiovascular system. A more marked pressor phase (without a subsequent depressor) developed more constantly in response to the first injection of the substances of group II if preceded by vagotomy and superficial anesthesia; in isolated cases it also appeared after injection of high concentrations ($1 \cdot 10^{-3}$ and over) of serotonin, acetylcholine, nicotine, and so on. The substances of group II had the effect more of stimulating the endings of the sensory nerves of the skin and mucous membranes, thereby frequently evoking a marked nociceptive reaction. Morphological investigations [4, 6, 7] have demonstrated the double afferent (vagus and spinal) innervation of the pulmonary vessels, and it has been shown that most of the spinal fibers pass through the stellate ganglia [6, 7]. These results, in conjunction with those of the present investigations, indicate that the afferent pathways for the pressor changes in the arterial pressure lie in the spinal nerves, while those for the depressor reactions and the changes in cardiac activity lie in the vagus nerves.

Series III (48 experiments). In response to stimulation of the arterial system of the lobe of the lung with the substances of group I in concentrations of $1 \cdot 10^{-6}$ - $1 \cdot 10^{-4}$, the arterial pressure fell by 2-5 mm Hg (in 22% of the experiments) but without changes in the cardiac activity. In response to stimulation of the veins by the same substances, the fall in arterial pressure was 5-14 mm (in 83%) and this was accompanied by slowing of the cardiac rhythm by 6-12 beats per min (in 45%) and by an increase in their amplitude (in 18% of the experiments). Stimulation of the intralobular arteries or veins by the substances of group II caused pressor-depressor reactions of the arterial pressure, although their magnitude (in absolute units) and their frequency were on the average smaller by 28 and 34% (for the arteries) and 21 and 18% (for the veins) than the corresponding indices in response to stimulation of the whole vascular system of the lobe ($P < 0.01$).

It can be concluded from comparison of the results of the experiments of series II and III that the greatest reflex changes in the circulatory system (this applies more to the depressor reactions and the changes in cardiac activity) developed in response to stimulation of the receptors of the pulmonary vessels of small caliber. Most probably, these receptors were in the capillaries. According to some reports [4, 6], these receptors are shared by the surrounding alveolar tissue (capillary-tissue receptors). The large area occupied by the capillaries in the vascular system of the lungs and the well developed innervation of the alveolar tissue [7] also indicate that the capillary-tissue zone is probably the main reflexogenic zone of the pulmonary circulation responding to chemical stimulation. It is clear from Fig. 2 that chemoreflexes from the receptors of the intralobular portions of the pulmonary veins were more marked than those from the intralobular arteries.

The role of the various parts of the pulmonary vascular system in the origin of chemoreflexes from them to the circulatory system is thus not equally important: the greatest changes are observed in response to stimulation of the receptors in the small vessels, and much smaller changes take place during stimulation of the pulmonary vessels of large and medium caliber (intralobular). No chemoreflexes on the heart or systemic arterial pressure can be observed to arise from the main trunk of the pulmonary artery and its bifurcation. The afferent pathways for the pressor changes in the arterial pressure lie in the spinal nerves, while those for the depressor changes and the changes in cardiac activity lie in the vagus nerves.

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