EFFECT OF SOME VASOACTIVE SUBSTANCES ON THE RESERVOIR FUNCTION OF THE PULMONARY VESSELS

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Injection of acetylcholine and histamine into the pulmonary vessels, with no direct hemodynamic connections with the systemic circulation, increases their blood volume. Noradrenalin and serotonin may either increase or decrease the blood volume in the lungs.

In the extensive literature of the action of chemical substances on the pulmonary vessels (see surveys in [2, 5, 8]) most of the data describe changes in the pressure or resistance in the pulmonary circulation, and information on changes in the blood volume in the lungs is small in volume and conflicting in nature [7, 9, 10].

The object of the present investigation was to study changes in the volume of the pulmonary blood vessels following injection of noradrenalin, acetylcholine, histamine, and serotonin into them.

EXPERIMENTAL METHOD

Experiments were carried out on 43 cats anesthetized with chloralose (0.05 g/kg) and urethane (0.5 g/kg). Thorocotomy was performed, artificial respiration applied under positive pressure, and heparin given. Blood was taken by means of a constant output pump [4, 6] from the main trunk of the pulmonary artery through a needle inserted into it, and injected into the peripheral end of an artery of the posterior lobe of the lung. The blood flowed from a catheter introduced into a vein of this lobe through an incision in the left auricle of the heart into a cylinder which had two outflow tubes in its lower part. Blood was withdrawn through one of them by the second channel of the pump at the same speed as the blood flowed into the cylinder, and was returned to the arterial system of the systemic circulation, while an electromanometer was connected to the second tube to measure changes in the hydrostatic pressure of the blood, after the cylinder had first been filled with blood up to an arbitrary level. Since the volume velocity of the blood flow through the lobe was stabilized by the first channel of the pump, and the output of both channels was made identical, changes in this hydrostatic pressure could reflect changes in the blood volume in the investigated lobe of the lung. These were expressed in milliliters, since the volume of blood producing a change in hydrostatic pressure of 10 mm water was known. Changes in the blood volume and perfusion pressure (resistance) of the pulmonary vessels were recorded by means of M-1030 oscillographic galvanometers.

To isolate the hemodynamics of the investigated lobe from the bronchial circulation, the bronchial and intercostal (the first three pairs) arteries were ligated at their origin from the aorta, together with the azygos vein. In some experiments changes in the blood volume of the lobe of the lung were determined by comparing the inflow and outflow of blood in its vessels when perfused under constant pressure [1].

The vasoactive substances, contained in 0.1 ml physiological saline, were injected instantaneously into the artery of the perfused lobe in the following doses: noradrenalin 30-100 μg, acetylcholine 1-10 μg, histamine 1-10 μg, serotonin 10-100 μg.

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TABLE 1. Changes in Capacity and Resistance of Pulmonary Vessels Following Injection of Vasoactive Substances into Them

Type of perfusion	Vasoactive substances	No. of expts.	No. of injections of substance	Dose of substance (in μg) for which changes	Changes in capacity of vessels: number of reactions — increase	decrease	magnitude of reactions (in ml) — absence	increase	decrease	Changes in resistance of vessels: number of reactions — increase	decrease	magnitude of reactions (in mm water) — absence	increase	decrease
Constant flow perfusion	Noradrenalin	12	41	50	24	5	12	2,3±0,8	1,7±0,4	30	2	9	25,8±4,7	7 and 4
	Acetylcholine	14	21	1and10	21	0	0	2,7±1,6	—	15	4	2	24,5±8,9	7,0±2,3 per 1 μg dose
	Serotonin	8	27	50	9	10	8	1,9±1,1	2,5±1,2	22	0	5	36,2±6,4	
	Histamine	7	24	5	24	0	0	3,2±1,3	—	21	0	3	34,5±7,3	—
Constant pressure perfusion	Noradrenalin	5	26	50	12	7	7	1,5±0,4	2,0±0,8	—	—	—	—	—
	Acetylcholine	6	21	10	18	0	3	1,9±1,0	—					
	Serotonin	6	20	50	5	7	8	1,4±0,7	2,2±0,9	—	—	—	—	—
	Histamine	8	18	5	16	0	2	2,3±1,1	—	—	—	—	—	—

EXPERIMENTAL RESULTS

The results given in Table 1 show that acetylcholine and histamine increase the blood volume in the perfused lobe of the lung, while serotonin and noradrenalin, besides producing changes of this type, also led in some experiments to a decrease in the blood volume of the pulmonary vessels. The reactions observed took place both when the innervation of the lungs was intact, and also after bilateral vagotomy in the neck and removal of the sympathetic chains at the level $C_5 - Th_5$.

It must be emphasized that changes recorded in the blood volume may have been the result not entirely of vascular effects, but also of bronchomotor effects and also changes in the tension of the alveolar walls. The role of these extravascular pulmonary factors in the formation of the changes in blood volume of the investigated lobe described above cannot be assessed quantitatively at this stage, for existing methods of measuring bronchomotor reactions, including the method of Konzett and Rössler [11] which is widely used, cannot differentiate the role of each of these factors in changes in the reservoir function of the pulmonary circulation. Changes in the outflow of blood from the vein of the investigated lobe could have depended to some extent on disturbances of capillary filtration, as shown by the fact that in approximately one third of all the experiments edema gradually developed in the lobe of the lung, most frequently after injection of histamine and acetylcholine. During perfusion of the pulmonary vessels under constant flow conditions, edema of the lobe was readily discovered, even when of slight degree, by the fact that the initial level of blood in the cylinder was not restored (see "Experimental Method"). Under these conditions of perfusion, changes in the outflow of blood due to changes in the capacity of the pulmonary blood vessels could be judged, in the writer's opinion, from the short latent period (3-5 sec) of changes in the outflow and the relatively high initial velocity of their development. Disturbance of capillary filtration, however, was evidently apparent somewhat later, and exerted its effect on the duration and magnitude of the outflow of blood from the pulmonary vein. The permeability of the pulmonary capillaries varied considerably from one experiment to another. This was confirmed by the fact that in some experiments, even after the first injection of histamine or acetylcholine, edema of the lobe developed, whereas in other experiments no signs of edema were present in the lobe even after repeated injections of these compounds in a larger dose.

The substances used are known to constrict both the arteries and veins of the pulmonary system [3, 9, 10]. The stability of the character of changes in the capacity of the pulmonary circulation following injection of acetylcholine and histamine into its vessels may perhaps be due to the constrictor action of these substances predominantly on the pulmonary veins [9], which would cause an increase in the blood volume in the lungs. Noradrenalin and serotonin, on the other hand, according to data in the literature, do not

produce any marked degree of venoconstriction. The fact that changes in the volume of blood in the lobe of the lung occurred in different directions despite qualitatively identical reactions in the resistance of its vascular system in response to injection of serotonin and noradrenalin (Table 1), and the marked variability in reactivity of these vessels are evidently dependent on the initial state of the individual segments of the pulmonary circulation in each experiment. The concrete mechanisms of this dependence will form the subject for future research.

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