EFFECT OF A MODIFIED GASEOUS MEDIUM ON THE PULMONARY CIRCULATION

N. V. Sanotskaya and D. D. Matsievskii

UDC 612.215.8-06:[612.223+612.273

KEY WORDS: pulmonary circulation; cardiac output; hypoxia; hypercapnia; ultrasound.

The pulmonary vasoconstrictor response to hypoxia is regarded as part of a self-regulating mechanism by which the capillary blood flow of the lungs automatically adapts itself to the level of alveolar ventilation. Adequate relations between ventilation and blood flow in the various parts of the lungs ensure normal arterialization of the blood. Changes in these relations lead, first, to the appearance of arterial hypoxemia [1, 2, 4, 13]. Constriction of the pulmonary vessels arising under the influence of acute hypoxia lies at the basis of the rise of arterial pressure (BP) in the pulmonary system. The importance of this mechanism has been demonstrated in man during certain diseases and in experiments on animals [3, 10, 11, 14]. There is some evidence to suggest that constriction of the pulmonary vessels in acute hypoxia takes place mainly at the level of the small arteries [12]. Many factors may be involved in the mechanism of development of the constrictor response. Their effect has been studied under different conditions and by the use of different methods [10, 13, 14]. It has been shown that the constrictor response to acute hypoxia can take place in totally denervated lungs, in a heart-lung preparation, and in isolated lungs [13, 14]. In most investigations perfusion of the lungs has been used. This accounts for the importance of a study of the effect of changes in the gaseous medium while the pulmonary blood flow remains normal.

In this investigation the blood flow was studied in different parts of the pulmonary vascular system in hypo- and hyperoxia, and also in hypercapnia.

EXPERIMENTAL METHOD

In acute experiments on 40 cats weighing 3-5 kg with an open chest and with artificial ventilation of the lungs, under pentobarbital anesthesia (30-40 mg/kg), the blood flow in different parts of the vascular bed of the lungs [8] was measured by an ultrasonic method [5]: in the infundibulum (output of the right heart), in a branch of the pulmonary artery supplying blood to the lower lobe of the left lung, and in the vein draining this lobe. The blood pressure in the pulmonary circulation was measured by means of a microelectromanometer [6]: the catheter was introduced through a branch of the upper lobe artery into the lumen of the left pulmonary artery. Some experiments were conducted on animals with a closed chest and with natural breathing. In these experiments the chest was opened, ultrasonic transducers were fitted to the corresponding pulmonary vessels, after which the chest wall was closed in layers and the animal's natural breathing restored. Respiratory movements of the chest were recorded with a piezoelectric transducer. To create conditions of hypo- and hyperoxia, and hypercapnia, the animals were made to breathe gaseous mixtures with a reduced oxygen concentration (5 and 10% O_2 in nitrogen) or with an increased CO_2 concentration (5 and 10% CO_2 in air), and also of oxygen. The gas mixture was supplied from a Douglas bag by means of an artificial respiration apparatus (in experiments with an open chest) or through respiratory valves (with a closed chest). Inhalation of the gas mixture continued usually for 10-12 min. In some experiments the effect of hypoxia and hypercapnia for a longer period (up to 1 h) was studied.

EXPERIMENTSL RESULTS

During inhalation of a mixture containing 10% O_2 the blood flow along the artery of the lower lobe of the lung fell by 10-15% below its initial level and the mean blood pressure in the pulmonary system rose from 5-8 to 15-18 mm Hg (Fig. 1a). The oxygen saturation of the

Laboratory of Pathophysiology of Respiration and Bioengineering Laboratory, Research Institute of General Pathology and Pathological Physiology, Academy of Medical Sciences of the USSR, Moscow. (Presented by Academician of the Academy of Medical Sciences of the USSR G. N. Kryzhanovskii.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 100, No. 9, pp. 286-289, September, 1985. Original article submitted October 3, 1984.

 0007-4888/85/0009-1182$09.50

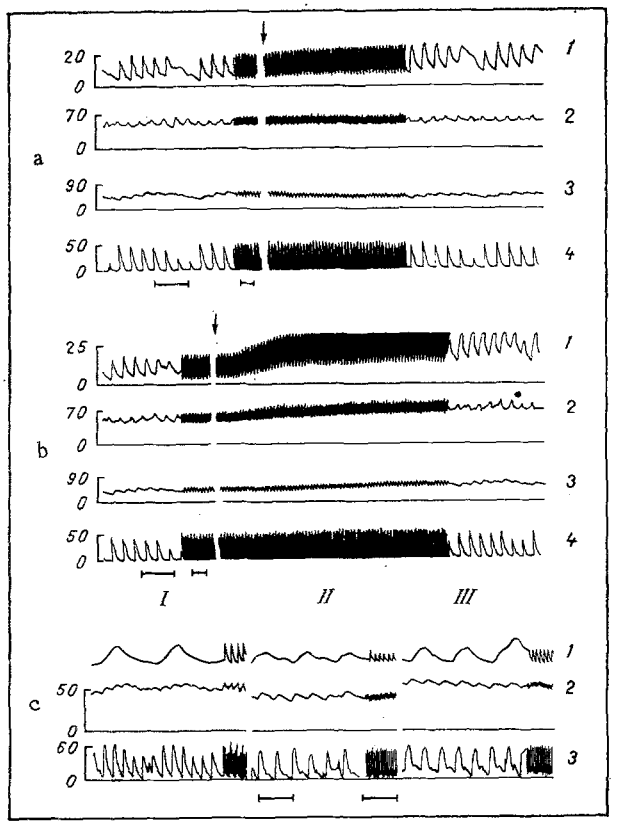

Fig. 1

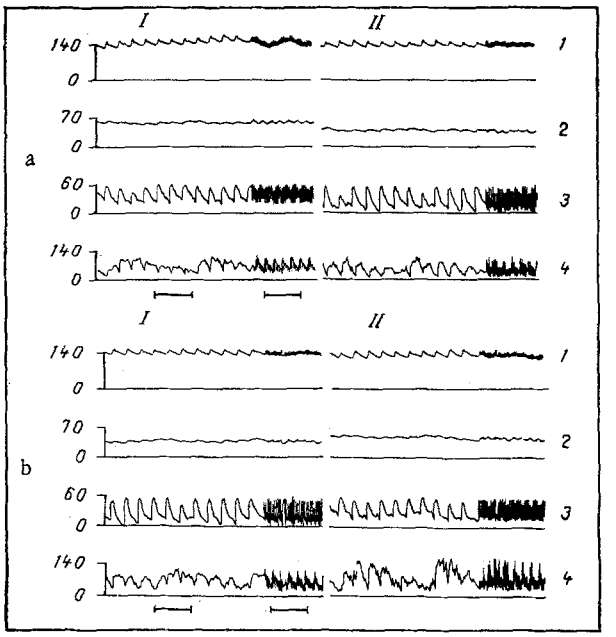

Fig. 2

Fig. 1. Effect of hypoxia on pulmonary circulation: a) inhalation of mixtures containing 10% O_2; b) inhalation of mixture containing 5% O_2, with open chest and artificial respiration; c) inhalation of mixture containing 10% O_2, with closed chest and natural breathing. a, b: 1) blood pressure in pulmonary artery (in mm Hg); 2) phasic blood flow in vein from lower lobe (in ml/min); 3) mean values of blood flow in artery of lower lobe of lung (in ml/min); 4) phasic blood flow in artery of lower lobe (in cm/sec). Time scale: 1 and 10 sec, arrow indicates beginning of exposure; c: 1) respiratory movements of chest (inspiration upward), 2) mean values of blood flow in artery of lower lobe (in ml/min), 3) phasic blood flow in artery of lower lobe of lung (in cm/sec). Time scale 1 and 10 sec. I) background, II) exposure for 5 min, III) recovery for 5 min.

Fig. 2. Effect of hypercapnia and hypoxia on pulmonary circulation: a) inhalation of mixture containing 5% CO_2; b) inhalation of mixture containing 5% O_2. 1) blood pressure in femoral artery (in mm Hg); 2) mean values of flow in artery of lower lobe (in ml/min); 3) phasic blood flow in artery of lower lobe (in cm/sec); 4) phasic blood flow in vein of lower lobe (in ml/min). Time scale: 1 and 10 sec. I) background, II) breathing gas mixture for 5 min. Note changes in diastolic flow in pulmonary artery (3), in the same direction as changes in mean values of blood flow in artery (2).

arterial blood (SaO_2) under these circumstances averaged 90% (from 87 to 92%) [9]. The systemic BP remained almost unchanged (Fig. 2a). In most experiments the cardiac output was unchanged under these conditions or increased a little (by 5-10%). This suggests that constriction of the pulmonary vessels takes place during moderate hypoxia.

Inhalation of a mixture containing 5% O_2 (more rigorous hypoxia) caused a varied response: in some experiments the reaction was biphasic (a fall at the beginning of exposure, followed by an increase in the blood flow), and in the other experiments the blood flow in the artery of the lower lobe increased by 10-15%. The mean blood pressure in the pulmonary artery rose to 23-25 mm Hg (Fig. 1b). SaO_2 fell under these conditions on average to 66% (from 51 to 81%).

Hypercapnia, like moderate hypoxia, usually caused the blood flow in the artery of the lower lobe of the lung to fall by 10-15% below its initial level, and the mean pressure in

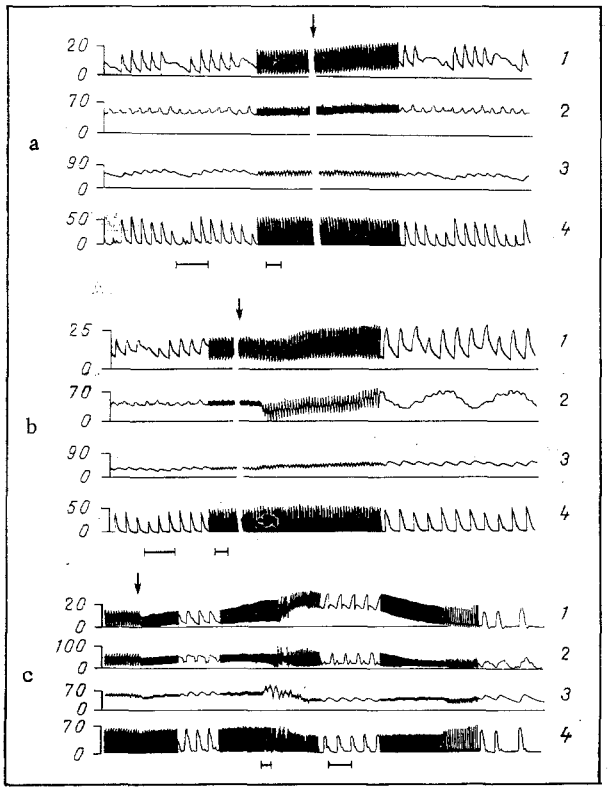

Fig. 3. Effect of hypercapnia and asphyxia on pulmonary circulation: a) inhalation of mixture containing 5% CO_2; b) inhalation of mixture containing 10% CO_2; c) asphyxia. Arrow indicates beginning of exposure. Remainder of legend as to Fig. 1a, b.

the pulmonary system to rise to 15-20 mm Hg (Fig. 3a). During inhalation of a mixture containing 10% CO_2, an increase in blood flow was observed in some experiments (Fig. 3b).

During inhalation of gas mixtures changes in the blood flow in the lobar artery and vein were often not parallel. Whereas during moderate hypoxia or hypercapnia the inflow of blood into the arteries fell, the outflow into the vein could be unchanged (Fig. 1a) or even increased (Fig. 3a). The relationship between these changes in blood flow in artery and vein indicates that during exposure to a modified gaseous medium the blood volume in the lobe of the lung studied (and also, probably, in the lungs as a whole) was reduced.

During hypoxia and hypercapnia changes took place in the character of the phasic blood flow in the lobar artery and vein. In the lobar artery of the lung there was usually a more or less conspicuous constant component of the blood flow (the diastolic flow) [8]. Experiments showed that quantitative changes in blood flow took place mainly on account of changes in this constant component. In those experiments in which the diastolic flow was more conspicuous, so also were the changes in the blood flow, i.e., reactivity of the pulmonary vessels is largely dependent on their initial functional state. When the blood flow was observed to decrease in hypoxia and hypercapnia, this was reflected in the curve as a decrease in the diastolic flow or its total disappearance (Fig. 1c, compare with Fig. 2a). It can be tentatively suggested that this was due to constriction of the intramural pulmonary vessels. With an increase in blood flow the diastolic flow increased (Fig. 2b). The phasic character of the blood flow ceased to be observed in the pulmonary vein during hypercapnia, and its respiratory fluctuations increased sharply (Fig. 3b). This could not be due in this particular case to changes in the intrapleural pressure, for the experiment was carried out with an open chest and with artificial respiration. This fact deserves special analysis.

In asphyxia caused by stopping the artificial respiration apparatus, the blood pressure in the pulmonary system rose to 25-30 mm Hg (Fig. 3c). The blood flow in the pulmonary vessels remained unchanged for 1-2 min or rose slightly, then began to fall parallel with extinction of cardiac activity and a reduction of cardiac output. Changes in the pulmonary venous flow were opposite in phase to changes in the flow in the pulmonary artery (Fig. 3c) (under

similar conditions the coronary blood flow is increased by 6-10 times compared with its initial level [9]).

In experiments with a closed chest a number of features were discovered which distinguished the character of the pulmonary blood flow under these conditions from that observed during artificial respiration. The respiratory waves of the blood flow were much weaker. Their direction was opposite to that observed during artificial ventilation of the lungs: in inspiration the blood flow increased, in expiration it decreased (Fig. 1c). The opposite relations were observed during artificial respiration [8]. The character of changes in the pulmonary blood flow in hypoxia and hypercapnia was the same as in experiments with artificial respiration, although the quantitative characteristics could be different: the responses in some experiments were greater (Fig. 1c).

In the intact organism, during moderate hypoxia (10% O_2) and hypercapnia, a very small reduction in blood flow took place in the lower lobe of the lung. This was evidently associated with constriction of the pulmonary vessels, due to the direct action of alveolar hypoxia and hypercapnia on them. In the case of more rigorous hypoxia (5% O_2) varied changes were observed in the pulmonary blood flow: either a biphasic reaction or an increase in blood flow.

The relative stability of the quantitative parameters of the pulmonary blood flow when investigated in the intact organism will be noted: even during quite rigorous procedures, but appropriate for the pulmonary circulation (hypoxia, hypercapnia), its changes usually did not exceed 10-15% of the original level. Meanwhile the shape of the phasic flow curve (particularly venous) and of the blood pressure curve in the pulmonary circulation could change considerably under these conditions. It can be tentatively suggested that this is the result of changes in contractile activity of the heart under the conditions studied [7].

LITERATURE CITED

1. A. M. Blinova and M. E. Marshak, in: Regulation of Respiration, the Circulation, and Gas Exchange, M. E. Marshak, ed. [in Russian], Moscow (1948), p. 214.
2. D. P. Dvoretskii, "Mechanisms of optimization of the hemodynamics and gas exchange in the lungs," Author's Abstract of Doctoral Dissertation, Leningrad (1978).
3. Ya. A. Lazaris and I. A. Serebrovskaya, The Pulmonary Circulation [in Russian], Moscow (1963).
4. M. E. Marshak, Usp. Sovrem. Biol., 36, No. 2 (5), 209 (1953).
5. D. D. Matsievskii, Byull. Éksp. Biol. Med., No. 9, 119 (1970).
6. D. D. Matsievskii, Byull. Éksp. Biol. Med., No. 3, 377 (1984).
7. R. Rushmer, Dynamics of the Cardiovascular System, ed. G. I. Kositskii [Russian translation], Moscow (1981).
8. N. V. Sanotskaya and D. D. Matsievskii, Byull. Éksp. Biol. Med., No. 12, 119 (1982).
9. N. V. Sanotskaya and D. D. Matsievskii, Byull. Éksp. Biol. Med., No. 3, 280 (1984).
10. A. I. Khomazyuk, Patol. Fiziol., No. 6, 23 (1978).
11. B. M. Shershevskii, The Pulmonary Circulation [in Russian], Moscow (1970).
12. E. H. Bergofsky, Am. J. Med., 57, 378 (1974).
13. A. P. Fishman, in: Handbook of Physiology, Section 2, Vol. 2, Circulation, Washington (1963), p. 1667.
14. A. P. Fishman, Circ. Res., 38, 222 (1976).