

5. E. I. Chazov, M. I. Titov, V. A. Vinogradov, et al., *Vopr. Med. Khim.*, No. 3, 47 (1984).
6. Yu. R. Sheikh-zade and M. V. Pokrovskii, *Byull. Éksp. Biol. Med.*, No. 4, 393 (1985).
7. G. Campbell, I. L. Gibbins, et al., *Neuroscience*, 7, 2013 (1982).
8. G. Chirlanda, L. Uccioli, P. Santarelli, et al., *Regul. Peptides*, 11, No. 4, Suppl., 231 (1985).
9. T. Hokfelt, D. Millhorn, et al., *Experientia (Basel)*, 43, No. 7, 768 (1987).
10. M. N. Levy, T. Iano, and H. Zieske, *Circulat. Res.*, 30, No. 2, 186 (1972).
11. R. Quirion, *Brit. J. Pharmacol.*, 66, No. 2, 251 (1979).
12. J. V. O. Reid, *Am. Heart J.*, 78, No. 1, 58 (1969).
13. S. C. Webb, *Brit. Heart J.*, 56, 236 (1986).
14. J. Wharton and S. Gulbenkian, *Experientia (Basel)*, 43, No 7, 821 (1987).

EFFICACY OF ARTIFICIAL VENTILATION IN OIL MICROEMBOLISM AND SUBSEQUENT PULMONARY EDEMA

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One of the causes of pulmonary edema (PE) is embolism of the lungs, including the fat embolism which arises as a result of the entry of yellow bone marrow into the blood stream after fractures of the long bones. When a model of fat-induced edema is created in order to study the mechanisms of onset of the condition and to develop adequate methods of diagnosis and correction, intravenous injection of olive oil is usually used, for this substance closely resembles yellow bone marrow in its content of saturated and unsaturated fatty acids [2]. The combination of therapeutic measures used in the treatment of patients with PE is artificial ventilation of the lungs (AVL).

The aim of this investigation was to study activity of the cardiovascular and respiratory systems in experimental oil microembolism of the lungs (MEL) and to evaluate the efficacy of AVL.

EXPERIMENTAL METHOD

Experiments were carried out on noninbred cats, male and female, weighing 2-4 kg, under pentobarbital anesthesia (35 mg/kg, intraperitoneally). The animals' rectal temperature was measured and was maintained at the initial level with the aid of an electric heater, with an accuracy of 0.5°C. Tracheotomy was performed at the level of one third of the trachea, and the systemic blood pressure (BP) was recorded through a cannula introduced into the femoral artery. In the course of the experiment the following parameters were determined with the aid of an MKh-01 polygraph, made in the former USSR: systemic HP, heart rate (HR), respiration rate (RR), and respiratory minute volume (RMV). Values of the partial pressure of oxygen in the arterial blood (p_aO_2) and its reaction (pH_a) were recorded continuously by means of a DS 67101 continuous flow cuvette, the temperature which was kept at 37.5°C

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TABLE 1. Survival Time with MEL and PE and Lung Parameters in Control Animals and Cats Dying after Injection of Olive Oil ($M \pm m$, $n = 7$)

Parameter	Experimental conditions		
	control	artificial ventilation of lungs	Natural breathing
Survival time, min	—	32 ± 9	$144 \pm 13^{***}$
Relative weight of lungs, g/kg	6.3 ± 0.5	$11.3 \pm 1.9^*$	$19.8 \pm 4.6^{**}$
Dry residue, %	24.6 ± 1.5	$20.1 \pm 1.0^*$	$17.8 \pm 2.1^*$
Edema fluid, g/kg	0.2 ± 0.4	2.1 ± 0.8	5.7 ± 3.0
Addition to blood volume, g/kg	-0.2 ± 0.7	2.9 ± 1.3	$7.8 \pm 3.6^*$

Legend. * $p < 0.05$, ** $p < 0.02$. For difference relative to control. *** $p < 0.05$ for difference between natural and artificial ventilation.

TABLE 2. Parameters of Respiratory and Circulatory Systems and Arterial Blood Composition after Injection of Olive Oil into Cats with Artificial and Natural Ventilation ($M \pm m$, $n = 8$)

Experimental conditions	Parameter	Initial value	Time after injection, min	
			5	15
AVL	RR, min^{-1}	26.1 ± 1.9	26.1 ± 1.9	26.1 ± 1.9
	RNV, ml/min	578 ± 47	578 ± 47	578 ± 47
	HR, min^{-1}	244 ± 27	239 ± 32	242 ± 21
	BP, mm Hg	99 ± 15	92 ± 22	90 ± 21
	pO_2 , mm Hg	90.9 ± 8.9	$39.9 \pm 3.6^{****}$	$48.1 \pm 3.8^{***}$
	SaO_2 , %	93.2 ± 1.2	$65.3 \pm 6.6^{****}$	$74.6 \pm 8.2^{***}$
Natural breathing	pHa	7.44 ± 0.03	7.41 ± 0.04	$7.32 \pm 0.04^*$
	RR, min^{-1}	24.8 ± 2.2	$39.9 \pm 5.9^*$	$64.6 \pm 7.1^{***}$
	RNV, ml/min	547 ± 51	590 ± 62	$826 \pm 91^*$
	HR, min^{-1}	215 ± 22	210 ± 35	219 ± 39
	BP, mm Hg	85 ± 22	78 ± 25	63 ± 22
	pO_2 , mm Hg	104.6 ± 9.9	$70.5 \pm 7.2^{**}$	101 ± 14.8
	SaO_2 , %	95.5 ± 1.0	85.3 ± 5.8	93.3 ± 5.7
	pHa	7.42 ± 0.02	7.40 ± 0.02	7.39 ± 0.03

Legend. * $p < 0.05$, ** $p < 0.02$, *** $p < 0.01$, **** $p < 0.001$. For difference compared with control.

(VT3 13 thermostat), with inbuilt electrodes. The partial pressure of oxygen was measured by means of an E-5046 electrode, and pH by a G 265C and KS 67053 electrode pair (all apparatus from "Radiometer International" A/S), and recorded on self-recording KSP-4 potentiometers. The oxygen saturation curve of arterial blood hemoglobin was determined with an OSM-1 instrument (Radiometer International). Blood was pumped into the cuvette by an NP-1M peristaltic pump from the femoral artery and reinjected into the femoral vein (blood flow 10 ml/min). To prevent the blood from clotting, the animal received a preliminary injection of heparin (200 U/kg intravenously). Oil MEL was induced by injecting olive oil (1 mg/kg, in the course of 2 min) into the femoral vein [1]. The survival time of the animals was determined, and after death, parameters of edema and the volume of blood in the lungs were measured after death, for which purpose the lungs were excised, weighed in the wet state, and again after drying for 2 weeks at 83°C. The above parameters were determined in the control animals, with spontaneous respiration and in animals with AVL associated with pneumothorax. The parameters of AVL were chosen to correspond to values of RR and RMV in these animals before thoracotomy: the value of RR with stepwise control was set as close to natural as possible, within the range from 20 to 34 cycles/min, whereas the value of RMV was controlled smoothly, at the same or a slightly higher value (so that the value of pO_2 did not fall by more than 20%). Under these circumstances the value of pH_a sometimes rose a little. Later, during the development of MEL, the initial volume–frequency character-

istics of AVL were maintained. The results were analyzed by standard statistical methods (a level of significance of $p < 0.05$ by Student's test for differences).

EXPERIMENTAL RESULTS

The results (Tables 1 and 2) show that on the whole animals with natural breathing were more resistant to MEL and subsequent PE than animals with AVL (survival time 144 ± 13 compared with 32 ± 9 min), and its volume--frequency characteristics were maintained at a pseudonormal level. Comparison of the parameters of the volume of edema fluid and of blood in the lungs of the two groups of experimental animals shows that the differences between them were not statistically significant. No significant differences likewise could be found during MEL in parameters of the systemic hemodynamics. However, analysis of the characteristics of external respiration and of the arterial blood composition revealed certain differences. The development of rapid superficial breathing in the animals with natural ventilation was noted. The increase in RMV which occurred under these conditions took place through a more than twofold increase in RR, and despite a fall in the tidal volume. This character of respiration during MEL and subsequent edema is evidently more favorable for the animal. The biomechanics of the lungs evidently makes its own contribution to the change in character of respiration, for during MEL and PE an increase in rigidity of the lungs may be expected.

Values of pH and the oxygen balance of the arterial blood can be seen to be better for animals with natural ventilation. The trend of changes in p_aO_2 and O_2 of both groups of animals is qualitatively similar, although a more marked degree of hypoxemia was observed in the animals with AVL. A significant difference in blood composition could be detected only by studying the trend of blood pH. Whereas in animals with AVL injection of olive oil very quickly leads to a linear increase in blood acidification, in animals with natural breathing the pH initially (the first 15-20 min) stabilized within the range of normal values. Thus in oil-induced MEL and subsequent PE rapid and superficial breathing is more effective, for it ensures an optimal ventilation/perfusion ratio. The use of AVL with fixed volume--frequency parameters corresponding to accepted views on the normal type of breathing at rest, under these conditions, may be useless or even harmful. The choice of concrete values for depth and frequency of AVL must ensure adequate flexibility of the adopted schedules, and suitability of the ventilation conditions for the requirements of the body can be monitored in terms of pH_a and p_aO_2 , which must be determined as continuously as possible.

LITERATURE CITED

1. A. M. Kulik, G. V. Kurygin, N. V. Sanotskaya, et al., *Byull. Éksp. Biol. Med.*, No. 11, 524 (1988).
2. V. V. Polikarpov, "Pathogenesis, prevention, and treatment of microembolic pulmonary edema," Author's Abstract of Dissertation for the Degree of Candidate of Medical Sciences, Moscow (1988).