# Effect of the Organophosphorus Compound Anthio on the Pulmonary and Systemic Circulation of Non-narcotized Cats

**N. V. Sanotskaya, Ya. K. Kurambaev, D. D. Matsievskii, and V. A. Safonov**

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Experiments on cats demonstrate the capacity of alert animals to compensate for disorders in pulmonary and systemic hemodynamics caused by organophosphorus compounds. Heart rate, systemic arterial pressure, and total peripheral resistance completely normalize on day 3 after exposure. Pulmonary vascular resistance and pulmonary blood pressure remain negligibly increased.

**Key Words:** *pulmonary circulation; systemic circulation; organophosphorus compounds; ultrasound; cats*

Previously we demonstrated that exposure of cats narcotized with pentobarbital to the organophosphorus compound (OPC) Anthio leads to the development of profound disorders of the pulmonary and systemic circulation and respiration and to an imbalance in the functioning of the right and left ventricles that is incompatible with life. The animals died 2 to 3 h after administration of the agent [4,5].

Some authorities report an ambiguous effect of anticholinesterase agents, to which OPC belong, on narcotized and alert animals. For example, exposure to anticholinesterase agents leads to a drop of arterial pressure (AP) and depression of respiration in narcotized animals [8,9,10]. In alert animals the opposite effects are observed: AP rises and respiration is stimulated [11,12]. However, no comprehensive studies of the pulmonary and systemic circulation of alert animals after exposure to anticholinesterase agents have been reported as yet.

Department of Respiration Pathophysiology, Bioengineering Department, Research Institute of General Pathology and Pathophysiology, Russian Academy of Medical Sciences, Moscow. (Presented by N. A. Agadzhanyan, Member of the Russian Academy of Medical Sciences)

The purpose of this research was to study the pulmonary and systemic circulation several days after administration of the OPC Anthio to animals not deeply narcotized.

## MATERIALS AND METHODS

Twenty-one mongrel cats of both sexes weighing 2.4 to 4.4 kg were used in the study. An emulsion of the OPC Anthio (Formathion) used in agriculture was administered through a tube into the stomach of animals under light short-term ether narcosis in the same doses as used previously in acute experiments, 20% $LD_{50}$ (42.6 mg/kg). Seven experiments were carried out 1 day after OPC administration, six after 2 days, and six more after 3 days. Twelve experiments were carried out during forced ventilation of the lungs and nine with the thorax closed and spontaneous respiration. Linear and volumetric bloodflow velocity in the ascending aorta and pulmonary artery cone were studied by the ultrasound method [1]. AP in the pulmonary and femoral arteries was measured with a microelectromanometer [2]. Real-time total peripheral vascular resistance (TPVR) and resistance

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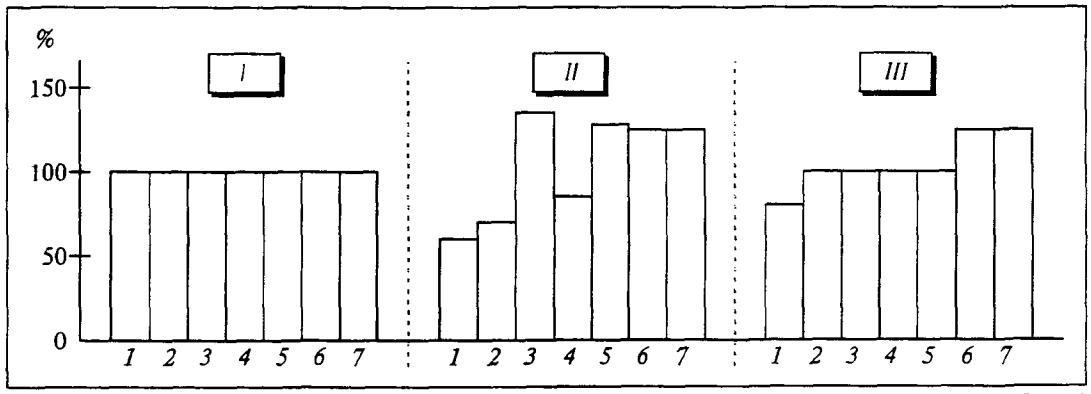


**Fig. 1.** Changes in systemic and pulmonary hemodynamics after exposure to OPC (in % of control level). Control (*I*), days 1 (*II*) and 3 (*III*) after exposure to OPC. *1*) cardiac index; *2*) heart rate; *3*) stroke volume; *4*) systemic AP; *5*) TPVR; *6*) pulmonary AP; *7*) pulmonary vascular resistance.

of the pulmonary vessels, heart rate, and left heart stroke volume were calculated using a microcomputer. The cardiac index was estimated. Initial values of pentobarbital-narcotized cats before OPC administration in acute experiments [4] were used as reference values.

## RESULTS

The animals did not die after OPC administration according to the method used in this study. Only one cat died right at the beginning of the operation (it was found to have pneumonia). On day 1 after OPC administration the animals were limp, reluctant to move, and refused to eat; hypersalivation was observed. In the days that followed their behavior normalized. It is noteworthy that the general status of animals and the time course of the parameters studied varied within a wide range in different animals.

On day 1 after OPC exposure, the cardiac index was reduced by 42%, on average, this reduction being particularly evident during forced ventilation of the lungs. A trend toward recovery of this parameter was observed on subsequent days, although the cardiac index remained lowered by an average 25% even on day 3 after OPC administration in the majority of animals in comparison with the control. It normalized on days 2-3 in three animals. This recovery was in good correlation with the positive time course of other parameters (systemic and pulmonary AP, heart rate).

The time course of the heart rate was particularly demonstrative: this parameter was reduced by approximately 30% in almost all the animals on days 1-2 after OPC administration. In the majority of animals the heart rate normalized on day 3 after OPC administration. In one animal with relatively high values of other characteristics (cardiac index and AP) the heart rate recovered on day 2. On the other hand, in two animals with lowered values of other parameters the heart rate remained lowered 3 days after exposure. The clear-cut reduction of the heart rate appears to be due to stimulation of the cholinergic systems resulting from the anticholinesterase effect of OPC [7].

In five animals the stroke volume was increased 35% on day 1 after OPC exposure because of the lowered heart rate, but in two cats it was lowered 55 and 32% *vs.* the control because of their extremely poor general status, which correlated with other parameters: low cardiac index, low systemic AP, and high pulmonary AP. On day 2 after exposure to OPC a tendency toward normalization of the stroke volume was observed: it was 12% higher than in the control. On day 3, when the heart rate normalized, the stroke volume was close to that in controls.

The systemic AP of animals under forced ventilation of the lungs was 17% lower in comparison with the control, but then tended to normalize. In animals with spontaneous respiration AP was within the normal range. Previously we demonstrated that in animals administered OPC under narcosis a gradual 62% reduction of systemic AP by the end of experiment was paralleled by a reduction of TPVR. In animals exposed to OPC without anesthesia TPVR showed a tendency toward hypercompensation; it was 30% increased on day 1, 22% increased on day 2, and almost normal on day 3.

Shifts in the parameters characterizing the pulmonary vessels were the most persistent. AP in the pulmonary arteries of the majority of animals was 25 to 30% increased and did not normalize till the third day after exposure to OPC. Pulmonary vascular resistance was approximately 25% increased in comparison with the control and did not normalize on day 3. This might be due to developing arterial hypoxemia found in experiments similar to ours [6]. On the other hand, pulmo-

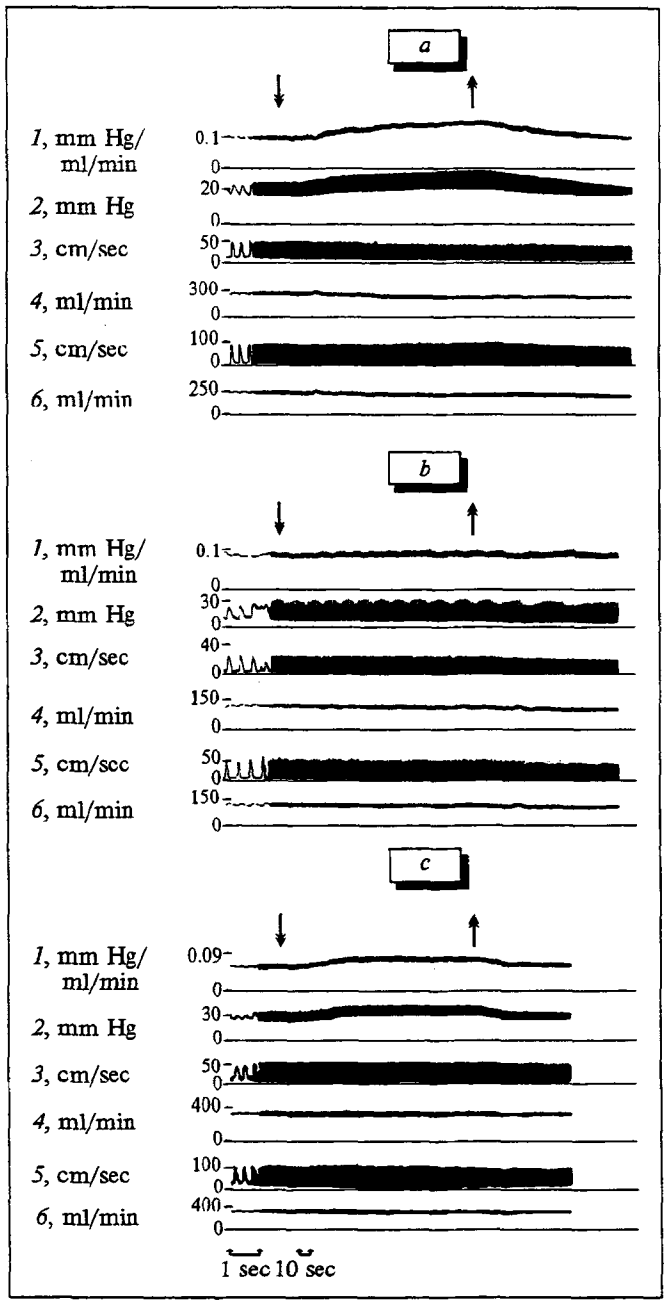


**Fig. 2.** Effect of inhalations of gaseous mixture with 7.5% $O_2$ on pulmonary circulation. Reaction to hypoxia in control animals (*a*) and in animals exposed to OPC 1 (*b*) and 3 (*c*) days after exposure. *1*) pulmonary vascular resistance; *2*) AP in pulmonary artery; *3*) linear bloodflow velocity in pulmonary artery cone; *4*) volumetric bloodflow velocity in pulmonary artery cone; *5*) linear bloodflow velocity in ascending aorta; *6*) volumetric bloodflow velocity in ascending aorta. Thin straight lines under each of the curves show the zero levels. Arrows show the beginning and end of gaseous mixture inhalation.

nary AP and pulmonary vascular resistance was close to the norm in 6 experiments: in one animal as early as on day 1 after OPC administration, in three on day 2, and in one on day 3 after exposure. These were the animals with the other favorable parameters mentioned above.

A functional test with short-term (3 min) inhalation of a hypoxic gaseous mixture (7.5% $O_2$ in nitrogen) was carried out to study pulmonary vessel reactivity. The experiments demonstrated no reaction of the pulmonary vessels to hypoxia on day 1 after OPC administration. A weak reaction became manifest on day 2 in some experiments, and on day 3 the reaction was more expressed (although not in all experiments): the characteristic reaction to hypoxia, presenting as an AP increase in the pulmonary artery and increased pulmonary vascular resistance, was observed (Fig. 2). Previously we noted a similar absence of reaction to hypoxia in animals with grave experimental pneumonia [3].

Effects on cell membrane structures and the enzymatic systems localized in them underlie the toxic action of pesticides [7]. This factor may contribute to the suppression of the reactivity of pulmonary vessels to hypoxia: some scientists report that cytochrome P-450 inhibition interferes with hypoxic vasoconstriction in the lesser circulation [13].

In a previous study of pulmonary circulation in animals with experimental pneumonia we demonstrated that the same intervention (intratracheal administration of 0.3 ml tarred turpentine) causes different diseases of the lungs, ranging from tracheitis to severe bilateral pneumonia, in different animals. The degree of functional disorders of pulmonary hemodynamics conforms to the severity of involvement of the lungs [3]. A similar phenomenon was observed in this study: the general status of animals after OPC administration and the degree of functional disorders of pulmonary and systemic hemodynamics varied in different animals. The differing individual tolerance for OPC observed in different animals appears to be related to the general functional status of the animals at the moment of exposure. At the same time, we succeeded in detecting certain tendencies in the time course of the pulmonary and systemic circulation after exposure to OPC.

Experiments demonstrated that the method of OPC administration which was used in this study did not incur large-scale death of animals, as was observed with administration of OPC to animals narcotized with pentobarbital. The alert animals showed a sufficiently high capacity to compensate for the disorders of the pulmonary and syste- mic hemodynamics caused by OPC. The heart rate, stroke volume, systemic AP, and TPVR normalized in the majority of animals on day 3 after administration of OPC. The cardiac index also showed a tendency toward normalization and the reactivity

of pulmonary vessels to hypoxia also exhibited a trend toward recovery. The slight increase of resistance in the pulmonary artery system and of the pulmonary AP were more persistent.

Hence, the findings suggest that pentobarbital narcosis exerts an inhibitory effect on the development of compensatory adaptive reactions in an organism exposed to OPC.

## REFERENCES


1. D. D. Matsievskii, *Byull. Eksp. Biol. Med.*, **76**, № 9, 119 (1973).
2. D. D. Matsievskii, *Ibid.*, **97**, № 3, 377 (1984).
3. N. V. Sanotskaya and D. D. Matsievskii, *Ibid.*, **101**, № 6, 671 (1986).
4. N. V. Sanotskaya, Ya. K. Kurambaev, D. D. Matsievskii, *et al.*, *Ibid.*, **117**, № 1, 18 (1994).
5. I. A. Tarakanov, Ya. K. Kurambaev, A. A. Khusinov, and V. A. Safonov, *Ibid.*, № 5, 470.
6. I. A. Tarakanov, Ya. K. Kurambaev, and V. A. Safonov, *Ibid.*, № 6, 587.
7. S. I. Fudel'-Osipova, Yu. S. Kagan, S. D. Kovtun, and U. A. Kuz'minskaya, *Physicological and Biochemical Mechanism of Pesticide Action* [in Russian], Kiev (1981).
8. A. Anzuetto, G. G. Berdine, G. T. Moore, *et al.*, *Toxicol. Appl. Pharmacol.*, **8**, 56 (1986).
9. J. H. De Neef, A. Manneke, and A. J. Porsius, *Arch. Toxicol.*, **50**, 241 (1982).
10. H. Edery, M. A. Geyer, P. Taylor, *et al.*, *J. Auton. Pharmacol.*, **6**, 195-205 (1986).
11. A. S. Foutz, E. Boudinot, and M. Denavit-Saubie, *Europ. J. Pharmacol.*, **142**, 207 (1987).
12. M. A. Miller and C. A. Hales, *J. Clin. Invest.*, **64**, 666 (1979).