gans of stress proteins that possess dispersive properties and can thus prevent protein denaturation and the associated damage to cellular structures responsible for the so-called "adaptive stabilization of structures" [12,14]. This latter phenomenon, in turn, underlies numerous protective effects of stress adaptation [5,13].

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Effects of an Organophosphorus Compound on Pulmonary and Systemic Circulations

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Shortly (30-90 min) after an intragastric administration of the organophosphorus pesticide Anthio to cats, their cardiac output begins to decrease and the right ventricular output decreased to a greater extent than the left. Blood is redistributed to the greater circulation with a diminution of blood flow in the pulmonary lobar vessels.

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

Organophosphorus compounds (OPC) are widely used for pest control in agriculture as well as in the home. Pesticides, however, may have health-damaging effects on humans and animals if applied in excessive amounts. For example, OPC used against plant pests inhibit cholinesterase activity in the blood and various tissues, which has been shown to be a major factor in the mechanism of OPC action on biological structures [1-3]. As a result of the impaired catalytic function of cholinesterase, conversions of acetylcholine are disrupted, leading to its accumulation in organs

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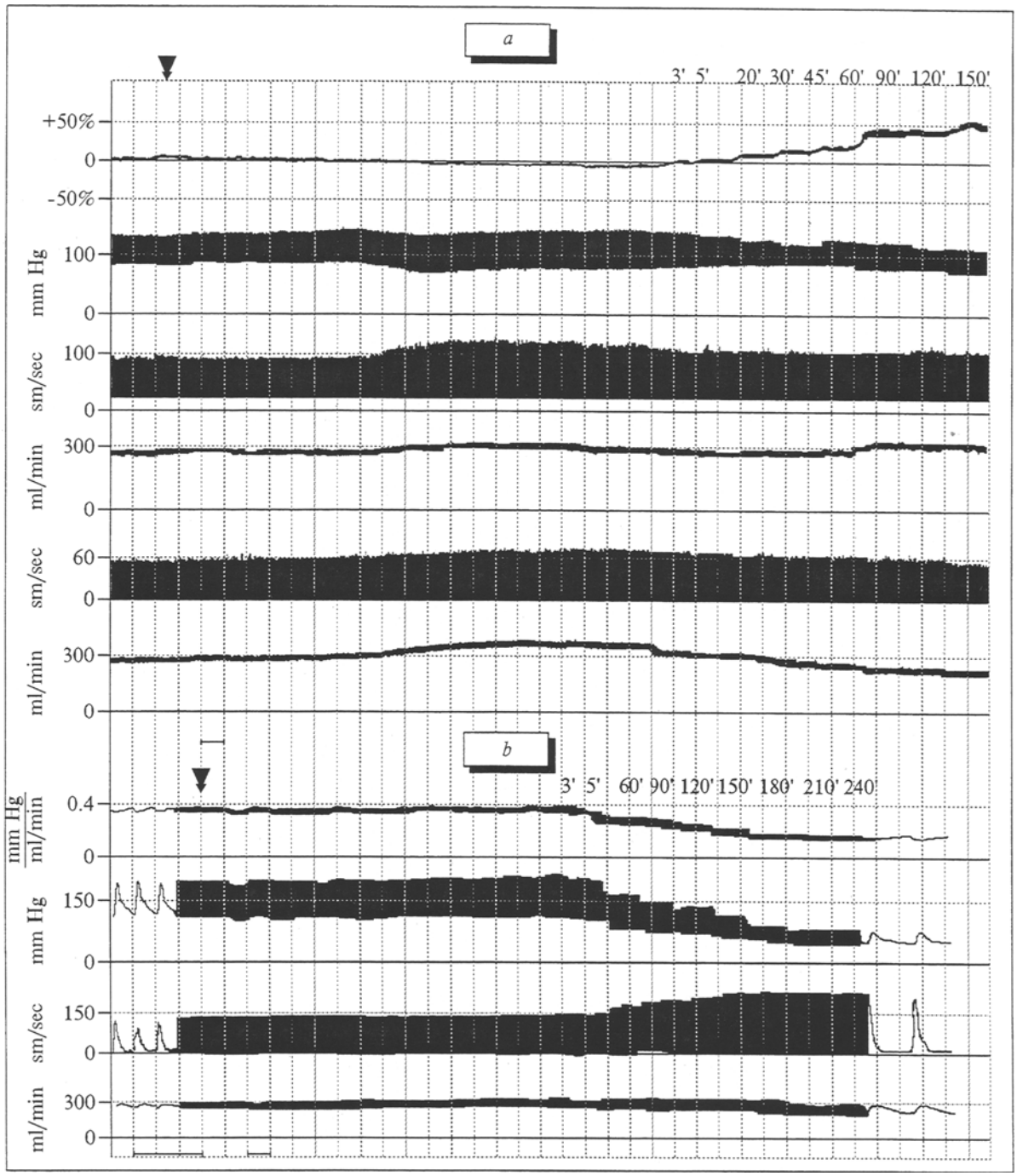

Fig. 1. Effects of Anthio on cardiac output and systemic blood pressure (BP) in artificially ventilated cats.From top down: *a*) balance between the right and left ventricular outputs in relative units (upward course of the curve signifies an increase of blood flow in the ascending aorta over that in the pulmonary cone); BP in the femoral artery; linear blood flow rate in the ascending aorta; volume blood flow rate in the ascending aorta; linear blood flow rate in the pulmonary cone; volume blood flow rate in the pulmonary cone; *b*) total peripheral vascular resistance; BP in the femoral artery; linear blood flow rate in the ascending aorta; volume blood flow rate in the ascending aorta. Here and in Figs. 2 and 3, the thin lines under each curve designate zero levels, while the arrows indicate the time of Anthio administration. Time scale: 1 and 10 sec.

and tissues with adverse consequences. While there are many published studies concerned with the impact of anticholinesterase agents on the activity of various organs and systems, including the respiratory and circulatory systems [1,3,7-9,13], relatively little is known about how OPC affect the relationships between the pulmonary and systemic circulations. The effect of these compounds on the state of the pulmonary circulation has not been investigated.

The purpose of this study was to examine the pulmonary and systemic circulations and the functioning of the right and left sides of the heart in cats exposed to an OPC.

MATERIALS AND METHODS

In acute tests on 20 Nembutal-anesthesized (30-40 mg/kg intraperitoneally) cats of both sexes weighing 2.1-4.2 kg, linear and volume blood flow rates in the artery and vein of the left lower lung lobe, in the ascending aorta, and in the pulmonary cone were estimated by an ultrasonic technique [4]; blood pressure (BP) in the pulmonary and femoral arteries was measured with a microelectromanometer [5]; further, in some cats, the balance between the right and left ventricular outputs was calculated with an analog computer as the difference between the mean blood flows in the pulmonary cone and the ascending aorta. Some of the tests were performed in artificially ventilated cats to evaluate hemodynamic changes uncomplicated by respiratory alterations, while other tests were run in spontaneously breathing cats. For the latter tests, ultrasonic sensors were placed on the appropriate vessels during artificial ventilation, after which the chest was sutured in layers and the animals were transferred to spontaneous respiration. Respiratory movements of the chest were recorded with a tensometer. The OPC used was the pesticide Anthio, which was administered orally via a gastric tube in a dose of 42.6 mg/kg.

RESULTS

In some of the cats, the administration of Anthio was followed immediately by increases in the frequency and amplitude of respiratory movements and in cardiac output, by small rises (10-20 mm Hg) in the systemic and pulmonary BP, and by the occurrence of extrasystoles (Figs 1, *a* and 2, *a*). In other cats, no such initial response to Anthio was observed (Figs. 1, *b* and 2, *b*); subsequently, however, alterations in the pulmonary and systemic hemodynamics were recorded, which differed in degree and time of onset in different cats but were of the same type in all animals.

The left ventricular output did not change significantly in most cats. In some animals it decreased but to a smaller extent than the right ventricular output. In a few cats linear blood flow rates in the aorta even increased, possibly as a result of diminished peripheral resistance (Fig. 1, *b*). Approximately 30 to 90 min postadministration, the right ventricular output began to decrease progressively, i.e., a redistribution of the blood to the greater circulation (Fig. 1, *a*) occurred, and this was reflected in the altered pulmonary and systemic hemodynamics. The administration of Anthio also resulted in decreased blood flows in the pulmonary lobar artery and vein. The pulmonary BP fell to 60% of its baseline value on average (range, 38-75%), whereas the pulmonary vascular resistance rose 3- to 10-fold (Fig. 2). The systemic BP fell progressively at a more rapid rate than the pulmonary pressure, to reach 38% of its baseline level on average (range, 20-70%), and the total peripheral vascular resistance (TPVR) also fell significantly to 39% of its baseline value on average (range, 19-66%). The heart rate decreased to 65% of its baseline value.

These findings indicate that the pesticide exerted opposite effects on the lesser and greater circulations: thus, it lowered TPVR in the greater circulation while considerably raising the vascular resistance in the lesser circulation.

A comparison of variations in cardiac output and BP values in the greater and lesser circulations led us to conclude that the reduction in systemic BP was due not so much to a weakened function of the left ventricle as to a drop in TPVR, i.e., to a general dilatation of the peripheral vessels. In contrast, the fall of BP in the pulmonary artery system occurred as a result of the reduced right ventricular output, and the pulmonary BP did not reach even lower values because the resistance of the pulmonary vessels was considerably increased. Blood was deposited in the greater circulation with a concurrent reduction in the amount of blood entering the lungs, probably again as a consequence of the increased resistance of the pulmonary vessels.

Of special note is the relationship between the alterations in blood flow along the pulmonary lobar artery and vein in response to Anthio: in more than one-half of the cats, blood supply by the lower lobar artery decreased by the end of the test to a greater extent than did the drainage by the vein originating from the lower lobe (Fig. 2). At the end of the test, blood supply by the lobar artery was in some animals close to zero, while venous drainage amounted to 20-30% of the baseline value. A similar response was observed in our earlier study on cats with experimental pulmonary embolism [6], although the etiology of the response to Anthio pesticide was very different. It seems likely that more blood was drained by the vein than was supplied by the artery because of an increased blood flow in the bronchial arteries, given that 2/3 of the venous outflow from the bronchial arterial system is effected via the pulmo-

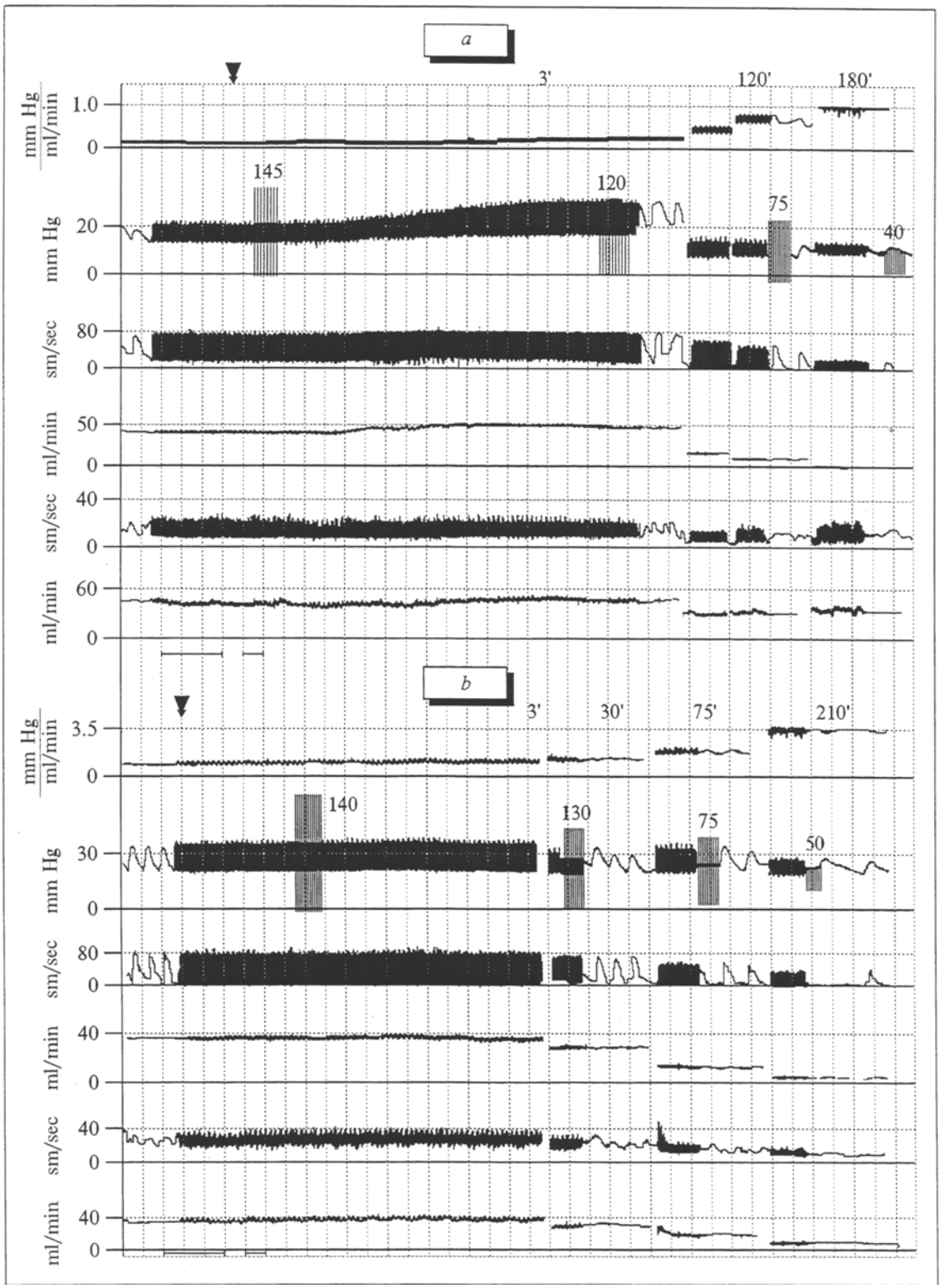

Fig. 2. Effect of Anthio on pulmonary circulation in artificially ventilated cats. From top down: pulmonary vascular resistance; BP in the pulmonary artery; linear blood flow rate in the pulmonary lower lobar artery; volume blood flow rate in the pulmonary lower lobar artery; linear blood flow rate in the pulmonary lower lobar vein. Bars indicate BP in the femoral artery; *a* and *b* illustrate differences in responses to Anthio administration.

nary veins (the so-called "bronchial systemic to pulmonary flow" [11]).

OPC can cause bronchospasm [1,3], and bronchoconstriction is known to result in an in-

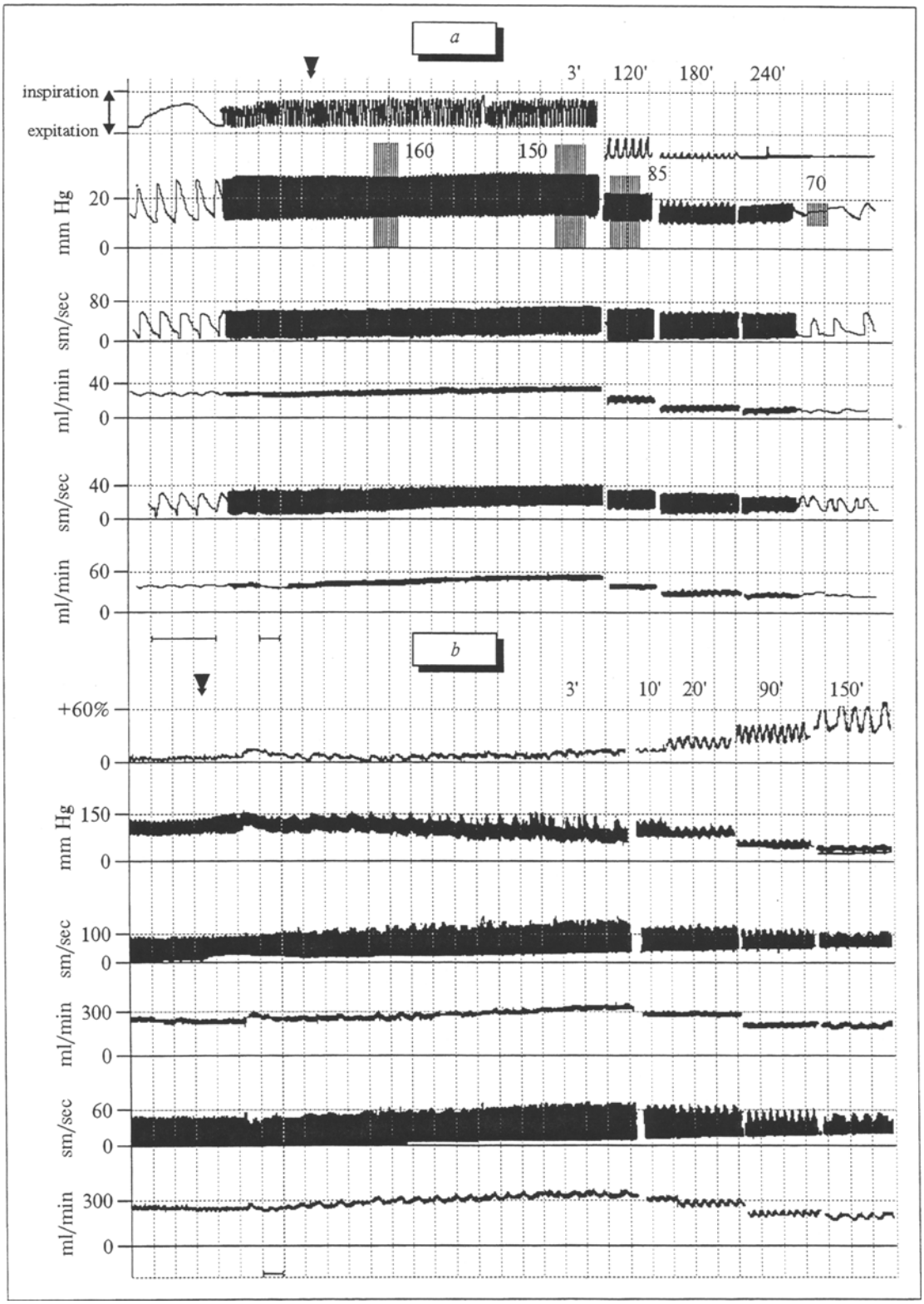

Fig. 3. Effect of Anthio on pulmonary (*a*) and systemic (*b*) circulations in spontaneously breathing cats. From top down: *a*) respiration; BP in the pulmonary artery; linear blood flow rate in the pulmonary lower lobar artery; volume blood flow rate in the pulmonary lower lobar vein; volume blood flow rate in the pulmonary lower lobar vein. Bars indicate BP in the femoral artery.

creased blood supply to the bronchial muscles in order to meet their metabolic needs [11]. The augmented blood outflow from the bronchial arterial system via the bronchial veins that enter the

left atrium may explain why the left ventricular output greatly exceeded the right ventricular output, which began to decrease 30-90 min after Anthio administration.

The tests with spontaneously breathing cats with closed chest enabled us to examine how alterations in respiration related to those in hemodynamics in response to Anthio. During the first few minutes after its administration, some cats exhibited increases in the frequency and amplitude of respiratory movements; 5 to 10 min postadministration, however, respiratory movements began to decrease in both frequency and amplitude and eventually ceased altogether (Fig. 3, *a*). In some cases, the complete respiratory arrest was preceded by the occurrence of a pathological respiration, or apnea. In spontaneously breathing cats, cardiac arrest followed the respiratory arrest. While the overall direction of hemodynamic changes in these cats was the same as in artificially ventilated animals, there were some differences. For example, the respiratory movements of spontaneously breathing cats administered Anthio were seen to involve much tension and appeared to be accompanied by substantial fluctuations in intrathoracic pressure, which was reflected in intensified respiratory waves of the pulmonary BP and blood flow (Fig. 3,*a*). Such respiratory waves were most conspicuous on the curve describing the balance between the right and left ventricular outputs (Fig. 3,*b*, upper curve), indicating that the balance of the entire respiratory cycle was upset in addition to the general disruption of the balance between the right and left ventricular outputs resulting in blood redistribution to the greater circulation (as reflected in an upward shift of the curve). Spontaneously breathing cats, unlike those ventilated artificially, showed a reduction in the left ventricular output, though to a lesser extent than that in the right.

In spontaneously breathing cats, respiratory arrest followed by cardiac arrest occurred 2 to 3 h after the administration of Anthio. Cats on artificial ventilation survived for longer periods - they were still alive when the observation was discontinued 3-5 h postadministration, at which time the systemic BP was as low as 30-40 mm Hg.

In some Anthio-treated cats, a functional test was performed involving a short-term (3 min) inhalation of a hypoxic gaseous mixture (7.5% O_2 in nitrogen) to evaluate the effect of Anthio on the responsiveness of the pulmonary vascular bed to hypoxia. The test showed that the pulmonary vasculature remained responsive to hypoxia for a long time after the exposure to this OPC: inhalation of the hypoxic mixture led to an elevation of BP in the pulmonary artery and to a rise in pulmonary vascular resistance ("pulmonary hypoxic vasoconstriction" [12].) This response disappeared only in the terminal phase, i.e., 20-30 min before the animal died.

In conclusion, this study has shown that the pesticide Anthio causes profound pathological changes in the pulmonary and systemic circulations and an imbalance in the functioning of the right and left ventricles. These changes are incompatible with life.

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