hibition of norepinephrine release from adrenergic terminals [9,15], direct cytoprotective effect [7,8,13], and prevention of vasoconstriction and thrombosis [11,12]. Our results suggest that the activation of protective PG may represent a mechanism responsible for the protective effect of adaptation to physical load during stress, ischemia, and other types of damage [1].

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Lipid Peroxidation After Acute Intoxication of Cats with Anthio and the Effect of Ionol on Their Survival

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Acute intoxication with the organophosphorus pesticide Anthio considerably increases the intensity of lipid peroxidation in Nembutal-anesthetized cats. Pretreatment with the synthetic antioxidant ionol prolongs the survival of the cats. Ionol has no appreciable effect on respiratory and hemodynamic parameters. Lipid peroxidation may contribute to the disturbances caused by Anthio.

Key Words: *organophosphorus pesticide; acute poisoning; lipid peroxidation; ionol; cats*

Organophosphorus compounds induce severe changes in tissue metabolism. Previously, we have shown that acute intoxication with the organophosphorus pesticide Anthio provokes pronounced metabolic acidosis, although pulmonary ventilation and blood Po_2 remained maintained within normal range [5]. This may be indicative of impaired tissue respiration. It was reported that the intensity of lipid peroxidation (LPO) is increased in people living in the areas where pesticides are widely used [1].

Our objectives were to determine LPO levels and examine the effects of the synthetic antioxidant ionol on respiratory and cardiovascular functions and on the survival of cats after acute intoxication with Anthio.

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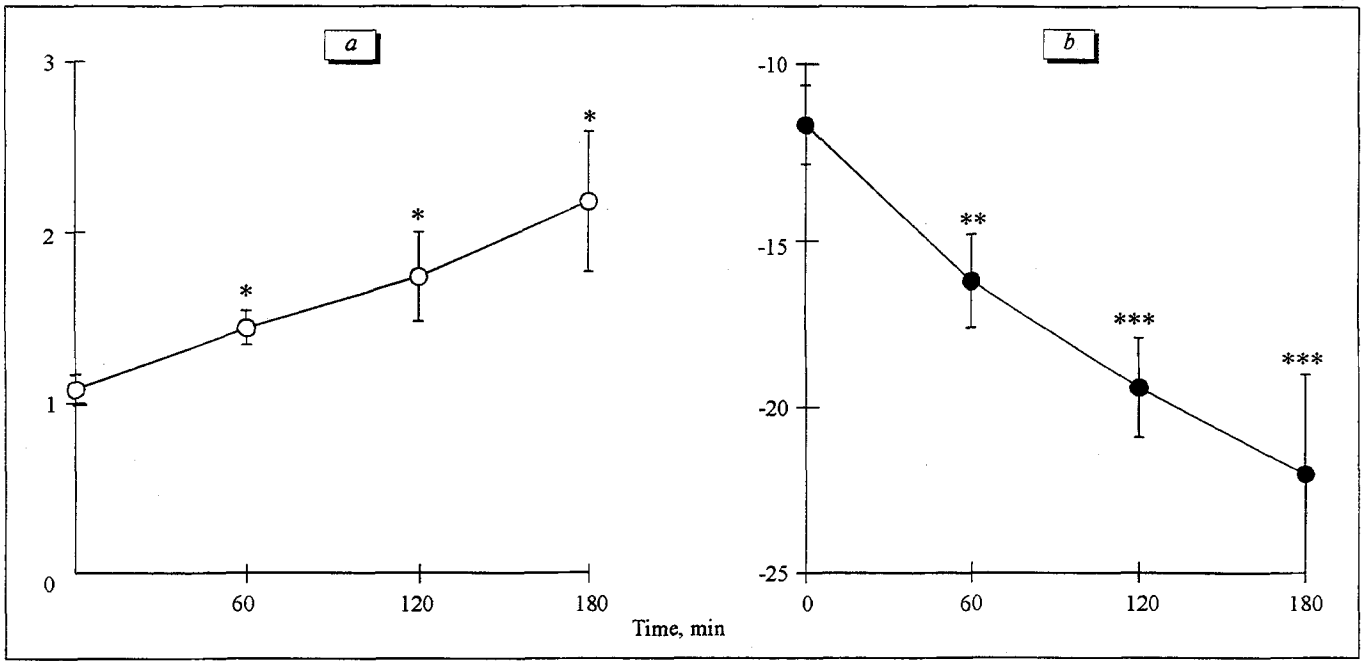

Fig. 1. Dynamics of LPO (*a*) and buffer base deficiency (*b*) in cats poisoned with Anthio. Ordinate: *a*) LPO products (mol MDA/mol phospholipids, $\times 10^{-3}$); *b*) deficiency of buffer bases (mmol/liter). Here and on Fig. 3: $^{*}p<0.05$, $^{**}p<0.01$, $^{***}p<0.001$ relative to baseline values.

MATERIALS AND METHODS

Experiments were performed on 13 Nembutal-anesthetized (40 mg/kg intraperitoneally) cats of both sexes weighing 1.95-3.25 kg. In the first series (control), LPO was evaluated after acute poisoning with Anthio [5] by the concentration of 2-thiobarbituric acid-reactive products [2]. The fluorescence of the malonic dialdehyde (MDA)—thiobarbituric acid complex (C) was calculated from the following formula: $C= [(F_t-F_c)/(F_s-F_c)]\times 1/V$ (nmol of plasma MDA), where F_t, F_s, and F_c is the fluorescence of test, standard, and control samples, respectively, expressed in relative units, and V is the volume of plasma in the sample. All the parameters were measured in a Hitachi-204 fluorimeter at an excitation wavelength of 530 nm and an emission wavelength of 545 nm.

Plasma concentrations of phospholipids were determined by the inorganic phosphorus content which was measured with the use of Boehringer Mannheim kits and expressed in μmol/ml plasma.

For analysis of the LPO dynamics, the concentration of LPO was standardized by the total phospholipid content.

In the second series, we attempted to diminish the Anthio-induced rise in LPO intensity. For this purpose, the phenolic antioxidant ionol (50 mg/ml in sunflower oil) was heated to 36-38°C and administered via a stomach tube in a dose of 50 mg/kg body weight. The tube was then washed with 0.5 ml normal saline, and the pesticide Anthio (Formation, Sandoz) was administered through it in a dose of 20% LD_{50} 2 h after ionol, after which the tube was again washed with saline. All other procedures and methods have already been described in detail [4,5].

The results were analyzed using Student's t test, and the differences were considered as significant at $p<0.05$.

RESULTS

It was found that Anthio markedly activates LPO in anesthetized cats, while ionol substantially increases the resistance of cats to this pesticide.

Within 2-3 h after administration of Anthio, plasma content of LPO products almost doubled in comparison with that of phospholipids (Fig. 1, *a*). The time course of LPO was similar to that of the buffer base deficiency (Fig. 1, *b*). The buffer base deficiency is the major manifestation of metabolic acidosis. It was analyzed in our previous study [5]. Both the rise in LPO and metabolic acidosis increase progressively and almost linearly until the death of the cat, suggesting a relationship between the intensity of LPO and the acid-base balance disturbances developing during acute intoxication with Anthio due to inhibition of tissue metabolism and mitochondrial respiration. This may be explained by the fact that changes in the phospholipid fraction studied partially reflect the total effect of Anthio on all the phospholipids of the body, including polyunsaturated fatty acids of cell membranes.

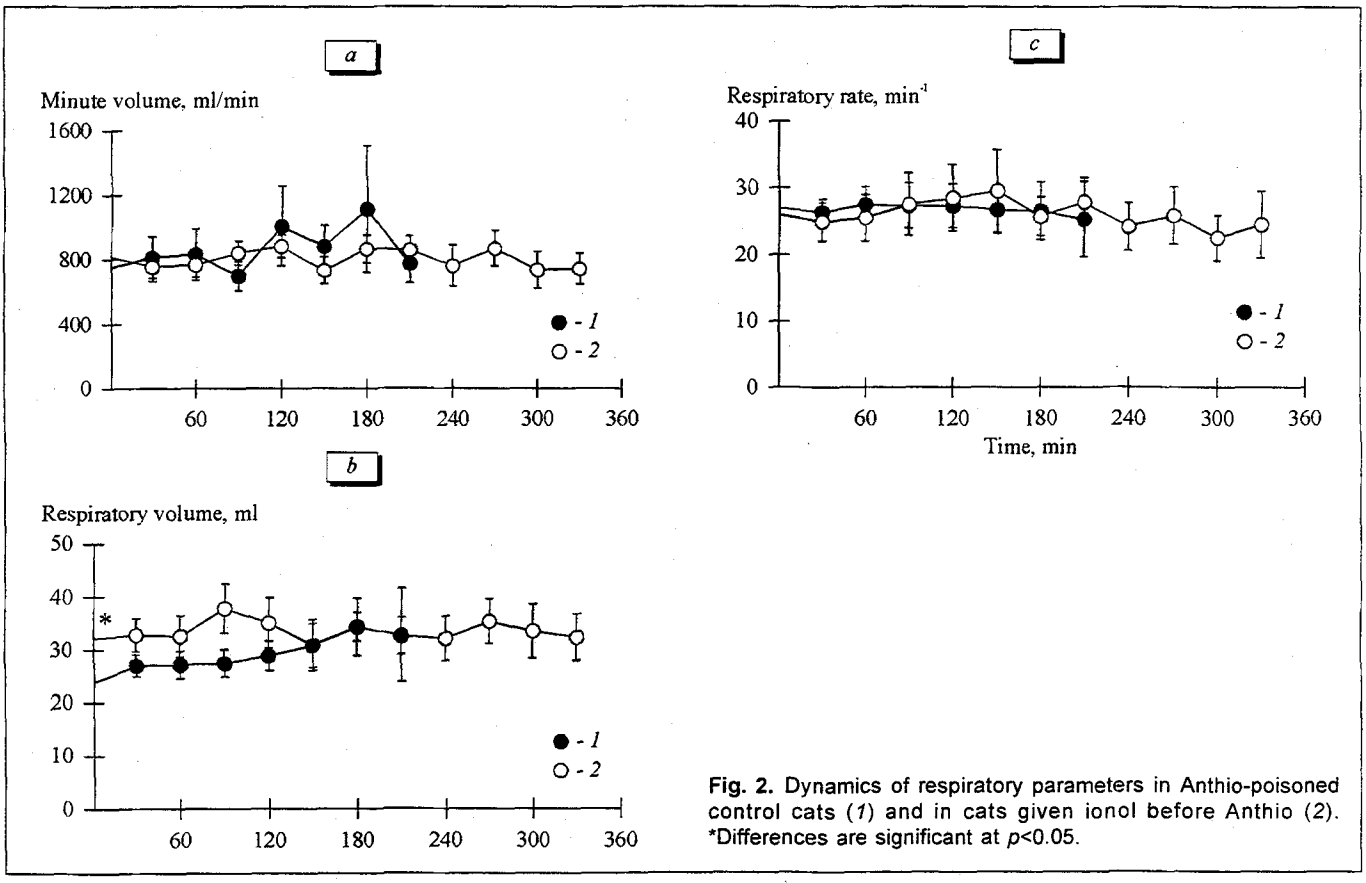

Fig. 2. Dynamics of respiratory parameters in Anthio-poisoned control cats (*1*) and in cats given ionol before Anthio (*2*). *Differences are significant at $p<0.05$.

Since damage to the CNS is the most dangerous consequence of intoxication with Anthio, it was important to examine the effect of LPO on the brain. Phospholipids make up 25% of the dry weight of the brain, which is 1.5- and 3- to 4-fold higher than the liver and heart content, respectively [6]. The highly oxidizable lipid fractions: such as phosphatidylethanolamine and phosphatidylserine amount to 38 and 14%, respectively, of total phospholipids [7]. Thus, LPO can inflict serious damage to brain structures, since in addition to the high content of phospholipids (LPO substrate), the brain has a powerful system of energy supply (source of oxygen radicals). It should be remembered that neurons, which occupy 5% of brain volume, utilize about 25% of brain oxygen.

Based on these considerations, we have hypothesized that the Anthio-induced intensification of LPO can be prevented by the antioxidant ionol. It

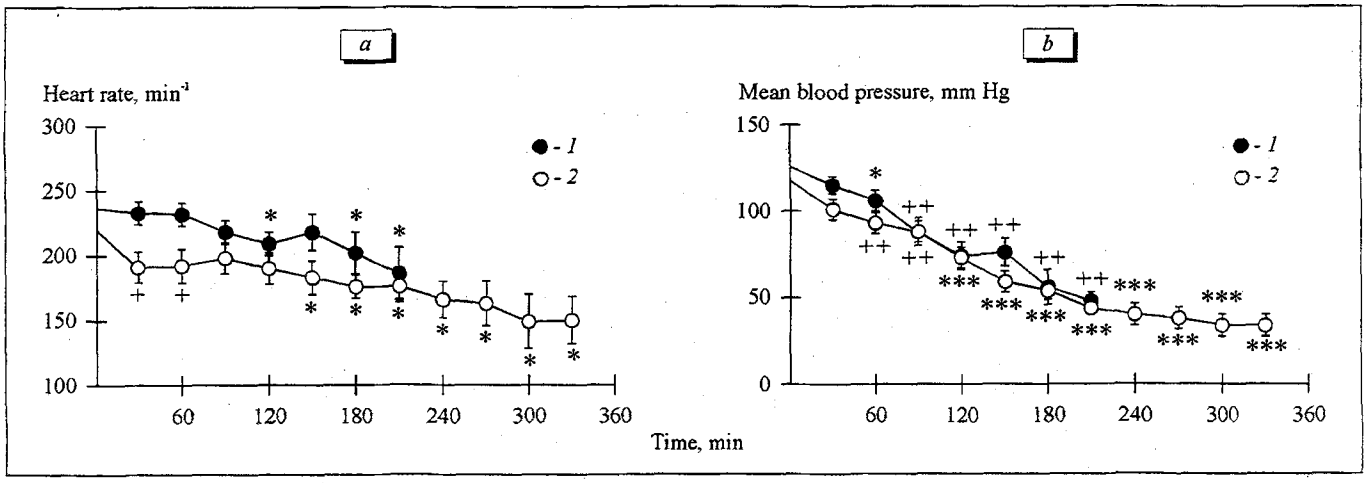

Fig. 3. Dynamics of hemodynamic parameters in Anthio-poisoned control cats (*1*) and cats given ionol before Anthio (*2*). Differences are significant at $^{*}p<0.05$ between the groups; $^{**}p<0.02$ compared with baseline values.

was demonstrated that a single administration of ionol before Anthio (instead of recommended 3-4 administrations [3]) prolongs the survival of the cats by 75% (320±36 min *vs.* 183±17 min in the control; $p<0.01$). Ionol had no effect on most of the measured parameters; it slightly increased the depth of breathing 2 h after administration (Fig. 2, *b*) and slightly decreased the heart rate 30-60 min after administration (Fig. 3, *a*). Since these changes have no principal significance, direct intergroup comparison is plausible. Ionol did not affect pulmonary ventilation in Anthio-treated and control cats (Fig. 2). However, it markedly reduced heart rate and blood pressure (Fig. 3). In our view, the almost identical changes in respiratory and circulatory parameters occurring in control and ionol-treated cats poisoned with Anthio indicate that ionol does not participate in the development of intoxication but increases the resistance of cats to the pesticide. Cats of both groups remained alive despite low cardiac activity (Fig. 3, *a*) and reduced blood pressure (Fig. 3, *b*). Presumably, conventional antioxidants (for example, α-tocopherol) will be helpful as an antidote against organophosphorus pesticides, since even a single administration of the antioxidant ionol produced a positive effect. Thus, together with conventional cholinolytics and acetylcholinesterase inhibitors, antioxidants can be used in the treatment of intoxication caused by organophosphorus pesticides.

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