Pathomorphological Investigation of Feline Lungs in Modeled Pneumonia

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The nature and specificity of the damaging effect of an Anthio-tarred turpentine combination and the changes it produces are studied in acute, subacute, and chronic experiments on cats. Anthio, a compound capable accumulating in adipose tissues and destroying lipid-containing structures (for example, surfactant), induces characteristic destructive effects on lung alveoli and causes dystelectasis and the formation of ectases, which are observed in acute experiments. The ectases contain an oxyphilic serous exudate and microfocal lymphoid-cellular clusters in the alveolar wall and are characterized by microcirculatory disorders such as edema, capillary and venous stases, and microhemorrhages. Study of the combined effect of Anthio and turpentine shows that the Anthio-induced destruction is persistent and probably creates conditions for secondary damaging factors which aggravate the pathological process and broaden the spectrum of the morphological alterations characteristic of acute pneumonia.

Key Words: *Anthio; turpentine; pneumonia; surfactant; ectases*

Lung pathology has been studied in acute animal experiments reproducing pneumonia induced with the organophosphorus compound (OPC) Anthio and turpentine, which cause severe pathology in human beings [1,2,5,6]. Chronic experiments show that Anthio has a moderate toxicity and is eliminated primarily via the lungs. Peribronchial atelectases, reduced or emphysemic alveoli, focal thickening of the interalveolar septa due to lymphoid-cellular infiltrates and capillary plethora, and perivascular accumulations of lymphoid-histiocytic cells have been observed in the lungs. On days 15-20, major bronchopulmonary destruction and the formation of bronchiectases have been documented [2,3]. Anthio induces circulatory disorders and concomitant destructive changes in the myocardium, liver, kidneys, adrenals, and brain [6].

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Under experimental conditions, tarred turpentine, used as an irritant [4,5,11], induces changes characteristic of spontaneously developing pneumonia and causes damage to the respiratory epithelium and some structures of the intraorganic (microcirculatory) component of the pulmonary vascular bed which form the air-blood barrier [11]. Destruction of this barrier results in serous exudation into the alveolar lumen [4], with concomitant pronounced hemodynamic disorders. This indicates the prevalence of the alterative component in the set of pathomorphological responses typical of pneumonia.

The aim of this study was to examine the damaging effect of Anthio, tarred turpentine, and their combination in acute and subacute experiments.

MATERIALS AND METHODS

Experiments were performed on cats of both sexes weighing 2.8-4.3 kg. The animals were maintained on a full-value diet. Prior to the experiments, they were

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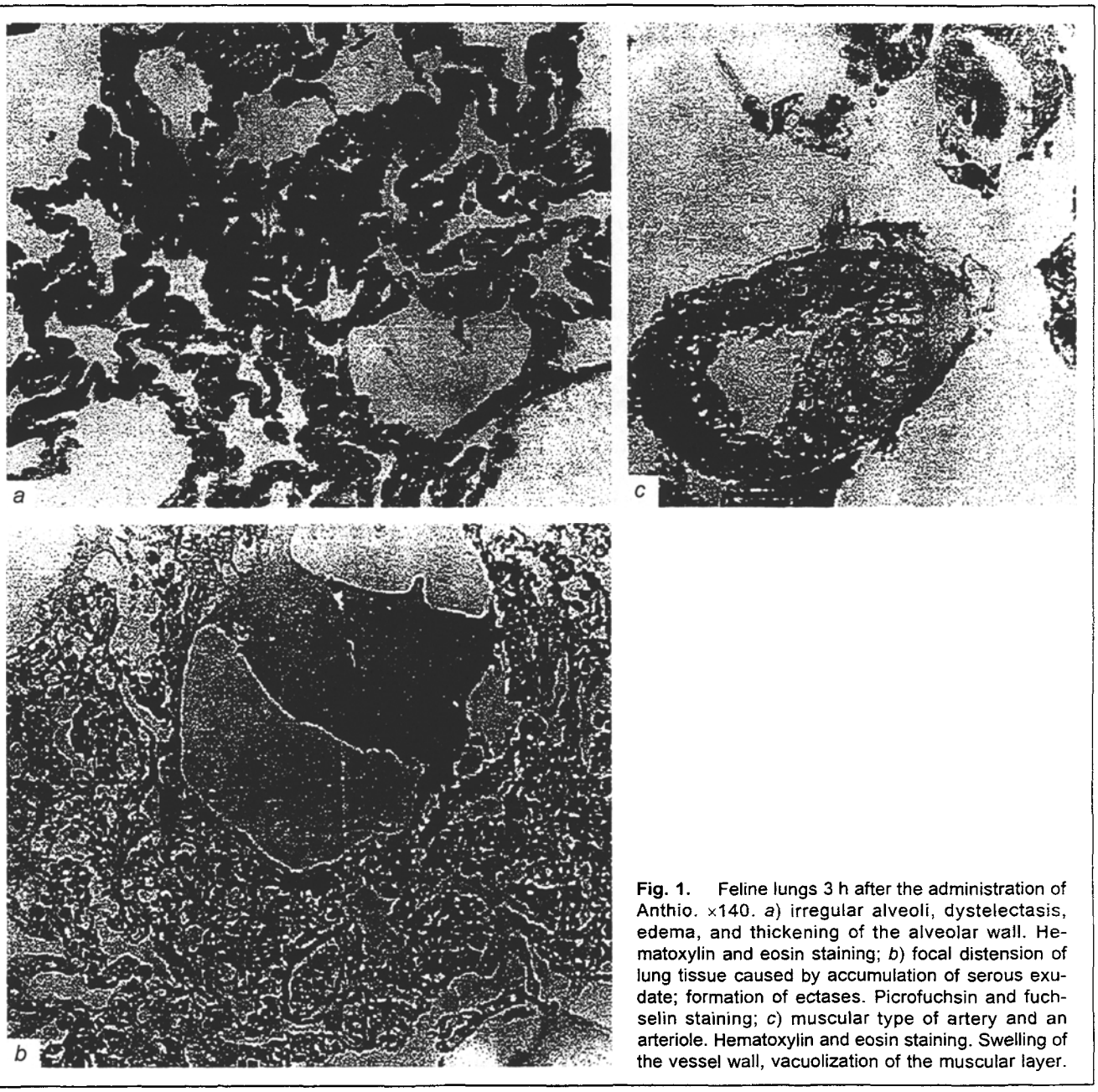

Fig. 1. Feline lungs 3 h after the administration of Anthio. ×140. *a*) irregular alveoli, dystelectasis, edema, and thickening of the alveolar wall. Hematoxylin and eosin staining; *b*) focal distension of lung tissue caused by accumulation of serous exudate; formation of ectases. Picrofuchsin and fuchselin staining; *c*) muscular type of artery and an arteriole. Hematoxylin and eosin staining. Swelling of the vessel wall, vacuolization of the muscular layer.

assigned to four groups, 3-5 cats in each. Anthio (1/5 of the lethal dose) was administered to group I cats via a gastral tube under Nembutal anesthesia (30-40 mg/kg, intraperitoneally). Functional changes in the lungs, myocardium, and brain were observed during a 3-h acute experiment [8-10]. The animals died against the background of lowered blood pressure [8,10]. In group II, Anthio was administered intragastrally under etherrausch narcosis, and then the animals were left for 72 h, after which they were examined in acute experiments. Turpentine was administered intratracheally to group III cats under etherrausch narcosis, and the animals were examined in an acute experiment 72 h later. In group IV, the Anthio-turpentine combination was applied: Anthio was administered intragastrally under etherrausch narcosis, after 72 h the cats were given turpentine intratracheally, and the acute experiment was performed after an additional 72 h. After the experiments, groups II, III, and IV animals were injected a lethal dose of Nembutal.

The thoracic and abdominal organs were examined at autopsy. Lungs with ligated trachea were excised and fixed in a 12% neutral formaldehyde solution. Sections were prepared from frozen or paraffin-embedded material and stained with hematoxylin and eosin, picrofuchsin-fuchselin, and Sudan III after Goldman.

RESULTS

Respiratory insufficiency probably caused by cerebral pathology [9,10] and other alterations typical of pneumonia: systemic and pulmonary circulation disorders, peripheral vascular dilatation presumably of a mosaic character, increased blood viscosity hindering microcirculation at sustained normoxia, and the development of hypercapnia associated with metabolic acidosis were observed in cats of groups I, II (Anthio against the background of Nembutal anesthesia), and IV (Anthio+turpentine).

Autopsy of group 1 animals showed moderate or diminished air-filling of the lungs, pale pink lungs with microfocal hemorrhages, plethora of major bronchial veins, and sometimes massive hemorrhages of the hepatization type. Vesicular (up to 5 mm in diameter) ectasic widenings containing transparent serous fluid were found in some animals. The liver was large and condensed, the spleen was anemic with subserous hemorrhages, the adrenal cortex was diminished, and there were hemorrhages in the adrenal medulla. Histological studies revealed damage to the epithelium of medium and small bronchi: exudate in the lumen, cell swelling, and peribronchial accumulations of serous fluid. Focal erythrocyte accumulation in alveoli, some swelling of alveolocytes, narrowing of alveolar lumens, and alveolar wall collapse, which could be interpreted as a tendency towards atelectasis or as a dystelectasis (Fig. 1, *a*), were seen. Presumably, the damaging action of Anthio, a substance capable of binding with fats, which is characteristic of OPC, affected primarily the lipid-rich alveolar surfactant. Destruction of the surfactant led to the col-

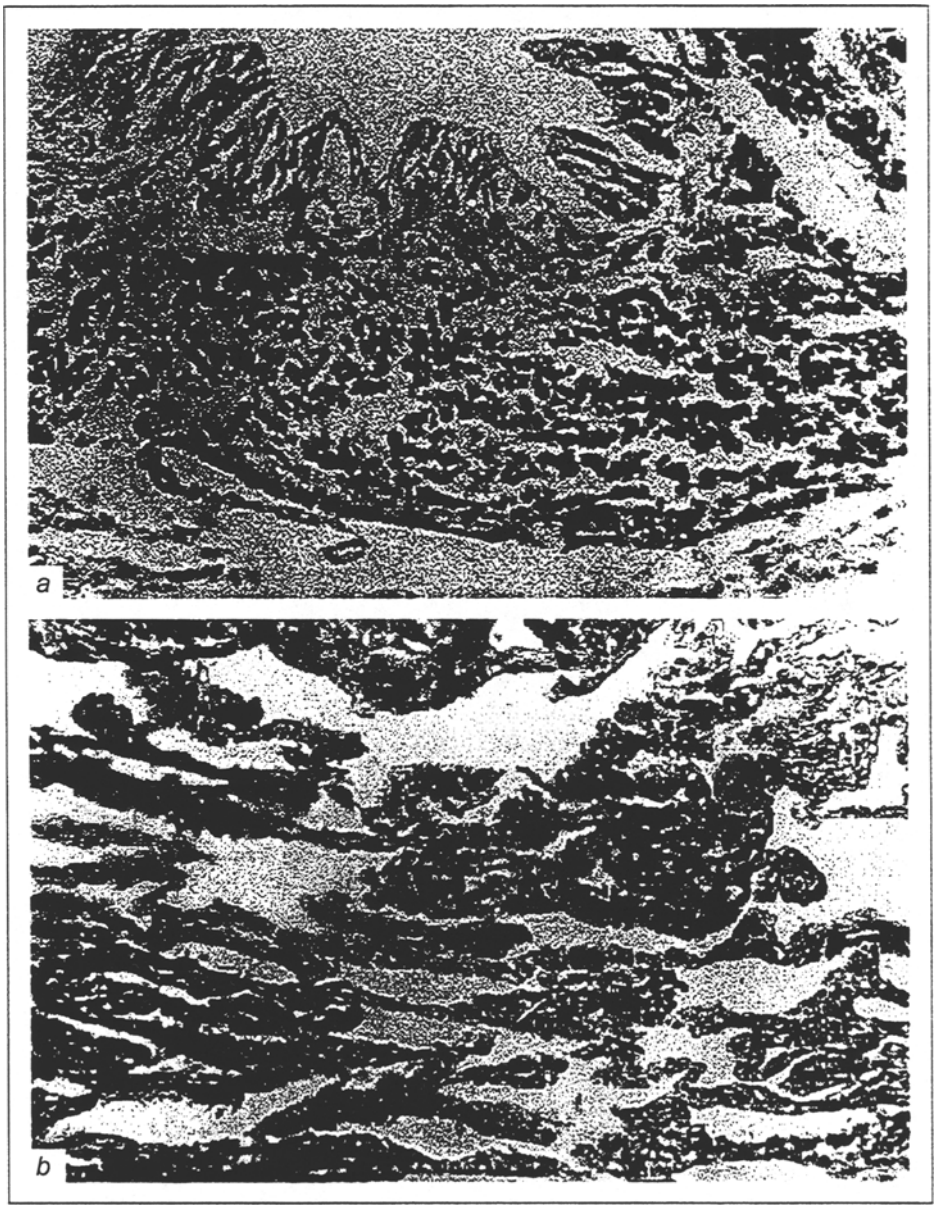

Fig. 2. Feline lungs 72 h after the administration of Anthio. *a*) medium bronchus. Mucous edema, lysis of the epithelium, and necrobiotic alterations in a peribronchial lymphatic follicle; *b*) irregular alveoli in the root area; edema and thickening of the alveolar wall; dystelectasis. Here and in Fig. 3: staining with hematoxylin and eosin. ×140.

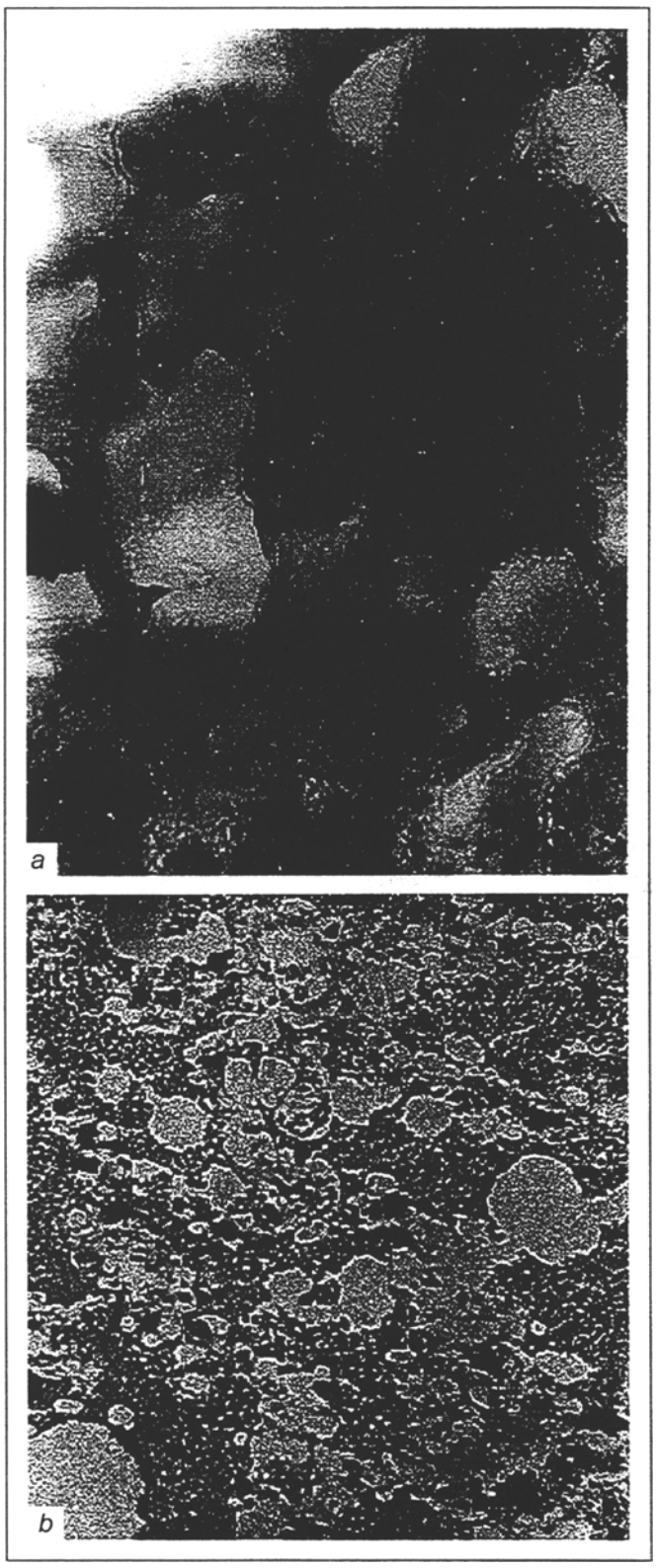

Fig. 3. Feline lungs 72 h after the administration of turpentine. *a*) lung alveoli. Thickening of the walls due to capillary plethora in interalveolar septa. Serous exudate in alveolar lumens. *b*) capillary and venular plethora and microhemorrhages.

lapse of the alveolar wall and promoted a tendency towards atelectasis, i.e., induced an instantaneous alterative response typical of inflammation.

This pathology was characterized by a widening of bronchial, bronchiolar, and alveolar lumens, focal distension of tissues, and the formation of ectases containing serous oxyphilic exudate (Fig. 1, *b*).

The walls of the lung arterioles (Fig. 1, *c*) and venules were swollen and showed perivascular edema. Presumably, Anthio also damaged the vascular wall by increasing its permeability, causing exudation of the plasma, its focal accumulation, and microhemorrhages, which were liable to appear in response to terminal hypoxia. In some cases, focal lymphoid-cellular infiltrates were found in thickened alveolar walls. This was probably the early manifestation of the delayed-type cell proliferation responses typical of inflammation.

Autopsy of group II animals revealed plethoric lungs with hemorrhages, plethora of large bronchial veins, and microfoci of whitish nodules half the size of a poppy seed on cross section. The liver was clayey. There were subserous hemorrhages in the spleen and other organs.

Histological studies revealed damaged epithelium of medium and small bronchi (Fig. 2, *a*). The damage to the alveolar epithelium manifested itself in cell swelling, the formation of a cellular multilayer, and cell desquamation into the alveolar lumen. There were alveolar ectases, dystelectases, and atelectases which, were often accompanied by focal lymphoid-cellular infiltration in the interalveolar septa (Fig. 2, *b*). Microcirculatory disorders (capillary and venular stases and microhemorrhages) were also observed.

These changes can be interpreted as the further development of Anthio-induced experimental pneumonia characterized by changes typical of inflammation: alterative, exudative, and proliferative.

The lungs of group III animals were plethoric, soaked with serous fluid, and hemorrhagic. Numerous hemorrhages were seen in the tracheal mucosa. The liver and spleen were plethoric or condensed with hemorrhages.

Histological studies revealed inflammatory alterations in the trachea and medium and small bronchi, as well as focal serous exudation in the alveoli (Fig. 3, *a*), focal lymphocyte reactions, capillary and venular plethora, and microhemorrhages (Fig. 3, *b*), which is characteristic of catarrhal pneumonia.

The lungs of the cats from group IV were plethoric and hemorrhagic. Nodules half the size of a poppy seed size were found in the lungs of all the animals.

Histological preparations showed sings of primary damage: edema of the bronchial epithelium, swelling of alveolocytes, narrowing of the alveolar lumen, and

dystelectases. Massive foci of parenchymal lysis were observed. There were small, diffusely scattered lymphoid-cellular infiltrates in the alveolar wall. Microcirculatory disorders were evident: capillary and venular stases, venular leukostasis, and microhemorrhages typical of pneumonia, probably resulting from the combined action of Anthio and turpentine.

From a comparison of the findings in groups II, III, and IV it can be assumed that the Anthio-induced destructive alterations could be aggravated, focal ectases could be transformed into focal parenchymal lysis, and proliferation of stromal elements could become multiple and focal or acquire other manifestations due to the action of other damaging factors (tarred turpentine in this study).

Comparison of groups I and II shows that Anthio rapidly causes damage to microvessels and alveolar surfactant, thus inducing the formation of atelectases and stimulating cellular-proliferative alterations in the lung stroma. The presence of parenchymal ectases and atelectases 72 h after intragastral administration of Anthio suggests that the pesticide probably accumulates in adipose tissues and, after being metabolized by certain structures of the internal organs, destroys their lipid-containing components, thus instituting a continuous damaging process.

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