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The Effect of Lead Inhalation on Rat Lung Morphology

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Abstract: Lead may exert toxic effects on several organ systems, but those in the lung are the most insidious. Therefore the aim of the present study was to investigate the morphological alterations caused by lead intoxication in rat lungs.

Twenty-five Wistar albino rats were divided into three groups: the control group consisted of five animals while the experimental groups contained ten animals each. The control group animals were not subjected to lead treatment, whereas the first experimental group animals were exposed to 500 µg /0.1 m^3 /day of lead for one week, and the second group had the same dosage of lead exposure for two weeks. All the animals were decapitated and the lung tissues were obtained from each animal. Tissue samples were processed for light microscopical examination.

In the lung tissue of the first experimental group, lymphocyte and monocyte infiltration and collagen accumulation were evident in the interalveolar septa, whereas in the second experimental group the animals had pneumonia in addition to exhibiting the same features as the first group animals.

In conclusion, the concentrations of lead, especially over a long period, may cause irreversible morphological alterations in the, rat lung tissue.

Key Words: Lead inhalation, lung, morphology, rat

Introduction

Lead is commonly used in several industrial fields by people who are unaware of its adverse effects on human health. In addition, lead is taken spontaneously from the lead polluted environment via water, air and food (1,2,3).

It is well established that lead intake, such as through lead vapour inhalation, may cause irreversible effects in several organ systems in mammals (4,5,6,7).

Previous studies have demostrated the effects of lead exposure on gastrointestinal and urinary systems, which were adversely affected by lead intake (6,8,9).

Although the effects of lead taken orally on gastrointestinal and urinary systems have been well established, it has been suggested that lead inhalation may be more dangerous than the effects mentioned above (10).

Therefore, the present study was designed to determine the effects of lead inhalation on the respiratory system, especially on lung histology.

Materials and Methods

In this study, 25 male Wistar albino rats weigh between 250g and 300g were used. In a closed glass chamber of approximately 0.1 m^3 volume (38 cm X 88 cm X 30cm), 500 µg/week lead was heated for 8 hours/day. In the upper surface of the chamber an opening of 1 cm was made. The first group of rats (ten) was put into the chamber and exposed to lead by inhalation, approximately 500 µg/0.1 m3/day for 1 week (11). The second group of rats (ten) was exposed to the same amount of lead for 2 weeks. The control group consisted of 5 rats not subjected to lead exposure.

After decapitation of the rats, lung tissue samples were taken by thoracotomy. The samples were fixed for 48 hours in buffered neutral formalin. Following the fixation procedure, the tissues were dehydrated through increasing concentrations of ethanol. They were then embedded in paraffin and 5-7 µm thick sections were cut from the paraffin blocks. These sections were stained with Hematoxylin-eosin for routine histological

examination, and stained with Van-Gieson's picric acid and acid fuchsin and Masson's trichrome stain for collagen fiber differentiation.

Results

Control Group

In the light microscopical examination of the control group lung tissue samples, bronchioli and their lumina lined with single layer columnar epithelium were observed together with the bronchial structures lined with pseudostratified epithelium and containing lymphocytes in their lamina propria. The bronchial structures were surrounded by a smooth muscle layer and segmented hyalin cartilage. Surrounding these structures the saccus alveolaris, alveoli with regular walls, interalveolar septa and Kohn pores connecting the alveoli to each other were observed in the lung parenchyma (Figures 1, 2).

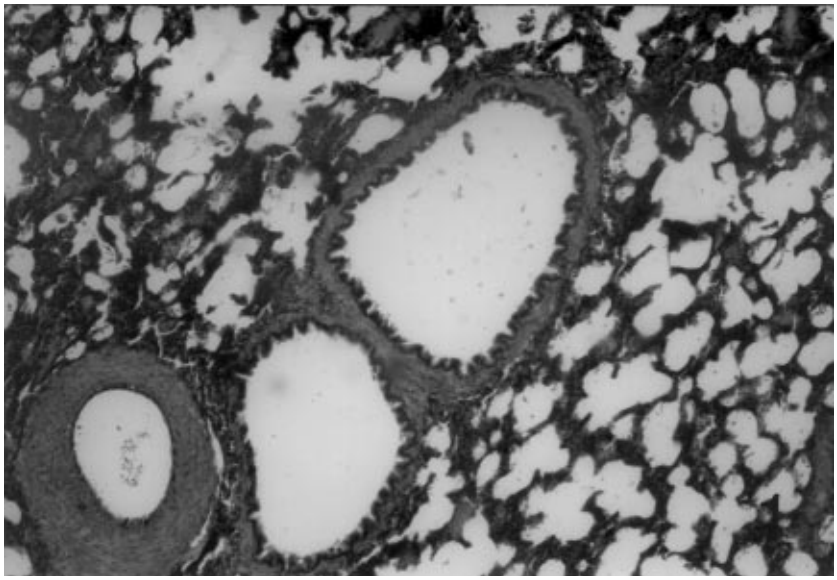

Figure 1. Bronchiolar and alveolar structures in the control group in their normal structures. A neighbouring muscular artery is also seen around the bronchioles. X40, H+E.

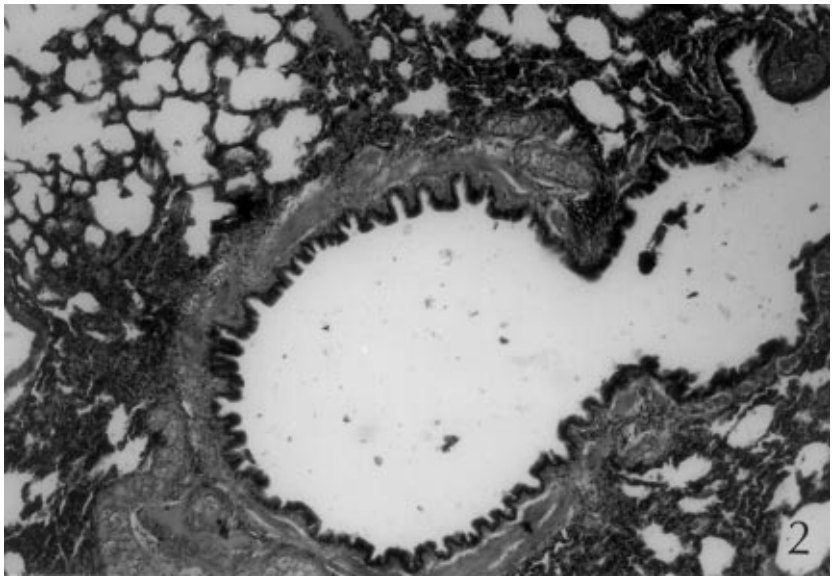

Figure 2. A bronchus lined with pseudostratified epithelium is shown in the control group rat lung. X40, H+E.

Experimental Groups

First Group

The light microscopic examination of the first experimental group, of rats exposed to one week of lead inhalation, revealed lymphocyte infiltration into the interalveolar septae and also into the bronchiolar lamina propria (Figure 3).

Clear histological findings such as mononuclear cell proliferation, mononuclear cell invasion and collagen fibre accumulation were also observed in the interalveolar septa (Figure 4). The structural organization of the alveoli seemed to be disturbed and the interalveolar septa were thickened. These findings may indicate that the lung tissue had undergone fibrosis.

Second Group

In seven out of ten rats, cystic areas isolated by a fibrous capsule were observed in the lung samples of the second experimental group (Figure 5). Numerous

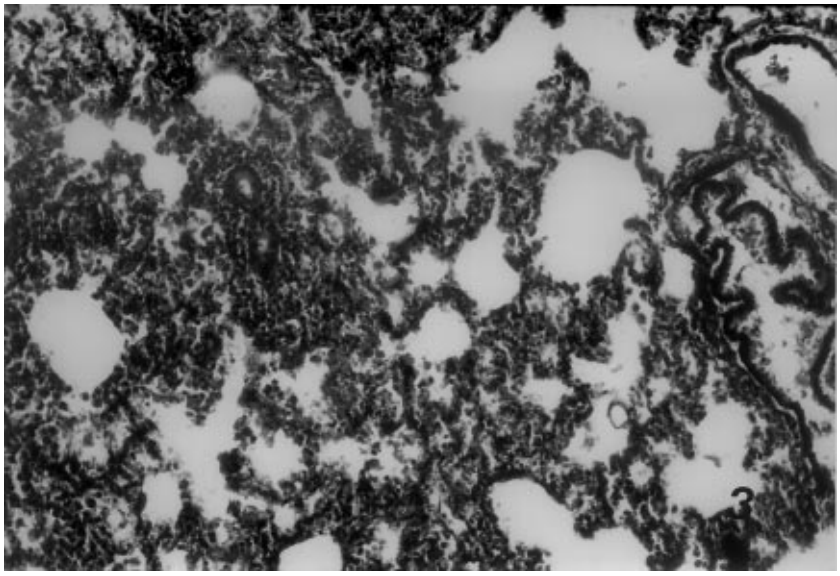

Figure 3. Lymphocyte infiltration both in alveoli and in bronchiolar connective tissue in the first experimental group. X40, Masson.

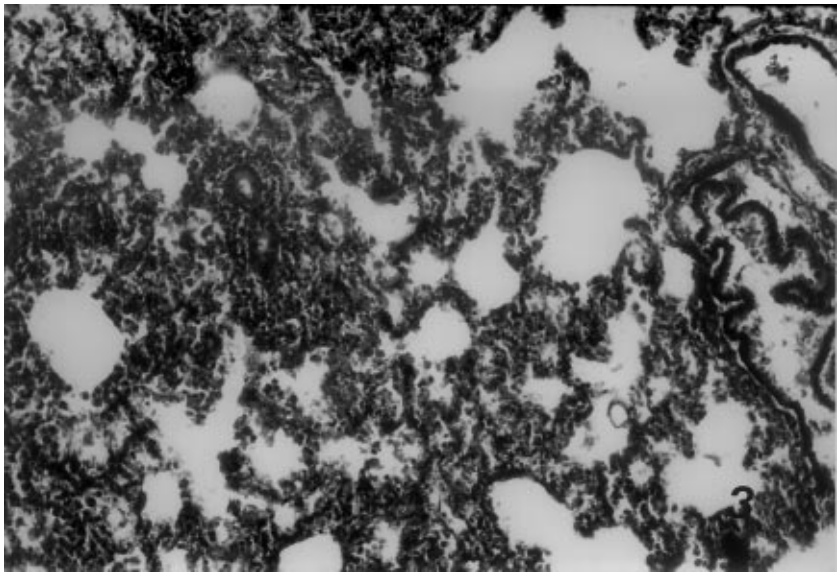

Figure 4. In the first experimental group, rat lung tissue containing collagen fiber accumulation along with distinctive cell proliferation and mononuclear cell invasion in the alveolar septa. X100, Masson.

lymphocytes and macrophages were observed in the bronchioli and bronchi lumina, alveoli lumina and interalveolar septa. Fibrosis and bronchopneumonia appeared to have occurred following lead administration (Figure 6).

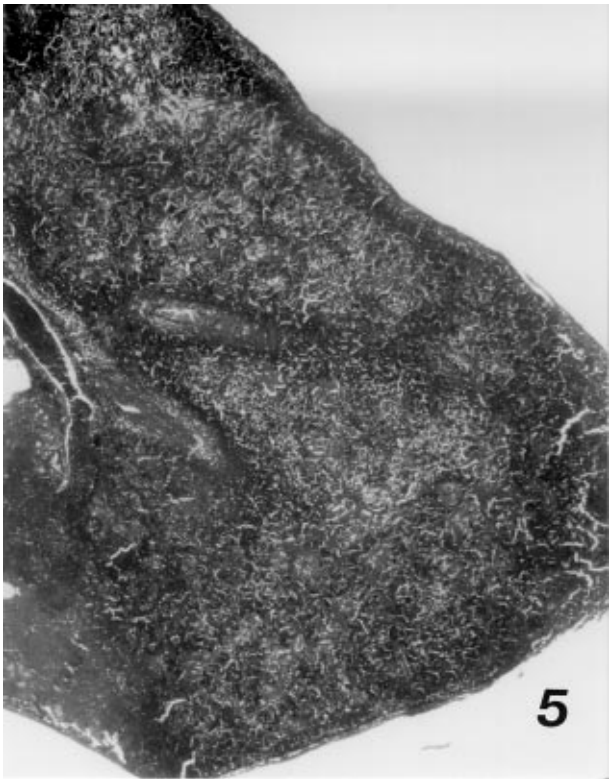

Figure 5. Seven out of ten rats in the first group demonstrated cystic structures isolated by a connective tissue capsule from the lung tissue. X10, H+E.

There was no evidence of bronchopneumonia in the rest of the group. However, the arterioles were contracted and epithelial cell debris was observed in the bronchiolar lumina. In the alveolar region, mononuclear cell proliferation in the septum alveolares, invasion of mononuclear cells, lymphocytes and an accumulation of collagen fibers were evident. These findings suggested a disorganized structure for the saccus alveolares and alveoli, which indicated fibrosis in these regions (Figure 7).

Discussion

It is well known that heavy metal dusts adversely affect human health in industrial areas and in the wider environment.

Previous studies on the effects of heavy metal dusts, especially lead, on the respiratory system have concentrated on humans and laboratory animals (1, 4, 5, 7,) The degree of the effects of inorganic dusts on lungs are thought to depend on the dosage, duration and dust type (12). The effects of heavy metal dusts are usually necrosis, interstitial fibrosis and degenerative changes in the lungs (4). However, the respiratory system has protective barriers and mechanisms against inorganic dusts. While the bigger particles are captured by nasal mucosa, the remaining particles are discarded by mucociliar mechanisms in the respiratory tract and also by macrophages in the alveolar parencyhma of the lung. Dusts of only 1-5 μm diameter can reach the lung parenchyma. However, dust particles that are smaller than 1 mm are discarded by expiration. Dust accumulation in the alveoli cancause fibrosis (12, 13).

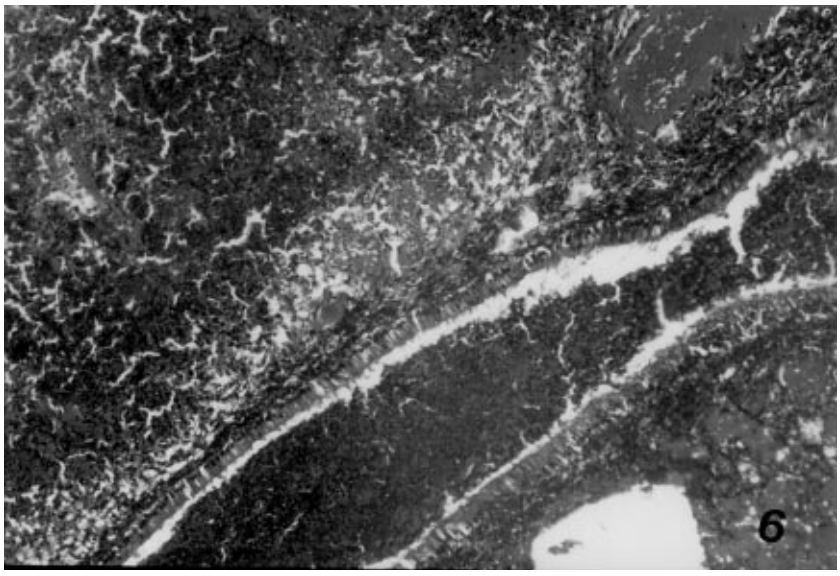

Figure 6. Bronchopneumonial features and fibrosis are evident in the lung tissue of the second experimental group. X40, Van Gieson.

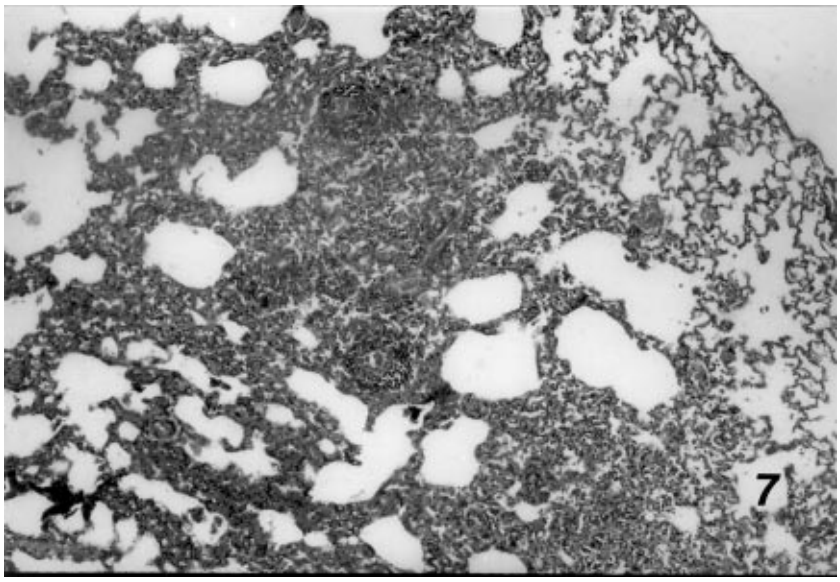

Figure 7. Similar to those seen in the first experimental group, the second experimental group contained cell proliferation and mononuclear cell and lymhocyte infiltration in the alveolar septa. X20, H+E.

Inhalation is the primary route for absorption of lead compounds. In the bloodstream, the majority of absorbed lead is bound to erythrocytes. The free diffusible plasma fraction is distributed to the brain, kidney, liver, skin and skeletal muscle, where it is readily exchangeable. Lead binds to sulfhydryl groups intracellularly and interferes with numerous cellular enzymes, including those involved in heme synthesis. This binding accounts for the presence of lead in hair and nails. Lead also binds to mitochondrial membranes and interferes with protein and nucleic acid synthesis . The maximum lead exposure limit is 0.05 mg/m according to OSHA PEL (Occupational Safety and Health Administration Permissible Exposure Levels) (14).

Morphological studies at the electron and light microscopic levels in different species have shown no structural differences between these species and human lung tissues (15,16).

Therefore, the present study investigated the effects of a high concentration and prolonged exposure to lead on rat lungs.

Pulmonary alveolar macrophages are known to have an important role in the phagocytisis of inhaled particles in the alveolar wall. In a study of heavy metal poisoning, a morphological analysis of bronchoalveolar lavage demonstrated pneumonia, multinuclear cell accumulation and fibrosis in lung tissue. In addition, investigation of the alveolar wall in the same samples revealed intensive macrophage accumulation and cell exfoliation into the alveolar lumen (17,18).

In the present study, rat lungs exposed to lead especially the interalveolar septa, contained mononuclear cell accumulation. As a result of cell invasion, the interalveolar septa were thickened, the alveolar surface became smaller and the alveoli were irregularly organized.

Mononuclear cell invasion seen in the interalveolar septa can be described especially by macrophage and lymphocyte accumulation. The histological findings for both the one-week and two-week exposure groups ixhibited no distinct differences.

It has been reported that the thickness of the interalveolar septa not only depends on cellular origin but also on collagen fiber accumulation and capillary changes (19). The present study also identified collagen fiber accumulation along with inflammatory cell invasion in the interalveolar septa, effects which have been suggested by previous studies of lung morphology following lead exposure.

It could be suggested that the above findings may indicate a reversible pathology associated with the inflammatory and immune process in the interalveolar septa whereas the collagen fiber accumulation characterized by fibrotic processes could indicate irreversible degenerative alterations.

Previous pathological studies of heavy metal poisoning from cobalt, carbide, titanium, tantalum, lead and aliminium have suggested fibrosis along with hyperplastic

alveolar epithelium in the lung tissue, as well as asthma and pneumonia (20).

However, while the findings of the present study showed no pneumonia in the one-week lead exposure group, the two-week lead exposure group exhibited fibrosis and bronchopneumonia characterized by lymphocyte accumulation in the alveolar and in the bronchiolar lumina.

In conclusion, it could be suggested that the high concentration of lead exposure caused fibrosis and alveolar disorganization in both experimental groups, whereas the long duration of lead exposure caused pneumonia.

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