

CONSEQUENCES OF METHYL MERCURY EXPOSURE ON LUNG HISTO-ARCHITECTURE IN RAT

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Abstract: The present study was conducted on 36 adult male Sprague Dawley rats of six weeks of age. These subjects were randomly assigned into three groups as control, 2.5 ppm and 5 ppm methyl mercury exposure. Exposed individuals were sacrificed at 14 and 35 days and lung tissue samples were collected and studied the effect of short time and long time exposure on lungs. Histological study of these samples revealed that the degeneration of alveolar architecture, disruption of respiratory epithelium and increased proliferation of collagen and elastic fibres around respiratory bronchiole in 2.5 ppm methyl mercury at 14 days post exposure group than 5 ppm group. Some individuals showed severe congestion of blood vessels, mild edema with no septal thickening of alveolar septa and congestion of alveolar capillaries in 2.5 ppm group at 14 days. Whereas in 5 ppm group, inter alveolar septal thickening in focal areas and at some places emphysematous changes were present. Some individuals showed haemorrhages and mononuclear cells in capillaries and septal thickening of alveoli, atelectasis and cellular infiltration within the alveoli at 2.5ppm in 35 days of exposure. While in 5 ppm group congestion of alveolar capillaries and blood vessels in the lung, mild thickening of alveolar septa and infiltration of cells in some respiratory bronchioles.

Keyword: Lung, Methyl mercury, Histology, Rat.

Introduction

There is a growing problem of worldwide contamination of the environment with mercury (Gilmore and Henry, 1991). The general population is most commonly exposed to methyl mercury primarily from eating fish and marine mammals that may contain some methyl mercury in their tissues. In the environment, inorganic mercury can be methylated by microorganisms to methyl mercury. Methyl mercury will accumulate in the tissues of organisms. The animals at the top of the food chain tend to accumulate the most methyl mercury in their bodies. Any source of mercury release to the environment may, therefore, lead to increased levels of methyl mercury in tissues of large fish and mammals (Weiner *et al.*, 2003). Once absorbed, metallic and inorganic mercury enter an oxidation-reduction cycle. Metallic mercury is oxidized to the divalent inorganic cation in the red blood cells and lungs

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of humans and animals. Recently, there has been much interest and discussion regarding the toxicity of methylmercury, the correlation with fish and shellfish intake, and methods of long-term management of the human health effects of methylmercury. What effects chronic exposure to a low concentration of methylmercury has on human health remains controversial (Young *et al.* 2012). Diminutive information was caring on respiratory effects associated with intermediate-duration exposures lead to undertake this present study to narrate the effect of methyl mercury on histological changes in lung.

Materials and Methods

The present study was conducted on 36 adult male Sprague Dawley rats of 6 weeks age. Rats were procured from National Centre for Laboratory Animal Sciences, National Institute of Nutrition, Hyderabad, India. After quarantine the rats were randomized and grouped (Table: 1). MeHg was fed in the form of Methyl mercuric chloride in drinking water given ad-libitum daily. All the three groups were fed with commercial pelleted rat diet (chow) ad-libitum daily. The animal experimental protocol followed the ethical principles as approved by the Institutional Animal Ethics Committee (through reference 4/IAEC/NTRCVSc/GVM-2013-14 dated 10.12.13).

Table 1: Experimental design

| Treatment groups | Number of animals sacrificed | |
|---------------------|------------------------------|---------|
| | 14 days | 35 days |
| Control (Group I) | 6 | 6 |
| 2.5 ppm (Group II) | 6 | 6 |
| 5.0 ppm (Group III) | 6 | 6 |

Exposed individuals were sacrificed at 14 and 35 days and lung tissues were collected, fixed in 10% neutral buffered formalin and processed for histological study. Paraffin sections of 4-5 μm thickness were cut and stained with Haematoxylin and Eosin staining for routine architecture, Vangieson's stain for collagen fibres, Weigert's elastic stain and Verhoeff's elastic stain for elastic fibres (Luna, 1968)

Results and Discussion

Mercury toxicity is known to affect the redox status of the victims' tissues through increased production of free radicals leading to oxidative stress (Ercal *et al.*, 2001). The concentration of mercury residues depends on the particular organ and the extent of damage probably depends on concentration, response and sensitivity of the organ. In the present study degeneration of alveolar architecture, disruption of respiratory epithelium, severe congestion

of blood vessels, mild edema, haemorrhages and increased proliferation of collagen and elastic fibres around respiratory bronchiole in 2.5 ppm methyl mercury at 14 days post exposure group than 5 ppm group (Fig.3). Lungs have shown diffuse infiltrates or pneumonitis in humans (Bluhm *et al.*, 1992 and Soni *et al.*, 1992). Airway obstruction, restriction and decreased vital capacity (McFarland and Reigel 1978) have been reported. However Rats exposed to 27 mg/m³ of elemental mercury vapors for 2 hours leads to dyspnea and death due to asphyxiation (Livardjani *et al.*, 1991).

Mild thickening of alveolar septa was noticed in 2.5 ppm at 14 days exposure compare with control group rats (Fig. 1 and 2). Whereas in 5ppm group, inter alveolar septal thickening in focal areas and at some places emphysematous changes were apparent. (Fig. 3). Congestion and intra alveolar septal thickening in the alveoli of 14 days post exposure of 5.0 ppm along with emphysematous changes was observed. Similarly, mercury vapor exposure resulted in alveolar dilation, emphysema, pneumothorax and death in humans (Jaffe *et al.*, 1983 and Kanluen and Gottlieb 1991).

Some individuals showed haemorrhages and mononuclear cells in capillaries and septal thickening of alveoli, atelectasis, adipose tissue near the respiratory bronchiole and alveolar ducts and cellular infiltration within the alveoli at 2.5ppm in 35 days of exposure (Fig. 4 and 5). Such functional impairment probably resulted from both vasoconstriction and a direct cytotoxic effect of mercury (Girardi and Elias, 1993; and Barregard *et al.*, 2010). While in 5 ppm group congestion of alveolar capillaries and blood vessels in the lung, mild thickening of alveolar septa and infiltration of cells in some respiratory bronchioles (Fig. 6). Congested lungs appeared in rats exposed to 1 mg/m³ metallic mercury vapors for 100 hours continuously per week for 6 weeks (Gage, 1964). However, 3 mg/m³ mercury vapor for only 3 hours a day, 5 days a week for 12–42 weeks, pathological examination revealed no significant changes in the respiratory system of rats (Kishi *et al.*, 1979).

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Illustrations

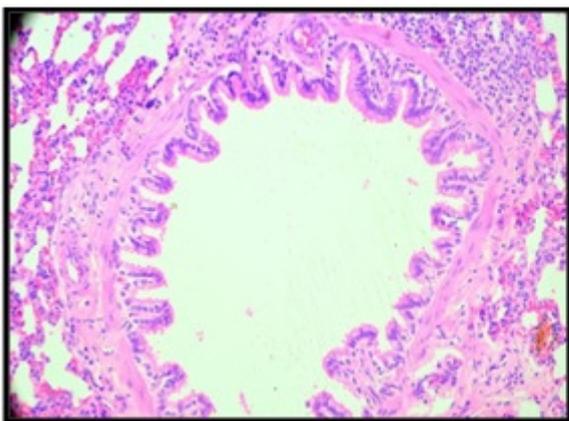


Fig. 1: Photomicrograph of lung showing normal respiratory bronchiole of control group of rats (14 days) **H&E X40**

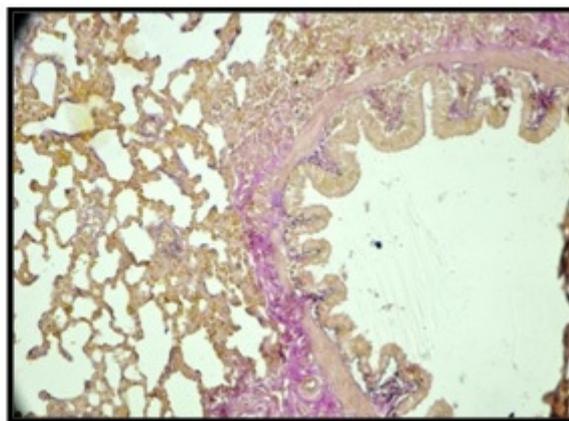


Fig. 4: Photomicrograph showing normal alveolar epithelium of control group rats (35 days) **Weigerts elastic stain X 40**

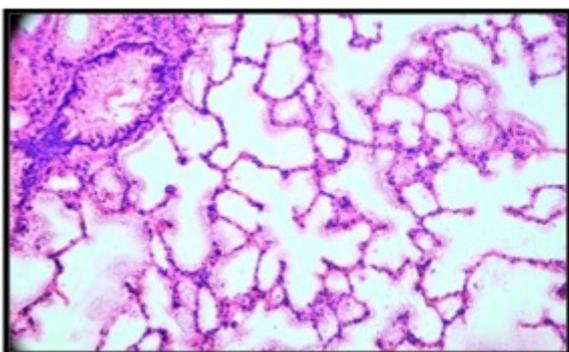


Fig. 2: Photomicrograph of lung showing desruption of alveolar sacs in rat (2.5 ppm at 14 days MeHg). **H&E stain X40**

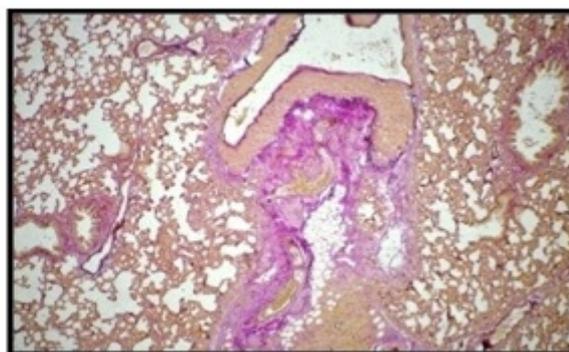


Fig. 5: Photomicrograph showing mild thickening of alveolar septa in rat (2.5 ppm for 35 days). **Weigerts elastic stain X 10**

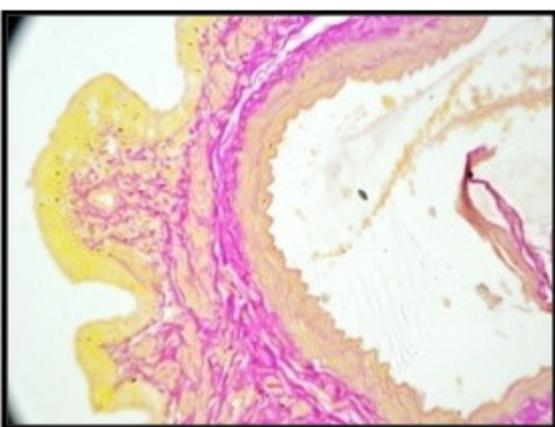


Fig. 3: Photomicrograph showing thickened respiratory bronchiole of lung in rat (5 ppm at 14 days MeHg) **Verhoeff's stain X 40**

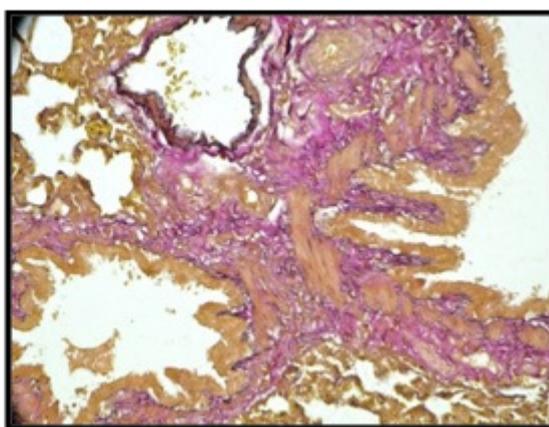


Fig. 6: Photomicrograph showing increased proliferation of elastic fibres in lung of rat (5 ppm at 35 days MeHg) **Weigerts elastic stain X 40**