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Pulmonary Toxicity of Beryllium in Albino Rat

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In view of the prevalent public and scientific concern about environmental and occupational factors in the etiology of human cancer metal toxicity, carcinogenesis specifically has attracted the attention of the scientists. Many secrets have been disclosed related to carcinogenic properties of the metals.

Arsenic compounds, if chronically exposed to human beings significantly increase incidences of epidermoid carcinomas of the skin and lung (NATIONAL INSTITUTE FOR OCCUPATIONAL SAFETY and HEALTH, 1973). According to SUNDERMAN and MASTROMATTEO (1975), nickel has been considered to be a important metallic carcinogen. Regarding beryllium, different opinions are held so far as its carcinogenic nature is concerned. While HASAN and KAZEMI (1974) have reported an equivocal increase in the incidences of respiratory cancers in patients with chronic pulmonary berylliosis, BAYLISS (1972) investigated the causes of increased deaths among workers of beryllium factory. He found no increase in the incidence of respiratory cancer. Among experimental animals, intravenous injections of suspensions of beryllium salts to rabbits have been shown to induce osteogenic sarcomas (GARDNER and HESLINGTON 1946, CLOUDMAN et al. 1949).

The present communication deals with the histopathological and enzymological study of lungs of albino rats after prolonged beryllium treatment.

MATERIAL AND METHODS

12 male albino rats of almost same weight (140 to 150 g) were selected and divided in two groups, the first group consisting of 4 animals. The animals of the first group were fed on standard pallet diet from Lever Brothers (India) Ltd. and water ad libitum and served as the control animals. The animals of the second group were given orally 20 mg of beryllium nitrate (Sigma) with the above pallet diet every third day. The experiment was allowed to continue for 2½ months when 40 doses had been given and the experimental animals came to comasate condition. The animals of both the groups were then sacrificed and the lung samples were fixed in buffered formalin, Rossman's fluid and chilled acetone. 6 to 8 micron thick sections were cut after paraffin embedding

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and were stained with haematoxylin-eosin-azure II to study histopathological lesions.

The activity of phosphatases including alkaline phosphatase (EC 3.1.3.1), acid phosphatase (EC 3.1.3.2) and 5'-ribonucleotide phosphohydrolase (EC 3.1.3.5) was estimated according to the methods of BODANSKY (1932 and 1933) and HEPPEL and HILMOE (1951) respectively. The activity of phosphatases has been expressed in terms of mg of phosphate liberated per hour per g. of the tissue.

RESULTS

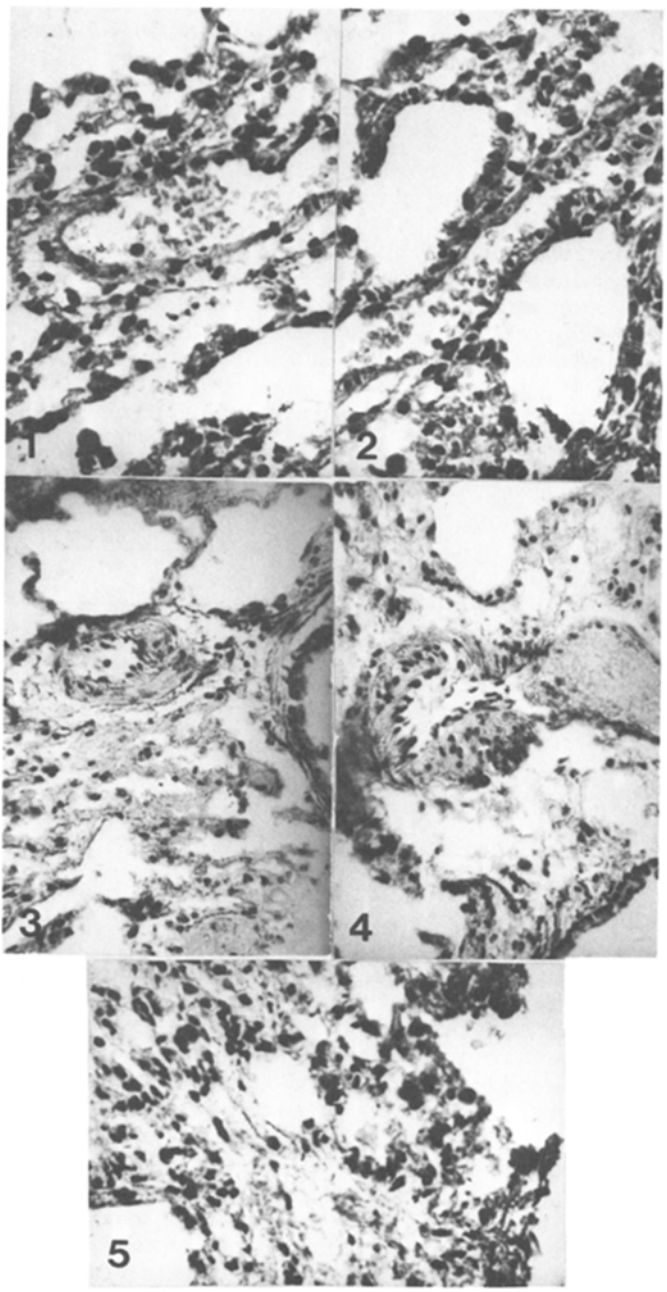
Histopathology:

Morphologically, the lung of the experimental animals was found to be more hard and stiff in comparison to control lung. The colour of the lungs of the experimental animals was found to be more opaque and turbid-white in contrast to pinkish-white of control animals.

Histologically, the lung showed many notable pathologic lesions. Most of the respiratory bronchioles get shrunk and filled with the jelly-like secretion depicting the condition of bronchiolar congestion. The wall of many respiratory bronchioles get damaged. At places, the ciliated epithelium get ruptured accompanied by the cytoplasmic infilteration, thus exposing the nuclei (Fig. 1). The nuclei of the damaged bronchiolar ciliated epithelium get enlarged at many places (Fig. 2).

Many of the alveoli in the lung of the experimental animals contain thickened epithelial cells (Fig. 3). At many loci, the alveolar epithelium shows severe degree of necrosis including rupture of the cell wall accompanied by karypycnosis. Such damage of alveoli is more frequent along perihaemal zones (Fig. 4). At these sites damaged alveolar cells are the remaining scars with only a few nuclei which are also under disintigration. Clumping of the nuclei also take place at these sites. On the whole, the cellular architecture is distorted in such a manner that in most of the zones no well defined alveolar ducts, atria and alveoli could be seen (Fig. 5).

It is interesting to note that the chronic pulmonary berylliosis includes damage of pulmonary blood vessels. Arterioles show damage of tunic intima (endothelium) (Fig. 4). The nuclei of degenerative endothelial cells show pycnosis and occupy more or less lumenal position. Many arterioles get so damaged that the 3 layers constituting arterioles are indistinguishable. Tunica adventitia also shows early signs of degeneration in some art-



Figs. 1 to 5 showing histopathic lesions in the lung of albino rat during Berylliosis.

erioles. The arterioles get enlarged.

The treatment by toxin also resulted in the damage of elastin fibres in the connective tissue of lung to a great extent which depicts the limited elasticity of the lung.

Enzymology:

The activity of the phosphatases including alkaline phosphatase (EC 3.1.3.1), acid phosphatase (EC 3.1.3.2) and 5'-ribonucleotide phosphohydrolase (EC 3.1.3.5) in the lungs increased during experimental berylliosis. Maximum increase was noted in the activity of alkaline phosphatase (approximately 50 per cent). The data for the phosphatases' reaction is shown in the Table below:

Phosphatases' reaction in the lung of albino rats

Enzyme	Enzymatic activity (mg. of phosphate liberated per hour per g. of tissue)	
	Control	Experimental
Alkaline phosphatase (EC 3.1.3.1)	1.43 ± 0.21	2.15 ± 0.13
Acid phosphatase (EC 3.1.3.2)	1.46 ± 0.03	2.00 ± 0.03
5'-ribonucleotide phosphohydrolase (EC 3.1.3.5)	1.68 ± 0.00	1.82 ± 0.06

DISCUSSION

Many metallic compounds have been known to induce cancers in experimental animals and human subjects. Epidemiological studies have demonstrated that certain occupational exposure of workmen to arsenic, chromium and nickel compounds are associated with increased incidences of specific type of cancer. Regarding carcinogenic property of beryllium, different views have been given. BAYLISS (1972) could not find any increase in the incidences of respiratory cancers after chronic pulmonary exposure but found increased rate of mortality during workmen berylliosis. However, MACUSO (1970) and HASAN and KAZEMI (1974) have reported an increased tendency of pulmonary cancers in the worker of beryllium factory. The present finding are in consonance with the reports of BAYLISS (1972) as death occurred of almost all the experimental animals preceded by the comasate condition after chronic induction of beryllium. The authors did not record any sign of

pulmonary malignancy in experimental animals and the death was caused due to severely damaged lungs. Intravenous injections of beryllium salts to rabbits and mice have been shown to induce osteosarcomas (GARDNER and HESLINGTON 1946, CLOUDMAN et al. 1949, KELLY et al. 1961). Similarly, inhalation of aerosols of beryllium salts in rats and monkeys has been reported to result in pulmonary carcinomas by NASH (1950), REEVES and VORWALD (1967) and KOMITOWSKI (1968).

Necrotic damage of lung tissue during beryllium disease has also been reported by GAENSTER (1959). According to him, bronchiolar congestion is the initial effect of berylliosis and these findings confirm present observations. LIEBEN et al. (1963) reported the deposits of beryllium in damaged alveolar cells after exposure to it. TOPPER et al. (1961) have shown the involvement of smaller pulmonary arteries with damaged endothelium in mammalian lungs after beryllium treatment.

It is interesting to note that the phosphatases' activity in lung during berylliosis increased. The maximal increase takes place in the pulmonary alkaline phosphatase reaction. Similar altered lactate dehydrogenase activity by beryllium induction has also been shown by REEVES (1967). This increase in phosphatase reaction in the lungs may perhaps be due to the toxic insult to the tissue cells by beryllium.

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