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Histomorphologic Changes Induced by Methyl Isocyanate in Lungs of Rats and Rabbits

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Methyl isocyanate is a highly reactive compound and its biological effects are due to its reactivity as acylating agent (Cohen and Oppenheimer 1977). It causes corrosive damage to tissue exposed by inhalation and topical application (Anonymous 1977). The available literature contains information on the gross morphological changes induced by MIC on the lungs (Kimmerle and Aben 1964). Discolored lungs with tissue necrosis and mottled red to reddening of entire lung surface have been reported following exposure to MIC (Dodd et al 1982). However, the effects of varying concentrations of MIC on the lung architecture has apparently not been studied in detail. This could delineate the possible mechanism of damage caused to lungs. The present study was undertaken with this aim in view.

MATERIALS AND METHODS

Male albino rats and rabbits were procured from the animal house of Defence Research and Development Establishment, Gwalior. The animals were fed a standard pellet diet (Hind Lever Feed, India). Rats weighing 100-130 g and rabbits 1200 to 1500 g were exposed for 30 min in a dynamically operated animal exposure chamber of 30 litre capacity. Methyl isocyanate was obtained from the chemical laboratories of Defence Research and Development Establishment, Gwalior. The monitored concentration of MIC was 3 mg/l in case of rabbits and 133 mg/l for rats. The chamber was ventilated with filtered air at the flow rate of 30 l/min. Control animals were housed similarly in the chamber exposed to filtered air only.

The second group of rats was exposed for 30 min to vapour of MIC in a spherical all glass static chamber of 21 litre capacity. Desired quantity of MIC was spontaneously evaporated in a small glass tube attached to the main

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body of the exposure chamber. The vapours were thoroughly mixed with the air inside the chamber by a pump with air displacement capacity of 30 l/min. The pump was operated periodically at 5 min interval during the exposure period. The monitored and metered concentrations of MIC vapours in the animal chamber were 1.04 mg/l, 0.50 mg/l and 0.32 mg/l (equal to 1 LC_{50}, ½ LC_{50} and 1/3 LC_{50} respectively) for an exposure period of 30 min.

Exposed and control groups of animals were sacrificed at 24 hours post exposure period with an overdose of sodium pentobarbital. The excised lungs of animals were inflated with air through a tracheal tube to an intra-pulmonary pressure of 10 cm H_2O. The whole lungs were fixed in a buffered formalin solution. Representative samples of tissue from different lobes of lungs were cut into small pieces and processed for embedding into paraffin. Tissue sections of 5-6 µm thickness were prepared, stained with haemotoxylin and eosin and examined under light microscope.

RESULTS AND DISCUSSION

Exposure of rabbits to MIC in a dynamically operated animal exposure chamber to a concentration of 3 mg/l for 30 min caused a 2-2.5 fold increase in the lung weight. Lungs had a cherry red colour and large haemorrhagic patches. The epithelial lining of the bronchioles was necrotic and sloughed (Fig.1). The alveoli were filled with oedematous fluid concomitant with marked congestion and thickening of alveolar septa (Fig.2). Cellular infiltration in the air spaces was evidenced by the presence of polymorphonuclear cells and red blood cells. Lungs of rats exposed to 133 mg/l concentration of MIC in a dynamically operated animal chamber showed comparable cellular damage to lungs (Fig.3 & 4). The most prominent feature was pulmonary edema in lungs of these animals.

Microscopic picture of lungs of rats that survived exposure to MIC (1.04 mg/l) caused granular deposition on the lining cells of bronchioles and epithelial cell necrosis together with infiltration of polymorpho-nuclear cells. Desquamation of epithelium of bronchioles and congestion in the small vessels and septal capilla-ries also resulted. In the rats exposed to 0.50 mg/l (MIC) the histomorphological damage was less. The epithelial cell lining of bronchioles was extensively damaged. In some specimens the lumen of respiratory bronchioles was found filled with exudate showing necrotic cells and inflammatory cells. The perivascular spaces were prominent with moderate degree of congestion

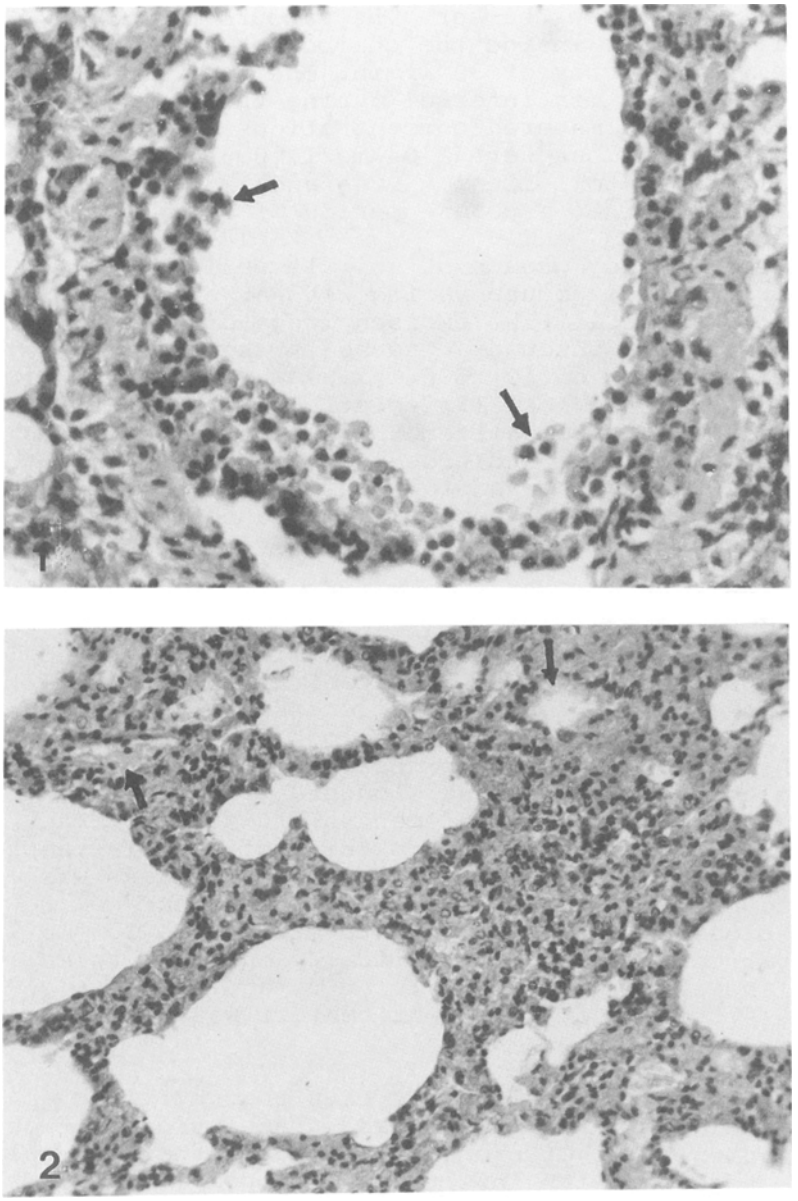
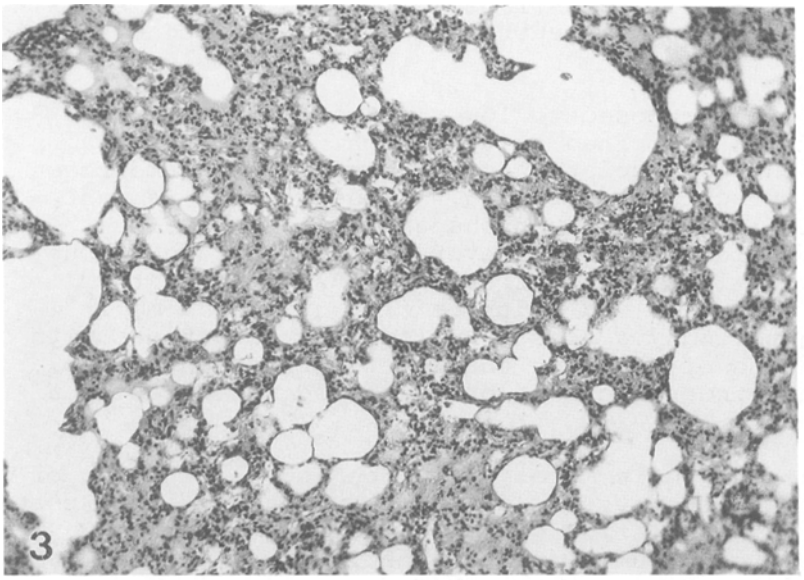


Fig.1 : Rat lung showing acute bronchiolitis H&E x 715.(top)
Fig.2 : Rabbit lung showing marked thickening of alveolar septa and alveolar spaces filled with oedematous fluid. H&E x 450.(bottom)



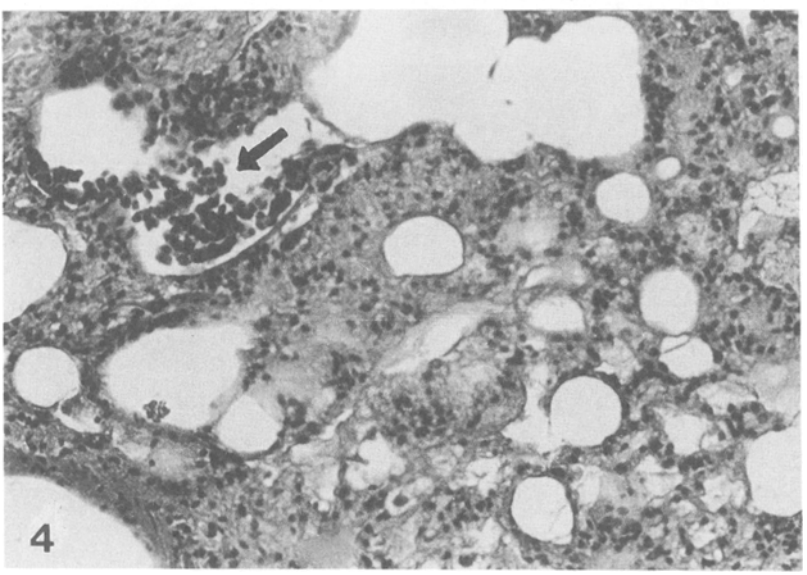


Fig.3 : Rat lung showing characteristic pulmonary oedema. H&E x 225.(top)

Fig.4 : Rat lung showing cellular infiltration. H&E x 715.(bottom)

as well as focal areas of haemorrhage. The most striking changes at higher concentration were acute bronchiolitis and congestion.

Lungs of rats exposed to lower concentration (0.32 mg/l) of MIC exhibited acute bronchiolitis with an area of intra alveolar and peribronchiolar haemorrhage with perivascular edema (Fig.5). Besides, there was severe inflammatory reactions and pulmonary edema caused by widespread and severe damage to lung tissue. However, at lower concentration (0.32 mg/l) or the animals that survived moderate exposure (0.50 mg/l) the lung parenchyma showed inflammatory reactions with infiltration of cells in the finer airways and alveolar air spaces independent of pulmonary edema and external haemorrhage.

It seems that inflammatory reaction and destruction of alveolar architecture leads to emphysema in rats exposed to lower concentration of MIC. Exposure to higher concentration results in the genesis of pulmonary edema. These findings suggest that MIC predominently damage the lung tissue due to its corrosive action.

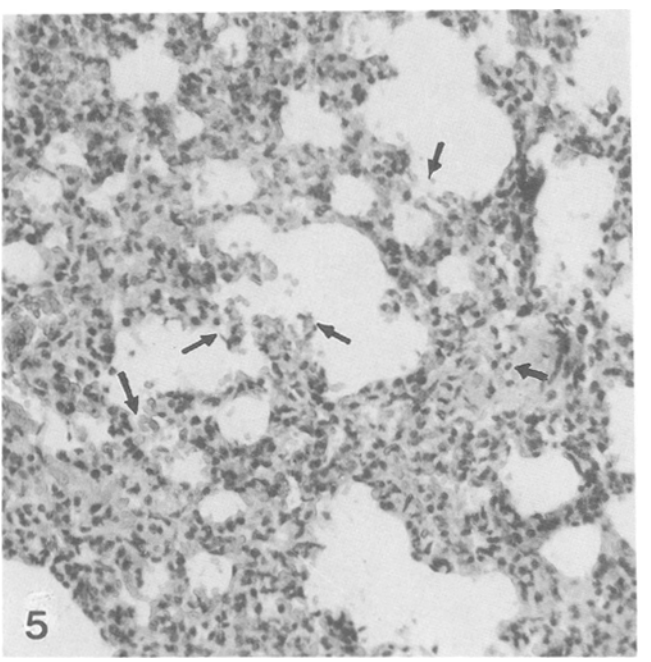


Fig.5 : Rat lung showing areas of haemorrhage and emphysema. H&E x 450.

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