Fibrosing alveolitis (pulmonary interstitial fibrosis) evoked by experimental inhalation of Gasoline vapours

A. W. J. Lykke[1] and B. W. Stewart

School of Pathology, University of New South Wales, P.O. Box 1, Kensington (NSW 2033, Australia), 17 August 1977

Summary. Rats exposed to an atmosphere contaminated with gasoline vapour for 6–12 weeks exhibit progressive focal interstitial fibrosis of the lung, which is associated with irregular alveolar collapse. It is suggested that this experimental model of diffuse fibrosing lung disease constitutes a useful tool for the study of the dynamics of pulmonary reactivity to atmospheric pollutants and which may facilitate an understanding of the pathogenesis of fibrosing alveolitis in man.

Rats exposed to an atmosphere containing gasoline vapour for periods of 6–12 weeks develop diffuse focal interstitial fibrosis associated with alveolar collapse. The gasoline used was commercial 'Super' grade (Octane Rating 98%) containing tetraethyl lead in a concentration of 0.45 g/l (w/v). 40 male Wistar rats (200–250 g) were enclosed for 8 h per day for 5 days per week in a 'perspex' box through which was circulated air containing gasoline vapour at an average concentration of 100 parts per million. For the 1st 5 weeks 2 rats were selected at random each week for sacrifice, whereas 4 rats were sacrificed weekly in the period 6–12 weeks. Under light ether anaesthesia, the thoracic cavity was opened and the pulmonary vascular tree perfused through the pulmonary trunk with 20 ml chilled Karnovsky's combined aldehyde fixative (pH 7.4) at a pressure of 100 cm water. Slices of lung from the lateral convexities of the R and L bases and the base of the R upper lobe were cut with a scalpel into blocks 2 mm thick and fixation was continued for a further 5 h by immersion in fresh fixative. After post-fixation in 2% osmium tetroxide, tissues were blocked in epoxy resin and sections cut with an LKB Ultramicrotome. 0.5 µm and ultrathin sections were studied by light and electron microscopy. Tissues from 5 untreated rats, prepared in similar fashion, served as controls.

Results. 22 of 28 rats exposed to gasoline vapour for periods ranging from 6–12 weeks exhibited pathological changes ranging from minor scattered foci to widespread sclerosis (figure 1). Of the 6 rats which did not show unequivocal pathology, 2 had been exposed to the gasoline fumes for only 6 weeks, 2 for 7 weeks and 1 each for 8 and 9 weeks. The changes in pulmonary parenchyma of advanced lesions consisted of aggregations of fibroblasts with an occasional macrophage in foci within the expanded interstitial plane, together with irregular deposition of collagen extending out into the surrounding parenchyma in the plane of the basement membrane (figure 1). With increasing frequency after the 6th week, irregular alveolar collapse (figure 2) accompanied the development of sclerotic foci and was associated with variable overdistension of the non-involved alveoli. Evidence of both hypertrophy and hyperplasia of type 2 pneumocytes was seen sporadically in the early periods of exposure but in lungs exhibiting more marked focal sclerosis, decreased numbers together with vacuolation of surfactant lamellae of type 2 pneumocytes was a common feature. There was no evidence of such change in lung tissue obtained from the control animals.

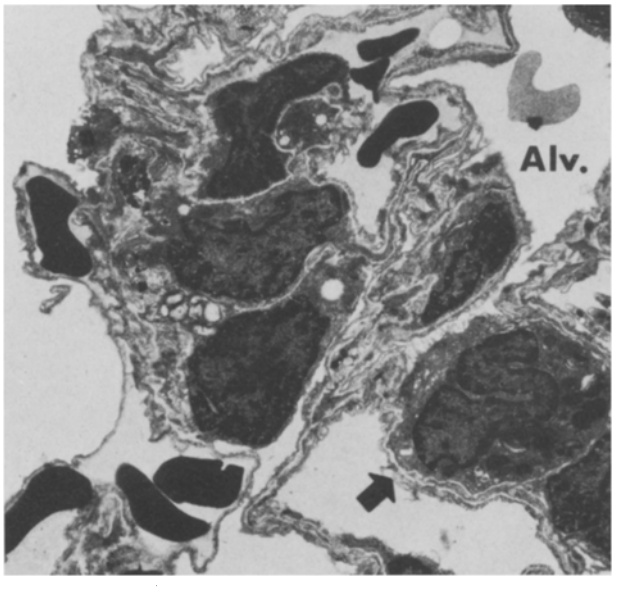

Fig. 1. Focus of interstitial fibrosis with distortion of alveolar pattern from lung of rat exposed to gasoline vapour for 10 weeks. A type 2 pneumocyte (arrow) is loculated within a collapsed alveolus (Alv.). Uranyl acetate and lead citrate. × 20,000.

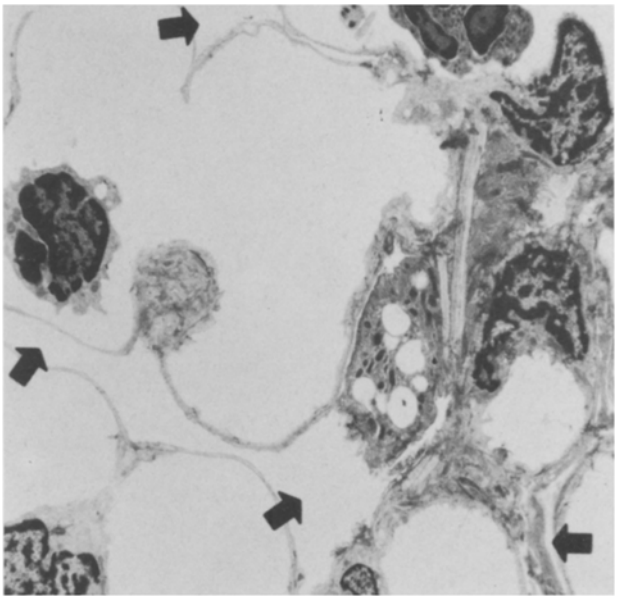

Fig. 2. Irregular interstitial fibrosis associated with collapse of alveolar spaces (arrows). The type 2 pneumocyte exhibits vacuolation of its surfactant lamellae. Uranyl acetate and lead citrate. × 20,000.

Animals exposed to gasoline vapour for more than 8 weeks exhibited a diminished tolerance characterised by prostration and tachypnea, from which animals usually recovered quickly when removed to a normal atmosphere. None of the animals exposed for less than 6 weeks showed unequivocal evidence of structural change in the lung.

Because of the rapidity with which lesions are induced in the lung of the rat exposed to gasoline vapour, this experimental technique provides an economical model for studying the sequential ultrastructural and biochemical events preceding the development of pulmonary fibrosis which might well provide an understanding of the pathogenesis of the enigmatic human syndrome of fibrosing alveolitis.

1 This work was supported by a grant from the National Health and Medical Research Council of Australia.