diffuse interstitial fibrosis with gradual increase in the density of the fibrous tissue, ultimately resulting in the replacement of most of the lung parenchyma by a dense collagen network surrounding distorted air spaces, many of which contain large clumps of granular pneumocytes which, in some areas, have lysed leaving foci of lipo-alveolar proteinosis.

The assessment of these lesions was based on 4 grades of fibrosis—minimal, slight, moderate and severe. Typical examples of slight, moderate and severe asbestosis are shown in Fig. 1–4. In addition, when carrying out the assessment it was found convenient to introduce the intermediate categories minimal/slight, slight/moderate and moderate/severe. The 7 resulting categories were scored 2–8 and the normal lung, in which there was no sign of asbestosis, was scored 1, and the assessments were averaged for each group of rats. The repeatability of this form of assessment was tested on 154 sections, reassessed in a different random order and 90% were assigned to within one category of the first reading.

Classification of tumours.—The tumours found in the lungs of rats after exposure to the various types of asbestos dusts were peripheral adenomata, widespread adenomatosis, adenocarcinomata and squamous carcinomata. The rarity of pulmonary tumours in rats has been stressed in the reviews by Kuschner and Laskin (1970) and Shabad and Pylev (1970). Further, these authors have described the development and morphological features of the tumours that we are reporting. All these tumours were peripheral and appeared to arise from the region of the respiratory bronchioles in which the asbestos fibre had accumulated.

The origin of the adenomata appeared to be from accumulation of type II epithelial cells that proliferated in the alveoli of the respiratory bronchioles (Fig. 5, 6). In many of the exposed animals these tumours were multiple, and in a number of animals, particularly those with the more severe grades of asbestosis, there seemed to be adenomata arising from numerous adjoining respiratory bronchioles, giving an impression of contiguous adenomata invading large areas of the lung. Dr Harold Stewart (personal communication) suggested that this type of lesion should be referred to as adenomatosis. In contrast to this, a few control animals were seen to have solitary adenomata which were small in size. The adenocarcinomata were of the same type and origin as the "alveolar adenocarcinomata" described by Shabad and Pylev (1970); many of these tumours were papillary adenoma–carcinomata. The squamous carcinomata appeared to originate from foci of squamous metaplasia occurring in the asbestotic lesions in the respiratory bronchioles (Fig. 7, 8). As far as can be ascertained, all these tumours were peripheral in origin and not bronchial papillomata. The classification of these tumours was discussed in some detail in Session VI at the Gatlinburg Conference on the Morphology of Experimental Respiratory Carcinogenesis in 1970; and the chapter by M. F. Stanton (1974) in the IARC Monograph on *Pathology of Tumours in Laboratory Animals* contains detailed descriptions of the tumours that we have illustrated.

The rats used in this experiment are from a caesarean derived, barrier maintained colony and fortunately they have been kept free of rat bronchitis; therefore the squamous metaplasia was not associated with bronchiectasis.

Metastases in the thoracic cavity to the chest wall, diaphragm, pericardium or the tracheo-bronchial lymph glands were seen in 14 animals; the majority had lesions invading 3 of the sites and in only 2 animals were metastases observed in the tracheobronchial glands. In one animal secondary deposits were seen in sections from a kidney. Eight adenocarcinomata and 6 squamous tumours had metastasized.

RESULTS

All except 2 of the rats in the groups with exposure of 12 months or less survived for the whole of their planned exposure. In the 24-month group there was appreciable mortality before the end of exposure and only 53% survived for the full period. Out of 1013 rats it was impossible to obtain adequate histological material in only 8 because of cannibalism.

Dust retention

The mean weights of asbestos dust in the lungs of animals killed at the

E. ×80.