

tial of mineral fibres and to serve as a substitute for animal studies.

Dr. HILLERDAL (Sweden) —→ Dr. MUHLE

Mice are not men, and investigations of the clearance of various inhalants in "healthy" smokers with chronic bronchitis actually show an increased clearance. So I doubt if your findings have any clinical importance for human beings.

Dr. MUHLE —→ Dr. HILLERDAL

The long-term lung clearance (alveolar clearance) investigated in our experiments resulted in a biological half-life of ca. 45 days. This important long-term clearance is also reduced in man after cigarette smoke inhalation, as indicate results of COHEN et al. (Science 204 (1979), p. 514). The experimental results concerning the effect of cigarette smoke on the short-term clearance are contradictory.

Dr. DUNNIGAN (Canada)

Does anyone know if adsorption of benzo(a)pyrene, present in cigarette smoke, would change the geometry of fibres?

I put this question in the light of the well recognized combined effects of asbestos and cigarette smoke. If the answer is no, then this would be another indication of the importance of surface chemistry of fibre reactivity

Dr. MUHLE

The multiplying effect of cigarette smoke and asbestos gives no evidence of the importance of the surface chemistry. Other mechanisms of the combined effect are possible, for example as described in our paper.

Mr. G.F. HERON (Great Britain)

I would like to suggest that this meeting gives more attention to the value and significance of animal experiments and in-vitro tests. Those of us who manufacture and sell asbestos products or their substitutes

rely on medical research, including animal experiments, to assess the relative harmful effects of existing and new fibres. I believe that animal experiments, (which must be used because we cannot do direct experiments exposing people to dust) may be giving us no correct answers - even where we choose animals - like the rat - which do at least produce the same diseases after fibre exposure - as man does, i.e. asbestosis, lung cancer - mesothelioma.

I would like to support my criticism of animal experiments and in-vitro tests by the following examples where I believe they do not rank the asbestos fibre in the correct order of harmful effect in man.

Amosite - was reported by Dr. DAVIS not to be carcinogenic to rats and yet the SELIKOFF studies of U.S. insulation workers and other studies show it to be highly carcinogenic in man.

Crocidolite - gives in-vitro test results which show that it is not very haemolytic nor very cytotoxic to many cell systems and it is ranked (by DAVIS and others) as only moderately carcinogenic to rats. Yet in man, as shown by the studies in South African mines and also the Nottingham (England) gas mask workers, it is very carcinogenic and gives a very high rate of formation of mesothelioma.

Chrysotile - by contrast - is shown by in-vitro tests to be very highly haemolytic, very cytotoxic to a number of cell systems (phagocytic and non-phagocytic) and is shown by some animal injection and inhalation experiments (DAVIS et al.) to be the most carcinogenic of all three commercial asbestos fibres. Yet human experience shows that it is much less implicated in the causation of mesothelioma (by studies of Canadian miners). Indeed many people believe that chrysotile does not cause mesothelioma.

These differences between man and animal need to be discussed and investigated. I believe they may be explained by the differences in solubility and dispersability of the fibre in the lung. Chrysotile is much more easily eliminated, but the very short life-span of the animal compared to man may not allow normal clearance/solution mechanisms to operate as they do during the much longer life-span in man. Tumours are generated only after a 20-40 year time-span in man. In rats they are generated in 1-2 years.

Dr. DAVIS

I believe that it is incorrect to talk of "anomalies" in this context. I believe that we have only one anomaly. In animal studies chrysotile appears to be much more dangerous than suggested by human studies.

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If chrysotile is excluded, then I believe that animal studies agree with human data and can be used to predict the relative harmfulness of a new material. In support of this suggestion I would point out that animal experiments show crocidolite to be more carcinogenic than amosite. I would also cite Dr. WAGNER's recent finding that erionite, which has produced an epidemic of human mesotheliomas in Italy, has caused by far the largest number of mesotheliomas so far found in an animal study.

Obviously it is extremely important to determine the results of animal studies using chrysotile as anomalous. At present, the most likely suggestion that while chrysotile is potentially the most carcinogenic of the main asbestos types, it does not remain long enough in human lungs to produce tumours. Future studies should aim to clarify this problem.
