

Pulmonary Tumors in Mice Exposed to Asbestos Dust

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Since the first case of carcinoma of the lung associated with asbestos was cited by Lynch and Smith in 1933,¹ there have been numerous reports in the literature of similar cases. Authors reviewing the literature describe an incidence of carcinoma of the lung associated with asbestosis ranging from 13% to 16%.²⁻⁴ Individual reports, usually dealing with relatively small numbers of cases, describe an incidence ranging from 2% to 50%.⁵⁻⁸ In an editorial in 1955, Huerper⁹ stated that 127 cases of asbestosis carcinoma of the lung were on record and described the occurrence of 114 cases of pulmonary carcinoma in 738 autopsies of asbestosis cases collected from the literature (1955).

Experimental work has not kept pace with the accumulation of clinical data. An increased incidence of pulmonary tumors has been recorded in mice following the subcutaneous injection,⁹ intratracheal injection,⁹ intravenous injection,¹⁰ and inhalation¹¹ of a variety of substances, but only one published statement has been found suggesting the induction of tumors in experimental animals by the inhalation of asbestos.¹²

The purpose of the investigation to be described in this report was to correlate, if possible, the effect of asbestos on the lungs of experimental animals with the suggested carcinogenicity for human subjects.

Received for publication Nov. 19, 1956.

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This work has been supported by a research grant, No. C-474, from the Public Health Service.

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Experimental Study

Animals.—Mice were selected for this work because the use of inbred strains would eliminate some of the uncertainties inherent in the use of other animals. Furthermore, the published report of Nordmann and Sörgel, which has been previously mentioned,¹² and unpublished data left by Dr. L. U. Gardner,¹³ of Sargass Laboratories, at his death suggested that mice might be suitable test animals. Dr. Gardner mentioned that of 22 mice inhaling short fiber asbestos for not more than 12 months, 3 (13%) developed lung tumors. Fifty-one mice exposed to other dusts for 10-12 months developed lung tumors in 2%. In both of these studies the number of animals used was small, and the strains employed were not mentioned or improperly varied.

In the study to be described, it was decided to use the F₁ generation offspring of Strain A male mice¹⁴ and Strain C female mice.¹⁵ It was felt that this hybrid strain would possess the genetic purity of the parent stock but would be harder and hence more suitable for long-term studies.

Strain A breeding stock was obtained from J. J. Blinn, of the University of Minnesota, and Strain C female breeding stock was obtained from Lloyd W. Law, of the National Cancer Institute. As soon as the Roscoe B. Jackson Memorial Laboratories had recovered from the disastrous fire of 1947, all breeding stock was obtained from that source.

AC7, animals from the breeding colony were divided into approximately equal groups, and at the age of 2 months one-half were placed in the cages exposed to asbestos dust. The other half were maintained as a control group. Male and female mice were kept in separate cages to avoid breeding in both the control and the dusted groups.

Of the hundreds of mice bred for this work, a great many succumbed to cannibalism, intercurrent infection, or other accidents, but 776 mice were subjected to perimortem examination. Of this number the largest groups were the control and test animals worked at 19 and 24 months of age. The observations in these groups will be emphasized in the discussion which follows.

In order to study larger animals with a tracheo-bronchial tree more comparable to that found in

DEPENDANT'S
EXHIBIT
USG-336

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