

STUDY OF EFFECT OF DIFFERENT KIND OF SHORT ASBESTOS ON LUNG OF RATS

YANG MEIYU • Zhao Jinduo • Ku Guihau • Zhao Xiuqing • Fu Bo • Zhang Jifang

Shenyang Research Institute of Industrial Hygiene and Occupational Disease, Shenyang, P.R. China

Asbestos has many properties which include acid and alkali resistance, fire resistance, and ability of electric resistance which make it indispensable in modern industry. It is well known that inhalation of asbestos dust can lead to pulmonary fibrosis and carcinoma of the lung or to the development of diffuse mesothelioma of the pleura and peritoneum. But the mechanism of asbestos carcinogenesis is not clear. Some authors believe that asbestos carcinogenesis depends on chemical action. Other authors think that the physical nature of asbestos fibre is the main factor. Especially long fibre asbestos is the main reason for either fibrosis or tumors of lung. In order to elucidate hazards of short asbestos fibre, an experiment study of effects of four kinds of short asbestos on lungs of rats was observed. (Figures 1-4)

MATERIALS AND METHODS

Dust

Chrysotile and crocidolite were obtained from a Shenyang asbestos processing factory and Qingdao No. 2 asbestos processing factory respectively. Tremolite and actinolite were obtained from mining department of a college. These fibres were prepared by grinding in a ceramic ball mill. The length and diameter distribution of these fibres were obtained by phase-contrast microscopy as in Table I. Morphology of fibres was observed by electron micrograph.

Animals

Wistar rats were used. Weights of rats were 180-220g with nearly equal number of male and female rats. They were divided into 5 groups: chrysotile, crocidolite, tremolite, actinolite and saline control group. There were seventy rats in each group. All rats were injected intratracheally with 20mg dusts suspended in 1 ml saline; one month later they were injected repeatedly with suspended dust of same dose. Total dose was 40 mg in each rat. Some rats were killed at the end of 2, 4, 6, 12 and 18 months respectively after the initial injection of dust. The one third rats were allowed to live out their full lifetime. The living condition of rats was observed. The body weight of rats was measured every other month. The wet and dry weight and collagen content of the lungs were determined. The lungs and hilar nodes were examined. The native death and the development of pulmonary neoplasms of the one third rats were observed.

RESULTS

The body weight of all the animals were increasing with time. There was no difference significantly among the experimental and control groups. The dry weights of lungs of rats in all groups are shown in Figure 5.

The increasing of wet weight and collagen of lungs was similar to that of dry weight of lungs, during the sixth to twelfth months after onset of injection dust. There was significant increasing of collagen in the lung. There was significant difference among experimental and control groups. The increasing of collagen in chrysotile group was the highest among the experimental groups as in Table II.

PATHOLOGY

Gross

There were a lot of small grey-white or brown-tan spots at the surface of lungs in every group, after 2-4 months of injection dust. In the crocidolite group, the spots often were grey-blue in color. There were obvious spots at the cut surface and slight pulmonary emphysema after 6-12 months. Lymph nodes in the experimental groups were larger and harder than those of control group, especially in the chrysotile group.

Microscopic Appearance

Chrysotile group: after 2-4 months, a lot of macrophages, dust cell, asbestos fibres and debris were seen in alveoli adjacent to respiratory bronchioles and there was increasing of reticulate fibre, thickness of bronchioles and arteriolas wall (Figures 6, 7). During 6-12 months, there was slight pulmonary emphysema, a few collagen fibres in the interstice (Figure 8). At the end of 18 months, these changes were similar to former. No asbestos bodies were found in the lungs. There were a few reticular fibres and dust in the lymph nodes (Figure 9).

In the tremolite and actinolite groups, pathologic changes were nearly the same and both slighter than chrysotile group (Figure 10).

Crocidolite group: Reaction of lung tissue was initially slighter than other experimental groups. Later there was also reticular fibres hyperplasia in pulmonary interstice.

At 18th months, the epithelium hyperplasia of bronchioles and alveolus in some rats was present in the crocidolite and chrysotile groups (Figure 11).

The incidence of pulmonary malignant tumor: The asbestos fibres produced pulmonary malignant tumor (the exclusion of spontaneous lymphoblastoma) in all experimental groups. No pulmonary malignant tumor happened in the control group. The first tumor was found in the chrysotile group; rat died after 15 months of injection dust. Later, two rats with cancer were found at 22 months after injection dust, two cases in the crocidolite group and one case in both tremolite and actinolite group separately, as in Table III and Figures 12, 13.

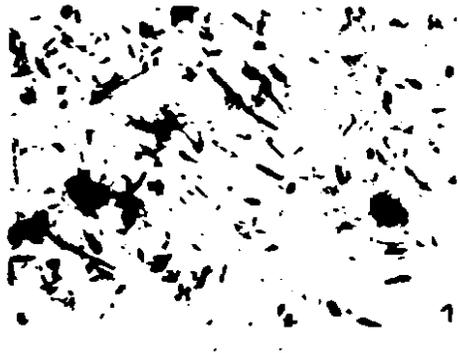


Figure 1. Electromicrograph of chrysotile ($\times 2500$).



Figure 3. Electromicrograph of tremolite ($\times 2500$).



Figure 2. Electromicrograph of crocidolite ($\times 2500$).



Figure 4. Electromicrograph of actinolite ($\times 2500$).

Table I
Length and Diameter Distribution of Different Asbestos and SiO₂

Asbestos Fibre	Length of fibre(%)					Fibre in diameter (%)					SiO ₂ %
	<3	-5	-10	-20	>20	<1.2	-1.6	-2.5	-5	>5	
Chrysotile	76	15	6	2	1	100					0.31
Crocidolite	88	8	3	1	0		100				4.7
Tremolite	88	6	3	3	0	19	55	20	4	2	0.13
Actinolite	76	14	7	2	1	26	55	11	6	2	0.34

Table II
Result of Collagen Content of Lungs in Every Group

Group	2			4			6			12			18		
	No. (T)	$\bar{X} \pm$ S.E. P)		No. (T)	$\bar{X} \pm$ S.E. P)		No. (T)	$\bar{X} \pm$ S.E. P)		No. (T)	$\bar{X} \pm$ S.E. P)		No. (T)	$\bar{X} \pm$ S.E. P)	
Cont	5	45.79 5.04		7	48.15 3.22		6	54.98 2.94		8	57.17 2.31		7	71.94 4.80	
Chr	4	53.66 3.74		5	68.40 6.40 (2.49, <0.05)		4	81.78 2.20 (6.59, <0.001)		8	80.10 1.40 (3.08, <0.01)		7	85.86 5.10	
Gro	4	35.59 2.70		6	48.64 2.33		6	55.89 3.37		8	72.26 6.29 (2.25, <0.05)		7	78.05 4.14	
Tre	4	49.20 3.88		5	53.30 6.46		6	69.30 3.93		8	71.20 4.21 (2.93, <0.01)		8	77.23 5.0	
Act	5	40.37 2.03		6	59.78 3.64 (2.32, <0.05)		5	71.71 6.70 (2.761, <0.05)		5	78.07 10.67 (2.396, <0.05)		6	79.10 5.18	

Table III
Pathologic Type and Time of Inducing Tumor

Group	No. of Animals	No. of Pulmonary Tumors	Time (Months)							
			15	17	19	21	23	25	27	
Chrysotile	38	3	sq					Fibro		Adeno
Crocidolite	39	2		Adeno				Fibro		
Tremolite	40	1					Adeno			
Actinolite	35	1				sq				
Control	38	0								

Sq, Squamous cell carcinoma;
Fibro, Fibrosarcoma;
Adeno, Adenocarcinoma;

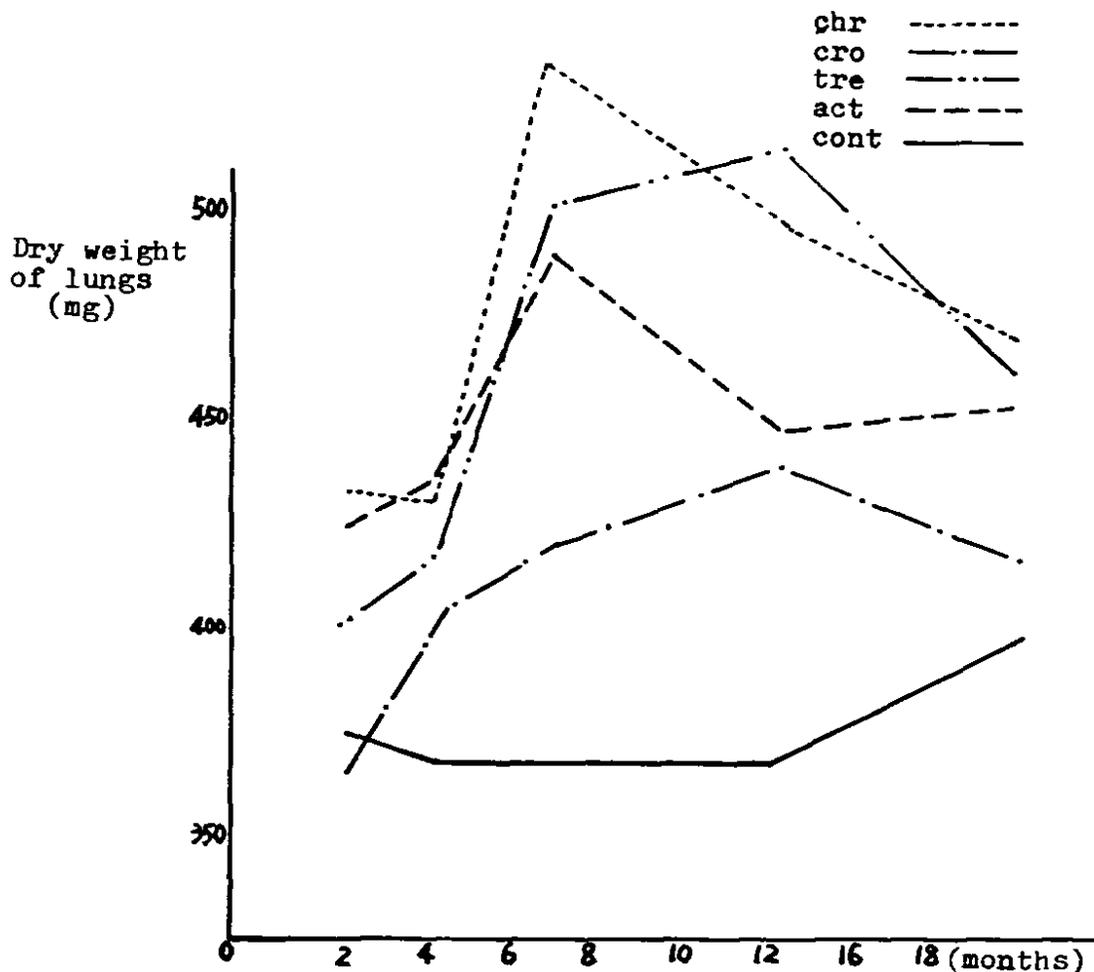


Figure 5. Changes of dry weight of lung in rats of every group.

DISCUSSION

For the different types of asbestos or the same asbestos type in different area, inhalation or injection asbestos can lead to various reaction of lung in the animal.^{1,2,3} In addition inhalation of same asbestos in different kinds of animals produced also various results. All four short asbestos in the experiment produced increasing of wet and dry weight of lung in rats. A lot of reticular fibres and a few collagen were found in the pulmonary interstice. These results correspond to Fu Shao Chang's report.^{4,5,6}

Inhalation of injection of asbestos fibres may produce pulmonary tumors.^{7,8,9} Seven rats with lung tumors in this experiment, the first lung tumor was found in a rat that had died at the 15th month after initial injection of chrysotile fibres. Most tumors were found during 21-25 months. No cancer happened in the control group. This experiment indicated that short asbestos fibres produced not only pulmonary fibrosis but also pulmonary cancer. This result corresponds with Gross's report. Besides, epithelium hyperplasia of bronchioles and alveoli was sometimes present. There changes were not seen in the control group. It seems possible that

pulmonary malignant tumors resulted from these changes.

Therefore, we hold that the effect of short fibre asbestos must be considered as recommended hygienic standard.

REFERENCES

1. Wagner, J.C., et al: Asbestosis in Experimental Animals. *Brit. J. Ind. Med.* 20:1-12 (1963).
2. Cooper, W.C., et al: Asbestos as a Hazard to Health. *Brit. Arch. Environ. Health* 15:285-289 (1967).
3. Gross, Paul, et al: Experimental Asbestosis. *Arch. Environ. Health* 15:343-355 (1967).
4. Fu Shaochang, et al: Experimental Study of the Effect of Asbestos on Lung of Rats. *J. Hyg. Res.* 10:118 (1981)..
5. Zhu Huilan, et al: An Experimental Study of Crocidolite-induced Fibrosis of Rat Lung. *Chinese J. Ind. Hyg. Occup. Dis.* 3:279-281 (1985).
6. Li Hongyang, et al: Pathological Changes of Lungs in Dogs Exposed to Asbestos under Mining Condition. *Chinese J. Ind. Hyg. Occup. Dis.* 2:138-141 (1984).
7. Wagner, J.C., et al: The Effect of the Inhalation of Asbestos in Rats. *Brit. J. Cancer* 29:252 (1974).
8. Shabad, L.M., et al: Experimental Studies on Asbestos Carcinogenicity. *J. Natl. Cancer Inst.* 52:1175-1187 (1974).
9. Davis, J.M.G., et al: Mass and Number of Fibres in the Pathogenesis of Asbestos-related Lung Disease in Rat. *Chinese J. Ind. Hyg. Occup. Dis.* 2:138-141 (1984).

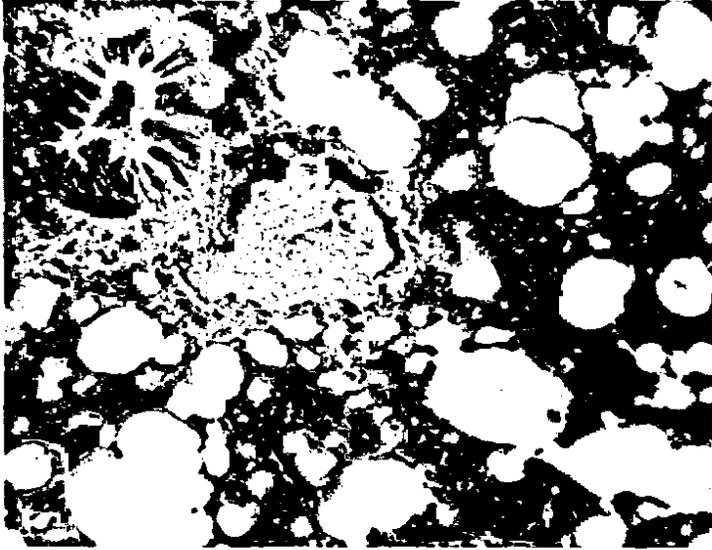


Figure 6. Chrysotile: Extensive areas of reticular fibre abutting on the terminal bronchioles and involving respiratory bronchioles. At the 2 months after injection of dust (H.E. $\times 78$).

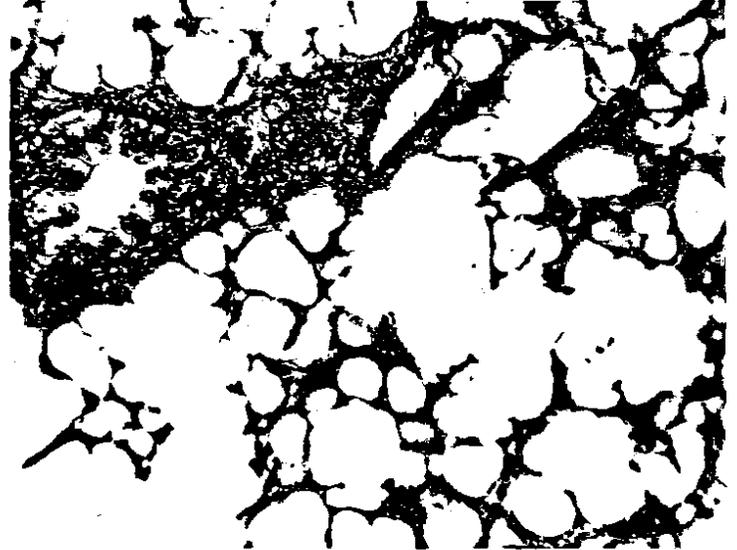


Figure 8. Chrysotile: Slight centrilobular emphysema and slight thickening of alveolar wall in different areas of the lungs. 6 months (G.S. $\times 78$).

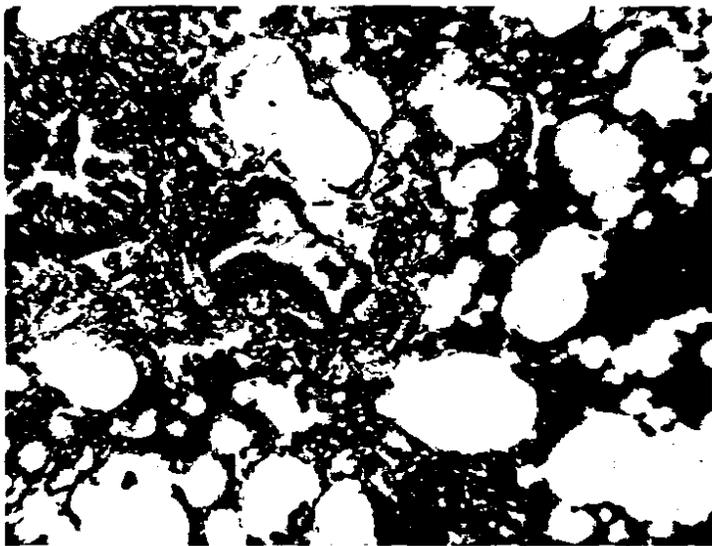


Figure 7. Bid (G.S. $\times 78$).

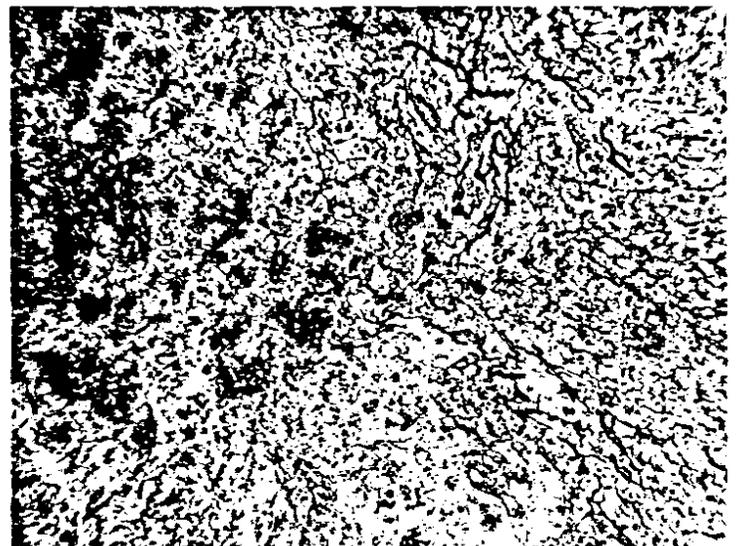


Figure 9. Chrysotile lymph node: Many more reticular fibres. 18 months (G.S. $\times 78$).

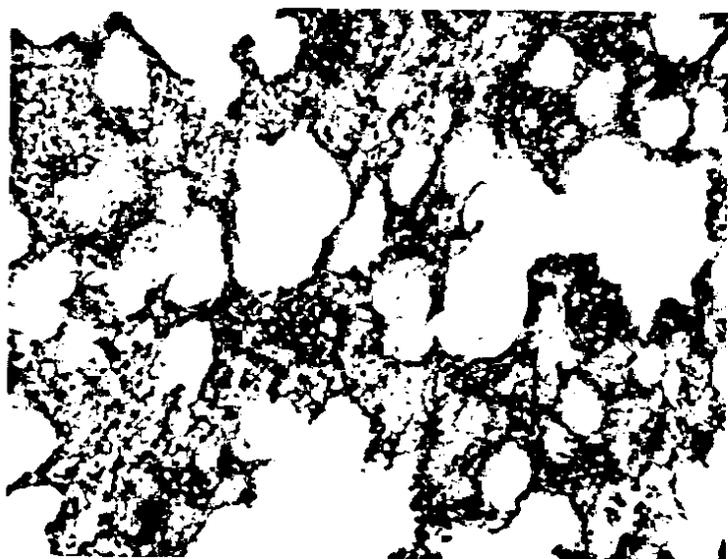


Figure 10. Tremolite: Extensive reticular fibres in pulmonary interstice. 12 months. (G.S. $\times 78$).

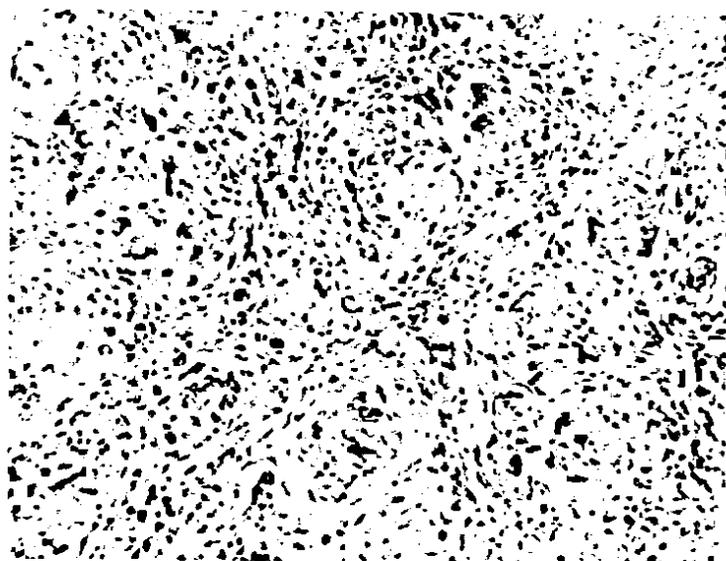


Figure 12. Chrysotile: Squamous cell carcinoma. 15 months (H.E. $\times 78$).

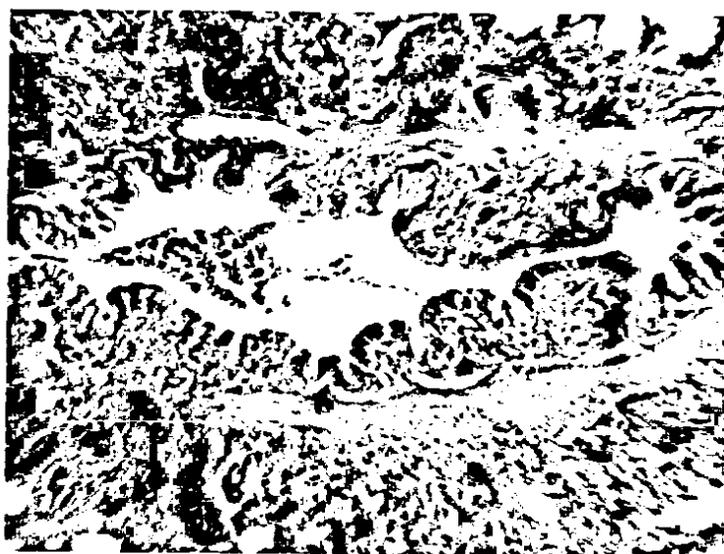


Figure 11. Chrysotile: Epithelium hyperplasia of bronchioles. 18 months (H.E. $\times 120$).

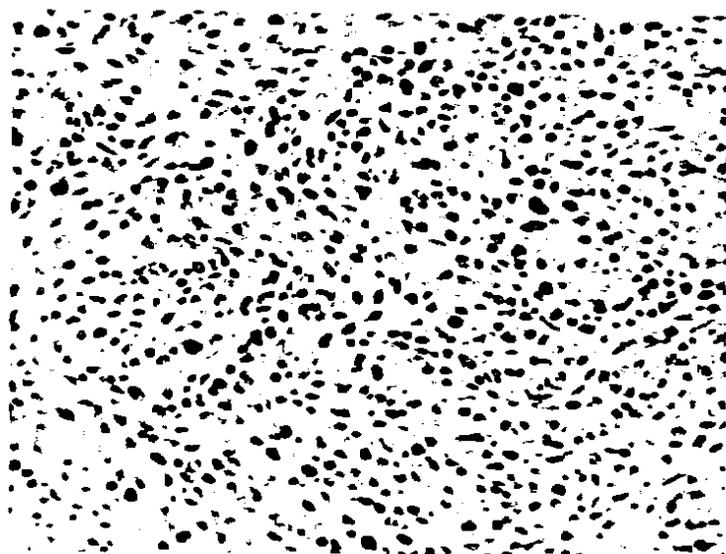
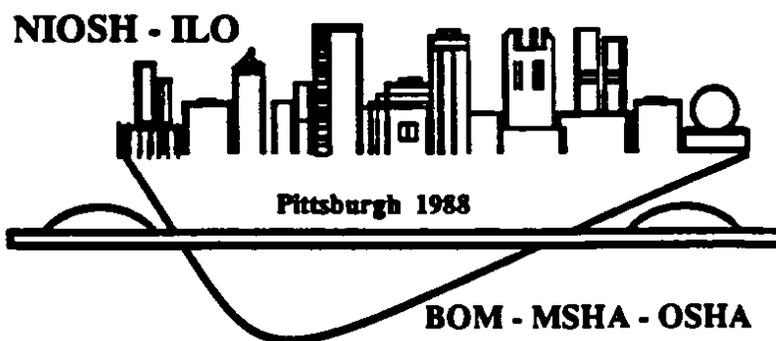


Figure 13. Chrysotile: Fibrosarcoma. 22 months (H.E. $\times 78$).

Proceedings of the VIIth International Pneumoconioses Conference Part
Transactions de la VIIe Conférence Internationale sur les Pneumoconioses Tome
Transaciones de la VIIa Conferencia Internacional sobre las Neumoconiosis Parte

II



Pittsburgh, Pennsylvania, USA—August 23–26, 1988
Pittsburgh, Pennsylvanie, Etats-Unis—23–26 aout 1988
Pittsburgh, Pennsylvania EE. UU—23–26 de agosto de 1988



U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
Public Health Service
Centers for Disease Control
National Institute for Occupational Safety and Health



Sponsors

**International Labour Office (ILO)
National Institute for Occupational Safety and Health (NIOSH)
Mine Safety and Health Administration (MSHA)
Occupational Safety and Health Administration (OSHA)
Bureau of Mines (BOM)**

November 1990

DISCLAIMER

Sponsorship of this conference and these proceedings by the sponsoring organizations does not constitute endorsement of the views expressed or recommendation for the use of any commercial product, commodity, or service mentioned.

The opinions and conclusions expressed herein are those of the authors and not the sponsoring organizations.

DHHS (NIOSH) Publication No. 90-108 Part II