

Review of Published Studies of Orally Administered Asbestos

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There has been great public concern about the adverse health effects resulting from the presence of asbestos fibers in municipal drinking water supplies. This article reviews and summarizes the experimental findings of 11 published papers that have evaluated the carcinogenic potential of asbestos following its ingestion. The long-term, high-level ingestion of various types of asbestos fibers in more than one animal species failed to produce any definite, reproducible, organ-specific carcinogenic effect.

Introduction

Prolonged industrial human exposure to asbestos has been associated with an increase in the incidence of certain forms of cancer. The relationship between inhaled asbestos and mesotheliomas of the pleura and peritoneum or pulmonary carcinoma is particularly strong; other cancers have also been implicated from inhaled asbestos (1-3). In order to explain why cancer may occur at remote sites following the inhalation of asbestos, it has been suggested that the asbestos fibers that are cleared from the lungs are swallowed and subsequently migrate through the gastrointestinal wall to the peritoneum where cancer may be initiated.

Originally the question of pathogenicity from asbestos exposure had relevance only to people occupationally exposed, but the discovery of amphibole fibers in municipal water supplies (4) indicated that asbestos was more widely dispersed through the environment than once believed. Asbestos from natural sources, as well as from mining activities, has been shown to contaminate bodies of water that are used as sources of drinking water. Asbestos fibers have been detected in commercial beverages, possibly resulting from the use of asbestos filters. The extensive use of asbestos cement pipe in municipal water systems has concerned officials of the U.S. Environmental Protection Agency. This paper summa-

rizes the various published asbestos ingestion studies that have attempted to answer the question of whether or not ingested asbestos is a health hazard. Other relevant topics such as gastrointestinal penetration by asbestos, the presence of asbestos in municipal drinking water supplies, and epidemiologic studies will be presented in subsequent papers of this workshop. The details of all but one of the cited experimental studies are summarized in Table 1.

Results of Published Studies

An abstract by Bonser and Clayson (5) initially reported experimental findings from an ingestion study. Asbestos was administered to Sprague-Dawley rats in their feed at a level of 0.15%. No malignant tumors were observed in the exposed animals, which may have been due to the low level of asbestos administered. The high mortality of the rats due to pulmonary infection seriously compromised the study.

Webster reported the only study conducted with primates (6). Because of lack of experimental detail, the findings of this article were omitted from Table 1. An unreported number of baboons were exposed to "heavy" concentrations of asbestos in food and drinking water for up to 5 yr. There was no evidence of any peritoneal or gastrointestinal tumors. The 5-yr exposure time appears too short for the carcinogenesis process to occur if the time element of the baboon's reaction to asbestos is similar to that of a human.

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Table 1. Summary of asbestos ingestion studies (continued).

Study	Species	Test material	Dose	Exposure time	Study duration	Number of animals, Initial/Examined	Malignant tumors		
							Number	Location	Type
Wagner (10)	Rat	Chrysotile	100 mg/day	101 days/ 5 mo.	619*	32/32	3	Node Stomach Uterus	L S S
		Talc	100 mg/day	101 days/ 5 mo.	614*	32/32	3	2 Uterus Stomach	S S
		Control	0	0	641*	16/16	0		
Smith (11)	Hamster	Amosite	0.5 mg/L <i>ad libitum</i>	To 23 mo.	To 23 mo.	60/60	1	Lung	C
		Amosite	5 mg/L <i>ad libitum</i>	To 23 mo.	To 23 mo.	60/60	3	2 Stomach Peritoneal mesothelioma	C
		Amosite	50 mg/L <i>ad libitum</i>	To 23 mo.	To 23 mo.	60/60	0		
		Taconite tailings	0.5 mg/L <i>ad libitum</i>	To 23 mo.	To 23 mo.	60/60	1	Uterus	S
		Taconite tailings	5 mg/L <i>ad libitum</i>	To 23 mo.	To 23 mo.	60/60	0		
		Taconite tailings	50 mg/L <i>ad libitum</i>	To 23 mo.	To 23 mo.	60/60	0		
		Control	0	0	To 23 mo.	120/120	1	Node	L
Donham (12)	Rat	Chrysotile	10% in diet <i>ad libitum</i>	To 32 mo.	To 32 mo.	240/189	4	3 Colon Abdominal mesothelioma	C
		Cellulose fiber	10% in diet <i>ad libitum</i>	To 32 mo.	To 32 mo.	242/197	2	Colon	C
		Control	0	0	To 32 mo.	121/115	3	Colon	C
Ward (13)	Rat	Azoxymethane	7.4 mg/kg wk	10 wk	34 wk	21/21	12	5 Ileum 7 Colon	C C
		Azoxymethane plus amosite	7.4 mg/kg wk 10 mg 3/wk	10 wk	34 wk	21/18	10	3 Ileum 7 Colon	C C
		Azoxymethane plus chrysotile	7.4 mg/kg wk 10 mg 3/wk	10 wk	34 wk	21/21	10	4 Ileum 6 Colon	C C

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Table 1. Summary of asbestos ingestion studies (continued).

Study	Species	Test material	Dose	Exposure time	Study duration	Number of animals, Initial/Examined	Malignant tumors		
							Number	Location	Type ^a
Bolton (15)	Rat	Amosite	250 mg/wk	25 mo.	Life	24/24	1	Stomach	S
		Crocidolite ^b	250 mg/wk	25 mo.	Life	22/22	1	Adrenal	C
		Chrysotile	250 mg/wk	25 mo.	Life	22/22	5	Fat	S
								Pleural histiocytoma,	
								2 Adrenal Plasma cell tumor	C
		Margarine control	0	0	Life	24/24	4	2 Adrenal Bladder Peritoneum	C C S
		Control	0	0	Life	23/23	2	Fat Lymphoma	S

^aType C = carcinoma; S = sarcoma; L = lymphoma.

^bMean survival time in days.

^cAzoxymethane given subcutaneously; saline administered by oral gavage or subcutaneously.

^dmfl = million amphibole fibers/L.

The results of a series of feeding experiments with different sources of chrysotile and crocidolite were reported by Gross et al. (7). This paper incorporated data from unpublished results of various studies conducted by three laboratories. Animals fed asbestos by gavage in butter or margarine for up to 21 months failed to provide evidence of a carcinogenic effect. The experiments were flawed for the following reasons: the number of rats in the experimental groups was small, the doses of asbestos were limited, significant information on experimental protocol was missing, and systematic histologic examination was not performed on a significant number of rats.

A study by Gibel et al. (8) was undertaken to feed asbestos filter material to rats because of the concern of the possible adverse health effects of erosion of asbestos from the filters used to purify commercial beverages. The filter material was composed of sulfated cellulose, a condensation resin and chrysotile asbestos (53%). The authors did not provide any information regarding the size and shape of the asbestos fibers that were incorporated into the filter material. Although 12 malignant tumors were noted in the asbestos-exposed group of rats and the mean survival time was decreased in the asbestos-treated group, the authors stated that no conclusions could be made from their test results regarding the pathogenesis of the tumors caused by the oral intake of asbes-

tos material. The relationship of this study to asbestos carcinogenicity was also confounded by the presence of several substances in the filter material, which were not clearly identified.

Cunningham and co-workers (9) conducted two limited feeding studies with male Wistar rats. Chrysotile asbestos (1% with 5% corn oil) was added to rat chow and fed to the animals for 24 months or 30 months. In the first study, 10 rats were exposed to asbestos. Six of the seven rats autopsied were found to have tumors, while only one malignancy was observed in the control animals. In the larger study of 80 animals, equal numbers of malignant tumors were noted in the exposed and the control groups. The authors stated that trace amounts of asbestos can penetrate the walls of the gastrointestinal tract, but evidence that asbestos causes cancer by the oral route of administration was inconclusive.

Wagner et al. (10) fed 32 Wistar rats 100 mg/day of chrysotile or talc in malted milk for 101 days over a 5-month period. A slight decrease in survival time was observed in the two experimental groups. One gastric leiomyosarcoma was detected in each exposure group. Interpretation of the results of this experiment is difficult because of the small number of animals included in the study.

A study in Smith's laboratory (11), which was the first study to utilize a large number of ani-

One can question the suitability of the animal models employed in evaluating the human response to oral exposure to asbestos, since sufficient time may be lacking between exposure and the development of malignancies during the animal's lifetime. However, exposure to asbestos by other routes has induced cancer in rats. For example, Wagner et al. (17) reported the development of lung cancer and mesothelioma from brief to lengthy inhalation exposure to various types of asbestos, while Gross (18) reported asbestotic lung cancers in 25 of 72 rats that survived 16 months of exposure to chrysotile dust. Based on the carcinogenic effects of asbestos from nonoral exposure routes (2,3), one would expect to be able to produce a neoplastic response within the lifetime of conventional laboratory animals with massive doses of ingested asbestos such as those employed in some of the studies mentioned in this paper. These studies also cast some doubt on the hypothesis that peritoneal mesotheliomas and gastrointestinal cancers result from the ingestion of asbestos fibers cleared from the lungs following inhalation exposure.

The research described in this paper has been peer and administratively reviewed by the U.S. Environmental Protection Agency and approved for presentation and publication. Mention of trade names or commercial products does not constitute endorsement of recommendation for use.

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