Commentary

Human Cancer Risk from Ingested Asbestos: A Problem of Uncertainty

by William J. Nicholson*

Human Health Effects

Although studies of populations exposed to high concentrations of asbestos fibers in drinking water appear attractive as research opportunities to define an asbestos-related risk, they are unlikely to provide a definitive answer to the question of whether asbestos in drinking water is associated with an elevated risk of malignancy. Consider, for example, a hypothetical 10-yr analysis of the deaths in a city of 1 million persons whose water supply is contaminated with 100 million fibers per liter (f/L) (a gross overestimate of any real situation). From the estimates in the asbestos criteria document (*1*), ingestion of this water over a 70-yr period would give rise to an added risk of death 3.3×10^{-3} per person.

To estimate the number of asbestos-related deaths in this population, using the above risk data, assume that the average residence time of those deceased in the contaminated area is 14 yr and that the distribution of residence times follows an exponential function, exp $\{t/14\}$. This distribution will certainly overestimate residence times compared with actual populations. Nearly half the census tracts in the U.S. EPA-sponsored San Francisco study, for example, showed more than 53% of the residents moving within 5 yr (*2*). Assume also that 7 yr is required for the risk of asbestos malignancy to manifest itself, as is the case for lung cancer. (See Fig. 1 for the expression of the relative risk of lung cancer in insulators.) This would appear to be so for gastrointestinal cancer (Fig. 2), but will lead to significant overestimates of risk for peritoneal mesothelioma because most such tumors do not appear until after 30 yr or more from first exposure. Approximately

100,000 deaths would be available for analysis over a 10-yr period from a population of 1 million persons. Table 1 lists the excess malignancies expected in this population from the above risk for each period of residence. Those alive will also carry a similar lifetime risk as they achieve the same exposure circumstances.
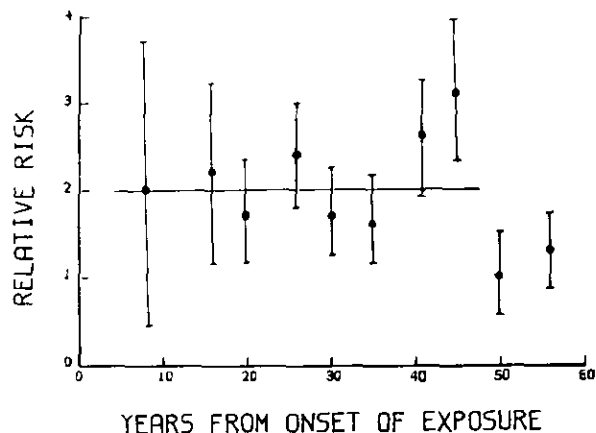

FIGURE 1. Relative risk of lung cancer due to asbestos in insulators.
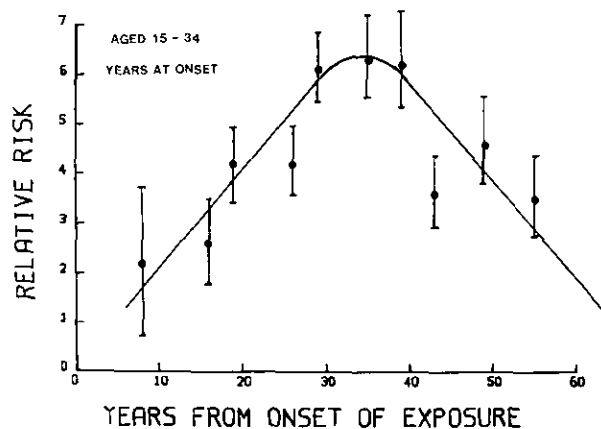

FIGURE 2. Relative risk of gastrointestinal cancer due to asbestos in insulators.

*Environmental Sciences Laboratory, Mount Sinai School of Medicine, City University of New York, New York, NY 10029.

Table 1. Estimated number of excess cancers in 100,000 deceased individuals.

Years exposed	Number exposed ($\times$ 1000)	Lifetime risk ($\times$ 10-4)	Excess deaths
0–6	39.4	0	0.0
7–13	22.7	1.6	3.6
14–20	15.6	4.9	7.6
21–27	8.8	7.2	6.3
28–34	5.3	10.5	5.6
35–41	3.2	14.8	4.7
42–48	2.1	18.1	3.8
49–55	1.2	21.4	2.6
56–62	0.7	24.7	1.7
63–65	0.5	28.0	1.4
70+	0.6	35.0	2.1
		Total	39.5

To simplify the calculations, the excess lifetime risk of the 900,000 alive will be attributed at the time of their deaths and will occur over the ensuing decades. As can be seen, the total additional cancers to be expected in this group is about 40. A cruder, but more direct, calculation is as follows:

$$\left[10^6\right] \times \left[3.3 \times 10^{-3} \times \frac{14}{70}\right] \times \left[\frac{10}{70}\right] = 94$$

Population   Average lifetime   Fraction of
exposed   risk from 14 yr   lifetime for
            of exposure   observation

The more detailed calculation takes better account of the population age distribution (less than 1% die annually, rather than 1/70) and more explicitly accounts for movement out of the area and death elsewhere (within the framework of the assumptions of the model).

If the distribution of excess malignancies parallels that of the working groups on which the risk estimates were made, 17 would be excess gastrointestinal tumors and 23 would be peritoneal mesotheliomas. However, since the risk estimates were based on mortality established by a review of all pathological material, the number of peritoneal mesotheliomas expected on death certificates would be no more than half a dozen. As can be seen, the low yield of excess malignancies expected in such a study would not achieve statistical significance. The expected number of gastrointestinal cancers would be about 4,100 in this population. Since the standard deviation of the expected number is 64, a study as described would show a statistically significant result only if the risk of the fiber concentrations were 7.5 times greater or if the population available for observation were 50 times greater. Thus, the upper limit of risk that can be established by negative studies

will be much higher than the risk estimated in the U.S. EPA criteria document (1).

The problem of confounding exposures is also of consequence. The excess projected could be accounted for by the excess mortality from a single shipyard employing 20,000 individuals in the study area (with no such facility in a control area). It is a happenstance coincidence that areas with high concentrations of asbestos in public water supplies also were (and continue to be) major shipbuilding areas. For example, the maximum shipyard employment in the combined San Francisco Bay–Puget Sound areas during World War II exceeded 300,000. Unless shipyard employment is specifically considered, e.g., by careful histories in a case-control analysis, positive studies on ingested water cannot be accepted uncritically.

Animal Studies and Carcinogenic Mechanisms

There is strong evidence that asbestos acts as a promoter for lung cancer in humans and probably in the same way for gastrointestinal cancer as well. In contrast, the fibers appear to act as initiators in the production of mesothelioma. Thus, the analysis of current animal studies should account for these different modes of carcinogenic action. In particular, species otherwise at low risk for gastrointestinal cancer are unlikely to show a significant asbestos effect if asbestos is acting as a promoter. The difference between humans and animals is particularly evident in the history of asbestos lung cancer research. In 1935, it was suggested that bronchogenic carcinoma was related to asbestos (3) and, in the forties, this was shown to be so (4). However, this was not demonstrated in animals until 1967. The synergistic effect of cigarette smoke, which acts as an inhibitor in humans, was not present in animal studies.

Control Strategies

The risk of asbestos cancer from ingestion cannot be verified by population studies, and animal experiments involve interspecies comparisons that are uncertain. Nevertheless, human data, albeit from a different exposure route, suggest significant risk for fiber exposures approaching 100 million fibers/L. Standard flocculation and sedimentation techniques can reduce asbestos concentration by about 90%. Such techniques should be adopted in areas with enormous fiber concentrations, since their cost (amortized over time) is relatively modest. Similarly, in aggres-

sive water systems shown to leach asbestos from asbestos-cement (AC) pipes, the water can be chemically treated to reduce the erosion, and new AC pipes can be coated to ensure safety from erosion.

Consider a system having 100 million fibers/L. In a population of 100,000 at exposure equilibrium,

$$\frac{100{,}000 \times 3.3 \times 10^{-3}}{70} = 4.7 \text{ deaths/yr}$$

might occur annually. While the potential deaths would, in general, occur out of the exposure area due to population mobility, their number could certainly justify the necessary system costs.

REFERENCES

1. U.S. Environmental Protection Agency. Water Quality Criteria: asbestos. NTIS, Springfield, VA, EPA 440/5-80-022.
2. Conforti, P. M., Kanarek, M. S., Jackson, L. A., Cooper, R. C., and Murchio, J. C. Asbestos in drinking water and cancer in the San Francisco Bay Area 1969-1974 incidence. J. Chron. Dis. 34: 211–224 (1981).
3. Gloyne, S. R. Two cases of squamous carcinoma of the lung occurring in asbestosis. Tubercule 17: 5–10 (1935).
4. Holleb, H. B., and Angrist, A. Bronchogenic carcinoma in association with pulmonary asbestosis. Am. J. Pathol. 18: 123–131 (1942).
5. Gross, P., and Harley, R. A. Experimental asbestosis: the development of lung cancer in rats with pulmonary deposits of chrysotile asbestos dust. Arch. Environ. Health 15: 343–355 (1967).