Letters

NIH Director: Recommendations

The Advisory Committee on the National Institutes of Health (NIH)* to the secretary of Health and Human Services (HHS) was asked to identify ways to enhance and strengthen the position of the NIH director, and thereby the NIH itself. This it did with remarkable unanimity and a real sense of urgency throughout four meetings, starting in December 1989. Simultaneously, a search committee was working and has now produced a short list of candidates for the second time (News & Comment, 20 Apr., p. 296). Nevertheless, the fate of the recommendations of the advisory committee is uncertain. A substantial number of the committee members came away from the final meeting on 25 April pessimistic about the possibility that the recommended changes would be made in time to encourage outstanding candidates to consider accepting the director's job.

Depoliticization of the job was topmost on the advisory committee's agenda. Last summer's fiasco, stemming from a White House test of a candidate's views on abortion, was only the most recent illustration of the need to reassert the fundamentally scientific responsibilities of the position. The committee recommended that, like the National Science Foundation (NSF) director, the NIH director be appointed for a 6-year term, renewable. This would require legislation.

The advisory committee urged that the NIH director have substantially increased authorities, including final appointment power for senior NIH scientific and administrative staff and for scientific appointments to NIH advisory committees, councils, and boards. Currently, the secretary of HHS has these authorities, and they could be delegated without legislation. A $20-million-dollar discretionary fund and the authority to transfer up to 1% of the budgets of the individual institutes would substantially improve the director's ability to provide leadership to biomedical research especially in times of emergencies, such as the AIDS crisis.

Adequate salary and compensation also received important attention. Current policy sets the director's salary at $83,600 (Executive Level IV), which is below the level for the director of NSF (Executive Level II, $96,500), the medical director, Department of Veteran's Affairs (Executive Level III and extra bonuses, $116,500), and the head of the Uniformed Services University of the Health Sciences (salary set at 50 to 70% of the mean paid to medical school deans in the northeast). An NIH director who chooses to be in the Public Health Service Commissioned Corps would be somewhat better compensated: approximately $98,000. Changes in compensation also require legislation.

By modifying the job description, the NIH director could become the HHS secretary's principal adviser on science policy and biomedical research program planning. Most biomedical scientists, both here and abroad, will probably be surprised to learn that the NIH director does not now hold that position. Indeed, the whole current picture, including salary, authority, and budget, hardly fits most people's concept of the NIH as the preeminent biomedical research institution in the world.

Neither HHS Secretary Louis Sullivan (who attended, briefly, only some of the meetings), nor committee chairman James O. Mason gave any indication of how they will react to the recommendations. Yet, a prompt and determined effort by the HHS secretary to effect the advisory committee's recommendations could rectify the disparity between the significance of the NIH directorship and the current reality. This effort is urgently needed if an outstanding biomedical scientist is to be successfully recruited as the next director. After 8 months without a director, the need for a timely appointment is obvious. Leadership is needed to deal with the current crisis in grant funding as well as the deteriorating morale of the intramural staff, not to mention myriad research policy issues. If the effort is not made, or fails, then perhaps it will be wisest to work to establish the NIH as an independent agency, like the NSF, so that our nation's splendid biomedical research effort is not continuously threatened by irrelevant bureaucratic and political considerations.

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Asbestos, Carcinogenicity, and Public Policy

Brooke Mossman *et al.*, in their generally excellent and informative article "Asbestos: Scientific developments and implications for public policy" (19 Jan., p. 294), propose that occupants of public buildings need not be concerned about chrysotile asbestos fibers when airborne fiber counts are low. The authors also state, "relatively young asbestos removal workers . . . should be protected." I am not sure that one can have it both ways, since in the last sentence of their paper Mossman *et al.* "acknowledg[e] that brief, intense exposures to asbestos might occur in custodians and service workers in buildings with severely damaged ACM [asbestos-containing materials]." The problem is that two essential elements are ignored in these conclusions: (i) a body of experimental data which shows that brief (1- to 3-hour), intense exposures to chrysotile asbestos fibers cause inflammatory, proliferative, and fibrogenic lesions in rats and mice within 48 hours after exposure (*1*), and (ii) damaged ACM is likely to leave on the top of false ceilings, pipes, and beams deposits of fibers that would not be found in routine airborne counts, but which could easily be aerosolized by numerous activities and could subsequently provide opportunities for the "brief, intense exposures." No one knows how many light bulbs a janitor must change or how many dusty corners a teacher must venture into before brief, intense exposures to chrysotile fibers will elicit a significant pathobiological response in the lung. The animal experiments suggest that only one such exposure is necessary; corresponding data for human exposures are not available. Thus, I am not convinced that it is prudent to consider chrysotile asbestos fibers innocuous and to leave ACM in situations where they eventually will deteriorate and provide a legacy for future generations of students, custodians, and removal workers. The authors make an excellent case for being cautious about unwarranted removal practices, but let us not think there is no problem just because airborne fiber counts in buildings are low.

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REFERENCES

1. L. Y. Chang, L. H. Overby, A. R. Brody, J. D. Crapo, *Am. J. Pathol.* **131**, 56 (1988); A. R. Brody and L. H. Overby, *ibid.* **134**, 133 (1989); P. D. McGavran, L. M. Moore, A. R. Brody, *ibid.* **136**, 695 (1990).

There may have been good reason not to let the reader know of the long-term asbestos industry associations of at least four of the five authors of the polemical article by Mossman and her coauthors, in which they advise that this industry not be required to remove asbestos from schools and public

buildings. Perhaps we can be told why this happened.

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The article by Mossman *et al.* is likely to mislead both the public and the scientific community about certain important issues concerning chrysotile asbestos. Since more than 95% of the asbestos used in the United States was chrysotile, this misdirection could have serious implications for public planning of the management of the asbestos in place in buildings throughout the United States. We present here a more complete discussion of some of the issues raised by Mossman *et al.*

Mossman *et al.* subscribe to the so-called "amphibole hypothesis," which they use to suggest that little, if any, cancer risk arises from exposure to chrysotile asbestos. They argue that the amphibole forms of asbestos—tremolite, amosite, and crocidolite—have substantially greater carcinogenic potential than chrysotile asbestos. They dismiss the "67 or more" mesothelioma cases that have occurred among Quebec chrysotile asbestos miners and millers (*1*) as "attributable to fibrous tremolite" because the lung burdens of tremolite in these individuals were higher than those of chrysotile. We believe that, as a parameter predictive of mesothelioma, "lung burdens" of fiber types are nearly worthless. As noted by Mossman *et al.*, chrysotile is a labile mineral that may disappear from lung tissue years before postmortem analysis is done. (Of course, the relevant carcinogenic mutations almost certainly occur years before cancer is detected.) This disappearance occurs because chrysotile, in contrast to amphibole minerals, splits apart longitudinally in tissue and can partially dissolve in body fluids. Mossman *et al.* imply that it is the 1% tremolite contamination of the chrysotile asbestos breathed by the miners and millers that caused the mesothelioma. We believe this argument is specious. Since the tremolite burden is proportional to the amount of chrysotile inhaled, it is also a measure of chrysotile dose. Thus, there is as strong a correlation with chrysotile dose as with tremolite burden.

The fallaciousness of the tissue burden argument can be seen further by considering mortality studies of asbestos-exposed workers when the results are analyzed in terms of exposure; it is essential to compare the risks of different fibers in terms of exposure. In

four studies (*2*) of asbestos-textile production workers, the exposure was primarily to chrysotile asbestos; the percentage of nonchrysotile fiber ranged from 0 to 2%, plus an additional 1% of tremolite contamination. In these studies the percentage increased in lung cancer ranged from 1.0 to 2.8% per fiber-year per cubic centimeter of cumulative exposure (*3*). In five other studies (*4*) where workers were exposed to asbestos containing 100% amosite—an amphibole, 60% chrysotile plus 40% amosite, and 80 to 90% chrysotile plus 10 to 20% crocidolite, amosite, or both, the risk of lung cancer per fiber exposure was the same as that for the predominantly chrysotile exposures, within the statistical uncertainties of the data. It ranged from 0.5 to 4.3% per fiber-year per cubic centimeter for mixed chrysotile-amphibole exposure circumstances. Even a pure crocidolite exposure to miners demonstrated a similar risk—2.1 to 5.8% increase per fiber-year per cubic centimeter (*5*). Were the "amphibole hypothesis" correct, the risks of cancer in the asbestos textile studies would have been up to 100-fold less than were seen. Mossman *et al.* suggest the high risks might be due to "solvents and oils used in textile production." There is no evidence for this.

There is a significantly lower lung cancer risk per fiber exposure associated with chrysotile mining and milling (*6*) than that associated with textile production in which only chrysotile (as mined) or predominantly chrysotile are used. The reason for this difference is not fully understood, but some, perhaps all, of the greater risk in textile mills may result from the presence of a greater percentage of thin, uncounted, but highly carcinogenic fibers that are produced during textile production in the carding process and in the high-speed spinning and weaving processes, where thin fibers may split off from the threads.

Similarly, the risk of mesothelioma per fiber exposure in three studies, where it can be estimated directly from exposure and incidence data, is identical to that for exposures to 98% chrysotile plus 2% crocidolite, 60% chrysotile plus 40% amosite, and 100% amosite, respectively. Moreover, in most other studies where the mesothelioma risk cannot be estimated directly, the ratio of the number of mesotheliomas to excess lung cancers is the same for exposures to predominantly chrysotile, to 100% amosite, and to mixtures of chrysotile, amosite and crocidolite, within the uncertainties of the estimation. The ratio for 100% crocidolite exposures is about twice as great (*3*).

These data on humans are corroborated by similar data obtained in experimental inhalation studies by Wagner *et al.* (*7*) with

rats. For equal exposures, the greatest numbers of cancers was produced in these studies by chrysotile asbestos. The amount of asbestos retained in the lung after conclusion of the 2-year inhalation experiment was also measured by Wagner *et al.*, who found that the mass of amphibole fibers in the lungs was about 15 times the mass of chrysotile fibers, although the air the animals breathed contained equal masses of each asbestos type. Thus, the chrysotile fibers, although conveying an equal (or greater) risk of malignancy than the amphibole fibers, were clearly less persistent in lung tissue than the amphiboles. Further, solvents and oils could not have played a role in these experimental results.

Mossman *et al.* state that "the rod-like amphiboles appear to penetrate the peripheral lung more readily than chrysotile fibers, which are curly, can occur in bundles, and can be intercepted at airway bifurcations." While a typical mine specimen of chrysotile contains a nonrespirable fraction, a substantial proportion is of a diameter that is respirable. This respirable fraction, including the thin, sublight microscopic, most highly carcinogenic fibers, increases in the successive stages of product manufacturing and use.

One of the authors of the *Science* article previously analyzed the fiber types found in lung parenchyma and parietal pleura of workers exposed to both chrysotile and amphibole asbestos. Contrary to the assertion of Mossman *et al.* that amphiboles more readily penetrate to the pleura than do chrysotile fibers, it was concluded that "in pleural tissues short chrysotile fibers frankly outnumber long fibers of amphibole type" (*8*). Why do Mossman *et al.* now repudiate this important finding? It should be noted that most mesotheliomas occur in the parietal pleura and that measurements of fiber levels in this tissue are likely to be a more relevant parameter than are lung tissue burdens.

It is not known precisely how asbestos—or any mineral fiber—interacts with cells to induce cancer. There are, however, recent data on how mineral fibers interact with a cell's genetic apparatus to cause mutations. Mossman *et al.* cite studies showing a lack of mutagenicity of asbestos fibers as demonstrated by the Ames test and other transformation assays. These assays were, however, performed by making a direct application of asbestos fibers, a route of exposure that may not be most relevant to human cancer. Also Mossman *et al.* de-emphasize recent evidence that chrysotile is mutagenic by means of its ability to transfer DNA into cells (*9*), apparently because no epidemiological studies have been done on kaolin or calcium phosphate. This capacity to transfect is, however, a recognized avenue for mutagenicity (*10*). In transfection studies conducted thus far, chrysotile asbestos has been seen to be more potent than calcium phosphate. Unlike calcium phosphate, chrysotile fragments the newly introduced DNA, a process now known to greatly enhance mutagenesis. It is likely that all cell transfectants are mutagens, but there are no published studies relating carcinogenesis to a particular tissue's accessibility to transfectants. This area should be further explored.

Mossman *et al.* review data on air concentrations of asbestos measured in buildings and in the outside air and use these data to derive estimates of risk for exposures in buildings. These data have two weaknesses. First, as evident by the fact that no asbestos fibers were observed in 83% of the samples analyzed, inadequate analytical techniques could have been used. In order to obtain a meaningful estimate of an asbestos concentration, at least four fibers should be counted in each sample analyzed. It would appear that at least ten times more filter area should have been scanned in these samples than was in fact examined. Second, as the authors of one of the air studies acknowledge (*11*), their results indicated building levels ten times lower than those of three other studies of airborne asbestos concentrations in buildings (*12*), which suggests the possibility of analytical error.

In addition, short-term air sampling is not likely to reflect actual long-term contamination levels in buildings. Contamination of the air in buildings comes largely from episodic releases during maintenance work or from physical abuse to the material. The very act of sampling alters the likelihood of such activities. Building maintenance or optional repair work will not be scheduled by a building manager when sampling is in progress. Sawyer (*13*) showed that the magnitude of episodic releases could be substantial. Concentrations ranging from 1 to 18 fibers per cubic centimeter were measured during the changing of light fixtures or removal of a ceiling panel. Both x-ray abnormalities and pulmonary function deficits have been associated with asbestos exposure among school custodians (*14*), demonstrating the fact of past, widespread exposures in buildings. Indeed Mossman *et al.* state that "brief, intense exposures to asbestos might occur to custodians and service workers in buildings. . . ."

Mossman *et al.* dismiss concern about asbestos exposures of 0.002 fiber per cubic centimeter, a level 1/100 the allowed occupational level and approximately ten times greater than background asbestos levels. However, it has been calculated by three U.S. agencies [the Consumer Product Safety Commission (CPSC), the National Academy of Sciences, and the Environmental Protection Agency (EPA)] (*3, 15*) that the lifetime risk for a 13-year exposure, beginning at age 5, ranged from 4 to 12 asbestos cancer deaths per 100,000 individuals exposed to a concentration of 0.002 fiber per cubic centimeter. For a school population of 20 million pupils, this translates into 800 to 2400 excess cases of cancer. When evaluating widespread environmental risks, one must focus on the population risks rather than the individual risks. Fortunately, because of action already taken, the average asbestos concentration in most school buildings is less than 0.002 fiber per cubic centimeter. However, even if the exposures in schools were as low as the 0.00024 suggested by Mossman *et al.*, the lifetime mortality for the current school population would still range from 100 to 300 asbestos cancers.

Finally, we consider the risk assessment projections of Mossman *et al.* in an ethical context. Rather than comparing asbestos risks (which are involuntary) with voluntary risks (smoking, school football) or risks that remain high despite expenditures of substantial public and private money (aircraft and highway accidents), we suggest comparing them with other involuntary, environmental risks that are controlled by regulatory agencies (pesticide exposures, drinking water contamination). In a review of regulatory actions taken by the Food and Drug Administration, the CPSC, and the EPA (*16*), it was found that when the population risk exceeded one death per year, the individual lifetime risk was usually regulated if it exceeded one per 1 million for a lifetime exposure. Only 8 of 31 carcinogenic exposures that exceeded this level were not regulated. The eight involved four agents: saccharin, aflatoxin, formaldehyde, and polycyclic organic matter. *Average* asbestos school building lifetime cancer risks range from 0.5 to 10 per 100,000 for only a 13-year exposure. In some schools with particular problems the risk could be higher. Thus, the risks that the EPA is attempting to reduce in school buildings by their Asbestos Hazard Emergency Response Act regulation (*17*) are in the mainstream of regulatory action taken by the U.S. government. The EPA does not require that asbestos be removed in school buildings or suggest that it be removed "haphazardly." It requires that buildings be inspected for asbestos and, if asbestos material is found, an operations and maintenance program be put in place. The program involves notification of the public and building occupants, training of workers to prevent release of asbestos during maintenance activities, and repair of damaged asbestos material or its replacement, if future

damage cannot be prevented. Removal is the option of last resort, and it is to be performed only when other approaches are not feasible or have failed. When removal must be undertaken, the EPA requires that it be conducted in a highly regulated manner that, if followed, will minimize risks to workers and prevent residual contamination.

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REFERENCES AND NOTES

1. The number of known mesotheliomas among Quebec asbestos miners was given as 67 by J. C. McDonald in a presentation at the Collegium Ramazzini Workshop on Disease Potential of Different Asbestos Varieties, Ottawa, Ontario, Canada, 22 March 1989.
2. J. M. Dement, R. L. Harris, Jr., M. J. Symons, C. Shy, *Am. J. Ind. Med.* **4**, 399 (1983); A. D. McDonald, J. S. Fry, A. J. Woolley, J. C. McDonald, *Br. J. Ind. Med.* **40**, 361 (1983); J. Peto *et al.*, *Ann. Occup. Hyg.* **29**, 305 (1985); A. D. McDonald, J. D. Fry, A. J. Woolley, J. C. McDonald, *Br. J. Ind. Med.* **40**, 368 (1983).
3. Details of the calculation of these unit exposure risks can be found in *Airborne Asbestos Health Assessment Update* (Environmental Protection Agency, Washington, DC, 1986).
4. H. Seidman, I. J. Selikoff, S. K. Gelb, *Am. J. Ind. Med.* **10**, 479 (1986); I. J. Selikoff, E. C. Hammond, H. Seidman, *Ann. N.Y. Acad. Sci.* **330**, 91 (1979); W. J. Nicholson, *ibid.* **271**, 152 (1976); V. L. Henderson and P. E. Enterline, *ibid.* **330**, 117 (1979); H. Weill, J. Hughes, C. Waggenspack, *Am. Rev. Respir. Dis.* **104**, 345 (1979); M. M. Finkelstein, *Br. J. Ind. Med.* **40**, 138 (1983).
5. B. K. Armstrong *et al.*, *Br. J. Ind. Med.* **45**, 5 (1988).
6. J. C. McDonald, F. D. K. Liddell, G. W. Gibbs, G. E. Eyssen, A. D. McDonald, *ibid.* **37**, 11 (1980).
7. J. C. Wagner *et al.*, *Br. J. Cancer* **29**, 252 (1974).
8. P. Sebastien *et al.*, in *Dusts and Diseases*, R. Lemen and J. M. Dement, Eds. (Pathotox, Park Forest South, IL, 1979), pp. 65–85.
9. J. D. Appel *et al.*, *Proc. Natl. Acad. Sci. U.S.A.* **85**, 7670 (1988).
10. L. Bardwell, *Mutagenesis* **4**, 245 (1989).
11. J. Chesson *et al.*, *Environ. Resh.* **51**, 100 (1990).
12. G. J. Burdett and S. A. M. T. Jaffrey, *Ann. Occup. Hyg.* **30**, 185 (1986); E. J. Chatfield, in *Asbestos Fibre Measurements in Building Atmospheres, Proceedings*, E. J. Chatfield, Ed. (Ontario Research Foundation, Mississauga, Ontario, 1986); D. J. Pinchin, *Asbestos in Buildings, Study No. 8* (Royal Commission on Matters of Health and Safety Arising from the Use of Asbestos in Ontario, Toronto, Ontario, 1982).
13. R. Sawyer, *Environ. Res.* **13**, 146 (1977).
14. L. C. Oliver, N. L. Sprince, R. E. Green, *Am. Rev. Resp. Dis.* **139**, A211 (1989).
15. *Report to the U.S. Consumer Product Safety Commission by the Chronic Hazard Advisory Panel on Asbestos* (Consumer Product Safety Commission, Washington, DC, 1983); National Academy of Sciences, *Asbestiform Fibers: Nonoccupational Health Risks* (National Academy Press, Washington, DC, 1984).
16. C. C. Travis *et al.*, *Environ. Sci. Technol.* **21**, 415 (1987).
17. Environmental Protection Agency, *Fed. Reg.* **52**, 41826 (1987).

Table 1. Average indoor concentrations of airborne asbestos fibers longer than 5 micrometers.

Sites	Number of buildings	Number of samples	Structures/ cm^3
GSA buildings			
No ACM*	6	42	0.0
Undamaged ACM*	6	42	0.00007
Damaged ACM*	37	256	0.00008
71 schools	71	328	0.00024
Minnesota universities	34	170	0.00003
Maryland public buildings	72	91	0.00009

*Differences in these concentrations among three groups of buildings are not statistically significant.

The article by Mossman *et al.* contains data on airborne asbestos in buildings from two sources: a survey conducted by the Environmental Protection Agency (EPA) of Government Services Administration (GSA) buildings and data from 71 schools involved in impending litigation regarding the presence of asbestos-containing building products. The levels reported by Mossman *et al.* for the GSA buildings were incorrectly identified as pertaining to asbestos structures longer than 5 micrometers, whereas in reality the figures were for total asbestos structures (*1*). Thus, the airborne concentrations in GSA buildings were lower than reported by Mossman *et al.* Table 1 contains the correct average levels from the GSA data along with data from the 71 schools. Also included are previously unpublished data from Minnesota state university buildings and Maryland state buildings; these data were generated in connection with impending litigation and were collected and analyzed by the same organizations employing exactly the same protocols as those used in the 71-school study.

On the basis of the study used by Mossman *et al.* to estimate annual death rates from asbestos exposure and other activities, the expected number of premature deaths among students exposed for 6 years to 0.00024 structure per cubic centimeter longer than 5 micrometers is 0.36 per million (*2*). By the same methods, the risk from 20 years of occupational exposure to 0.00007 structure per cubic centimeters longer than 5 micrometers is 0.43 per million.

In comparison, by combining the National Council on Radiation Protection estimate of the radiation exposure from naturally occurring radionuclides in masonry building products (*3*) with the BEIR V committee's potency estimates (*4*), one obtains a lifetime risk of 15 per million from 6 years of school, and 46 per million from 20 years of work in masonry buildings. These risks, which do not include the much larger risks from radon (*4*), are 40 to 100 times larger than the corresponding risks from exposure to asbestos in buildings.

Concern has been raised that airborne levels may be increased during brief periods due to disturbance of asbestos materials and that these increases may not be reflected in routine monitoring. However, the data in Table 1 are based on a total of 1185 samples, each collected over a period of two consecutive days during normal building activities, which cumulatively are equivalent to more than 3 years of continuous sampling. These data therefore suggest that such disturbances either occur infrequently or else do not produce high exposures.

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REFERENCES

1. K. Crump and D. Farrar, *Reg. Toxicol. Pharmacol.* **10**, 51 (1989).
2. J. M. Hughes and H. Weill, *Am. Rev. Res. Dis.* **133**, 5 (1986).
3. National Council on Radiation Protection and Measurements, *Radiation Exposure of the U.S. Population From Consumer Products and Miscellaneous Sources* (Report No. 95, Bethesda, MD, 1987).
4. National Research Council, *Health Effects of Exposure to Low Levels of Ionizing Radiation, BEIR V.* (National Academy Press, Washington, DC, 1990).

Response: Brody presents his work with mice and rats as "a body of experimental data" showing a "significant pathobiological response in the lung" after a single, intense exposure to chrysotile asbestos (*1*). He then attempts to compare these rodent inhalation studies to asbestos exposures encountered by janitors changing light bulbs and teachers venturing into "dusty corners." His arguments are flawed. While Brody's work shows morphometric changes and an increase in incorporation of tritiated thymidine by a variety of cell types in rodent lungs after inhalation of chrysotile, he does not mention that labeling in asbestos-exposed lungs returns to normal levels that persist throughout the 30-day observation period. Brody demonstrates no fibrotic lesions by accepted functional and histopathologic criteria (*2*). These asbestos-induced mitogenic responses reflect acute reversible changes and have no necessary relation to the development of pulmonary fibrosis. In Brody's experiments, animals were exposed for 1 and

5 hours to astronomical airborne concentrations (hundreds of billions of fibers per cubic meter of air) (*3*) of chrysotile. We are hard-pressed to envision a comparable situation in which teachers or students would remain for extended periods of time in dust clouds where vision would be significantly impaired.

Brody appropriately raises the issue of potential exposure of maintenance and custodial staff to asbestos-containing materials (ACM) in buildings. The Occupational Safety and Health Administration (OSHA) has said that these workers are entitled to the coverage of the OSHA Asbestos Standard for Construction (*4*). This permanent standard has provisions for initial determination of exposure, a permissible exposure limit for airborne asbestos, work practices, personal protective equipment, and medical surveillance procedures. As with other OSHA standards, the employer is responsible for ensuring adherence to the provisions of the standard. In buildings, this responsibility falls to the school board. The asbestos standard was amended in 1986 (*4*). The agency usually allows 60 days for those covered to comply. Building owners and School Boards not using operations and maintenance (O&M) plans that protect maintenance and custodial personnel are in technical violation of the standard. Each building must be evaluated for appropriate protective measures. Our experience indicates that some buildings require few and relatively simple procedures, while others require more elaborate procedures. There is no "universal" O&M plan to effectively protect maintenance and custodial personnel.

We appreciate the opportunity to reply to the misinterpretations of data and arguments presented by Nicholson *et al.* We were unable to contact McDonald concerning the "67 or more" cases of mesothelioma that have occurred among Canadian chrysotile miners and millers. Unfortunately, abstracts and papers from McDonald and other presenters at the referenced conference (*5*), which was organized by the Mount Sinai group, were neither invited nor published individually or in a summary. However, the recent review (*6*) cited in our article shows that among the 53 chrysotile-induced pleural mesotheliomas recorded in the literature, 10 were from industry (with suspicion of mixed chrysotile and amphibole exposure) and 41 were miners in geographic areas where tremolite was a natural contaminant of the chrysotile ore. We note that "the relative *ratio* of tremolite to chrysotile fibers in the lungs of Canadian miners and millers is related directly to their risk of developing mesothelioma (*7*)."

Nicholson *et al.* present criticisms concerning the "fallaciousness of the tissue burden argument" in drawing conclusions about the importance of fiber type in the development of mesothelioma. Our conclusions are based primarily on a review of the epidemiology of mesothelioma mortality in cohorts of workers exposed predominantly to "chrysotile-only," amphiboles alone, or mixed concentrations of fibers (amphibole plus chrysotile). We emphasize that most mesotheliomas judged in "chrysotile only"–exposed individuals were actually amphibole-related, as confirmed by lung tissue fiber types and geological data. If tremolite contamination is indeed the agent of mesothelioma in Canadian miners and millers, then it is logically necessary that extremely high concentrations of chrysotile deliver a critically important dose of tremolite to the lung. We do agree that the data on the different pathogenic potential of asbestos types in the causation of lung cancer is less compelling than that for mesothelioma.

As we stated, South Carolina asbestos textile workers exhibit "a striking increase in lung cancers with duration of exposure when compared to Canadian chrysotile miners and millers." Most of the asbestos to which the textile workers were exposed was Quebec chrysotile. However, airborne dust levels in the textile plant were estimated (as air concentrations of fibers were unavailable) as one-tenth of those encountered in mines and mills, an observation supporting the data that numerical concentrations of asbestos fibers in lung were higher in miners and millers than in textile workers. Length and diameter distributions of chrysotile and tremolite fibers in these worker populations were similar (*8*). Thus, one cannot attribute lung cancers in these textile workers to increased exposure or differences in fiber size. However, there are two potential explanations for increased lung tumors in workers in this textile plant. First, mineral oils and hydrocarbons may be inculpated, as was first suggested by Harington (*9*) and later by the McDonalds (*8*). We realize that this explanation has not been verified. Second, the plant in question was unusually dirty, as burlap bags were employed to trap asbestos fibers and were beaten by workers to recycle these fibers.

Nicholson *et al.* incorrectly interpret the rodent inhalation studies by Wagner *et al.* (*10*) as concluding that the greatest numbers of cancers were produced in these studies by equal exposures to chrysotile. In fact, numbers of asbestos-induced mesotheliomas in these rats were low (four in crocidolite-exposed rats, none in Rhodesian chrysotile-exposed rats, and four in Canadian chrysotile-exposed rats) and equivalent to numbers occurring spontaneously in this species (*11*). The majority of asbestos-induced lung tumors were adenomas also occurring in control rats. We emphasized that rodents were exposed to greater *numbers* of chrysotile fibers in comparison to amphibole fibers on an equivalent weight basis (*3*).

We do not make the assertion that amphiboles more readily penetrate the pleura, nor do we repudiate a publication by one of us (J.B.) showing that short chrysotile fibers outnumber long amphibole fibers in pleural tissues (*12*). In this study, all fibers found in the parietal pleura were short (1 to 2 micrometers in length) Fibrils inactive in bioassays of cell transformation and carcinogenesis (*12*). No reference is provided by Nicholson *et al.* to substantiate their statement "that most mesotheliomas occur in the parietal pleura."

Nicholson *et al.* dismiss the results of in vitro experiments that used bacterial systems and mammalian cells because asbestos fibers are added to intact cells. They quote studies from their laboratory in which chrysotile fibers pre-incubated with naked DNA were used to transfect monkey kidney cells as a mechanism related to human cancer (*14*). We cited this paper and a similar study exploring asbestos-mediated transfection by viral RNA into mammalian cells (*15*) in our article. In the latter work, the efficiency of chrysotile asbestos fibers in transfection was compared with that of a number of asbestos and nonasbestos particulates. Under these circumstances, chrysotile asbestos was intermediate in rank (as was calcium phosphate) when compared with equal concentrations of a number of insoluble particles and fibers. The most efficient facilitators were kaolin and talc. Several epidemiologic studies on kaolin and talc workers exist, none of which have documented an increased cancer risk in individuals exposed to asbestos-free minerals. (*16*).

To assert that analytical techniques measuring asbestos-in-air on filters are "inadequate" because asbestos fibers were not observed in 83% of the samples, is incorrect. This observation merely indicates that fibers, if present, are at concentrations below the analytical sensitivity. As we indicated, the concentrations of asbestos-in-air reported in recent studies differ from those reported earlier, presumably because of differences in transfer techniques associated with sample examination in the transmission electron microscope, and not because of the possibility of analytical error. Comparisons between four studies of asbestos-in-air concentrations were recently presented by Chesson (*17*), who discussed the reasons for discrepancies in results and concluded that "levels are generally low," which is one of the major points of our paper.

The concept of "episodic" releases in buildings to support criticisms of air sampling as "snapshots in time" does not bear close scrutiny. Crump and Farrar (*18*) used a statistical approach to demonstrate that it was unlikely that not a single elevated concentration resulting from episodic release was detected in the Environmental Protection Agency (EPA)–sponsored study of buildings. It is more likely that releases of fibers resulting from intrusion of ACM creates elevated airborne fiber concentrations in close proximity to the source, but mixing with air results in rapid decrease of the concentration distant from the source. Thus, O&M programs are targeted to protect maintenance personnel from these short-term potential releases. The work of Sawyer (*19*) was based on phase contrast microscopy, a technique incapable of differentiating between asbestos fibers and other fibers. This is the more than likely explanation for the high concentrations he reported for short-term episodic releases.

Nicholson *et al.* cite an abstract by Oliver *et al.* (*20*) upon which they base their conclusions that "x-ray abnormalities and pulmonary function deficits have been associated with asbestos exposure among school custodians." We agree that some plaques occur in maintenance workers, but asbestosis is rare and, if present, is mild. We emphasize that this situation of asbestos exposure must be addressed under OSHA standards.

The lifetime risk estimates by U.S. government agencies in the past have been calculated from amphibole or mixed-fiber exposures and at fiber concentrations greater than actual fiber levels in buildings and schools. Regardless, the EPA estimate of risk for exposure to mixed fibers at 0.00024 fibers per cubic centimeter of air starting at age 5 and lasting for 13 years is approximately 4.8 *lifetime* deaths per million. Averaged over 70 years of remaining life (from age 5), this is less than 0.1 per million on an annual basis, or less than one in 10 million (and most of these are late in life) (*21*).

We understand the distinction for regulators between voluntary and involuntary health risks and recognize that society must make these choices. However, for both the general public and schoolchildren, all available scientific evidence indicates that ambient asbestos levels in air cannot cause asbestosis. In the 17,800 insulation workers with mixed-fiber exposure, 467 of 471 lung tumors were found in smokers (*22*). Whether the four tumors observed in nonsmokers occurred in smokers who quit or in those exposed to smoking passively is not clear. Nevertheless, if these observations are extrapolated to the environmental situation where concentrations of asbestos fibers in air are many thousands of times lower than those in past occupational settings, the apportionment of risk resulting from smoking increases dramatically. For these reasons, to suggest that asbestos in buildings causes lung cancer in the absence of smoking (a voluntary risk) is ill-founded. We emphasize that the risk of mesothelioma in the absence of amphibole exposure in schools and buildings is miniscule. Nicholson is on record as stating that "a few fibers [asbestos] will eventually cause disease" (*23*). Furthermore, his colleagues have described (*24*) asbestos in buildings as "the third wave of asbestos disease." Such emphasis is, in our opinion, scientifically invalid.

We agree that the EPA is now indicating that, in most cases, the best solution to ACM in buildings is to leave it in place and manage it with an O&M plan (*25*). The EPA now states that "the health risks to building occupants. . . appears to be low," and "removal is often not a building owner's best course of action" (*26*). When the agency issued its initial guidelines, school administrators were instructed to use an algorithm, later demonstrated to be invalid (*27*). The algorithm did not appear in later asbestos guidance documents from the agency, but it set the tone for subsequent emphasis on removal because its use usually resulted in a score that dictated that action, namely removal, be taken. The growth of the asbestos removal industry to its present $\$3.5 \times 10^9$ gross sales per year (in 1989) stems largely from this early approach to the problem—an approach that ignored the role of air sampling in risk assessment that would place the problem in perspective. To imply that the asbestos removal industry operates on the principle that "removal is the option of last resort" is incorrect. Before publication, we discussed with the *Science* editors our public, governmental, consultative, and legal activities that have been on behalf of labor, school boards, and industry. The vague accusations of Samuels are politically orientated and unfounded. Our main objective as scientists in this field has been (and will continue to be) to protect the health of workers exposed to asbestos.

We thank Crump for the additional information and corrections to air sampling data provided in table 1 of our article.

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REFERENCES AND NOTES

1. L. Y. Chang, L. H. Overby, A. R. Brody, J. D. Crapo, *Am. J. Pathol.* **131**, 56 (1988); A. R. Brody and L. H. Overby , *ibid.* **134**, 133 (1989); P. D. McGavran, L. M. Moore, A. R. Brody, *ibid.* **136**, 695 (1990).
2. J. E. Craighead *et al.*, *Arch. Pathol. Lab. Med.* **106**, 541 (1982).
3. Ten milligrams of the International Union Against Cancer reference sample of chrysotile asbestos contains approximately 11.5×10^{10} fibers [G. Monchaux *et al.*, *Carcinogenesis* **2**, 229 (1981)]. Brody's experiments were done at 410, and 13 milligrams of chrysotile per cubic meter of air.
4. 29 Code *Fed. Reg.*, part 1911, sect. 1926, 58, as amended in *Fed. Reg.* **51**, 22612 (20 June 1986).
5. Collegium Ramazzini Workshop on Disease Potential of Different Asbestos Fiber Varieties, Ottawa, Ontario, Canada, 20 to 22 March 1989.
6. A. Churg, *Chest* **93**, 621 (1988).
7. A Churg *et al.*, *Am. Rev. Respir. Dis.* **130**, 1042 (1984).
8. J. C. McDonald and A. D. McDonald, in *Asbestos-Related Malignancy*, K. H. Antman and J. Aisner, Eds. (Grune & Stratton, Orlando, FL, 1987), pp. 57–59.
9. J. S. Harington, *Nature* **193**, 45 (1962).
10. J. C. Wagner, G. Berry, J. W. Skidmore, V. Timbrell, *Br. J. Cancer* **29**, 252 (1974).
11. J. C. Wagner, D. Griffith, D. Munday, *Br. J. Ind. Med.* **44**, 749 (1987).
12. P. Sebastien *et al.*, in *Dusts and Diseases*, R. Lemen and J. M. Dement, Eds. (Pathotox, Park Forest South, IL, 1979), pp. 65–85.
13. T. W. Hesterberg and J. C. Barrett, *Cancer Res.* **44**, 2170 (1984); M. P. Stanton *et al.*, *J. Natl. Cancer Inst.* 67, 965 (1981); F. Pott, in *Assessment of Inhalation Hazards*, U. Mohr *et al.*, Eds. (Springer-Verlag, New York, 1990), pp. 242–251.
14. J. D. Appel, T. M. Fazy, D. S. Kohtz, J. D. Kohtz, E. M. Johnson, *Proc. Natl. Acad. Sci. U.S.A.* **85**, 7670 (1988).
15. G. R. Dubes and L. R. Mack, *In Vitro Cell Dev. Biol.* **24**, 175 (1988).
16. M. Kleinfeld, J. Messite, M. H. Zaki, *J. Occup. Med.* **16**, 345 (1974); G. F. Rubino, G. Sconsetti, G. Piolatto, C. A. Romano, *J. Occup. Med.* **18**, 186 (1976); G. Sheers, *Br. J. Ind. Med.* **21**, 218 (1964).
17. J. Chesson, J. Hatfield, B. Schultz, E. Datro, J. Blake, *Environ. Res.* **51**, 100 (1990).
18. K. S. Crump and D. B. Farrar, *Reg. Toxicol. Pharm.* **10**, 51 (1989).
19. R. Sawyer, *Environ. Res.* **13**, 146 (1977).
20. L. C. Oliver, N. L. Sprince, R. E. Green, *Am. Rev. Respir. Dis.* **139**, A211 (1989).
21. J. M. Hughes, personal communication.
22. W. Rom, paper presented at the Banbury Conference on Molecular Mechanisms of Fiber Cytotoxicity and Carcinogenesis, Cold Spring Harbor, NY, 14 to 17 March 1990.
23. Hartford *Courant*, 28 March 1990, p. 1.
24. "The Third Wave of Asbestos Disease: Exposure to Asbestos in Place. Public Health Control," meeting to be held in New York, NY, 7 to 9 June 1990.
25. *The ABC's of Asbestos in Buildings* (Environmental Protection Agency, Washington, DC, 1989).
26. L. J. Fisher, Office of Pesticides and Toxic Substances, Environmental Protection Agency, before

the Subcommittee on Health and Safety, Committee on Education and Labor, U.S. House of Representatives, Washington, DC, 3 April 1990; testimony before the Subcommittee on Toxic Substances, Environmental Oversight, Research and Development, Committee on Environment and Public Works, U.S. Senate, Washington, DC, 26 April 1990.

27. *Asbestos Containing Materials in School Buildings: A Guidance Document, Part 1* (Office of Toxic Substances, Environmental Protection Agency, Washington, DC, 1979); M. E. Findley, V. E. Rose, G. R. Cutter, R. A. Windsor, *Am. J. Publ. Health* **73**, 1179 (1983).

Cooling Towers, Not "Smokestacks"

Unless engineering practices in East Germany differ substantially from those in the West, the figure accompanying Jeremy Cherfas' article "East Germany struggles to clean its air and water" (20 Apr., p. 295) shows cooling towers, not the smokestacks the caption indicates. The distinction is more than semantic: the visible plumes from cooling towers are principally water, rather than the smoke that is the article's subject. Cooling towers are a sign that water is being recycled, actually minimizing a plant's impact on at least the aqueous environment.

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Erratum: In the report "Genomic sequencing and methylation analysis by ligation mediated PCR" by G. P. Pfeifer, S. D. Steigerwald, P. R. Mueller, B. Wold, and A. D. Riggs (10 Nov. 1989, p. 810), reference 7 should have read, "P. R. Mueller and B. Wold, *Science* **246**, 780 (1989)."

Erratum: In the research article "In vivo footprinting of a muscle specific enhancer by ligation mediated PCR" by P. R. Mueller and B. Wold (10 Nov. 1989, p. 780), an error was introduced after the galley proofs were approved by the authors. The ninth sentence of the legend for figure 2 contained an error in the concentration of deoxynucleoside triphosphate. It should have read, "Hybridization was stopped by transferring to ice; a solution of 7.5 μl of 20 m*M* $MgCl_2$, 20 m*M* dithiothreitol (DTT), and 0.2 m*M* of each deoxynucleoside triphosphate (dNTP) was added. . . ." The printed version read, ". . . 0.02 m*M* of each deoxynucleoside triphosphate (dNTP). . . ." This erroneous tenfold reduction in dNTP concentration may have a significant negative impact on the efficiency of the first strand synthesis reaction and therefore on the ultimate success of the ligation mediated PCR procedure.

Erratum: In Robert Pool's article "Freshman chemistry was never like this" (News & Comment, 13 Apr., p. 157), the description of physicist Theodore Ducas' teaching at Wellesley College contained an error. The last sentence of the second paragraph on page 158 should have read, "They [the students] can see for themselves that masses in a gravitational field really do move in a parabola . . . and also that their *horizontal* [not vertical] velocity remains constant throughout the motion."

Erratum: The photograph of a mechanical Triceratops in the issue of 20 April (Briefings, p. 307) was taken by Chip Clark of the Smithsonian Institution.