Case Report

Fatal Asbestosis 50 Years after Brief High Intensity Exposure in a Vermiculite Expansion Plant

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The authors report the case of a 65-year-old accountant whose only asbestos exposure was during a summer job 50 years earlier in a California vermiculite expansion plant. Vermiculite is a silicate material that is useful in building and agriculture as a filler and insulating agent. He developed extensive fibrocalcific pleural plaques and end-stage pulmonary fibrosis, with rapidly progressive respiratory failure. Careful occupational and environmental history revealed no other source of asbestos exposure, and the initial clinical diagnosis was idiopathic pulmonary fibrosis; open lung biopsy shortly before his death confirmed asbestosis. Electron microscopic lung fiber burden analysis revealed over 8,000,000 asbestos fibers per gram dry lung, 68% of which were tremolite asbestos. Additional asbestiform fibers of composition not matching any of the standard asbestos varieties were also present at over 5,000,000 fibers per gram dry lung. Comparison analysis of a sample of Libby, Montana, vermiculite showed a similar mix of asbestiform fibers including tremolite asbestos. This case analysis raises several concerns: risks of vermiculite induced disease among former workers of the more than 200 expansion plants throughout the United States; health effects of brief but very high-intensity exposures to asbestos; and possible health effects in end-users of consumer products containing vermiculite.

Keywords: asbestosis; respiratory failure; tremolite; vermiculite; electron microscopy

Vermiculite is used extensively in the insulation and building industry, as well as in horticulture. It is useful as a bulking agent in animal feed and as a carrier or vehicle for fertilizers. It is a hydrated magnesium–aluminum–iron sheet silicate mineral. It differs from crystalline silica, which causes silicosis, and contains no other elements in chemical composition. Native vermiculite is usually converted to a very low-density material by heating in expansion plants. The native vermiculite is loaded into ovens and rapidly heated in furnaces, much like popcorn, at temperatures above 1,500° F. After heating, the appearance of vermiculite is similar to a small, brown, accordion-shaped granule. It is particularly useful because the heat-expanded lightweight form is up to 12 times the bulk of the native, unexpanded form. Other useful properties include the fact that it is chemically inert, noncombustible, and has a high surface area (1, 2).

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Until recently, vermiculite has been viewed for regulatory purposes as a nuisance dust, one that does not chemically interact with the lungs or produce specific long-term adverse effects. Mines in Libby, Montana, have been a major source of United States vermiculite. The Libby, Montana, vermiculite ore has significant tremolite asbestos associated with it. It is the presence of the tremolite that has caused significant morbidity and mortality in miners and in community members living in this area (3–6). Therefore, vermiculite is now viewed more cautiously (1). Because vermiculite is widely used and often dispersed in deposits of naturally occurring tremolite, there must be concern about significant disease and mortality in nonmining settings (7, 8).

We report the case of a man who died of respiratory failure due to asbestosis as a direct result of asbestos-containing vermiculite exposure 50 years earlier. Lung biopsy helped distinguish between usual interstitial pneumonitis and the pneumoconiosis that developed in this man. This case is also significant because it suggests a brief, but intense exposure can cause significant fibrotic disease after a long latency period. As Libby vermiculite was shipped to over 200 expansion plants throughout the United States, it seems likely that other former workers at these plants may be at risk for disease (and, that there should be concern even about community exposures in the vicinity of these expansion plants).

CASE REPORT

The patient worked for a Southern California insulation company during two consecutive summers when he was 18 and 19 years old (1951–1952). Vermiculite ore was shipped from mines in Libby, Montana, to the Southern California expansion plant where he worked. His duties included unloading the vermiculite ore, operating a forklift, shoveling ore into canvas bags and, occasionally, shoveling ore into ovens. Although he sometimes wore a cotton mask, he recalled a heavy dust burden on his clothes and snorting black dust from his nostrils in the evenings after bathing. He subsequently served three years in the Navy before college. He served as a deck officer on two ships and attended flight school. He was unaware of any specific asbestos exposure during his naval duty; his service did not include engine or boiler room work, nor was he present during significant overhauls. He became a certified public accountant and had no further occupational asbestos exposures for the remainder of his life. He smoked cigarettes for approximately 20 years, averaging a pack of cigarettes per day, quitting at age 40.

At age 50, a routine chest radiograph showed extensive bilateral pleural fibrocalcific disease. At age 60, his chest radiograph showed interstitial disease and extensive pleural calcification. Pulmonary function tests at that time showed restrictive

TABLE 1. PULMONARY FUNCTION TESTS

Date	Age Years	FVC*	FEV_1*	FEV_1/FVC (%)	TLC*	D_LCO*	$\dot{V}O_2$*	pH	P_{CO_2}	P_{O_2}
Mar-93	59	66	70	85	77	73				
May-96	62	65	70	84	71	71				
Sep-97	64	61	61	78	56	64				
Oct-97	64						85			
Jul-98	65	49	56	88		56	59			
Nov-99	66							7.42	42	74

Definition of abbreviations: D_LCO = lung diffusing capacity; FEV_1 = forced expiratory flow at one second; TLC = total lung capacity; $\dot{V}O_2$ = oxygen consumption.
* Percent predicted.

ventilatory defects (Table 1). He remained asymptomatic until age 65, even though pulmonary function declined. He skied regularly at attitudes of 10,000 ft. In September 1999, he traveled to the Mediterranean and reported snorkeling without any problems. He developed shortness of breath in October 1999. Examination at that time showed use of accessory muscles of respiration, mild clubbing, and crackles. Pulmonary function tests showed progression of previously noted restrictive ventilatory defects.

Chest radiographs (Figures 1 and 2) showed progression of fibrocalcific changes. Computed tomography (CT) of the chest (Figure 3) showed extensive fibrocalcific disease of the pleura and basilar interstitial lung disease. The radiographic appearance of the interstitial disease was mild on CT, and consideration was given to the possibility of idiopathic pulmonary fibrosis.

To help establish a specific diagnosis and guide decisions about therapy such as antiinflammatory/immunosuppressive drugs, a lung biopsy was performed. An initial sixth interspace incision was made in anticipation of the possible use of video-assisted techniques. However, the pleura was densely calcified and there was, in fact, fibrous adhesion of the underlying lung to the parietal pleura. Accordingly, the incision was enlarged to allow limited thoracotomy and direct open biopsy of both lung and pleura. Extensive parietal pleural calcification and some visceral pleural calcification were noted. Most remarkable was the appearance of the diaphragm, which was completely covered with calcific plaque and appeared to be virtually immobile. With difficulty, specimens were obtained from the left upper lobe of the lung. The surgeon felt that decortication would likely be unsuccessful, particularly in view of the involvement of the diaphragm.

Immediately following the lung biopsy, the patient was able to resume his usual activities and reported feeling better than before the biopsy. However, two weeks later, he developed rapid atrial fibrillation, and his ventricular rate was slowed with diltiazem and digoxin. About a week later, he presented with severe respiratory failure and hypercapnia. There was no obvious cause for his deterioration. He was treated with antibiotics

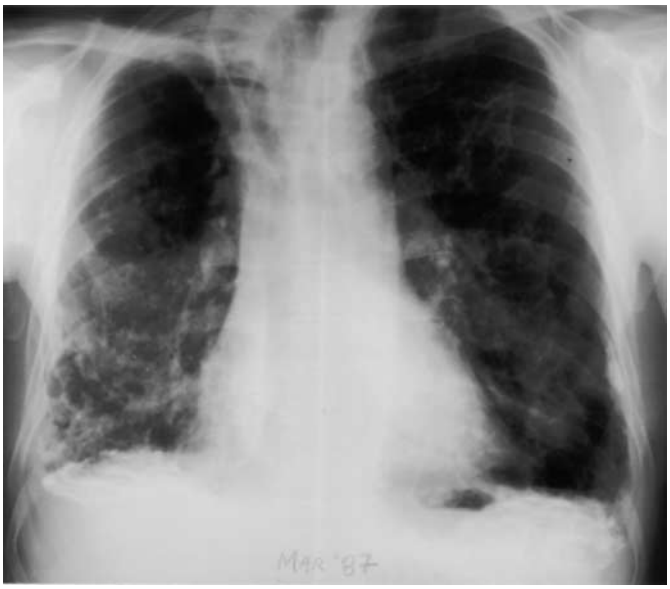

Figure 1. Chest radiograph of patient taken at age 54, 35 years after his work in a vermiculite expansion plant and 13 years before death. It shows extensive pleural fibrocalcific disease.

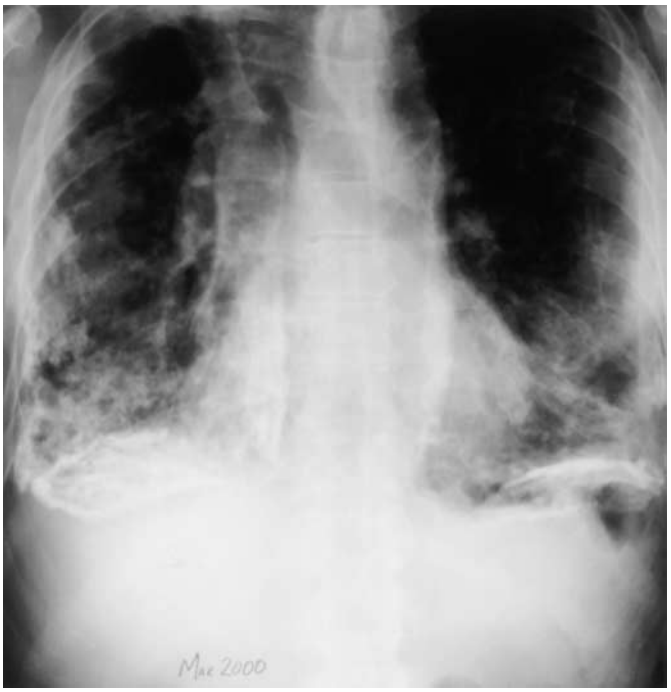

Figure 2. Chest radiograph taken shortly before death at age 66, showing progression of pleural fibrocalcific disease.

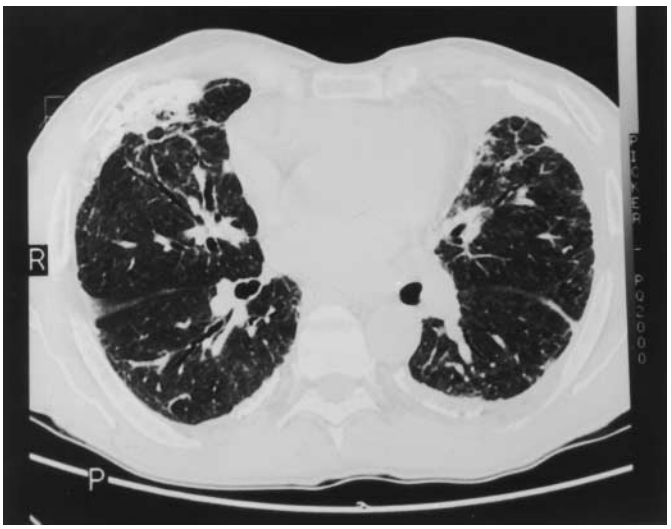

Figure 3. High-resolution chest tomography taken before lung biopsy at age 66, demonstrating both pleural fibrocalcific disease and mild basilar fibrosis.

but remained gravely ill. After extensive discussions, the patient opted for comfort care only. The patient died two months later of hypercapneic respiratory failure at home. No autopsy was performed.

The biopsy showed extensive interstitial and subpleural fibrosis, interpreted as consistent with usual interstitial pneumonitis (Figure 4). Asbestos bodies were easily found in the sections, thus confirming the diagnosis of asbestosis. Lung tissue was subsequently analyzed for mineral fiber burden. A mineral sample of Libby, Montana, vermiculite was also obtained and analyzed for comparison with the fibers retained in the patient's lung.

TISSUE AND MINERAL SAMPLE ANALYSIS METHODS

The lung tissue analysis used standard bleach digestion and filtration (9). Lung parenchyma was taken from paraffin blocks, deparaffinized, rehydrated, and digested with sodium hypochlorite, with the residue collected on Nuclepore filters for analysis by light microscopy for asbestos body counting or scanning electron microscopy (SEM) and energy dispersive X-ray spectroscopy for mineral fiber analysis and counting. In the SEM analysis, at a magnification of ×4,000, all fibers at least 3-μm length were analyzed, with a detection limit of 47,800 fibers per gram dry lung.

RESULTS OF TISSUE ANALYSIS

Asbestos bodies. Filter preparation examined by light microscopy revealed numerous classic asbestos bodies (Figure 5). The concentration was determined to be 178,000 asbestos bodies per gram dry lung. In the SEM analysis the concentration of asbestiform fibers was determined to be 14.5 million fibers per gram dry lung. The types of asbestiform fibers and their concentrations are presented in Table 2. The 'other' asbestiform category includes the series of sodium-calcium magnesium silicates characteristic of the Libby vermiculite. It is noteworthy also that no commercial amphibole asbestos fibers (amosite or crocidolite) were detected.

In addition, a vermiculite sample from Libby, Montana, (verified in an independent analysis by the United States Environmental Protection Agency [U.S.E.P.A.], personal communication, C. Weis to J.L.A., May 2001) was dispersed and analyzed for comparison to the lung fiber burden of the vermiculite-exposed patient. The distributions of elemental ratios in the various asbestiform fiber types were similar in the mineral sample and from the lung, in keeping with the mixed solution series of asbestiform minerals characteristic of the Libby vermiculite material. (Figure 6).

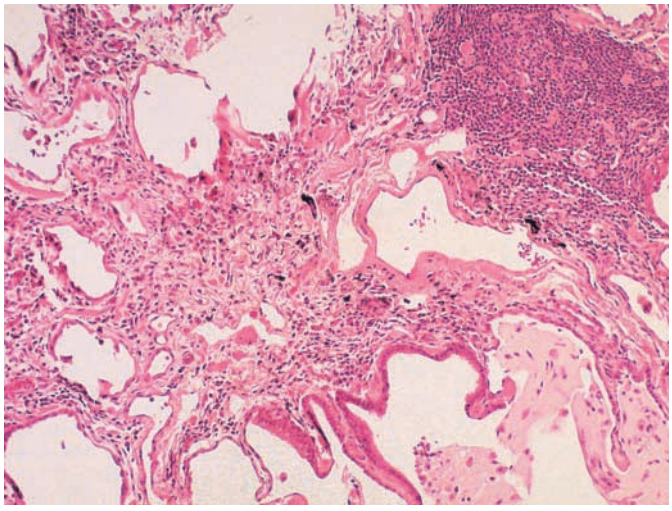

Figure 4. Lung biopsy from the left upper lobe, H&E stained section showing interstitial fibrosis.

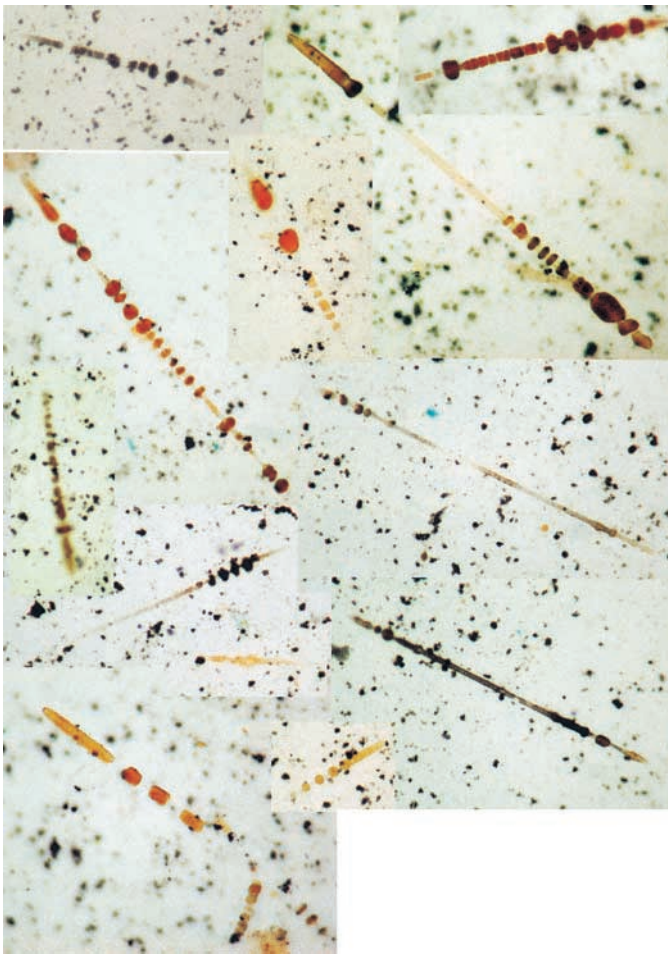

Figure 5. Montage of light microscopic images of asbestos bodies noted on filter preparation of lung digestate.

DISCUSSION

Asbestos refers to a family of naturally occurring, flexible, fibrous silicate minerals that are relatively heat resistant and relatively indestructible. They share the property of having a crystal habit in which the asbestos minerals crystallize with a high aspect ratio (ratio of length to diameter), forming fibers (10). There are two major classes of asbestos fibers, chrysotile and amphibole. Chrysotile (serpentine) has been most widely used commercially in the United States Amphibole, the second class, includes several types: the 'commercial amphiboles': amosite and crocidolite; and tremolite, actinolite, and anthophyllite. Crocidolite has been considered by some to be the most dangerous, but tremolite's toxicity is also recognized. Recog-

TABLE 2. FIBER ANALYSIS OF LUNG

Tremolite	5.94 million fibers per gram dry lung
Actinolite	1.78 million fibers per gram dry lung
Chrysotile	0.99 million fibers per gram dry lung
Anthophyllite	0.05 million fibers per gram dry lung
Other asbestiform fibers	5.75 million fibers per gram dry lung

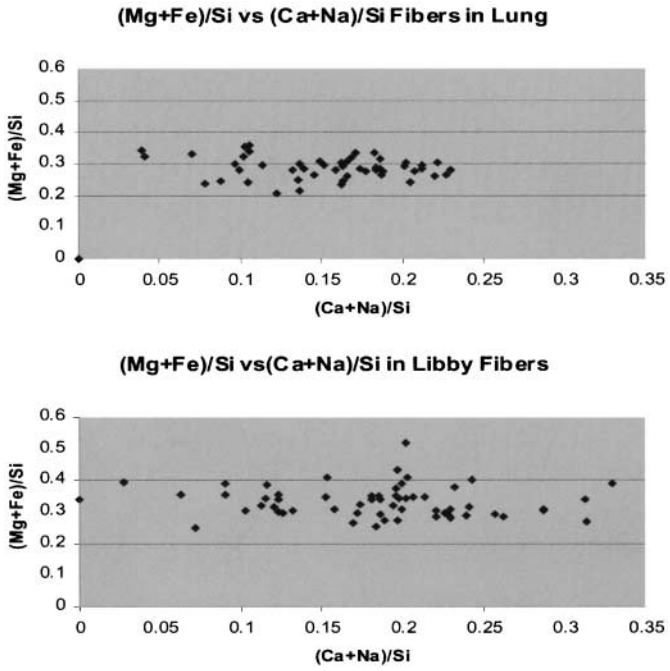

Figure 6. Graphs of comparison of fibers in lung digestate (*top graph*) with fibers in Libby vermiculite preparation (*bottom graph*). Each point represents the EDXA elemental intensity ratios for a single fiber. These results indicate there is not one pure chemical fiber type but rather both the fibers in the patient's lungs and the Libby vermiculite show a range of compositions that are remarkably similar to each other. Pure tremolite would have a much narrower and only partially overlapping distribution on this type of graphical presentation. Pure standards of tremolite do not reveal Na or K, and the Mg/Si and Ca/Si ratios in tremolite are generally higher than in vermiculite.

nition of the effects of tremolite contamination of vermiculite has increased public health concern (6, 11).

Vermiculite is a naturally occurring sheet silicate, with particles generally ranging from 1 mm to 1 cm in diameter. When these particles are rapidly heated above 230° C, they expand and form lightweight particles, much like popcorn, and are useful for filler and insulation.

Other than a nuisance dust effect, there is scant evidence of a harmful effect from inhalation of respirable vermiculite dust *per se*. Studies in South African vermiculite workers showed little, if any, pulmonary damage from mining vermiculite (12). Similarly, cancer mortality studies of workers exposed to South Carolina vermiculite have demonstrated that its risk is lower than the Montana material (13). Vermiculite from South Africa and South Carolina are minimally contaminated with asbestos, unlike vermiculite mined in Montana and Quebec. In these latter two areas, vermiculite ore deposits contain other minerals including tremolite. It is the tremolite and other asbestiform fibers that have significant implication to human health.

There is increasing concern about the threat of asbestos contamination of vermiculite. The U.S.E.P.A. recently compiled a comprehensive survey and analysis of commercial vermiculite products (2). Contamination of the products by asbestos, including tremolite, was found. The E.P.A. initially surveyed 16 vermiculite products in the Seattle area and detected asbestos in five of these. Subsequently, the E.P.A. expanded its survey nationally and analyzed 38 products. Of these, 17 had detectable asbestos. Furthermore, the E.P.A. conducted experiments with these products to simulate consumer use scenarios. Although the study concluded that there is little health risk to consumers, it did not discount the possibility of ill effects among workers using these materials. We have shown that such an exposure in our patient did, indeed, have a fatal effect.

The danger of tremolite asbestos exposure in vermiculite was first recognized in the miners of Libby, Montana. Since the early reports of bloody pleural effusions in these miners in the 1950s, concern was increased by reports in the 1980s describing significant morbidity and mortality in miners exposed to tremolite-contaminated vermiculite (3–6). In addition, animal investigations have shown that tremolite produces mesotheliomas and carcinomas (14, 15). Tremolite asbestos, like other amphiboles, also causes lung parenchymal fibrosis (16).

Tremolite asbestos inhalation has been associated with significant morbidity and mortality in miners, family members of miners, or individuals living in proximity to the mines. A recent series of investigative articles from the *Seattle Post-Intelligencer* newspaper further enhanced concerns about the many deaths in Libby, Montana, miners and their family members. Although the data has not been peer reviewed in a scientific journal, they reported 192 deaths attributable to asbestos exposure in these townsfolk, and another 375 were diagnosed with terminal lung disease (17).

Many aspects of this case demonstrate that our patient's lung disease was related to his vermiculite work: the combination of extensive pleural findings with interstitial fibrosis is much more consistent with asbestos-related disease than with idiopathic pulmonary fibrosis. This is particularly so in view of the bilateral nature of the pleural findings. No alternative source of significant asbestos exposure was discovered. Although there may have been an opportunity for asbestos exposure during his years as a deck officer in the Navy (e.g., sleeping below decks), it is very unlikely that this produced enough exposure to produce asbestosis.

In this case, lung biopsy and tissue analysis were key to proving a causal relationship between inhaled vermiculite many years ago and disease later in life. The lung tissue analysis is particularly persuasive. The predominance of tremolite and the proportions of various and characteristic asbestiform fibers in both lung and Libby vermiculite sample strongly supports the Libby vermiculite rather than other asbestos sources as the origin. As noted earlier, most other asbestos sources in the United States have a predominance of chrysotile. It is generally known that ship insulation in the Navy often contained amosite in addition to chrysotile. Our analysis of the patient's lung tissue excludes significant amosite exposure, and thus the argument for substantial asbestos exposure from his Navy experience, in comparison to his exposure from his vermiculite work, is rather weak.

Our case is unique and has significant implications for several reasons. First, the patient worked thousands of miles from the Montana vermiculite mine in an expansion and packing facility. Thus, whereas much attention is focused in Montana, the threat to public health is more widespread.

Second, there was a latency period of nearly 50 years between his exposure and symptomatic illness. This reinforces the need to obtain a thorough occupational history for all patients with apparent idiopathic pulmonary fibrosis.

Third, his exposure was relatively brief, but intense. Nevertheless, this led to both extensive fibrocalcific disease of the pleura and fatal fibrosis. These effects of such limited, albeit intense, exposures have not been described before. The long latency period, the brief duration of exposure, and the lack of general awareness of vermiculite as a source of asbestos exposure, make us concerned that many former workers and their

physicians may not even be aware of the dangerous exposures that occurred earlier in life.

Fourth, there was a very long period between the appearance of the pleural findings and the development of extensive interstitial fibrosis. Even though chest radiographs had shown pleural fibrocalcific disease over 20 years earlier, he did not develop significant symptoms until the last 6 months of life. Preceding his terminal illness, he was physically active and asymptomatic.

Finally, workers from former vermiculite expansion plants and other industries packaging or using vermiculite should be considered at risk. In addition, there is possible risk to persons who have had community exposures near expansion plants and secondary exposures to material brought home on the clothing of former workers. Some end-users of products are likely at risk as well.

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