



University of Texas Health Center at Tyler

# An Unusual Case of Mixed-Dust Exposure Involving a "Noncommercial" Asbestos

### Ronald F. Dodson<sup>1</sup> and Jeffrey L. Levin<sup>2</sup>

<sup>1</sup>Department of Cell Biology and Environmental Sciences and <sup>2</sup>Department of Occupational Health Sciences, The University of Texas Health Center at Tyler, Tyler, Texas, USA

Our health center evaluated an individual for suspected pneumoconiosis, which had resulted from exposures in a foundry/metal reclamation facility. Appropriate consent forms were obtained for the procedures. Historically, individuals who work in foundries have been exposed to various types of dusts. The clinical findings in this case were consistent with silicosis with a suspicion of asbestos-induced changes as well. A sample from this individual, analyzed by electron microscopy, showed both classical and atypical ferruginous bodies. The uncoated fiber burden in this individual indicated an appreciable number of anthophyllite asbestos fibers. This finding, coupled with analysis of cores from ferruginous bodies and the presence of ferruginous bodies in areas of interstitial fibrosis, pathologically supported the diagnosis of asbestos-related disease. The unique factor associated with this case is that unlike in some settings in Finland where anthophyllite was mined and used commercially, this mineral fiber is not commonly found in commercially used asbestos products in the United States. Although the actual source of the asbestos exposure in this case is still being sought, it should be recognized that anthophyllite is a contaminant of many other minerals used in workplace environments, including foundries. The fiber burden indicates a unique type of exposure, differing from that usually construed as typical in occupational settings in the United States. Key words amphibole, anthophyllite, asbestos, microscopy, pneumoconiosis. Environ Health Perspect 109:199-203 (2001). [Online 29 January 2001]

### http://ehpnet1.niehs.nih.gov/docs/2001/109p199-203dodson/abstract.html

# Case Report

This individual was first seen in early 1996 for respiratory symptoms of cough and mild shortness of breath; these prompted a chest X-ray, which was abnormal. The radiograph showed a diffuse reticulonodular pattern worse in the upper lung zones with some pleural thickening noted on the right. Breath sounds were clear, heart exam unremarkable, and extremities without cyanosis or clubbing. The hematocrit was 37.8. Other than a diagnosis of hypertension, there had been no specific history of cardiovascular disease.

The patient's occupational history at that time consisted of 32 years of work in an iron pipe foundry, with the last 28 spent in a highdust environment as a core maker—an individual who prepares silicate forms around which castings are founded. He had worked without respiratory protection until the last few years, and he had never smoked tobacco. Pulmonary function studies were consistent with a mild restrictive pattern: forced vital capacity (FVC) = 2.72 L or 73% of predicted; forced expiratory volume (FEV<sub>1</sub>) = 2.24 L or 75%; FEV<sub>1</sub>/FVC = 82%; forced expiratory flow (FEF) 25–75 = 57% of predicted (14 March 1996). Based upon this history and the X-ray findings, a differential diagnosis of silicosis, sarcoid, or tuberculosis was considered. Purified protein derivative (PPD) skin testing was positive at  $22 \times 15$  mm of induration. The patient was treated with isoniazid, rifampin, and pyrazinamide pending results of sputum stains and cultures for acid-fast bacilli (AFB). When these studies were negative, he was changed to prophylactic treatment with 6 months of isoniazid.

In late 1997, almost 2 years later, the patient experienced increased cough and shortness of breath accompanied by rales on examination and progression of chest radiograph findings. Films had been read on two separate occasions by two separate chestradiograph readers and found to be consistent with pneumoconiosis. Despite a probable diagnosis of pneumoconiosis, objective evidence of disease progression prompted an effort to secure a tissue diagnosis. Via video-assisted thoracoscopy, therefore, wedge biopsies of the lung were taken from the right middle and lower lobes. The initial pathology produced a clinical diagnosis of silicosis that was later expanded to include

asbestosis. Although asbestosis is predominantly a lower lung disease radiographically, the presence of asbestos bodies in regions of parenchymal fibrosis supports this diagnosis pathologically as outlined elsewhere in this paper. A more recent chest radiograph (early 2000) demonstrated a stable pattern of severe interstitial lung disease, pleural and parenchymal scarring, and mild hyperinflation (Figure 1). Spirometry and lung volumes (2 June 2000) are consistent with mild restriction: FVC = 2.47 L or 67% of predicted;  $FEV_1 = 1.85$  L or 62%;  $FEV_1/FVC$ = 75%; residual volume (RV) = 1.32 L or 78%; total lung capacity (TLC) = 3.96 L or 74%; and RV/TLC = 33%. Diffusion capacity was mildly reduced at 18.4 mL/mmHg/min or 67% of predicted.

# Detailed Pathologic Examination

Hematoxylin and eosin-stained tissue sections were screened via an A O Micro Star Light microscope (American Optical Corporation, Buffalo, NY) at 100/400x magnification. The open lung biopsy material submitted for tissue analysis via digestion was collected in glutaraldehyde fixative that had been prefiltered through 0.2 µm polycarbonate filters. The tissue submitted for analytical assessment was prepared in accordance with a procedure described elsewhere (1). The digestion pool was made from approximately one-half of the eight pieces of submitted tissue. The sample of material contained 1.18 g wet (0.143 g dry) tissue. The procedure used for analysis by analytical transmission electron microscopy is described elsewhere (2). The direct method of sampling enabled a scan of a cleared mixed cellulose ester (Millipore Corporation, Bedford,

Address correspondence to R.F. Dodson, The University of Texas Health Center at Tyler, 11937 U.S. Highway 271, Tyler, TX 75708 USA. Telephone: (903) 877-7552. Fax: (903) 877-7558. E-mail: rdodson@uthct.edu

Received 2 May 2000; accepted 27 October 2000.

MA) filter (pore size  $0.22 \ \mu m$ ) by light microscopy, to assess the presence of particulates and ferruginous bodies.

We used a classification system applied in our earlier study of foundry workers (3) to distinguish the various types of ferruginouscoated particles as observed by light microscopy. A replica preparation was made of the surface material collected on a polycarbonate filter (0.2  $\mu$ m pore size Nucleopore; Nucleopore Corporation, Pleasanton, CA). The grids from this preparation were scanned in a JEOL 100cx ATEM instrument (JEOL USA, Inc., Peabody, MA) at 16,000× magnification for fibers. Additional scans were made at 10,000× to assess the nonfibrous particulate burden. A 1,600× additional scan permitted greater area assessment to detect ferruginous bodies. We performed core analysis on the various types of coated structures.

We analyzed fibrous particulates as well as the core of the ferruginous bodies by selected area diffraction and X-ray energy dispersive analysis (EDAX-NX-2 analyzer; EDAX, Inc., Mahwah, NJ). All fibers  $\geq 0.5$  µm with an aspect ratio greater than five to one were evaluated in the scans.

# Results

### **Light Microscopy**

*Tissue sections.* A review of the tissue section by light microscopy revealed areas of parenchymal involvement characterized by appreciable numbers of macrophages. Interstitial fibrosis occurred adjacent to the areas of greater tissue involvement.

We observed small polarizable particulates within the macrophages. These crystalline structures varied in shape. Occasionally we found in the presence of the diffuse interstitial fibrosis one or more ferruginous bodies that were morphologically consistent with asbestos bodies (Figure 2). This observation supported a diagnosis of asbestosis based on pathologic criteria (4,5). Orientation within the tissue sections occasionally permitted recognition of a ferruginous coating deposited on a thin black filament (Type B) as shown in Figure 3. A thick, black rod was also occasionally found as a core structure. An example of this Type C ferruginous body is shown in Figure 4. We observed no ferruginous bodies in the tissue sections that suggested formation on larger plates or "flake-like" structures (Type D).

**Digested Material.** A light microscopy assessment of a cleared wedge of mixed cellulose ester filter revealed a heavy particulate burden consisting predominantly of small black particles. We saw occasional larger aggregates of the same density as the smaller structures. Many of the smaller particulates as well as larger structures were birefringent in polarized light. There was a mixture of ferruginous body (FB) types found on the slides (Table 1). There were 132 classical ferruginous bodies whose typical appearance (clear, elongated fibrous core) suggested that these were formed on asbestos (asbestos bodies). Tissue concentration was equivalent to 5,280 FB/g wet weight (ww) of tissue



Figure 1. Postero-anterior chest radiograph demonstrating diffuse, reticulonodular, and interstitial changes.



Figure 2. Classical ferruginous body morphologically consistent with an asbestos body. It is associated with alveolar macrophages.



**Figure 3.** Ferruginous body containing a thin black filament that extends out of the area of ferruginous coating and into the adjacent region (arrow). Magnification x6,100.



Figure 4. Ferruginous body within the cluster of macrophages containing an obvious thick black rectangular structure (arrow) as its central core.

(43,560 FB/g dry weight [dw]). The limit of detection was 40 FB/g ww (330 FB/g dw).

Applying the classification scheme used earlier (3) to distinguish types of ferruginous bodies from foundry workers, we found that the digested material contained seven Type B ferruginous bodies (a core consisting at the light microscopy level of a thin black filament). The cores of these ferruginous bodies were determined by analytical transmission electron microscopy to be formed on an organic filament. There were 19 Type C ferruginous bodies (having a core of thickened black rod), which were also determined to be of a carbon composition. There was one ferruginous body found by light microscopy, formed on a "flake-like" or plate material which had varying degrees of ferruginous deposits along its periphery. This body, which was not elongated, could not be confused with an asbestos body based upon its morphology.

# **Electron Microscopy**

The material collected on the polycarbonate filter for ATEM analysis represented 0.04 g ww (0.00485 g dw) aliquot of the digestion pool. A high magnification scan  $(16,000\times)$  of 0.36 mm<sup>2</sup> revealed 98 fibers. These fibers were analyzed by both X-ray dispersive analysis (XEDS) and selected area diffraction. There were 24 uncoated amphibole asbestos fibers [23 anthophyllite (Figure 5) and one tremolite] in the scanned area (Table 2). Figures 6 and 7 show the respective X-ray energy dispersive analysis spectrum and an amphibole diffraction pattern of a typical anthophyllite fiber. The 24 asbestos fibers were equivalent to 641,667 fibers/g ww (5,293,750 fibers/g dw). The limit of detection at  $16,000 \times$  was 26,736 fibers/g ww (220,573/g dw). Seventy-four other nonasbestos fibers were found in the screen. These included 47 aluminum silicates, some of which had iron and other ions as components, 8 titanium fibers, 6 crystalline silica fibers, and 2 organic fibers. The remaining fibers were of mixed magnesium silicates with combinations of other ions. The total burden of nonasbestos fibers consisted of 1,978,472 fibers/g ww (16,322,386 fibers/g dw).

An additional lower magnification scan at  $1,600 \times \text{over } 7.02 \text{ mm}^2$  yielded six elongated ferruginous bodies. The respective core of each was comprised of anthophyllite (Figure 8), tremolite, crystalline silica, one organic fiber (Figure 9), a fiber rich in magnesium aluminum silicates (MgAlSi) and one totally coated core (unidentifiable). There was one Type D ferruginous body which we determined was formed on aluminum silicates (Figure 10).

All of the nonasbestos fibers were shorter than 5  $\mu$ m. Sixty-nine percent of the

anthophyllite fibers were shorter than 5  $\mu$ m, whereas the average length of the remaining 31% was 14  $\mu$ m (Table 3).

A particulate analysis carried out at 10,000× revealed an overall moderate burden. Crystalline silica comprised 8% of the particulate burden. The low concentration of silica did not coincide with the pathologic and clinical suspicion of silicosis. However, the tissue received for electron microscopy analysis was not fully representative of involved lung zones originally determined clinically to support this diagnosis. The highest percentage of particulate was iron-rich particles (35%) and aluminum silicates (45%).

#### Discussion

A 53-year-old man was evaluated for suspected pneumoconiosis as suggested by occupational history and reticulonodular pattern on chest radiograph with pleural thickening. The individual had worked in a foundry/metal reclamation facility for 32 years. By their nature, these facilities are dusty work environments, which can create accumulation in the lung of mixed dust burdens including silica, various silicates, ferrous material, as well as fiberglass (3,2). The morphology of the inhaled particulates consists of both fibrous and nonfibrous dust.

In a previous study, lavage material from five individuals who worked in similar foundries revealed the presence of four morphologically distinct types of ferruginous bodies as seen by light microscopy (*3*) and classified as Types A,B,C, or D. These included typical-appearing ferruginous bodies (Type A), formed predominantly on asbestos, as revealed by analytical electron microscopy. Infrequently, the cores were fiberglass or thin transparent sheet silicates.

The second form of ferruginous body as defined by light microscopy had as its core a thin black filament determined by electron microscopy to be composed of amorphic organic material (Type B). The filament was sufficiently thin that its detection would be in question at lower magnification scans by

Table 1. Ferruginous body (FB) concentration as types by light microscopy.

	FB concentration		Detection limit	
Туре	FBs/g ww	FBs/g dw	FBs/g ww	FBs/g dw
Classical FB	5,280	43,560	40	330
Type B FB	280	2,310	40	330
Type C FB	760	6,270	40	330
Elongated sheet silicate FB	320	2,640	40	330



Figure 5. Electron micrograph showing an elongated uncoated anthophyllite fiber collected from digested tissue.

Fable 2. Uncoated asbestos fiber	concentration by	y types using	electron microscopy
----------------------------------	------------------	---------------	---------------------

	Uncoated asbestos fiber concentration		Detection	Detection limit	
Asbestos fiber type	Fibers/g ww	Fibers/g dw	Fibers/g ww	Fibers/g dw	
Anthophyllite	614,931	5,073,177	26,736	220,573	
Tremolite	26,736	220,573	26,736	220,573	



Figure 6. X-ray energy dispersive spectrum from the anthophyllite fiber in Figure 5.



Figure 8. Ferruginous body. Core is anthophyllite asbestos.



**Figure 10.** Electron micrograph showing an example of a nonfibrous dust. Deposits of material (arrows) are iron rich. By light microscopy, this material conforms morphologically to a nonfibrous ferruginous body.

light microscopy. Another form (Type C) appeared to be composed of the same material, but contained a much thicker black core. These were easily distinguished by light microscopy and subsequently confirmed by electron microscopy as organic. material comprising the cores in these entities were plates or "flake-like" structures, and often displayed a yellowish dark golden coloration. The striking feature among these five patients, as well as in lung tissue from other foundry workers submitted to our facility, is the abundance of

The final form of fer-

ruginous body (Type

D) was not confused

with the other elongated forms of fer-

ruginous bodies that

occur on fibrous

cores because the



Figure 7. Amphibole diffraction pattern from anthophyllite fiber in Figure 5.



Figure 9. Ferruginous body, defined by iron coating on the upper end (arrows) on the long central filament. When analyzed, the filament was found to be organic in composition and represents the thin black filaments found in some ferruginous bodies as seen by light microscopy.

Table 3. Geometric mean of unce	oated asbestos fiber din	nension
---------------------------------	--------------------------	---------

Asbestos fiber type	Length	Width	Aspect ratio
Anthophyllite ( <i>n</i> = 23) <sup>a</sup>	3.13 μm (0.8–34 μm) <sup>b</sup>	0.22 μm (0.02–1.3 μm) <sup>b</sup>	14.41
Tremolite ( <i>n</i> = 1)	`3μm	0.2 μm	15

<sup>a</sup>Total of 23 anthophyllite asbestos fibers found in the area scanned. <sup>b</sup>Values in parentheses are ranges.

ferruginous-coated material within the lung. In light of the present patient's work history and his pulmonary status, tissue samples were submitted for digestion and analysis by light and electron microscopy.

This case has consistent findings as well as unique factors when compared with observations from the previous study of foundry workers (3).

The lung tissue from the present case was found to contain "classical ferruginous bodies" which by morphologic definition could be considered asbestos bodies by light microscopy (5) and occurring at levels above that observed from general populations (6-8). Similar to our previous observations (3), this individual had nonasbestos cored ferruginous bodies, most of which, by light microscopy, could easily be distinguished from asbestos bodies.

Analysis by ATEM identified the core material of ferruginous bodies to include nonasbestos (organic material, crystalline silica, MgAlSi) and "noncommercial" asbestos (anthophyllite, tremolite) fibers. The latter contrasts with the findings of the previous study (*3*) where asbestos bodies were formed on amosite cores—an amphibole considered a "commercial" asbestos.

Exposure to various dusts has long been recognized in foundry settings ( $\mathcal{9}$ ). The rare occurrence of a nonelongated ferruginous body in this case differs from our findings of their common occurrence in samples from workers from another East Texas foundry ( $\mathcal{3}$ ).

Other distinctions between this case and our previous report exist in the uncoated fiber burden. Uncoated chrysotile or amosite asbestos fibers were found in lavage from four of the five previously studied workers.

The anthophyllite form of asbestos has been reported to be of no commercial significance in the United States (10). To our knowledge, the use of anthophyllite in the United States consists largely of two manufacturing facilities in Delaware and a small facility in Minnesota. The anthophyllite was brought to the facilities from Finland. In fact, Finland, through its mining opportunities in a quarry at Paakkila, represented the world's commercial mining output of this type of asbestos (11). No records have been found that indicate that products manufactured with anthophyllite were ever used in the foundry where the patient in this case worked.

Not surprisingly, limited data exist in the United States about cases where elevated exposure to anthophyllite has occurred. The significant presence of ferruginous bodies formed on anthophyllite in women has been linked to products such as cosmetic talc, or anthophyllite-contaminated clay where this asbestos was considered a component of the primary mineral used in the product (6,7,12-15)

Churg and Warnock (15) have noted that from a medical viewpoint the "noncommercial" types of asbestos such as anthophyllite are most likely to be encountered as natural contaminants of other minerals. When such noncommercial fibers are found in tissue from the general population, they are usually shorter than 5  $\mu$ m (8,15). The population of anthophyllite fibers in this individual is represented by considerable numbers of fibers longer than 5  $\mu$ m. The presence of longer fibers of anthophyllite is more consistent with findings from individuals with a history of asbestos exposure in the workplace where 67% of the anthophyllite was longer than 5  $\mu$ m (*1*). In the present case, 23 of the 24 asbestos fibers were anthophyllite; the remaining uncoated fiber was tremolite.

The limited data have shown that in the United States elevated exposures to anthophyllite have occurred among talc workers (16) and in commercial talc manufacturing (17). The presence of anthophyllite and tremolite in talc from the Gouverneur Talc District of New York has been verified by several studies, including a Bureau of Mines Report of Investigations in 1985 (18). A report by the government of British Columbia has noted that talc was used in the United States in 1996 in numerous products, including ceramics, paint, paper, plastics, roofing, and cosmetics. Additional applications included insecticides, rubber, refractories, and other products (19). It has also been reported that there is direct use of talc in some foundry applications (20). While a material containing talc could be suspect as a source of the anthophyllite in this case, a specific product has not yet been identified.

In the present case, we found no uncoated fibers of the "commercial types" of asbestos, in contrast to findings from previous studies involving foundry workers (3). Key observations in this case included the levels of tissue burden of anthophyllite as well as the qualitative composition of the fibers, appreciably different from expected findings in the general population (8,15). Further, the type of asbestos found was inconsistent with those described in most published observations of workplace exposures reported in the United States. It is reasonable, therefore, that this individual's exposure occurred from a product that, by content, consisted mostly of a nonasbestos mineral in which there was an appreciable component of anthophyllite.

Prognostically, this individual is at risk for progression of silicosis as well as fibrosis due to asbestos. The presence of asbestosis also places him at increased future risk of cancer. Adding to the complexity in this case is the identification of a considerable burden of "noncommercial" asbestos with a yet-tobe defined exposure source.

The instructive nature of this case centers around the concern with how many other similar exposures may occur in which asbestos is not considered a contributor to disease or risk of future disease. This omission may occur because historical links of exposure to asbestos-containing products in the workplace or environment are not immediately evident. This realization may have significant implications for clinical prognostic reasons as well as medical and legal concerns.

#### **REFERENCES AND NOTES**

- Dodson RF, O'Sullivan M, Corn CJ, McLarty JW, Hammar SP. Analysis of asbestos fiber burden in lung tissue from mesothelioma patients. Ultrastruct Pathol 21:321–336 (1997).
- Dodson RF, O'Sullivan MF, Corn C, Williams MG, Hurst GA. Ferruginous body formation on a nonasbestos mineral. Arch Pathol Lab Med 109:849–852 (1985).
- Dodson RF, O'Sullivan M, Corn CJ, Garcia JGN, Stocks JM, Griffith DE. Analysis of ferruginous bodies in bronchoalveolar lavage from foundry workers. Br J Ind Med 50:1032–1038 (1993).
- Craighead JE, Abraham JL, Churg A, Green FH, Kleinerman J, Pratt PC, Seemayer TA, Vallyathan V, Weill H. The pathology of asbestos-associated diseases of the lungs and pleural cavities: diagnostic criteria and proposed grading schema. Arch Pathol Lab Med 106:544–596 (1982).
- Churg A. The diagnosis of asbestosis. Hum Pathol 20:97–99 (1989).
- Roggli VL, Pratt PC, Brody AR. Asbestos content of lung tissue in asbestos associated diseases: a study of 110 cases. Br J Ind Med 43:18–28 (1986).
- Dodson RF, Greenberg SD, Williams MG, Corn CJ, O'Sullivan MF, Hurst GA. Asbestos content in lungs of occupationally and nonoccupationally exposed individuals. JAMA 252:68–71 (1984).
- Dodson RF, Williams G, Huang J, Bruce JR. Tissue burden of asbestos in nonoccupationally exposed individuals from east Texas. Am J Ind Med 35:281–286 (1999).
- McLaughlin AIG, Harding HE. Pneumoconiosis and other causes of death. Arch Ind Health 14:350–378 (1956).
- Alleman JE, Mossman BT. Asbestos revisited. Sci Am 227:70–75 (1997).
- Huuskonen MS. Health hazards of asbestos exposure in Finland. In: Sourcebook on Asbestos Diseases, Medical Legal, and Engineering Aspects (Peters GA, Peters BJ, eds). New York:Garland STM Press, 1980;299–312.
- Churg A, Warnock ML. Analysis of the cores of ferruginous (asbestos) bodies from the general population. III. Patients with environmental exposure. Lab Invest 40:622–626 (1979).
- Churg A. Fiber counting and analysis in the diagnosis of asbestos-related disease. Hum Pathol 13:381–392 (1982).
- Churg A. Nonneoplastic diseases caused by asbestos. In: Pathology of Occupational Lung Disease (Churg A, Green FHY, eds). New York:Igaku-Shoin, 1988;213–277.
- 15. Churg A, Warnock ML. Asbestos fibers in the general population. Am Rev Respir Dis 122:669–678 (1980).
- Gamble J, Fellner W, Dimeo MJ. An epidemiologic study of a group of talc workers. Am Rev Respir Dis 119:741–753 (1979).
- Kleinfeld M, Messite J, Langer M. A study of workers exposed to asbestiform minerals in commercial talc manufacture. Environ Res 6:132–143 (1973).
- Virta RL. The Phase Relationship of Talc and Amphiboles in a Fibrous Talc Sample. Bureau of Mines Report of Investigations 8923. Washington, DC:U.S. Department of the Interior, 1985.
- Simandl GJ, Paradisl S. Carbonate-Hosted Talc. In: Selected British Columbia Mineral Deposit Profiles Vol.
  Industrial Minerals (Simandl GJ, Hora ZD, Letebure DV, eds). Vancouver:British Columbia Ministry of Energy and Mines,1999.
- Roe LA, Olson RH. Talc. In: Industrial Minerals and Rocks (Lepond SJ, ed). New York:Society of Mining Engineers of the American Institute of Mining, Metallurgical and Petroleum Engineers, Inc., 1983;1275–1301.