as·bes·tos (ăs bĕs′təs, ăz-), *n.* **1.** *Mineral.* **a.** a fibrous amphibole, used for making incombustible or fireproof articles. **b.** the mineral chrysolite, similarly used. **2.** a fabric woven from asbestos fibers, used for theater curtains, firemen's gloves, etc. **3.** *Theat.* a fireproof curtain. Also, **as·bes′tus.** [t. L, t. Gk.: unquenchable; r. ME *asbeston*, t. OF] —**as·bes·tine** (ăs bĕs′tĭn, ăz-), *adj.*

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Sputum cytopathological findings in former asbestos workers

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Cigarette smoking asbestos workers constitute a high-risk group for the potential development of lung cancer. The Tyler Asbestos Workers Program was begun in July 1974 to examine 890 former asbestos workers, approximately 90% of whom are cigarette smokers. As of April 1975, 456 former workers had been studied by sputum cytopathology; 217 (48%) were found to have mild squamous epithelial atypias, 20 (4%) severe atypias, and 1 (0.3%) malignant cells of a squamous carcinoma. Sputum cytopathology has been found to be an excellent, simple, noninvasive, painless, and inexpensive means of early detection of premalignant and malignant lesions of the lungs.

One-third (33%) of these former asbestos workers had ferruginous bodies in their sputum. The ferruginous bodies were most numerous in aerosol-induced sputa specimens and could be readily identified by the routine Papanicolaou stain.

Introduction

The Tyler Asbestos Workers Program has been developed for former asbestos workers in order to provide them the most up-to-date care for the early detection and treatment of pulmonary diseases, particularly carcinoma. Approximately 90% of these men are also cigarette smokers, and this along with their previous occupational asbestos exposure renders them 90 times more likely than the general population to develop carcinoma of the lung.[1,2] The cohort for the program is composed of 890 former amosite asbestos workers, most of whom still live within a 150-mile radius of Tyler, Texas. The plant operated between 1954 and 1972. The program began in July 1974, and is ongoing. Each former worker is scheduled for a complete interview, physical examination, and laboratory diagnostic studies including complete blood count and urinalysis, roentgenogram of the chest, electrocardiogram, spirometry, and sputum cytopathology which serves as the heart of the program. Through April 1975, 1,184 sputum specimens from 456 workers had been studied and the results serve as the basis of this report.

Material and Methods

Sputum is collected by both aerosol inhalation during the initial clinic visit and early morning cough at home. All sputa are collected directly into 60% alcohol which serves as an instant fixative. Three sequential early morning home-collected sputa are mailed to the cytopathology laboratory and pooled into one. Sputum induction is carried out by transoral inhalation of a few breaths of an ultrasonic aerosol mist of 8% solution of sodium chloride in water. After inhaling as few as three to five breaths, the patient yields an adequate specimen which is collected directly into 60% alcohol in the sputum container. The sputum specimens are poured into a Petri dish and the cytotechnologist, using curettes, selects out portions of cellular aggregates, debris, and particulate matter and transfers them onto four prelabeled microscopic slides which have been coated with a thin layer of albumin. The cellular material is spread thinly and evenly over the slide by a second slide which is not albumin coated. The

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slides to be stained are then placed in 95% ethyl alcohol in a Coplin jar and subsequently stained in the routine manner by the Papanicolaou technique. The remainder of the specimen is utilized for preparation of a cell block. The sediment for the cell block is placed into a tissue embedding bag, passed through the routine tissue fixatives, and embedded in paraffin. The paraffin blocks of the sediment are sectioned and stained with hematoxylin and eosin and Prussian blue for iron.

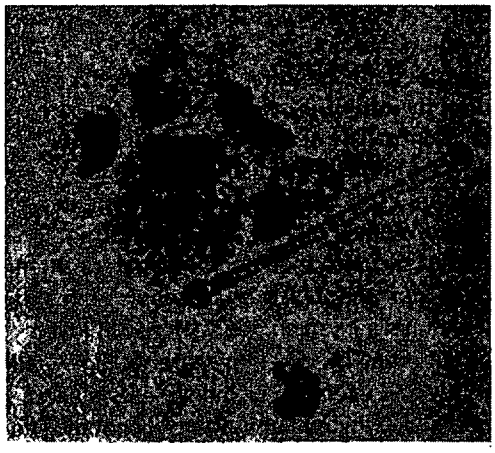
Screening of the Papanicolaou-stained sputum smears averages five to seven minutes per slide. Black ink dots are placed by atypical cells and green ink dots by ferruginous bodies. The total number of ferruginous bodies per specimen (four slides) is reported as follows: few, 1 to 14; moderate, 15 to 29; and many, more than 30. For quality control, the cytopathology slides of 10% of all negative sputa specimens are rescreened.

The sputa specimens are reported as unsatisfactory (saliva), no atypia, mild atypia, severe atypia, and positive for carcinoma. Free alveolar macrophages must be identified in order for the specimen to be considered adequate; otherwise it is presumed to be unsatisfactory. Mild atypias include squamous metaplasia and mild dysplasias. Severe atypias include moderate and severe dysplasias. The term "dysplasia" is used to imply dyskaryosis. The squamous metaplasia and the dysplasias are thought to be reversible atypias of the bronchial epithelium. "Positive for carcinoma" includes both carcinoma in situ and invasive carcinoma. We are applying this nomenclature of descriptive terminology to represent the progression of epithelial atypias from the mildest change of simple squamous metaplasia to the development of frank squamous carcinoma.

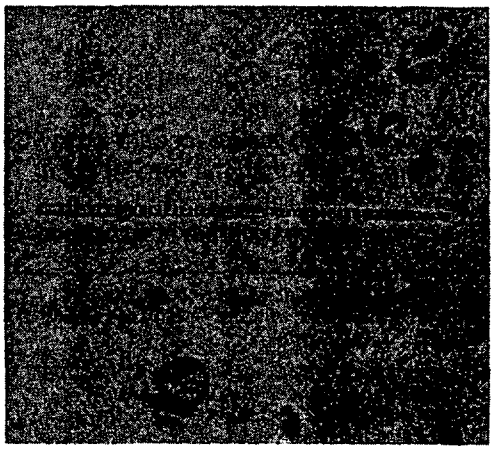
Results

Ferruginous bodies have been found in the sputa of approximately one-third of the former asbestos workers. Less than

1. Photomicrograph of sputum showing a dumbbell-shaped ferruginous body. Note the adjacent cluster of free alveolar macrophages. Papanicolaou stain, X 260.



2. Photomicrograph of sputum showing a lance-shaped ferruginous body. Papanicolaou stain, X 260.



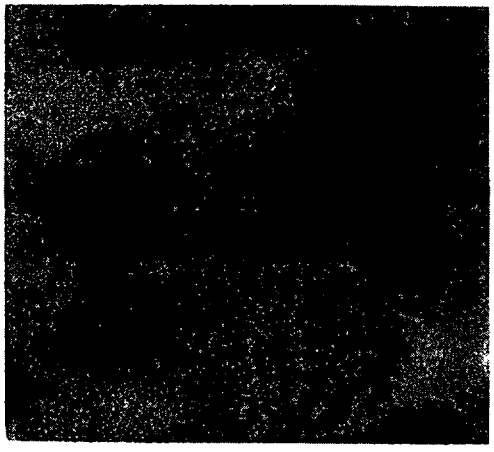
1% of those tested have failed to produce satisfactory specimens. Thus far, only one former worker has been found to have cells positive for squamous carcinoma in his sputa. He was a 76-year-old Caucasian man who had worked in the asbestos plant from 1954 to 1961. He was also a chronic cigarette smoker of 180 pack years.* Initial sputum examination disclosed both ferruginous bodies (Figs 1, 2) and malignant cells of squamous carcinoma (Fig 3). A roentgenogram of the chest showed reticular infiltrates consistent with interstitial fibrosis in the lower lobes of both lungs; however, no localizing lesion was seen. Fiberoptic bronchoscopy revealed an ulcerating lesion of the bronchus intermedius which, by brushing, washing, and biopsy, was positive for squamous carcinoma (Fig 4). Mediastinoscopy and other routine laboratory studies showed no metastasis, and a right exploratory thoracotomy was performed. When visceral pleural metastases were discovered, the carcinoma was considered to be unresectable and the operation was terminated. The patient refused both radiation therapy and chemotherapy, and died of probable ventricular fibrillation six months after diagnosis. Necropsy revealed the squamous cell carcinoma of the bronchus intermedius (Fig 5) with metastases to right bronchial lymph nodes, right visceral pleura, and pericardium. Asbestosis with interstitial fibrosis was present in both lower lobes of the lungs (Figs 6, 7) and centrilobular emphysema was present in the upper lobes.

Twenty former workers (4%) have had sputa with severe epithelial atypias, and 48% have had mild atypias, the majority of which are squamous metaplasia.

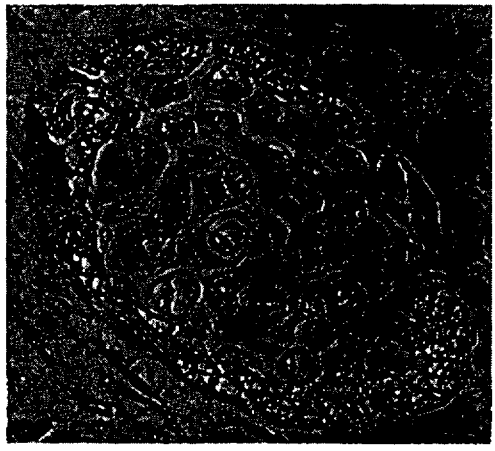
In the group of former workers whose sputa has yielded ferruginous bodies, the aerosol method of sputum specimen induction has provided for more frequent recovery of the bodies than spontaneous sputa alone. Also, by our methods of quantitation, the aerosol-induced sputa specimens contain a larger number of

*Three packs of cigarettes/day/50 years.

3. Photomicrograph of sputum revealing two large malignant cells of squamous carcinoma. Papanicolaou stain, X 260.



4. Photomicrograph of the tissue preparation of the bronchial biopsy. Note nest of malignant cells of squamous carcinoma. Hematoxylin and eosin stain, X 145.



5. Gross photograph of a coronal section of the right lung. Note the irregular white squamous carcinoma (arrow) involving the bronchus intermedius.

6. Gross photograph of coronal section of right lung. There is diffuse interstitial fibrosis of the lower lobe (arrow).

ferruginous bodies. This appears to be even more significant when one considers that the aerosol-induced specimen is a single specimen, while the spontaneous specimen is a pool of three. The sputa specimens with severe epithelial atypias were equally distributed between aerosol-induced and spontaneous specimens.

Discussion

While the first cases of pulmonary fibrosis caused by asbestos inhalation were reported in 1929,[3] and the first case of lung cancer associated with asbestos in 1935,[4] it was not until 1968[2] that epidemiologic studies established the role of asbestos in the development of lung cancer in cigarette smoking asbestos workers.

The Tyler asbestos plant was in operation between 1954 and 1972, employing 890 men who processed amosite asbestos mined in South Africa.

For many years, sputum cytopathology has been known to be a useful clinical laboratory means of early detection and diagnosis of lung cancer, yielding positive results in up to 80% of cases.[5] Only recently, however, has the role of fiberoptic bronchoscopy been established in the localization of superficial endobronchial carcinomas.[6] Serial roentgenograms of the chest will not permit truly early detection of lung cancer because such a cancer must grow and double for more than five years before it becomes large enough to be seen by the radiologist.[7]

Thus far, in the Tyler Asbestos Workers Program, only one of 456 former workers has had a sputum cytopathologic diagnosis of squamous carcinoma. Although the roentgenogram of this man's chest showed no localizing lesion, the cancer found by fiberoptic bronchoscopy in the bronchus intermedius had already metastasized to the visceral pleura and was nonresectable for cure. Twenty of these 456 former workers have severe atypia of epithelial cells in their sputa. Close clinical and cytologic follow-up of these 20 patients is presently in progress. As the program continues, all 890 former workers will be examined and reexamined

routinely at six-month intervals or more often depending upon cytopathologic and clinical findings in each case.

As yet, no statistical correlations can be made between the association of ferruginous bodies (Fig 8) and atypical epithelial cells in the sputa, but in the future, as more data are gained, this will be of great interest. Even now, one can state that the finding of ferruginous bodies in such numbers indicates significant asbestos exposure, because from 1972 to 1975, not one such body had been found in similar cytopathologic examinations of 12,000 sputa specimens from the general public in the Cytopathology Laboratory of the Harris County Hospital District, Houston, Texas.

Conclusion

Sputum cytopathology is an excellent, simple, noninvasive, painless, and inexpensive means for early detection of malignant and premalignant lesions of the lung, and no special techniques are necessary for the identification of ferruginous bodies.

7. Photomicrograph of tissue preparation from right lower lobe of lung showing a deeply stained ferruginous body with associated free alveolar macrophages and fibroblasts. Prussian blue stain, X 170.

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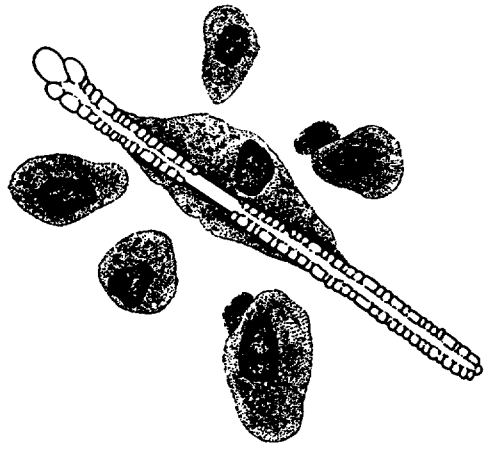
8. Artist's sketch of a club-shaped ferruginous body with associated free alveolar macrophages.



Editorials

THE SMALL BEAUTIFUL TIME BOMB

The asbestos fibril is such a tiny thing—so tiny that 1 million of them laid side by side will measure only an inch. It resists time, water, acids, fire, and body fluids. And these properties make it a time bomb. It enters the body through the nose, throat, or mouth. It lodges in the lung, pleura, pericardium, peritoneum, or gastrointestinal tract.

This beautiful mineral (that's what shimmers in tiger's-eye) lies quietly ticking in the body. It may take 20 years for the explosion to occur, but that is not long for asbestos.

A Bantu child is made to work filling jute bags with amosite asbestos. Before the age of 12 he will die of pulmonary fibrosis (asbestosis) and cor pulmonale.

A native woman has lived near an asbestos mine for 15 years. A mesothelioma develops in her pericardium; the pathologist finds asbestos fibrils (ferruginous bodies) in the resected specimen.

In England, workers with more than 20 years' experience in an asbestos-textile factory have 11 times as much cancer as men in the general population.

A housewife in Texas gets a chest x-ray. Her doctor finds scars in her lungs and pleurae. No, she never worked with asbestos, ". . . but my husband has been an insulator (using asbestos) for 20 years. His clothes sure are dusty, and I always shake them out before I wash them."

In Pennsylvania, 42 people died of mesothelioma between 1958 and 1963. Ten of the 42 had known exposure to asbestos. The other 32 were relatives of the workers, lived in the vicinity of an asbestos factory, or had some minor exposure to asbestos.

Now we come to Tyler, Texas, where an asbestos insulation plant opened in 1954. By the time it closed 18 years later, it had employed 890 workers who were exposed to asbestos (amosite) for varying periods. In this issue of *Texas Medicine*, Greenberg and his co-workers present their account of a continuing evaluation of the health of these men. This study reports the results of sputa examinations of 456 former employees. Twenty (4% of those tested) had sputa with severe epithelial atypias, and 217 (48%) had mild atypias of squamous metaplasia. One worker's sputum specimen was reported to be positive for bronchogenic carcinoma.

True, one person with lung cancer out of 456 examined is not impressive, but that is only the first sputtering of the time bomb. Usually, 10 to 20 years pass before asbestos affects the body. Pleural effusion and calcification, pulmonary fibrosis, lung cancer, intestinal cancer, and mesothelioma eventually appear. As time passes and the bomb explodes, more of the workers will succumb to incurable diseases—fibrosis and cancer.

Deplorable! Were the asbestos workers told their jobs were dangerous? Didn't they know of the danger to others in their households from the asbestos dust that they brought home? Were they provided rooms in which to change clothes? To all of these, the answer is, "No."

Was industry informed? From the moment the alarm was sounded at the Tyler plant in 1962 to the day of its closing ten years later, the management denied that asbestos was dangerous. Its scientists and physicians denied that the concentration of asbestos to which the workers were exposed was toxic to the body. The Industrial Hygiene Foundation of America refused to declare the plant safe. The company, nevertheless, fought the Department of Labor and then the Bureau of Occupational Safety and Health. After a long, hard struggle, the plant was forced to close.

Whose responsibility is it to keep the air clean of asbestos? The government is ponderous and irresolute. Industry is more interested in staying in business. To quote Paul Brodeur, science writer for *The New Yorker* magazine, "The responsibility is clearly up to men and women . . . who are the independent medical and scientific community. Only you, after evaluating the problems and after apprising yourselves of the dangers of asbestos, can say, 'No, I will not countenance such a situation.' "

Daniel Jackson, MD, Houston.

Quotation from Mr. Brodeur used with permission.