Asbestos in Lung Cancer

To the Editor:

The article by Kishimoto and Okada merits several comments ("The Relationship between Lung Cancer and Asbestos Exposure," Chest 1988; 94:486-90). The study's intent is admirable and important; however, it calls into question the adequacy of review prior to publication. First, the methods are inadequately described. Are the results of asbestos body counts reported on a number per gram wet or dry lung? What were the instrumental conditions of the scanning electron microscopy (SEM) analysis? Second, not enough data is given to interpret the results. The dimensions of the asbestos bodies were not reported. Were the asbestos bodies analyzed or were the areas of uncoated fibers analyzed? No standard energy dispersive x-ray spectra are shown, and the one spectrum illustrated closely resembles tremolite asbestos (with nearly equal Mg and Ca peaks, both of which are roughly 25 percent the intensity of Si peak) rather than chrysotile (which would have more nearly equal Mg and Si peaks and less or no Ca). Thus these results must be seriously questioned, which leads to questioning the conclusion that chrysotile was the most widely found component. This subject is too important and sensitive. I refer the reader to the recent article by Churg (Chest 1988; 93:621-28). There is a great discrepancy with results from most laboratories (the cores of asbestos bodies are rarely chrysotile fibers). Perhaps the author's reference chrysotile (which they did not document) was heavily contaminated with tremolite (or mislabeled).

Quantitation of chrysotile and amphiboles is needed. It is not surprising that chrysotile is the dominant asbestos type (assuming for the moment that the undocumented analytic results are as stated); Values for normal subjects in California show ≥10 chrysotile fibers/gm dry lung and ≤10,000 crocidolite and amosite fibers/gm dry lung. It is essential to document the concentrations and dimensions of asbestos fibers. One could then assess whether the amphiboles or the chrysotile fibers were abnormal in concentration and/or dimension.

In the abstract, the authors state that "residents of Kure had high exposure to the inhalation of asbestos bodies". Does this type of sentence reflect a lapse in editorial reviews and assistance?

There is no mention of asbestosis in these cases. Was it observed? Was it graded?

The Figures have cases missing or misplaced in plotting.

The text is poorly proofread: "cases with right lung involvement (4,065) had more asbestos bodies than those of the left side (19,952)".

The references are certainly not current. The most recent is 1984. Some citations of literature are dangerously inaccurate (eg. citation of references 18 and 19). References 8 has a nongrammatical title.

Unless retracted or corrected, this article could lead to much unnecessary muddying of the literature.

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McFadden on exercise-induced asthma which stresses the importance of bronchial vasculature in the pathogenesis of exercise-induced asthma (EIA).1 Nasal blood vessels (as well as bronchial blood vessels) are important structures for conditioning luminal gas temperature and humidity. Functionally, nasal vasculature resemble bronchial vasculature in their response to environmental, physical, chemical, nervous and hormonal stimuli.

We have extensively studied several factors which regulate nasal airflow resistance (Rnaw) and nasal blood flow (Qn) in man, including nasal or oral hyperventilation and physical exercise.2 If bronchial blood vessels react similar to nasal blood vessels (as we believe), rebound bronchial vascular congestion (RBVC) 5 to 10 min postexercise could explain the hypotension suggested by McFadden1 and Gilbert et al3 in the pathogenesis of at least the early phase of EIA.

Nasal blood vessels in patients with allergic rhinitis (with or without bronchial asthma) are hyperplastic and hypertrophied; so are bronchial blood vessels in patients with bronchial asthma. The response of these blood vessels to various stimuli is also exaggerated.

The usual response of physical exercise in both healthy subjects and patients with allergic rhinitis (with or without bronchial asthma) is an immediate decrease in Rnaw due to an increase in sympathetic nervous activity, causing vasconstriction of the precapillary and capacitance vessels in the nose.4 This response is initiated in the hypothalamus.5 The prompt decrease in Rnaw is followed by a recovery phase, which is faster in patients with allergic rhinitis with bronchial asthma, especially in those who develop EIA.3

In about 60 percent of patients with allergic rhinitis and bronchial asthma there is a pronounced rebound in Rnaw which is due to rebound nasal vascular congestion (RNC). This occurs 5 min postexercise in patients who develop EIA; at the same time, these patients begin to experience symptoms of exercise-induced bronchoconstriction.2

If bronchial blood vessels reacted similar to nasal blood vessels during and following exercise, there would be vasconstriction of bronchial precapillary and capacitance vessels, all aimed at conserving expiratory heat and water loss. This could be followed by rebound bronchial vascular congestion (RBVC) similar to RNC a few minutes after exercise. Rebound bronchial vascular congestion could itself lead to bronchial mucosal edema and swelling, hypomobility of bronchial mucosa which could trigger mediator release and promote postexercise-induced bronchoconstriction.

The mechanisms underlying RNC and RBVC in patients with allergic rhinitis and bronchial asthma are less clear but this response is consistent with a high degree of vascular and mucosal lability in these patients.

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The Editors:

Dr. Abraham's comments partly relate to the methodology of our work. Our methodology was not described in details since these methods have been described before elsewhere,1,4 and we felt it was adequate simply to reference them. However, since the points are raised we can answer them in detail:
1) Asbestos body counts were done per gram of wet lung.
2) Instrumental condition and dimension are ZAF correction 15.00 KV, VFS 2,048.
3) For SEM sample, we used uncoated fibers. Samples we examined were lysed with sodium hypochlorite and partly modifications of uncoated fibers were observed. Because of this, we examined these asbestos fibers by TEM also, confirmed the typical structure "scroll" in these asbestos and determined these fibers to be chrysotile.
4) Dr. Abraham is oblivious to the fact that the spectrum of tremolites in x-ray spectrum analysis is very similar to that of chrysotile. This explains why we did not emphasize the x-ray spectra of asbestos fibers. It is clear that our conclusions and interpretations were well within the scope of our data.
5) In this paper, almost all data were dependent on light microscopy; only 20 asbestos fibers were examined by x-ray analyzer. We want to examine much more asbestos uncoated fibers obtained from cases with lung cancer and have now started this study using TEM.
6) Dr. Abraham questions the exposure of Kure City residents to asbestos bodies, but more than 40 years have passed since such exposure could have occurred. How can one quantify exposure 40 years after an event?
7) There are five cases of asbestos in these 51 lung cancer cases, but all of these have a low grade of lung fibrosis.

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Diagnosing Thymic Neoplasia

To the Editor:

I am having great difficulty accepting the diagnosis of thymic neoplasia in the report by Dr. Asamura and co-workers (Chest 1988; 94:947-49). Case 1 appears to be a case of T4N2 lung cancer, and its light micrograph includes a structure which seems possibly to be a rosette of a malignant carcinoid tumor. Case 2 appears also to be lung cancer T3 as best I can tell—and large cell anaplastic not otherwise classifiable on the light micrograph.

The criteria used by the authors to diagnose thymic epithelial origin seems to have been: tumor involvement of the thymus, lymphocytes admixed with epithelial tumor cells (particularly in case 2), and epithelial cells both leu 7 and keratin positive.

Both tumors look cytologically malignant from the photographs and thus qualify as thymic carcinoma provided that thymic origin was proven. To prove this, it is generally accepted that lung origin must be excluded, since tumors of the lung and tumors of the thymus are known to be histologically similar.1 Lung origin has not been excluded in these two cases (indeed, it seems most likely).

Lung cancer quite often is associated with a mononuclear host response which has been shown to be primarily T cell.4 Thus, while thymic epithelial tumors often are accompanied by T lymphocytes, one cannot conclude that an intrathoracic epithelial tumor with admixed T lymphocytes is necessarily a thymoma.

While the authors’ reference 10 does state that leu 7 decorates epithelial cells of the normal thymus and thymomas, that reference also clearly points out the nonspecificity of leu 7. Leu 7 is known to be present in small cell and non-small cell lung cancer. Again, I would argue that, while thymic epithelial tumors are typically leu 7 positive, one cannot conclude that an intrathoracic epithelial tumor which is leu 7 positive is necessarily thymic.

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To the Editor:

The question raised by Dr. Miller seems to be, in part, due to limited space for the text, including information regarding the immunohistochemical study and microphotographs.

Indeed, as Dr. Miller pointed out, lung cancer is often associated with T lymphocytes as a host response to the tumor. Our previous study demonstrated that these infiltrating T lymphocytes are subset of OKT6-negative and Leu 4-positive mature T lymphocytes. However, many T lymphocytes seen in association with thymoma are immature and OKT6-positive. Immunohistochemical study of the two present cases revealed a significant number of OKT6-positive immature or cortical T lymphocytes in the tumors; especially in case 2 numerous immature T lymphocytes were seen throughout the tumor (not shown in the article). No OKT6-positive immature T lymphocytes were shown in any of lung cancers examined. OKT6-positive cells in lung cancers were not lymphocytes but Langerhans' cells. Therefore, these two cases presented are definitely thymomas.

Furthermore, in case 1 the only site of lymph node involvement by the tumor was the anterior mediastinum. Neither pulmonary nor hilar nodes were involved. Considering the route of lymphatic drainage in the lung, the lung is least possible as an origin of the tumor.

Histologically and cytologically, tumors of both cases displayed only slight atypia. The microphotograph of case 1 was presented

FIGURE 1. Histologic appearance of the tumor in case 1. Tumor is composed predominantly of epithelial cells with minimal atypia, indicative of the predominantly epithelial thymoma. H. & E. X179.