

Correspondence

Diagnosis and Initial Management of Nonmalignant Diseases Related to Asbestos

To the Editor:

The Ad Hoc Statement Committee submits that the American Thoracic Society currently recognizes no confounding by cigarette smoking in the radiographic presentation of asbestosis (1). This challenges the current state of science in this field. Small, irregular opacities are recognized to be present on the posteroanterior chest X-ray in a significant number of individuals (~5%) without any prior history of exposure to either particles or fibers. There is voluminous investigation defining the capacity of cigarette smoking to result in such a profusion of irregular opacities (summarized in Reference 2). This association between cigarette smoking and chest X-ray findings of an interstitial lung injury is also supported by computed tomography that similarly demonstrates these opacities (3). Furthermore, there are pathologic data delineating the relationship between collagen deposition and fibrosis in the human lung and cigarette smoking (4). This manifests as microscopic foci of fibrosis in areas of emphysematous destruction, peribronchiolar fibrosis as an aspect of small airway disease, or the more generalized fibrosis observed with respiratory bronchiolitis-associated interstitial lung disease. Finally, there is postulated to be a shared mechanism of injury between cigarette smoking and fiber inhalation. Exposures to all particles and fibers can present as an oxidative stress in the lung and effect a fibrotic injury to the respiratory tract. Those particles associated with cigarette smoking are comparable to other particles and fibers in that oxidant generation follows *in vitro* and *in vivo* exposures (summarized in Reference 5). Such free radical production has been proposed as the common avenue for fibrosis in a tissue exposed to either cigarette smoke or asbestos.

Decades of investigation have provided the insight that cigarette smoking can confound the diagnosis of asbestosis. To disregard this evidence discredits the American Thoracic Society as a scientific body and contradicts the Society's recognition of interstitial lung disease associated with cigarette smoking (6).

Conflict of Interest Statement: A.J.G. earns \$10,000 annually in providing opinions to both plaintiff and defense law firms and functioning as an expert witness for both plaintiff and defense law firms; V.L.R. earns approximately \$100,000 per year as an expert in asbestos litigation and this comes from both plaintiff and defense attorneys and involves numerous law firms and is about equally divided between plaintiff and defense firms.

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To the Editor:

The American Thoracic Society (ATS) publishes official statements with the expectation that these statements will be balanced, scientifically rigorous, and reflect a comprehensive review of the medical literature. In our opinion, the recent ATS Statement, “Diagnosis and initial management of nonmalignant diseases related to asbestos” (1), did not fully consider alternative points of view and all of the available literature in several important areas.

Since space does not permit a point-by-point rebuttal of the Statement, we have elected to briefly consider examples of the Committee's treatment of two high-impact asbestos-related issues: the question of benign pleural thickening as a risk factor for future malignancy, and whether clinically relevant chronic obstructive pulmonary disease is a likely consequence of asbestos exposure. In the case of the former, the Committee's citing of evidence is selective, and with the latter, there are internal inconsistencies that are likely to leave readers confused and unable to independently draw their own evidence-based conclusions.

With regard to pleural plaques being associated with increased malignancy risk, the authors state, “The presence of plaques is associated with a greater risk of mesothelioma and of lung cancer compared with subjects with comparable histories of asbestos exposure who do not have plaques.... Therefore, the presence of pleural plaques should be interpreted as a marker for elevated risk of malignancy, which may be higher than the occupational history alone might suggest.” To support this point, two studies were cited (2, 3). Weaknesses of these studies have been pointed out in a more recent publication (4). In addition, other (one could argue, more powerful) data were not included in the Statement. For instance, in a longitudinal study of asbestos cement workers, the presence of pleural plaques (in the absence of asbestosis) was not associated with an increased lung cancer risk (5). The strength of this study was its prospective cohort design in which radiographic and exposure data were available in a large at-risk population subsequently followed for cause-specific mortality. Additionally, a meta-analysis by Weiss (6) concluded that the weight of the evidence favors the position that persons with asbestos-related pleural plaques do not have an increased risk of lung cancer in the absence of asbestosis. This viewpoint is not considered in the Statement. Further, although risk of malignancy is considered in relation to pleural plaques, the question of whether asbestosis is required to attribute lung cancer to asbestos exposure is not addressed. Given that the most persuasive scientific evidence (5, 7, 8), extensively reviewed by Weiss (9), supports the hypothesis that asbestosis is required to assign causation of lung cancer to asbestos, it is a glaring omission that this document chose not to review this area of the literature. Instead, the document addressed only the unproven association between pleural plaques and malignancy.

In the section on chronic airway obstruction, the Statement implies that clinically significant chronic airway disease can be caused by asbestos exposure alone. However, the studies cited

are unable to support that conclusion given their lack of dose-response information and failure to control for other factors (e.g., smoking, radiographic abnormalities, and age) that impact lung function. Despite this, the Committee reached conclusions that are contradictory and that were not based on a comprehensive review of the available literature. As an example of the former, the Committee states, "In general, the magnitude of the asbestos effect on airway function is relatively small. This effect, by itself, is unlikely to result in functional impairment or the usual symptoms and signs of chronic obstructive pulmonary disease." We agree. However, in the next paragraph, the Committee states, "Asbestos exposure independently contributes to accelerated decline in airflow over time, whether or not exposure ceases...." Finally, in the concluding paragraph of the airway disease section, the claim is made that "[t]he association between airway obstruction and exposure to asbestos has been well demonstrated in nonsmokers...." However, when excluding nonsmoking patients with radiographic evidence of asbestos-related lung disease and when adhering to the definition of COPD (reduced FEV₁/FVC ratio) as put forth by the GOLD initiative (10), there is no evidence of an association between clinically significant airway obstruction and asbestos exposure alone. Comments made by the Committee to the contrary are misleading and are not based on the published data.

There is very little doubt that asbestos inhalation can cause small airway abnormalities, detected both histologically (11) and physiologically (12). But when the Committee cited studies suggesting the presence of obstruction in exposed populations (either by small reductions in midexpiratory flow rates, FVC, or FEV₁/FVC ratio), it made strong assertions about the clinical implications of these changes with very little evidence to support its claims. In fact, contrary to the opinion sometimes expressed in the Statement, these changes lack proven clinical importance, and the airway effects of asbestos exposure alone are small compared with the effects of cigarette smoking, when the latter causes symptomatic, progressive chronic airway obstruction (COPD). It has been demonstrated in a study with exposure and radiographic and pulmonary function information that no decrement in FEV₁/FVC ratio was seen in relation to exposure, even while showing dose-dependent declines in FEF₂₅₋₇₅ (e.g., see Reference 12). The Statement did not include these data.

We take no satisfaction in concluding that the process leading to this Statement has failed to result in a useful and credible summary of current knowledge on causal aspects of asbestos-related health effects. The ATS imprimatur demands great rigor in the development of official statements, particularly those that have substantial potential influence on assessment of public and occupational health risks and related public policy decision-making, and are likely to be controversial if they are not balanced.

Conflict of Interest Statement: D.W. is involved in consulting and testifying for parties involved in litigation regarding occupational lung diseases; H.W. for many years has consulted with and occasionally testified for interested parties in litigation involving occupational lung diseases including those caused by asbestos.

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From the Committee:

We thank our correspondents for their interest and for articulating the ideals that we strove to follow in writing the Statement (1). We offer one clarification before addressing their individual points: The Statement was never intended to be a comprehensive review of the literature on asbestos, a task that would require years and multiple volumes. It is what its title describes: an update of the clinical criteria for making the diagnosis of non-malignant asbestos-related disease. Where a dispute, controversy, or uncertainty affect clinical management, it is discussed; otherwise, we cite the reference that was most relevant.

Ghio and Roggli suggest that the Statement does not recognize confounding by cigarette smoking in the radiographic presentation of small opacities and may lead to misdiagnosis. We direct their attention to page 700, column 1, paragraph 3, where we address this issue. Given that the criteria require evidence for nontrivial exposure to asbestos, the limited effect of even relatively heavy cigarette smoking on the profusion of small opacities (at most one minor category [2]), and the criterion requiring exclusion of alternative diagnoses, misdiagnosis is unlikely in practice.

Weill and Weill make one general and two specific points. The general point is that nonmalignant asbestos-related disease is a marker of risk for lung cancer. The Committee agrees and this point is emphasized in the introduction to the Statement and throughout, specifically with respect to management of the patient after the diagnosis is made. The Statement was not written, nor intended to review, causation of malignant disease.

The first specific point is the observation that pleural plaques are an independent marker of risk for lung cancer, which Weill and Weill dispute, relying on the work of Weiss (3, 4). Weiss wrote in his 1993 paper: "...whether pleural disease in workers exposed to asbestos is a marker for increased risk of lung cancer compared with the answer of pleural disease in exposed workers . . . is not the question considered in this review" (4). It is, however, the essential question addressed in the Statement. The 1997 review by Hillerdal and Henderson cited in the Statement examines 10 studies and comes to a different conclusion than that of Weiss (3, 4), a conclusion that has since been confirmed by the findings of Karjalainen and colleagues (5) in a 1999 study not then avail-

able to Weiss. A new study that also confirms this finding has been published (6). The Committee believed that clinicians should be aware of this association, which is now supported by a substantial body of evidence. On the other hand, the Committee did not address the reported association between pleural plaques and coronary artery disease, which requires confirmation and does not lead to an obvious recommendation for management at this time (7).

Weill and Weill actually appear to agree with the Committee on the association of chronic airway disease and asbestos exposure on almost every point. They do raise the question of whether these changes are of clinical importance and allege that the Statement makes "strong assertions" about the clinical implications of these changes. In fact, the Committee was careful to describe the magnitude of the asbestos effect on airway function as "relatively small" and provided supporting documentation demonstrating that the asbestos effect, in isolation, is quite limited. The possibility of clinically significant impairment is suggested only when the asbestos effect is "superimposed on another disease process... in persons with low levels of lung function," and as a possible factor in accelerated loss of lung function observed among asbestos-exposed workers.

The alert reader may detect a disproportion between the particular objections raised by the correspondents and the blanket denunciations of the Statement, and by extension the Society itself, in the closing paragraphs of both letters. We invite Weill and Weill, as well as Ghio and Roggli and any others who may be interested, to provide the Committee with the "point-by-point rebuttal" they propose in their letter. The Committee is prepared to discuss these issues in a suitable ATS forum and is planning such an opportunity for the 2005 Annual Meeting.

Conflict of Interest Statement: Neither T.L.G. nor any member of his immediate family or, to his knowledge, extended family have a financial relationship with any commercial entity that has a substantial interest in asbestos, exposure to asbestos liability, or business that would be affected by the Statement of this committee. During the period of deliberation of the Committee, he declined to participate in personally remunerative activities directly related to asbestos, in order to avoid the perception of conflict of interest. During this period, the George Washington University Medical Faculty Associates received fees for his professional services in a few cases in which exposure to asbestos could have been an issue, including a small number of individual cases and cases referred by the U.S. Department of Energy for evaluation (value, less than \$7,000). Dr. Guidotti receives a small revenue from royalties derived from books, one of which, *Science on the Witness Stand* (2001), contains an appendix discussing asbestos; future sales of this book are not expected to be affected (value in 2004, less than \$200). C.A.B. has never served as an expert for a commercial sponsor in the course of his occupational medical practice, he has served as an expert witness for individuals with asbestos-related disease involved in workers compensation and litigation represented by various attorneys and legal firms and has no contractual financial relationship with these individuals or their legal representatives with all work performed on an hourly fee for service basis; D.C. does not have a financial interest with a commercial entity that has a substantial interest in the subject of the deliberations of the Committee or the manuscript published as the Statement of the Committee. No member of his family has a financial relationship with such a commercial entity. The following represents disclosure of asbestos-related income for the years 2001 to the present: in 2001 he received \$2,750 in consulting fees from asbestos plaintiff attorneys and approximately \$4,000 from insurers, Medicare, Medicaid, work compensation and commercial insurers for evaluating asbestos-exposed individuals in his clinical practice; in 2002 he received \$4,600 in consulting fees from plaintiff attorneys and \$4,000 from third party payers for evaluating asbestos-exposed individuals in his clinical practice; in 2003 he received \$2,000 in consulting fees from asbestos plaintiff attorneys and approximately \$3,000 from third party payers for evaluating asbestos exposed individuals in his clinical practice; in 2004, he received \$1,225 in consulting fees from plaintiff attorneys and approximately \$2,000 from third party payers for evaluating asbestos-exposed individuals in his clinical practice; M.R.H. presented at the White House and the U.S. Congress on aspects of the Hyde-Ashcroft Asbestos reform bill; his airfare and hotel were paid for by Public Citizen and he received no other compensation. He wrote a position statement for the Association of Occupational and Environmental Clinics which set ethical guidelines for physician participation in asbestosis screening. In the early 1990s, he participated in an asbestosis screening program which was associated with investigations from multiple government agencies. No impropriety or wrongdoing was found. G.H. does not have a financial relationship with a commercial entity that has an interest in the subject of this letter; J.R.B. does not have a financial relationship with a commercial entity that has an interest in the subject of this letter. He has been an expert witness for plaintiffs who have

filed asbestos-related disease claims, but has not personally received remuneration for work on these cases. Remuneration has always gone to his employer, e.g., Regents of the University of California; P.H. and his employer, University of California, Los Angeles, have received approximately \$10,000 from Conwed Corp. for a project and payment for medical consultation and expert witness services and approximately \$7,500 from multiple insurers and attorneys in 2001–2004; F.H.Y.G. is employed full time jointly by the University of Calgary where he is a Professor of Pathology & Laboratory Medicine and by Calgary Laboratory Services where he is the Chief of the Autopsy Service for the Calgary Health Authority. He has not been employed by a commercial entity that has an interest in the subject of the statement and does not perform consultant work. In the past three years, his medical/legal consultations involving claimants in the United States have been entirely in the area of black lung compensation and none of the cases have involved asbestosis. He is also employed infrequently (once or twice a year) to review potential cases of occupational lung disease for the Alberta Workmen's Compensation Board; in the last three years two of these cases have involved the pathologic diagnosis of asbestosis at autopsy. He is paid for these opinions at the rate of Can \$200 per hour and has also been paid to give lectures by commercial sponsors; in the last three years the only sponsorship has been by the 3M Company to give a talk on the pathology of asthma at the European Respiratory Symposium in 2002; asbestos was not part of the presentation or discussion. With Dr. Sam Schurch he has a patent pending on a treatment of asthma involving surfactants and perfluorocarbons and this has no relationship to asbestos or asbestos-related injuries. He also receives royalties from a textbook co-edited by Dr. Andrew Churg entitled "*The Pathology of Occupational Lung Disease*," published by Williams & Wilkins. This book covers numerous areas of occupational lung disease pathology including asbestosis. However, the chapters on non-neoplastic and neoplastic lung disease associated with asbestos exposure are entirely authored by Dr. Churg and thus the opinions expressed in this book regarding asbestos are largely those of Dr. Churg. He has no stock ownership or options in any company that would be related to the subject of this letter; W.N.R. has a contract with Con Edison to perform CT scans on employees, some of whom have had asbestos exposure; G.R.W. does not have a financial relationship with any commercial entity that has an interest in the subject of this letter; A.M. has reviewed medical/scientific aspects of proposed administrative guidelines or legislation for asbestos-related claims for the American Bar Association in 2002 receiving no fee, for the Province of British Columbia Workers Compensation Board for a fee of Can \$150 and for law firms for a standard per-hour fee. He lectured for the Defense Research Institute for their standard honorarium and for a symposium on law and medicine for a Federal District Court, receiving no fee. He is a designated "impartial expert" for the New York State Workers Compensation Board, receiving their standard fee. He served on a NIOSH expert panel on the B Reader Program in 2004, receiving no fee. He has reviewed clinical cases for plaintiff and defense law firms and served as an expert witness in three mesothelioma trials in the past three years, the last being 10/2/02. All his publications on asbestos-related disease have been supported solely by the academic medical centers at which he was employed.

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ON BEHALF OF THE AD HOC COMMITTEE
 TO UPDATE THE 1986 ATS CRITERIA FOR
 THE DIAGNOSIS OF NONMALIGNANT
 ASBESTOS-RELATED DISEASE

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This series of letters discussing the ATS document “Diagnosis and initial management of nonmalignant diseases related to asbestos” will be continued in an upcoming issue of the Journal.