Editorial

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Asbestos-related Diseases of the Lungs and Pleura

Current Clinical Issues[1]

Asbestosis, or fibrosis of the lungs, occurring in those with exposure to asbestos, had been recognized by the early years of this century (1) and was the subject of careful investigation and report in the United Kingdom in 1930 and in the United States in 1938 (2, 3). This was followed by legislation on environmental control measures and health examinations in the United Kingdom, and recommendations on Threshold Limit Values in the United States, measures that it was hoped would result in disease control (1). However, by the 1960s it was apparent that this hope had been premature. Factors such as wartime stringencies, which had allowed increased useage with lax controls, postwar demolition of old buildings, including their asbestos lagging, and the construction of high-rise buildings requiring spray-on insulation, had resulted in the reemergence of asbestos-related disease as a major health hazard (1). Furthermore, new risks associated with exposure, such as cancer of the lung and pleura, had now become recognized; its role in the production of other cancers was also suspected (1). In addition, more acute parenchymal and pleural reactions, such as desquamative interstitial pneumonia and acute pleural effusions, had been described (1).

Over the last 20 yr the relationship of asbestos and disease has been the subject of intense study by scientists of many disciplines (4). Scientific investigation has been accompanied by close attention from increasingly concerned work forces and manufacturers, from an increasingly informed public, and from governments sensitive to the health implications of the issues and concerned as to the role they should play. Nevertheless, the application of current scientific knowledge to personal health issues must inevitably remain in the hands of the individual physician dealing with his or her patient.

This editorial addresses some current clinical issues from the perspective of the practicing physician and in light of present knowledge. Developments since an earlier clinical review in this Journal (5) will be emphasized. Public health issues have recently been reviewed elsewhere (6–9).

Most physicians (and many members of the public) are now aware that there are several varieties of asbestos. The main commercial fiber is chrysotile, accounting for approximately 95% of world use, with the commercial amphiboles—crocidolite in the United Kingdom and amosite in the United States—accounting for most of the rest (10). Anthophyllite has a small commercial use and exposure to tremolite occurs because it contaminates other exploited materials, e.g., chrysotile in Quebec, talc in New York state, or agricultural land, as in certain areas of Europe and the Middle East (10).

In the earlier review (5) it was noted that exposure response relationships were demonstrable for the major asbestos-associated diseases despite the fact that all measurements of exposure developed could be regarded as no more than a poor reflection of dose delivered to the target organs. The question of whether fibers differed in their disease potential was also reviewed; at the time there was already evidence of a fiber gradient for mesothelioma, less evidence of a gradient for lung cancer, and least for fibrosis (5). For mesothelioma, exposure to crocidolite appeared to carry the greatest risk, exposure to chrysotile, a lesser risk, with amosite probably in between (11). Anthophyllite, though recognized as carrying a lung cancer risk, had not been associated with mesothelioma production (11). In addition, the mesothelioma risk, at least for amosite and chrysotile, was thought to be higher in manufacturing than in mining and milling (11).

A review of relevant present knowledge is obviously beyond the scope of an editorial. However, the task is made easier by recent reviews (1, 7–9) and the published proceedings of two recent international conferences (12, 13). Contributions to knowledge have come mainly from (*1*) epidemiologic studies in exposed populations addressing for the main part etiologic issues (*14*), (*2*) the quantitative as well as qualitative analyses of lung dust content (15), and (*3*) studies focused on the cell and its response to exposure (16).

Lung Dust Assessments

Lung dust burden may be assessed quantitatively, using fiber counts of ashed lung material, and qualitatively, by fiber identification. A conference in 1964 drew attention to three important points. First, lung dust content of asbestosis cases was much lower than that of silicosis cases and did not increase with increasing degrees of fibrosis. The explanation offered was that asbestos fibers were dissolved in the lung over time and, on the basis of the physiochemical properties of the different fibers, it was suggested that chrysotile would be the most easily attacked, amosite the least, with crocidolite in between (17). Second, using electromicroscopy it was shown that the bulk of lung dust in laboratory animals and in humans consisted in small particles less than 1 μnm in length (18). Third, the widespread prevalence of coated fibers (asbestos bodies) in routine autopsy material (19) raised two issues, the apparent indestructibility of fibers in the lung and the universal nature of exposure clearly involving the general public. The latter issue was

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Of particular concern in view of the relatively recent (at that time) recognition of the mesothelioma risk, including its association not only with occupational but also with nonoccupational exposure such as domestic contact.

By 1972, there had been impressive developments in the qualitative assessment of individual fibers (20), and by 1978, there was ample confirmation that the bulk of the lung dust burden was in short fibers less than 5 μnm, and that fibers over 25 μnm were rarely seen. In addition the dimensional characteristics of lung dust were shown to vary with fiber type, chrysotile fibers appearing as the shortest and finest, amosite as the longest and coarsest, and crocidolite fibers being of an intermediate range (21). Subsequent studies have shown that only the longer fibers are likely to undergo the process of coating (22), hence it follows that coated fiber counts in human lungs tend to reflect the amphibole load and uncoated fiber counts the chrysotile load (23–25).

Subsequent studies have also strengthened the evidence that fibers dissolve out of the lungs over time, the loss occurring preferentially in chrysotile fibers. Thus, though chrysotile accounts for the bulk of commercial use and hence human exposure, it is the amphiboles that constitute the core of the majority of asbestos bodies found in human lungs, even in those known to have had occupational exposure to chrysotile (23, 24, 25). In addition, studies of lung dust residues in Quebec chrysotile miners have shown the presence of almost as much tremolite, even though the latter fiber is a contaminant occurring only in small amounts in the chysotile deposits worked (26). Finally, the results from two mesothelioma case control studies, one in the United Kingdom and one in the United States, reported in preliminary form in 1980 (14) (one was subsequently reported in full (27)), also suggest the preferential loss of chrysotile. Thus, both studies showed the quantities of chrysotile in cases and their controls to be comparable (chrysotile also accounted for most of the lung dust burden); however, there was an excess of crocidolite in the United Kingdom and of amosite in North American cases in relation to their respective controls. All these findings strengthen the evidence that chrysotile is cleared more readily from the lungs than other fibers and may explain, in part at least, the fiber gradient in health effects (28).

Quantitative and qualitative assessment of lung dust residues provide (with obvious caveats as to degradation and clearance) a much closer measure of dose delivered to the target organ than indexes of exposure available to date for epidemiologic research. Often these have been no more than duration of employment since first exposure (5). Even a more complicated index such as cumulative exposure has to be based on incomplete past information obtained usually from area (not personal) sampling (7). More important, no index can in fact take account of any let alone the many factors, environmental and personal, that must determine whether or not inspired material will be retained and if so for how long (6).

Asbestos-related Diseases of the Lungs and Pleura

Acute pulmonary reactions to asbestos exposure. Appreciation of the promptness and character of these reactions, in particular those in the short-term (within days or weeks), comes from research on animal models (29), from *in vitro* cell studies (16), and from observations on bronchoalveolar lavage material in animals (29) and in humans (30, 31). Thus exposure is followed by a reaction sequence that includes macrophage activation and release of chemotactic factors for neutrophils, as well as a protein factor that disturbs collagen balance; this sequence of events is thought to "cause chronic irritation in the sense of intrinsic activity depending on the kind of fiber and its geometry" (16). Indeed, it is now difficult to accept that any airborne dust inhaled into the lung is truly inert, including dusts not generally believed to be fibrogenic or oncogenic. However, the link between reactions at the cellular level and at the organ level remains to be established. An important question is whether any components of the exposure reaction are reversible in humans, as is suggested by animal work (32). For instance, in one 7-yr prospective study in humans, certain clinical abnormalities such as basal rales, particularly if present on their own at the time of the first examination, were often not present on the next examination, a finding consistent with the possibility of regression of certain components of the human response (33).

Parenchymal fibrosis. The clinical indicators of parenchymal fibrosis include breathlessness, basal rales, pulmonary function changes, and small, mainly irregular, opacities on the chest radiograph (33). A relationship between exposure and prevalence of all these indicators, either individually and/or in combination, has been shown in most sectors of the asbestos industry, including mining and manufacturing, as well as in the application and use of asbestos materials (5). Experimental evidence suggests that effects are proportional to the number and dimensions of fibers rather than their dose by weight (16). Direct measurements of lung dust recently reviewed (34) tend to confirm the dose relationship between lung dust burden and fibrotic changes. However, it is not clear what determines progression from the initial cellular reaction mentioned above to what has graphically been described by Turner-Warwick and coworkers (31) as the "perpetuating circuits of fibroblastic proliferation or collagen condensation no longer dependent on the primary agent." Implicated are certain changes in the immune system (35, 36) but probably not genetic factors (37). Epidemiologic data showing that radiologic progression is only poorly related to exposure (38–41) also point to the importance of individual characteristics in determining a subject's response to exposure. In addition, after withdrawal from exposure, not only may existing abnormalities progress, but in a not unimportant number of cases, as much as 10% in one study (38), new changes may appear. As regards between-fiber differences in fibrogenic potential, the evidence is only very modest in contrast to that for between-fiber differences in oncogenic potential (7), which is considerably stronger (see subsequently).

Cancer of the lung. The first case of death from lung cancer in a man with asbestosis was reported in 1935; some 60 cases were reported over the next 20 yr (42). The first study to test the causal hypothesis was reported in 1955, and since then some 16 or more major cohort studies have been carried out and all showed an excess of lung cancer in relation to exposure (42). All major commercial types of asbestos have been implicated (7, 43, 44), though all probably do not carry the same risk (7, 14). In addition there is some evidence that risks may be greater when expo-

sure occurs in the manufacture of asbestos products and their use and application than when exposure occurs in mining (7). The lag-time between first exposure and the development of lung cancer is long, seldom less than 10 and usually over 20 yr (7, 14). Today's cases are thus the result of the exposures of yesteryear; cases will no doubt continue to appear but should, it is hoped, eventually level off in view of the general improvement in working environments.

It is still not clear whether the distribution of cell types in asbestos-related lung cancers differs from that seen in nonexposed persons (35). Some asbestos-related lung cancers appear to be scar cancers, i.e., a complication of asbestosis, as in other forms of pulmonary fibrosis such as scleroderma. Their cell type (adenocarcinoma), as well as their location (peripheral, usually lower lobe) and origin (often *multicentric*), are consistent with this suggestion. Others, usually squamous cell types, occur often in association with only minimal fibrosis, are centrally located, and are usually seen in workers who smoke. Similarly, in epidemiologic studies, parenchymal radiographic abnormality, and by implication pulmonary fibrosis, predates the appearance of cancer in some but not all subjects who later died of cancer (45). These findings are also not inconsistent with the possibility of more than one etiologic mechanism operating in the production of asbestos-related lung cancers. The role of cigarette smoking, more than additive to the exposure risk in some epidemiologic studies, and *multiplicative* in others (14), cannot be assessed with certainty in the individual case.

Lung cancer risk is related to exposure, and most studies suggest that the relationship is linear and almost certainly without a threshold below which there is no risk (7, 44). Risk differs from work force to work force, differences that do not appear entirely explained by quantitative differences in exposure (7, 46). In addition a recent report on Australian crocidolite miners (47) serves to strengthen the existing evidence for a fiber gradient in lung cancer production, the risk being greater for crocidolite than for chrysotile (14). Industrial exposures also appear to carry a higher risk than mining and milling (7).

Malignant mesothelial tumors. An association between mesothelial tumors and asbestos exposure was first reported in 1959 (10). By 1963, it was recognized that most commercial fibers were implicated, and a fiber gradient was suggested (48). By 1979, information on mesothelioma rates for work forces exposed to Australian crocidolite at source (47), as well as in its use in the manufacture of wartime gas masks (49, 50), together with information on the differences in the recovery rate of the various fiber types from the lung (see above), had greatly strengthened the evidence for a fiber gradient. The amphibole fibers (crocidolite in the United Kingdom and amosite in North America) are more strongly implicated than chrysotile (14). Experimental evidence shows that the carcinogenic potential of fibers, given access to the cell, is primarily determined by particle size (10, 51). Exposure to tremolite may be associated with mesotheliomas if the particles are in the oncogenic size range, less than 2.5 μnm in diameter and greater than 9 μnm in length (10).

Evidence for a dose relationship to exposure for this malignancy is still modest. What is available supports the concept of increasing risk with increasing dose without a threshold (7, 44), but with age at first exposure an important determinant (46). Cigarette smoking is not apparently related to its development. The long lag time, the often low levels of exposure in the remote past, and the occasional history of domestic and/or environmental exposure (accounting for as much as 10 (52) and 15% (6) of cases, respectively) remain the most disturbing aspects of this tumor. Concern was increased by the recent report of what can reasonably be termed an epidemic of mesotheliomas in rural Turkey (53). The cases cluster in certain villages (pleural mesotheliomas dominating in some areas, peritoneal in others), while high rates for other types of pleural reaction including plaques and calcification are seen in yet other areas. The soil and rocks in some regions contain not asbestos but zeolite minerals in fibrous form (erionite), with dimensions in the range believed to have oncogenic capacity (see above), and these materials are frequently used in stucco applied to the local buildings (10).

Nonmalignant pleural disease. Nonmalignant pleural disease associated with asbestos exposure may take several forms (54). Thickening of the visceral pleura (usually occurring as part of parenchymal fibrosis) and parietal pleural plaques had been recognized as being associated with nonoccupational as well as occupational exposure prior to 1964 (55) and likely influenced by fiber type. Exudative pleurisy (pleural effusion) and progressive pleural fibrosis were described later (5, 54).

In 1979 attention was drawn to the high prevalence of pleural changes in workers in certain parts of the industry, including mining (56), construction (54), and, in particular, shipyard occupations (57, 58) where the prevalence of these changes may exceed that of parenchymal disease. In one study smoking appeared to influence the prevalence of pleural reactions (57). There is underdetection of pleural plaques by the chest radiograph (59) and their effects on lung function are modest compared with those of the pleural thickening and fibrosis that not infrequently follows active pleural reactions (60). They may, however, predict mortality (45).

Pleural plaques had been dubbed the visiting cards of asbestos, a term implying minimal health effects and in line with the views expressed in 1972 (61). However, it was clear from subsequent reports that some pleural reactions, such as those associated with dockyard exposures (57, 58), may be less innocent than originally believed; workers with these changes are more likely to develop progressive parenchymal fibrosis than those without (57), and may have an increased risk of developing mesothelioma (62).

Pleural plaques and/or calcification (detected by radiologic methods) have been reported in rural populations in a number of countries, including Czechoslovakia, Bulgaria, Finland (10), and recently in Greece (63), as well as in Turkey as discussed above. These pleural reactions are attributed to exposure to fibers and/or other materials found in the soil, the fibers implicated being mainly tremolite and anthophyllite, but unlike the situation in Turkey, these exposures do not appear to evoke malignant pleural reactions (10).

Airway responses. Evidence that occupational exposures to respirable particles play a role in the development of bronchitic symptoms (in particular, increased cough and sputum) has led to the acceptance of the term industrial bronchitis (64). The relationships be-

tween occupational exposure and cigarette smoking on the one hand, and bronchitic symptoms and airflow limi- ·tion on the other hand, have been .died in some detail in coal miners in ıom the deposition of the larger in- ıaled particles in the major airways is believed to be responsible for the mucous hypersecretion; these airways are also thought to be the site for airflow limitation if it occurs (64). In contrast, small airway limitation in coal miners is believed to be more closely linked to smoking (64).

The same spectrum of airway responses (mucous hypersecretion and/or airflow limitation in large and/or small airways) has been reported in asbestos workers (65–72) with the evidence linking these changes to occupational exposure being more or less strong. Thus studies in a general population have shown an increased prevalence of bronchitic symptoms, such as wheezing, in workers exposed in a variety of occupations, including those with asbestos exposure (65). Studies of asbestos-exposed work forces have also shown an increase in bronchitic symptoms in relation to exposure consistent h the presence of an industrial bron- ·.tis; this occurs not only in the min- sector (66), where the environmental pollution usually includes a certain amount if not a lot of rock dust, but also in the manufacturing section (67) where the environmental pollution is usually primarily in the form of fibers with or without other contaminants.

Function profiles suggesting large airway obstruction are not infrequently seen in subjects with asbestosis in whom a restrictive pulmonary function profile would be anticipated on clinical grounds (68). Where such changes cannot be attributed to smoking, it is not difficult to make a case for a role, contributory or even causal, of the occupational exposure; such a role may also be as important even in the presence of a smoking history, though further research is required to clarify the relationships of exposure, smoking, and airflow limitation in appropriate work forces. In addition, small airway abnormality has been shown to relate to exposure in subjects who have no ologic abnormality (69); such ·' ·nges may therefore reflect the sence of peribronchiolar fibrosis, which on the basis of both animal (32) and human (73) studies is believed to be the characteristic early lesion of asbestosis.

Finally, documentation in animal studies of the promptness of the lung cellular reactions (see above) to asbestos fibers and their nature (16, 74) has suggested potential mechanisms that might evoke parenchymal reactions to fiber inhalation other than fibrogenesis; for instance, endogenous elastase release leading to lung tissue destruction. Indeed, there appears to be good reason to review the role of all dusts, including asbestos dust, in evoking not only airway responses but also their possible role in the causation of airflow limitation. Research in this area is indicated, however difficult, and is in line with the hope expressed in a recent task force report (75) that it might be possible to "lessen the contribution of workplace (exposures) to disorders that are highly prevalent, such as chronic bronchitis."

Exposure-Response Relationships

Epidemiologic studies have in general confirmed the relationship of respiratory abnormality and/or disease to exposure in most industrial settings (5), so that the physician can reasonably assume this to be the case for most plants even if the plant or industry from which the patient comes has not been directly examined. Nevertheless, as pointed out above, there is considerable variation between subjects in response to what appear to be comparable doses, so that at high exposure levels there are those who do not respond (5), and at low exposure levels there are those who do. This may be due merely to imprecision in the measurements of exposure (as the use of personal rather than area sampling seems to suggest (76)) or to imprecision in the measurements of response or to both. Alternatively, they may be due to real modifiers of response by individual characteristics that make up a subject's "susceptibility" to react to exposure. Indeed, as exposure levels fall (and they have been doing so in many workplaces over the last 20 yr (77–79)), individual characteristics may well assume a greater importance in determining not only the actual amount of material delivered to the target site and retained there, but also the nature of the response.

Environmental Control Limits

Control limits have in general been based on assessments of the risk of developing pulmonary fibrosis. For instance, the 1968 recommendations of the British Occupational Health Society for chrysotile, 2 fibers per cm^3 averaged over 3 months (80), would allow, it was hoped, no more than a 1% risk of developing asbestosis, as evidenced by basal crepitations, in a 50-yr working lifetime. The study underlying these proposals had been carried out in an asbestos textile plant. Subsequent 10-yr follow-up measurements in the same plant showed higher prevalence rates of basal crepitations at all exposure levels, and in the investigators' opinion "left no room for complacency," although they felt at that time that it was "impossible to state definitely that the standard is inadequate" (77). In 1979 an advisory committee in the United Kingdom recommended that the control levels be reduced to 1 fiber per cm^3 (78). The increasing importance of lung cancer as a cause of death in asbestos workers was emphasized in the medical review of the ill effects of asbestos on health prepared for this committee (7). For crocidolite, a control level of 0.2 fiber per cm^3 was recommended (78).

In a recent REVIEW, Finkelstein (79) reports asbestosis rates in workers in an Ontario asbestos cement factory in relation to exposure, and compares his findings with those reported by Berry and associates (77) in the British textile factory referred to above. Finkelstein (79) used certification by the compensation authorities as his diagnostic criterion for asbestosis, and estimated that the risk of developing asbestosis would reach 1% after a cumulative exposure of only 10 fiber-yr/cm^3. This value is considerably lower than the figure of 43 fiber-yr/cm (95% confidence limits, 34 to 52) estimated by Berry and associates (77) for reaching a 1% risk of developing, not certifiable asbestosis but only one clinical indicator of this disease, basal crepitations. For possible and certified asbestosis the figures were 55 and 72 fiber-yr/cm^3, respectively.

The studies are not of course directly comparable for a number of reasons. Workers seeking compensation are more likely to be symptomatic than those who do not seek such assessments, and their assessors are less likely to give awards for short exposure. In consequence, Finkelstein's study may even have underestimated the overall risk to workers in the plant while exaggerating the slope of the overall exposure response relationship (76). Both studies assume the absence of any clini-

cal indicators of asbestosis (i.e., breathlessness on exercise, rales, parenchymal opacities, and pulmonary function abnormality) in the absence of exposure, whereas all have also been shown to occur with cigarette usage (33, 81, 82). In addition, in both studies the fiber levels used in the calculation of exposure indexes of the older men and covering the earlier years of operation of the plants are based on estimates, not measurements, of fibers in the environment, because at that time in both plants only particle counts were carried out. The indexes used, therefore, inevitably incorporate all the inaccuracies attendant on such extrapolation (76), and though they are appropriate for within-plant comparisons, they are much less likely to be valid for between-plant comparisons. Indeed, the character of the environmental pollution in a British textile mill is unlikely to be directly comparable to that in an Ontario plant manufacturing other asbestos products.

These uncertainties serve to underline the difficulties of extrapolating the health experience from one working environment to another. In addition, they underline the difficulties for scientists in attempting to supply quantitative information on exposure-response relationships and for legislators in using such information to set control limits (76). As a consequence, such limits should be regarded as no more than estimates based on the best available information of levels that will protect human health within the limits stated. As for any other estimate, they have to be updated in light of new information. Physicians need to appreciate the nature of such standards, if for no other reason than to avoid the mistake of excluding asbestos exposure as the relevant agent in a particular case because it is claimed that the environmental levels to which the patient was exposed were "in compliance with control levels." Cases that appear to have developed under such circumstances should always serve to direct attention back to the environment and its careful reevaluation.

Some Unresolved Issues

Among the important unresolved issues is the *risk associated with low level exposure*. The issue is pertinent because even the latest engineering technology is capable of controlling fiber emissions to indeterminably low levels only in certain operations; others continue to remain dusty. Furthermore, many, many tons of asbestos materials are incorporated in buildings round the world where it will continue both to delay the fire hazard on the one hand, and on the other hand, to pose a health risk if friable or if removed without appropriate care. Furthermore, some fibers will be released into the work environment as long as asbestos is mined and processed. Current knowledge on the risks associated with low level exposure depends on backward extrapolation of the findings associated with high exposure. With the lower levels of exposure for most current work forces, lag time may be longer and, perhaps, responses less aggressive, factors that will tend to make the research approaches used with success to date (e.g., cohort studies with mortality as the end point) less useful in the future. To address the issue of low level exposure, new approaches to the measurement of exposure (76, 83), including exploiting external counting methods such as magnetopneumometry for directly assessing lung dust burden (84, 85), as well as new methods of measuring response (86) and new methods in design and analysis (87, 88), should be sought. Likewise, the suggestion made in another context (89) to concentrate on what protects one person and not another, given comparable exposure to a risk factor (in this instance, asbestos exposure), might pay dividends.

A second issue, related to the first, is the *evaluation of the impact of the control measures* that have been introduced over the last 15 to 20 yr; it would be unforgivable not to learn from the experiences of the 1930s. Here, appropriate studies should exploit to the fullest the techniques of evaluation research that have been developed in recent years (87).

A number of *etiologic issues* have also been raised in this editorial. These include the following: the relationship between fibrogenesis and carcinogenesis in the pleura as well as in the lung parenchyma; what modifies exposure favorably and unfavorably for the individual and what personal characteristics collectively determine "susceptibility" to respond unfavorably to exposure; whether the concept of an inert dust can be sustained, not only as far as the lung parenchyma is concerned, but also, and particularly, as far as the airways are concerned. Finally, there is the question of *what causes the gradient in biologic effects between different fibers and/or different types of exposure*. The best explanation remains that of Timbrell (90), namely, that biologic activity relates to the degree of penetration and deposition of inhaled asbestos particles (which primarily depends on their physical characteristics); however, in light of the current knowledge, biologic response is likely to be modified by how long these particles survive in lung tissue (which probably depends on their chemical characteristics). Research throwing light on any of these issues may, by providing explanatory information, also have useful practical implications.

Clinical Issues

The clinical issues have for the most part remained the same over the last decade (5) and are concerned with (*1*) establishing the presence and nature of the disease, (*2*) assessing impairment and disability (91), (*3*) assessing cause and/or helping to establish attributability (92), and (*4*) recommending measures to protect or improve health. Only for the last two issues does the approach differ if the disease diagnosed (reactive, fibrotic, or neoplastic) is known or suspected of being linked to asbestos exposure.

Attributability (in the medical sense) depends largely on establishing exposure, which can be done by history, by an environmental enquiry conducted at the work site, or by recovery of fibers from biologic fluids or other material. A good exposure history, carefully taken, remains the most powerful of the chest physician's tools (34). It should cover (*1*) all occupations ever held, including short-term and summer jobs and military or other service (with start and stop dates, job titles, job descriptions including process and agent(s) used, as well as plant health services and worker health experience) (*2*) occupations of all household members, including their exposures, and whether clothes were brought home for laundering; (*3*) residence history, with particular reference to potential sources of neighborhood pollution (e.g., mines, plants). Although it is usual clinical practice to pursue the exposure history in face of a diagnosis of parenchymal fibrosis, it is less usual to do so in face of a diagnosis of lung cancer, unless there are specific indications. However, failure to do so in the 1980s may well be deemed negligent in view of the increasing number

recognized human carcinogens (43), many of which are released into the working environment.

The vigor with which attempts to identify asbestos in biologic material is pursued will vary with the clinical context. For instance, in a case of pulmonary fibrosis with long exposure in a plant with a known risk, it would hardly be necessary for the purposes of clinical diagnosis (or indeed for establishing legal attributability) to seek further evidence. However, when the exposure history is inconclusive, particularly if it was short in duration and remote in time, identification and/or counting of fibers in biologic material, including sputum (93), bronchoalveolar lavage fluid (94), and biopsy or autopsy specimens, may provide evidence of past exposure (95). Coated fibers are readily seen under the light microscope without special expertise; their presence indicates exposure, often but not always recent, and usually to a heavy dust cloud containing long fibers. But their absence in no way excludes past exposure, particularly if this has been to fine fibers (34). Coarse, uncoated fibers can also be seen with phase contrast microscopy; for identification of the fibers less than 0.2 μm in diameter, which constitute the bulk of the lung dust burden (see above), the electron microscope is required. Qualitative identification of fiber type by energy dispersive X-ray analysis is rarely necessary in the clinical context, though it may obviously provide useful additional information.

The application of qualitative and quantitative lung dust assessment to clinical decisions of diagnosis and etiology is attractive (96). However, such measurements should clearly be used with caution until more information on unexposed subjects, as well as more information on exposure-response relationships, becomes available (34). In addition, techniques will need to be standardized to reduce between-laboratory differences (97), and simplified (98). At present, to count all the fibers, coated and uncoated, in 3 to 4 samples from one lung represents approximately 1 wk of work for a trained technician. In light of the evidence that chrysotile is leached from the lung, it is obvious that although high counts of any fiber indicate important exposure, low counts by no means rule it out.

Given evidence of exposure and disease, it is reasonable in the clinical context to attribute the second to the first. The issue of attributability in law is beyond the scope of this editorial; it is, however, always the physician's job to bring the case to the attention of the appropriate health authorities. This is not only for purpose of possible compensation but, more important, to be certain that appropriate protection of others exposed in the same workplace is carried out, particularly if the workplace is one not previously recognized to be hazardous.

Undoubtedly, the most important issue in case management is whether or not the individual patient should be advised against further exposure; it is also one of the most difficult. The advice given should depend on the stage of the disease (within the physician's expertise) and on the current workplace environment (often outside the physician"s expertise). These issues have been discussed in greater detail elsewhere (34). In many workplaces current environmental levels are low or asbestos usage has been discontinued. Clearly, it would be immoral not to recommend withdrawal if the workplace environment counts were not in conformity with current control levels.

On the other hand, withdrawal from exposure is no certain protection against progression of already existing disease or development of new disease (38–41). Nor is it realistic to underestimate what the loss or change of a job may mean to a person for both economic and social reasons, particularly if he or she is without symptoms and believes himself or herself to be in good health. Nevertheless, few would disagree with the view expressed by Weill in his summing up at the most recent Lyon conference (99) that "radiographic evidence of fibrosis should lead to the prudent course of avoiding further exposure." However, it is uncertain whether this course of action should also be recommended for workers who exhibit limited benign pleural abnormalities only (99). Nor is it known whether removal from exposure will also influence favorably future risk for developing lung cancer; nevertheless, because it seems to be cumulative dose that is relevant and, though withdrawing from exposure may not diminish this risk, continuing exposure must surely increase it. For subjects who smoke there is good evidence (100) that quitting will favorably influence their cancer risk, as it would if they were engaged in an occupation without asbestos exposure. As always, it is up to the individual to make the final decision, and it is the physician's role to provide him or her with the medical facts as far as they are known.

MARGARET R. BECKLAKE[2-4]
Departments of Epidemiology and Health, and of Medicine
McGill University
Montreal, Quebec, Canada

[2] Career Investigator, Medical Research Council of Canada.

[3] Requests for reprints should be addressed to Margaret R. Becklake, M.D., Department of Epidemiology and Health, McGill University, 3775 University Street, Montreal, Quebec, Canada H3A 2B4.

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