# The radiographic pleural abnormalities in asbestos exposure: Relationship to physiologic abnormalities

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The effects of asbestos-induced benign pleural conditions on pulmonary function have been controversial since this subject was first studied in the mid-1960s. Firm conclusions have been difficult to reach because of (1) the difficulty of taking into account asbestos exposure, which may have effects on pulmonary function other than those mediated through pleural lesions, (2) the disagreement over the type and extent of radiographic pleural abnormalities, (3) the imprecision in measuring pulmonary function, and (4) the numerous potential confounding factors of reduced pulmonary function, such as cigarette smoking, age, concurrent occupational exposures, and prior chest diseases or trauma. This article critically evaluates the published reports on the functional significance of asbestos-induced pleural conditions. The results of this analysis lead to the conclusion that (1) pleural plaques are not associated with clinically significant reductions in pulmonary function, (2) diffuse pleural thickening, when extensive, can severely impair ventilation, and (3) restriction with a preserved diffusing capacity is the expected pattern when pleural lesions are responsible for reduced pulmonary function.

## INTRODUCTION

Several benign pleural conditions can result from asbestos exposure. These conditions have been demonstrated radiographically and pathologically, and have been linked to asbestos exposure by numerous epidemiologic studies over many years. Most of the epidemiologic studies have been based on radiographs. Two recent reviews by pathologists of the effect of asbestos[1,2] benign pleural conditions only briefly, but are consistent in categorizing them as follows:

- *Hyaline plaques of the parietal pleura.* These lesions are often found without adhesion to or fibrosis of the visceral pleura, and in persons without asbestosis. They are discrete lesions, no matter how numerous or large. Asbestos-induced pleural calcification is dystrophic calcification of older plaques.
- "*Pleural fibrosis*"[1] or *fibrosis of the visceral pleura.*[2] This is an adhesive process that can, when widespread, obliterate large areas of the pleural space.
- *Pleurisy with effusion.*

According to Churg, the pathologist has little to offer in the diagnosis of these pleural lesions, beyond ruling out cancer.[1] The lesions are of more interest to clinicians, radiologists, and other practitioners concerned with occupational and public health.

With access to many more cases, investigators using the radiographic response variable have supplemented and extended the observations of benign pleural lesions by pathologists. Most studies of the incidence and progression of these lesions and their relationship to antecedent asbestos exposure have been based on radiographic surveys. Some radiographic abnormalities (eg, rounded atelectasis, calcified plaques in fissures, and fissural thickening in the absence of generalized pleural thickening) are not yet fully defined as to their pathologic anatomy or relationship to asbestos exposure and, of these, only fissural thickening, because it is relatively common, will be considered below.

Plaques have a long latency period, or time from the initial exposure to their radiographic visibility. They are usually found on the lower chest wall and the central parts of the hemidiaphragms, and are sometimes seen against the left cardiac border (Fig 1a).[3] They often occur in the paravertebral "gutters" but are rarely seen there on plain radiographs. They are not found over the lung apices or in the costophrenic angles. Because calcification is a degenerative change in hyaline plaques, these plaques have an even longer latency period (Fig 1b).

Diffuse pleural thickening is a less common manifestation of asbestos exposure than are plaques. In some of the older literature, diffuse thickening was

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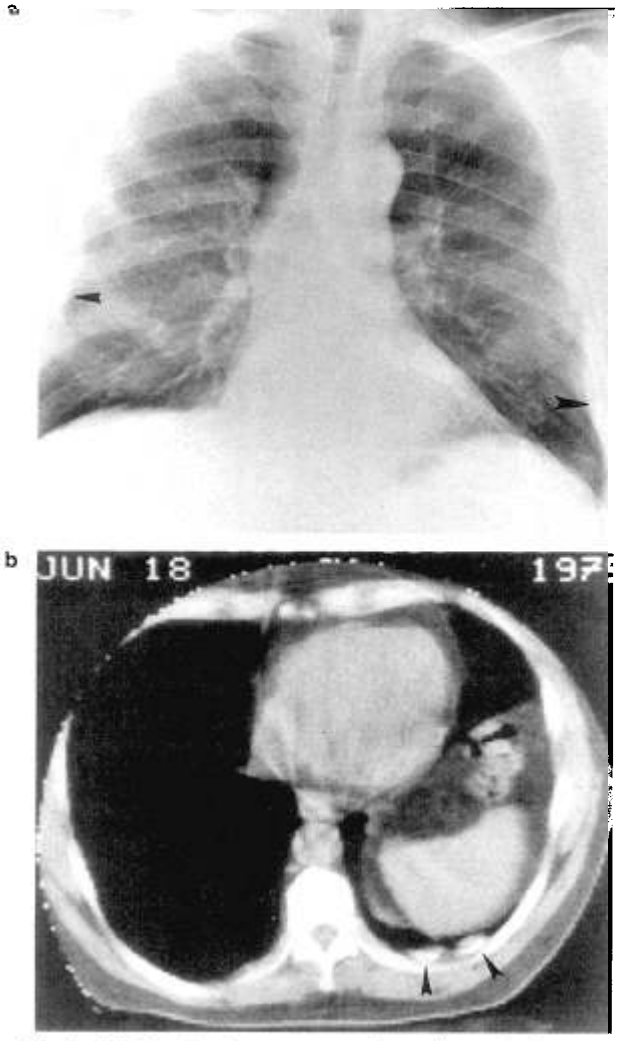


**Fig 1. (a)** Standard posteroanterior radiograph demonstrating circumscribed plaques. They consist of focal, plateaulike areas of pleural thickening that are seen in profile along the lateral chest wall (arrowheads). **(b)** Computed tomographic (CT) scan of a different patient showing calcified plaques above the left hemidiaphragm (arrowheads).

said to represent an extension of pulmonary fibrosis (asbestosis) to the visceral and parietal pleura.[4,5] Becklake,[6] in her state-of-the-art review, distinguished parietal pleural plaques from an exudative reaction that is usually widespread and involves both the parietal and visceral pleura and, usually, the lung parenchyma, obliterating the pleural space.[6]

However, in a review of 185 cases of diffuse thickening in persons exposed to asbestos, McLoud et al[7] found that the radiographic appearance of diffuse thickening was most often a residual sign of benign asbestos-related pleural effusion (Fig 2). The preceding effusion was documented in almost one third of the cases of diffuse thickening. Epler et al[8] demonstrated 35 cases of benign pleural effusion among a survey group of 1,135 asbestos-exposed workers, for an incidence of 3.1%. Residual diffuse thickening, usually with a blunted angle, was noted in more than half (54.3%) of those cases. Histologically, such cases were easily distinguished from thickening due to plaques or an extension of parenchymal fibrosis.

The spectrum of radiographically detectable asbestos-induced pleural abnormalities is shown in Fig 3. These abnormalities range from diffuse fissural thickening (Fig 3**a** and **b**) to thickening as part of a diffuse pleural reaction (Fig 3**c**) or localized plaque formation in the absence of diffuse pleural changes (Fig 3**d**). The radiographic abnormality in pulmonary asbestosis is an increase in pulmonary parenchymal small opacities, linear or irregular in shape and initially detectable mainly in the pulmonary bases. Advanced cases resemble diffuse interstitial disease of several other types, including idiopathic fibrosis. In the early stages of asbestosis, the opacities are difficult to detect radiographically,[9] and asbestosis has been diagnosed histologically in some patients with radiographically normal lungs.[10–14] Any of the pleural abnormalities described above may occur in the absence or presence of asbestosis.

## SOURCES OF IMPRECISION IN RADIOGRAPHIC-FUNCTIONAL CORRELATIONS

It is difficult to study the functional concomitants of radiographic pleural abnormalities independent of other factors that are related or unrelated to asbestos exposure. Some of these confounding factors are avoidable, others unavoidable. A discussion of the potential problems will make the approach taken in the critical review of the literature that follows easier to understand. It may also be helpful to those who are planning similar studies.

### Differences in asbestos exposure

If the investigator is interested primarily in the isolated functional effects of the pleural lesions themselves, he or she must take into account differences in asbestos exposure. If the investigator is interested in pleural lesions as indicators of past exposure or as a reflection of the intensity and duration of exposure, the details of the exposure are even more important.

Characterizing asbestos exposure has pitfalls for the unwary. For example, the designation "shipyard worker" says very little about the degree of asbestos exposure. Workers in a few shipbuilding trades (eg, insulating, lagging, pipe covering) are exposed to consistently heavy or moderately heavy levels. Boilermakers, outside machinists, and shipfitters are exposed to various levels depending on the nature of their work. Ripping out insulation produces enormous levels of airborne fibers, meaning that ship repair or modernization involves higher exposures than does new ship construction. The exposures of welders,

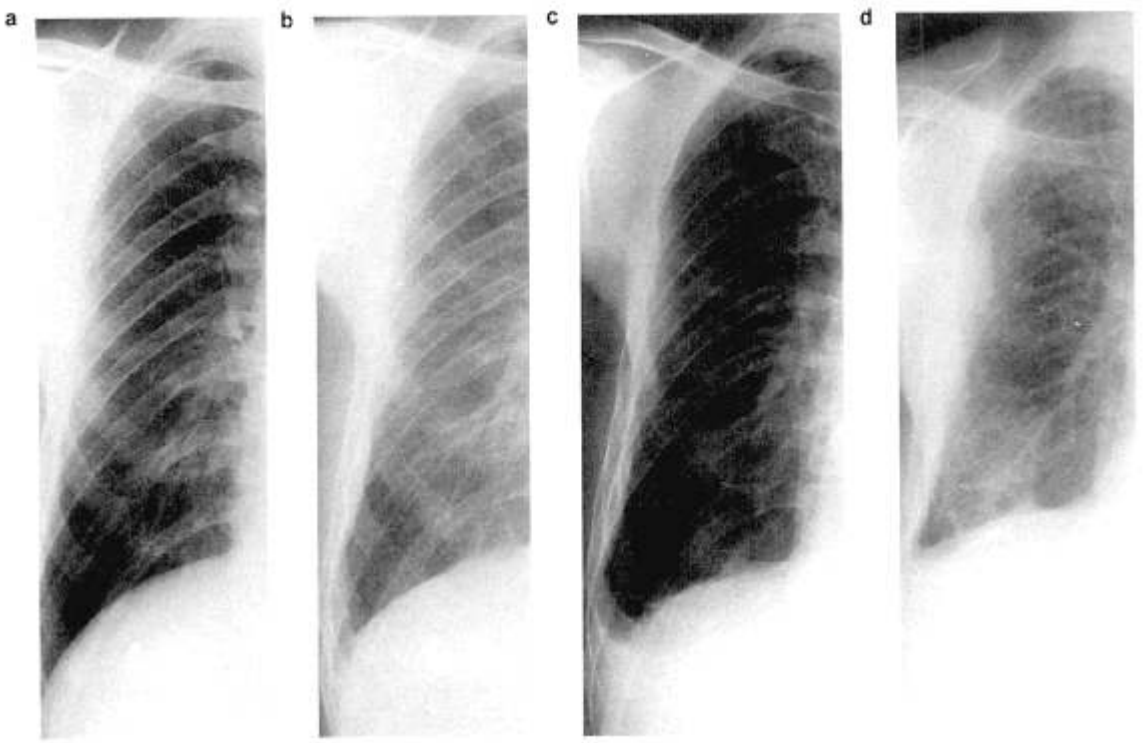


**Fig 2.** Asbestos-related pleural effusion in a 54-year-old pipe coverer who had been exposed to asbestos since 1951. **(a)** Normal film after 13 years of exposure. **(b)** Evidence of pleural plaques four years later. **(c)** Meniscus indicating pleural effusion the next year. **(d)** Film from 11 years after (c). Plaques have enlarged and there is also diffuse thickening above the costophrenic angle. Reprinted with permission from McLoud TC, Woods BO, Carrington CB, et al: Diffuse pleural thickening in an asbestos-exposed population: Prevalence and causes. AJR 1985;144:11. Copyright by American Roentgen Ray Society, 1985.

tackers, carpenters, and laborers are evidently highly variable.

However, despite this manifest diversity, more than one writer has implied that the shipbuilding trades constitute a homogeneous category of moderate-to-heavy exposure. For instance, Jarvholm and Sanden[15] aver that asbestos-cement manufacturing workers probably have a "much lower exposure" than shipyard workers, a proposition not supported by data on the relative amount of fiber either utilized in production or measured in the air in the general work place. The same diversity of exposure must certainly apply across the various construction trades, and within most of them. Insulators may be presumed to have been exposed to *uniformly* moderate to heavy levels in past decades, but the same presumption would be dubious if applied to sheet metal workers or pipe fitters, and implausible if applied to carpenters or ironworkers.

In fact, the amount of data on air sampling in both the shipbuilding and the construction industries is meager in relation to that needed to estimate accurately a person's exposure level by job or job activity. Faced with this problem, many researchers have used length of time in the industry or in a trade as a surrogate measure of cumulative asbestos exposure. This practice is acceptable to a point, but estimates based on duration alone remain inferior to those based on both duration and intensity; such estimates are also more open to being confounded with aging and with the duration-related effects of concurrent exposures. Concerning the latter, researchers should be aware that many building trades involve daily exposures to various types of smoke, silica, nonasbestos silicates, and a variety of other noxious or potentially noxious inhalants. If length of time in a trade is a surrogate measure of one type of exposure, it will be a surrogate measure of the other types. Moreover, the expression of pulmonary function test results as percentages of the predicted values ("percent predicted") does not always reflect the effects of the passage of time. This becomes important when length of time in a trade is used as the only index of asbestos exposure, and when the exposure period may cover an entire adult lifetime.

### Variability in classifying radiographically evident pleural abnormalities

The most noteworthy feature of the radiographic pleural abnormalities considered here is their varying specificity as indicators of the effects of asbestos. Included are abnormalities that are virtually certain in-

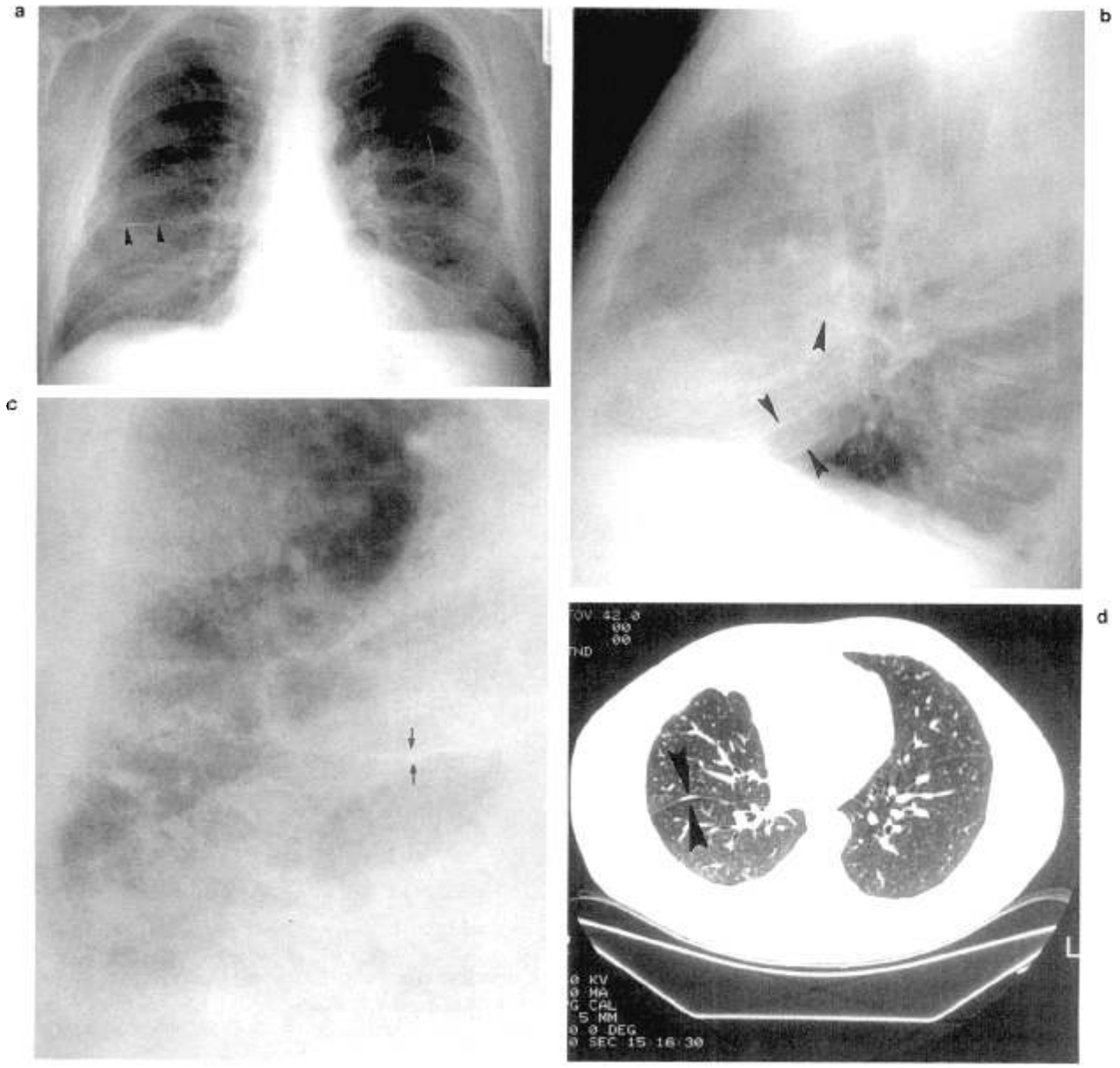


**Fig 3. (a,b)** Frontal and lateral radiographs of the chest showing bilateral major and minor fissural thickening (arrowheads) associated with bilateral pleural plaque formation, but in the absence of diffuse pleural thickening. Note that the costophrenic angles are clear. **(c)** Oblique radiograph illustrating diffuse pleural thickening associated with underlying asbestosis. This thickening most likely involves the minor fissure (arrows). **(d)** CT scan of different patient showing isolated visceral pleural plaque formation (arrowheads) in the right major fissure.

dicators of asbestos injury: highly distinctive patterns of chest-wall and central diaphragmatic calcification, and sharply raised plaques shown in a good tangential projection. Also included are nondescript bilateral pleural thickenings on the chest wall of limited extent. These are sometimes caused by asbestos but sometimes by trauma, infection, or infarction; in some persons, they represent subpleural fat.[16] Nondescript unilateral pleural thickenings on the chest wall are even less specific for asbestos. The least specific effect is pleural thickenings in the costophrenic angle, an abnormality that is more prevalent in asbestos-exposed populations but is likely, in any individual case, to have some other cause.

Before 1980, the International Labour Office (ILO) classification[17] did not advocate distinguishing between pleural plaques and diffuse thickening in the classification of abnormalities on the chest wall. The 1980 version introduced a distinction between "circumscribed" thickenings, corresponding to plaques, and "diffuse" thickenings, which may nonetheless be quite limited in extent (according to the examples provided in the ILO standard radiographs). Thickenings on the diaphragm, to be detectable, must of necessity

be circumscribed (ie, must represent plaques). In typical patterns and locations, calcifications always indicate plaques. Plaques do not occur in the costophrenic angles, and thickening in that location is thus diffuse; the low specificity of such thickening has been mentioned.

Some investigators have chosen to disregard the distinction and analyze their radiographic data by combining all classifiable pleural abnormalities into one inclusive variable, with each subject's pleural appearance then being either normal or abnormal. Others, trying to focus on what is more certainly the result of asbestos exposure, have encountered the problem of observer variability. Since the late 1970s, the use of multiple experienced readers has become the norm for radiographic surveys. Experienced readers will often differ on whether an instance of pleural thickening on the chest wall is circumscribed or diffuse, and they will sometimes differ on its thickness or extent, or whether it is calcified. Some of this variability is due to shortcomings in the instructions, definitions, and standard films in the ILO classification. Also, plain radiographs, however interpreted or classified, are relatively insensitive in detecting small plaques.[18] Obviously, the radiographic assessment of the pleural response to asbestos exposure contains sources of imprecision.

### Imprecisions in pulmonary function testing

Pulmonary function testing has quite a low specificity for the diagnosis of dust diseases. The commonly found patterns of obstruction and restriction have numerous possible causes, some of which are far more common than effects due to exposure to inorganic dust. Examples include cigarette smoking (a cause of obstruction) and technical errors (a cause of spurious restriction). A considerable effort is required in the design and analysis of population surveys to control for confounding variables. An even greater effort is required to ensure the validity of the measurements. The analysis of the results is complicated. Expressing the results as "percent predicted" may not, as stated above, adequately control for changes associated with aging, and may not completely control for differences in body size. Expressing them as the average or mean pulmonary function values requires adjustments for observed differences in the age, size, and smoking history of the groups being compared; furthermore, mean values are open to inordinate influence by the results from a few exceptional persons. All of these problems can be dealt with, but prior articles on this topic show that the problems are not always recognized, and if recognized, are not always adequately handled.

## LITERATURE REVIEW

Published studies of the functional effects of benign, asbestos-induced pleural abnormalities date only from the middle 1960s. The evidence presented in them does not always provide abundant support for their authors' conclusions. Subsequent citations are usually even less constrained by the data, and the occasional result is an assertion that a certain article proves the opposite of its findings. Moreover, there is no single article or group of articles that provides a definitive exposition on the subject. All of the articles, to greater or lesser degrees, have the methodologic shortcomings inherent in clinical and epidemiologic research. Far and away the commonest shortcoming is *selection bias*, the effect of some extraneous factor that distorts the composition of a group of subjects. This factor undermines the subsequent comparisons made between or among groups because such comparisons rest on the assumption that the groups were constituted only through the operations of the formal selection criteria and the laws of chance. Epidemiologists generally give more weight to dose-response relationships within an exposed or experimental group than to relationships between exposed subjects and nonexposed controls, precisely because the former is less sensitive to selection bias. There are, of course, other shortcomings based on the confounding factors reviewed in the preceding discussion. The critical reader (or reviewer) has no choice but to draw bits and pieces of evidence from a number of articles.

In 1965, Kiviluoto[19] reported on the radiographic effects of asbestos in a number of "cases," presumably drawn from radiology department files. In the study of those with plaques, there were 38 cases and 23 controls. The experimental subjects had a lower mean vital capacity (VC). The controls were selected on the basis of age, and there was no analytic control for the effects of different exposure levels, smoking status, or size of subjects in the groups.

In 1966, Hourihane et al[20] compared the diagnosis of pleural plaques by autopsy and by chest radiography. There was an incomplete overlap between the population with autopsy-detected plaques and the one with radiographically detected plaques. Subsets of subjects were drawn from several different sources, and the results were not always identified in terms of those sources. One conclusion was that only 15% of the cases of plaques detected at autopsy were diagnosable from antemortem radiographs. The authors suggested that radiographically visible plaques were associated with asbestosis, but the data indicate a strong possibility of selection bias. Most cases of plaques detected at autopsy did not have pulmonary fibrosis.

In 1970, Bader et al[21] reported the results of a survey of 598 members of an asbestos workers' union. Of 100 workers with abnormal radiographs, 37 had films showing pleural abnormalities alone. Nineteen of these 37 showed a decreased VC. However, about the same proportion of those with radiographic pleural abnormalities plus pulmonary changes of asbestosis had a reduced VC, an unexpected finding. Moreover, 155 of the 498 with neither pulmonary nor pleural abnormalities also had a reduced VC. Thus, there may have

been difficulty both in separating pleural from pulmonary radiographic abnormalities and in measuring pulmonary function.

Also in 1970, Becklake et al[22] examined the relationship between radiographic abnormalities and pulmonary function in an age-stratified random sample consisting of 1,069 men employed in the mining and milling of chrysotile asbestos. Men were counted as having a pleural abnormality if their radiographs showed pleural calcification or thickening, including thickening in the costophrenic angle. The number of men with pleural abnormalities was not given. The pulmonary function values were standardized for age and height. Comparisons were controlled for the degree of pulmonary abnormality, as assessed using the ILO classification. There was no control for differences in smoking or dust exposure. Small but significant differences between those with and without pleural thickening were found for residual volume (RV), total lung capacity (TLC), one-second forced expiratory volume ($FEV_1$), and alveolar volume ($V_A$); differences, however, were found only among those with no radiographic pulmonary abnormality (ie, an ILO category of 0/0). This might only reflect the greater statistical power of the larger numbers in category 0/0, but it might also indicate that the effects of pleural abnormalities on pulmonary function are slight compared with those of parenchymal abnormalities.

In 1971, Langlands et al[23] studied the effects of asbestos in a survey of 272 working insulators. They found evidence of restriction in association with radiographic pulmonary abnormalities, particularly in workers with pleural abnormalities alone. Because of differences in the mean ages of those with and without pleural abnormalities, direct comparisons of pulmonary function test results were (according to the authors) valid only in the age range of 40 to 59 years; those comparisons showed no difference in pulmonary function between men with pleural abnormalities only and men with normal chest radiographs.

In 1972, Muldoon and Turner-Warwick[24] reported a study of 75 persons referred to the pneumoconiosis medical panel for evaluation of their disabilities. Restriction, defined as a reduced TLC with normal specific conductance (a measure of airway function), was found in six of eight persons with pleural abnormalities only. Despite the cautious interpretations by its authors, this article has been cited as showing the clinical importance of pleural abnormalities. There were, however, nine persons whose radiographs showed neither pleural nor pulmonary abnormalities; of these, only two had normal pulmonary function, and five had restriction or mixed restriction and obstruction. Moreover, the proportion of subjects with normal pulmonary function was highest in the group with advanced grades of radiographic pulmonary abnormalities, indicating that subjects with lesser degrees of radiographic pulmonary abnormalities were not likely to be referred unless they had nonradiographic manifestations of disease, such as symptoms or pulmonary function abnormalities. This is an example of selection bias that affects comparisons among subsets of the experimental group, as well as the implicit comparison of the entire group to the general population.

In 1977, Lumley[25] published the results of a study of dockyard employees with asbestos-related pleural conditions detected in a large radiographic survey. Pulmonary fibrosis was found to be accompanied by more functional abnormalities than any of the pleural abnormalities. Diffuse pleural thickening was associated with more adverse functional effects than were pleural plaques; and pleural calcification was not accompanied by any significant functional abnormalities. Plaques and calcification were found to correlate better with length of exposure and time since the initial exposure to asbestos than was diffuse pleural thickening. Diffuse thickening was thought to often result from a "pleural reaction," described as a relatively sudden event that sometimes occurred in younger men. The author was clearly referring to pleural thickening being a consequence of benign asbestos-related pleurisy with effusion.

In 1977, Seaton[26] published a study of six subjects with asbestosis, five subjects with bilateral calcified pleural plaques but no evidence of asbestosis, and nine normal subjects. Radioactive xenon scanning showed impaired ventilation of the lower pulmonary zones in the subjects with asbestosis, but not in the subjects with pleural plaques alone.

In 1978, Zitting et al[27] reported a cross-sectional study of patients previously certified as having asbestosis. Pleural abnormalities, mainly diffuse and extensive, were found in 88 of 133 films. They were associated with a decreased VC and $FEV_1$ in cases of mild pulmonary fibrosis (ie, an ILO category of 0/1 to 1/1). Because 64% of the cases of pleural thickening had a maximal width of pleural thickening greater than 10 mm, and because 63% had a linear extent greater than half of one chest wall, the observed differences in pulmonary function may well have resulted from cases of frank fibrothorax. A bias similar to that previously discussed was also likely, wherein persons referred for certification with milder degrees of radiographic asbestosis were likely to have more nonradiographic findings in support of their disability claims.

In 1978, Weiss and Theodos[28] collected radiographic data on workers in two asbestos-products manufacturing plants. One of the plants used chrysotile asbestos only, while the other used chrysotile and amosite. Workers in the latter plant had approximatey twice the incidence of pleural thickening. In the same plant, there was a definite relationship of smoking to radiographic pulmonary disease, and a possible relationship of smoking to pleural thickening. Weiss has been a strong advocate of the hypothesis that smoking causes pulmonary fibrosis; he has not argued that smoking alone produces pleural fibrosis.

In 1979, Solomon et al[29] showed a correlation between increasing length of employment in South African asbestos mines and thickening of pleura in the interlobar fissures. The effects of pleural thickening on pulmonary function were not studied.

In 1980, the doctoral thesis of Hillerdal[30] was published in book form by the faculty of medicine of the University of Uppsala in Uppsala, Sweden. The book is entitled *Pleural Plaques,* but the larger part of it is occupied by a literature review, with 815 references, on the medical problems of asbestos exposure. The section on the clinical importance of pleural plaques is introduced with the statement that pleural plaques are in themselves harmless. There is no mention of their effects on pulmonary function.

The book also contains a piece of original work entitled "Lung parenchymal changes in persons with pleural plaques" by Fridriksson et al that was published in similar form in 1981 in the *European Journal of Respiratory Diseases.*[31] The study examined persons found to have pleural plaques in a community-wide health screening program. There were 45 presumably healthy men whose radiographs showed only pleural plaques. Persons with plaques who could not confirm histories of asbestos exposure were excluded. The pulmonary function test results of the 45 men were compared with smoking-specific values derived from a relatively small reference population, selected by criteria not described in either version of the work. The group with plaques showed about a 15% lower mean $FEV_1$, TLC, VC, and RV, and about a 30% lower mean specific compliance. In general, however, there was an absence of effects of the differing extent of plaques on pulmonary function. The work's major deficiency is the lack of assurance that cases and controls were subjected to the same criteria of healthiness.

In 1980, Artz et al[32] reported a study of patients with asbestos-related conditions. Patients with pleural abnormalities alone had a lower VC than those with normal films. They did not, however, have a lower static or specific compliance, which should have been observed if the low VC had resulted from pleural or pulmonary fibrosis. There was no control for differences in smoking or dust exposure. The lack of information about patient selection is the main defect of the article.

In 1980, Jones et al[33] reported a prospective longitudinal study of chest radiographs and pulmonary function measurements in a cohort of current and former asbestos-cement manufacturing workers. The radiographic progression of small opacities in the pulmonary parenchyma was found to depend on the average and cumulative exposure, whereas the progression of pleural thickening or calcification depended on the time since the initial exposure or the total length of time of the exposure (both of which were highly correlated in this cohort). The progression of pleural thickening was associated with significantly larger annual declines in forced (expiratory) VC (FVC) and $FEV_1$. The more important finding is the time dependency of pleural abnormalities, which suggests a weak relationship to cumulative exposure.

In 1980, Wright et al[34] demonstrated a pronounced restrictive effect of diffuse pleural thickening in six patients, four of whom had no radiographic evidence of asbestosis. Because gas transfer was preserved, the authors felt that the major cause of the restriction was the pleural abnormality, which they thought might have been related to benign asbestos-induced pleurisy rather than (subpleural) pulmonary fibrosis.

In 1980, Sterling and Herbert[35] reported six cases similar to those of Wright et al but with additional proof of the absence of coexisting asbestosis in the form of normal results from lung biopsies. The low compliance in their patients was explained by a restrictive effect of pleural thickening, rather than by pulmonary fibrosis. The authors pointed out, however, the probability of some overlap between purely restrictive pleurisy and typical asbestosis, the latter of which usually also has some pleural involvement.

In 1981, Hedenstierna et al[36] published a study based on health surveillance examinations of construction workers, with comparisons made with controls. In an analysis of 36 pairs of subjects matched for age, height, and smoking status, those with plaques had a worse closing volume, expressed as percent VC, and lower instantaneous flow rates at low pulmonary volumes, than did the nonexposed controls. There was no significant difference in spirometric test results between smokers with plaques and smokers with neither plaques nor prior asbestos exposure.

In 1981, Gefter et al[3] published a lengthy review of the radiographic evaluation of asbestos-related chest disorders. The review considered not only the radiographic abnormalities, but also their relationship to other biologic effects and to prognosis. In the section on pleural plaques and parenchymal fibrosis, the fact that plaques are more common than asbestosis is emphasized. In the section on benign asbestos-related pleural effusion, the contribution of this disorder to the prevalence of diffuse pleural thickening is mentioned.

A 1982 article by McMillan and Rossiter[37] primarily covered radiographic progression, but touched on points likely to be of importance in the effect of pleural plaques on pulmonary function. The main question was whether pleural plaques were associated with an increased risk of developing parenchymal opacities (ie, a higher incidence of asbestosis). The authors presented evidence supporting such an association, but their control for differences in asbestos exposure in their survey population of shipyard workers was relatively crude. In the group presumed to have the heaviest asbestos exposure, a similar incidence of asbestosis was observed for those with and without plaques. There was no evidence of a consistent relationship between smoking and the development of small opaci-

ties, the subject of another controversy and a potential confounding factor in radiologic-physiologic correlations.

In 1982, Britton[38] studied a group of 88 asbestos workers, many of whom had been referred for evaluation of compensation claims. He concluded that pleural thickening as an isolated radiographic finding can, particularly when severe, contribute to a diminished VC.

In 1983, Miller et al[39] reported seven cases of severe ventilatory impairment from asbestos-induced pleural fibrosis. Direct examination of the thoracic organs showed minimal or no pulmonary fibrosis in three of five patients, and less severe involvement of the lung than the pleura in the remaining two. The extent and width of the pleural thickening shown and described in this article indicate that the patients suffered from fibrothorax.

In 1983, Cookson et al[40] reported a study of pleural thickening and gas transfer in patients with radiographically diagnosed asbestosis. TLC and $V_A$ were reduced in patients with more severe grades of pleural thickening. Pleural thickening in patients with small opacities in ILO profusion category 1 did not influence the diffusing capacity of the lung.

In 1984, Andrion et al[41] studied the relationship between pleural plaques found at autopsy, smoking habits, and asbestos exposure. Smoking was found to be associated with a higher prevalence of plaques, but only in men older than 50 years.

In 1984, McGavin and Sheers[42] reported data from 37 asbestos workers with diffuse pleural fibrosis but no asbestosis. Most were identified through a radiographic survey, but some were drawn from clinic referrals. Persons with more extensive pleural thickening had a significantly lower VC.

In 1985, Kilburn et al[43] reported the results of examining 339 male shipyard workers who were recruited through advertising for volunteers. This method of selecting a population is biased toward obtaining participants who believe that they have health problems. In light of this, their finding of little evidence for functional impairment beyond that attributable to cigarette smoking may be given considerable weight. Thirty-seven percent of the patients with radiographic abnormalities had pleural abnormalities alone, and another 35% had pleural and pulmonary abnormalities.

In 1985, Baker et al[44] examined the significance of asbestos-associated pleural conditions in 314 members of a sheet-metal workers' union, who were the earliest responders from a target population numbering 1,413. (This selection criterion is not entirely free of the "volunteer" bias mentioned immediately above.) Pleural abnormalities were associated with a significantly lower mean FVC (99.5% versus 103.2% predicted). There was no effect of the duration of employment on the FVC, but there was a strong correlation between the duration of employment and the presence of pleural abnormalities. There was only a slight correlation between the width and extent of the pleural thickening and reductions in FVC and $FEV_1$. The authors felt that smoking increased the rate at which pleural abnormalities developed but that it had no effect on the final prevalence rates in workers with a long exposure.

A longitudinal study published in 1985 by Ohlson et al[45] showed no effect of plaques on the annual changes in spirometric values.

In 1986, Jarvholm and Sanden[15] reported a study of 202 older nonsmoking male shipyard workers with varying exposure to asbestos, 87 of whom had no radiographic abnormality other than pleural plaques. Three of the 115 workers with normal radiographs and 13 of the 87 with pleural plaques had FVC values below the reference limits. Those with plaques had a 6.9% lower mean FVC than those without plaques, and larger differences were found between those with and without plaques in the subgroup with heavy asbestos exposure.

In 1987, Hilt et al[46] reported the results of a community-based population screening for asbestos-related disorders. Two hundred persons under 70 years of age had pleural plaques as the only radiographic finding. Compared with a group of 90 persons who had not been exposed to asbestos, the persons with plaques had a greater likelihood of having an FVC below 90% predicted. Because the same study showed that asbestos exposure in the presence of a normal chest radiograph was associated with an increased prevalence of symptoms and a reduced FVC and $FEV_1$, the above comparison is biased toward finding greater impairment in those with plaques.

In 1987, Picado et al[47] studied six patients selected because of asbestos-related pleural fibrosis, in whom pulmonary disease was thought to be excluded by gallium and computed tomographic scanning. Functional abnormalities were suspected as being caused by increases in the chest-wall impedance, which in turn were attributed to the reduced compliance of the parietal pleura. There was, however, no anatomic difference between visceral and parietal pleural fibrosis, and it is doubtful whether physiologic testing could distinguish the two. The results seem only to support the proposition, abundantly supported by other reports, that extensive pleural fibrosis can have clinically important consequences for pulmonary function.

In 1987, Rockoff et al[10] studied fissural thickening (ie, visceral pleural thickening) on the plain radiographs of a group of asbestos-exposed sheet-metal workers and pipe fitters and a group of nonexposed controls. The exposed group had an incidence of fissural thickening of 54.5%, compared with 16% for the controls. In the exposed group, the time since the initial exposure to asbestos had a strong effect on fissural thickening beyond the effect attributable to age. Eighty-five percent of the exposed persons with plaques and 36% of the exposed persons without plaques showed fissural thicken-

ing occurred in 45% of those without radiographic evidence of pulmonary fibrosis and in 85% of those with pulmonary fibrosis. An analysis showed that being exposed to asbestos for 21 years was associated with having a 50% chance of developing fissural thickening, while being exposed for 31 years was associated with having a 50% chance of forming pleural plaques, indicating that fissural thickening is an earlier sign of asbestos exposure than plaque formation.

In 1988, Jarvholm and Larsson[48] reported that asbestos-related symptoms were more prevalent in workers with plaques than without, but not significantly so, after the workers' ages and smoking habits were controlled for. These authors' speculation about subroentgenologic fibrosis—that it is the cause of dyspnea associated with lower lung function—should have been withheld pending a controlled study for possible exposure differences, an independent measure of fibrosis, or both.

In 1988, Bourbeau et al[49] studied insulation workers with plaques or costophrenic angle thickening. Their findings indicate that the insulators had lower mean FVC (402 mL) and $FEV_1$ (222 mL) after controlling for the subjects' ages, heights, smoking habits, and lung abnormalities (as assessed by plain radiographs and gallium 67 scans). Pleural abnormality did not produce diminished exercise capacity, but it was associated with differences in some exercise ventilation parameters and with the complaint of shortness of breath on strenuous exertion.

Also in 1988, Delclos and Wilson[50] reported that there was no independent association between plaques and lung function at rest or during exercise. Their study comprised 67 subjects with plaques and 35 subjects with exposure but no plaques. People with radiographic lung abnormalities were excluded from the study.

In an article accepted in 1988 for publication, Jones et al[51] reported on ten years' follow-up of the asbestos cement–manufacturing cohort. After controlling for smoking, asbestos exposure, and radiographic pulmonary abnormalities, the investigators found significant adverse effects of pleural abnormalities on base-line spirometric tests and RV (in percent predicted), but no meaningful effect of pleural radiographic worsening on longitudinal changes in the pulmonary function.

## CONCLUSION

The discordant findings in the literature result mainly from selection bias and from imprecisions in characterizing and controlling for different exposure levels and confounding influences, and in detecting and measuring responses. A critical review of the literature provides us with reasonable grounds for the following conclusions:

- Pleural plaques, as an isolated radiographic finding, do not by themselves produce clinically significant reductions in pulmonary function.
- In groups of persons, plaques are probably associated with small reductions in mean pulmonary function after the study has controlled for other influencing variables. Most of the published studies of the effects of plaques, however, have not adequately controlled for the effects of other factors on pulmonary function.
- Diffuse pleural thickening resulting from asbestos exposure can produce clinically severe impairment of ventilation.
- When pleural thickening is the sole or major cause of impaired pulmonary function, the impairment will usually consist of restriction with preserved diffusing capacity.
- The exposure relationships and the effects of fissural thickening on pulmonary function have not been fully explored.

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