Abnormal pulmonary function associated with diaphragmatic pleural plaques due to exposure to asbestos

Kaye H Kilburn, Raphael H Warshaw

Abstract
Pulmonary function was measured in 79 men with diaphragmatic pleural plaques (DPP) as the only abnormality characteristic of asbestos disease on chest radiographs. They were selected from 4572 construction and shipyard workers exposed to asbestos. Abnormalities of pulmonary function in 21 non-smokers and 43 current smokers were compared with referent values adjusted for height, age, and duration of cigarette smoking. In the non-smokers, flows (FEV₁, FEV₁/FVC and FEV₁/FVC) were reduced and TGV and RV/TGV were raised. Current smokers had similar significant reductions. Thus by contrast with some current opinion that plaques are "an index only of past asbestos exposure," workers with plaques, even limited to the diaphragm, have functional impairment typical of pulmonary asbestosis. This suggests that they have pulmonary asbestosis, which is below the threshold of radiographic recognition.

The functional effects of pleural thickening and plaques identified on chest radiographs in a population exposed to asbestos remain unclear. In fact, there is controversy as to whether pleural plaques merely indicate exposure to asbestos, or are associated with impairment of function similar to that seen in pulmonary asbestosis. Beyond impairment of function is a key question as to the nature of the physiological abnormality. Is it "restrictive" as defined by a reduced thoracic gas volume (TGV) or a reduced vital capacity (VC), which, in the absence of obstruction, has been considered to be a measure of reduced total lung capacity; or is it an obstructive disorder of the airways in which a reduced forced vital capacity (FVC) is due to air trapping and not to restrictive disease?

Diaphragmatic pleural plaques (DPP) are signs of minimal pleural asbestos disease when compared with the other end of the spectrum—namely, extensive thickening that extends up the thoracic walls associated with bilateral obliteration of the costophrenic angles. Thus to assess the effects on pulmonary function of minimal pleural disease we carried out measurements on men with diaphragmatic plaques. The study was designed to determine whether there are effects of DPP alone on pulmonary function and to distinguish whether these are obstructive or restrictive. Subjects with DPP were selected from a large study of American workers exposed to asbestos.

Methods
Seventy nine men with diaphragmatic plaques as the only sign of asbestos disease visible on chest radiographs were selected from 4572 men at 20 sites in the United States. Most of them were members of boilermakers', pipefitters', metal, or chemical unions. The criteria for study were 15 or more years from initial exposure to asbestos and five or more years of exposure. The study was approved by the Human Subjects' Institutional Review Board of the University of Southern California and informed consent was obtained from each worker. The men were studied at appointment by a single travelling medical team who presented questionnaires and carried out physical examinations of the chest, chest radiographs, and spirometry. A questionnaire administered by trained interviewers asked for information on occupational history, proximity to and duration of exposure to asbestos, and medical, pulmonary, and cardiovascular history. The chest was examined for size, shape, deformity, and the presence of normal, decreased, or absent breath sounds, rales, and wheezing. Extremities were examined for cyanosis, clubbing, and oedema.

Spirometry was performed on rolling seal spirometers (Ohio 820). The subjects were standing
Pulmonary expiratory flows and lung volumes as percentage of predicted in 64 men with diaphragmatic pleural plaques compared with referents

<table>
<thead>
<tr>
<th>Subjects with diaphragmatic pleural plaques</th>
<th>p Value</th>
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<tbody>
<tr>
<td>No</td>
<td>167</td>
</tr>
<tr>
<td>FVC</td>
<td>95-8</td>
</tr>
<tr>
<td>FEV1-FVC</td>
<td>95-2</td>
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<tr>
<td>FEV1/FVC \times 100</td>
<td>77-4</td>
</tr>
<tr>
<td>FEF25-75</td>
<td>95-1</td>
</tr>
<tr>
<td>FEF75-85</td>
<td>106-8</td>
</tr>
<tr>
<td>TGV</td>
<td>101-3</td>
</tr>
<tr>
<td>RV/TGV \times 100</td>
<td>34-0</td>
</tr>
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</table>

<table>
<thead>
<tr>
<th>Non-smokers</th>
<th>119</th>
<th>21</th>
</tr>
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<tbody>
<tr>
<td>No</td>
<td>99-0</td>
<td>96-0</td>
</tr>
<tr>
<td>FVC</td>
<td>99-2</td>
<td>92-1</td>
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<tr>
<td>FEV1-FVC</td>
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<td>FEF25-75</td>
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<tr>
<td>FEF75-85</td>
<td>102-1</td>
<td>72-3</td>
</tr>
<tr>
<td>TGV</td>
<td>100-1</td>
<td>110-8</td>
</tr>
<tr>
<td>RV/TGV \times 100</td>
<td>30-3</td>
<td>46-8</td>
</tr>
</tbody>
</table>

Results

The mean age of the 79 men with DPP was just over 60, with over 30 years of exposure to asbestos. The 43 men with 30 years of cigarette smoking had a prevalence of chronic bronchitis of 16-5% and of asthma of 7.1%. The 21 non-smokers had a similar prevalence of chronic bronchitis. The 15 ex-smokers were not considered further.

Expiratory flows (forced expiratory volume in one second (FEV₁), forced expiratory flow (FEF 25-75, FEF 75-85), volumes (FVC, TGV, and residual volume (RV)), and FEV₁/FVC for subjects with DPP were compared with those for the non-asbestos exposed referents by smoking specific groups (table). In 43 current smokers with DPP expiratory flows and FVC were reduced, TGV was increased, and RV/TGV was raised compared with 167 current referent smokers, after adjustment for duration of smoking.

To sharpen these comparisons, the 21 non-smokers were compared with the 119 non-smoking men in the referent population. Differences were significant for expiratory flows, FEV₁, FEV₁/FVC, and FEF 75-85 but not for mid flows or FVC. Total lung capacity and air trapping (RV/TGV) were significantly increased in the group with DPP. The group of 15 ex-smokers had more impairment of function and more variability than the other groups so that further comparisons were not useful.

Discussion

Limitation of expiratory airflow and air trapping with a slightly increased TGV was the physiological pattern in men with DPP as their only radiographic abnormality due to asbestos. As thoracic gas volume was increased, there was no evidence of restrictive
Impairment. Thus diaphragmatic pleural plaques in men exposed to asbestos were associated with limitation of expiratory flow, an obstructive physiological lesion in which the anatomical locus is in small airways. The physiological impairment in men with this “subclinical asbestosis” resembled that of men in a large epidemiological study who had pulmonary asbestosis recognised by irregular opacities (ILO categories 1/0 and greater) on chest radiographs (K H Kilburn and R H Warshaw, unpublished observations). The subjects with DPP had less severe obstruction of the airways, however, than the 202 current smokers and 108 non-smokers who had pleural plaques on their chest walls,13 and considerably less impairment than those with thickening of the lateral chest wall affecting the costophrenic angles; this suggests an orderly continuum.

Opinions as to the functional significance of pleural plaques have been polarised. Parkes2 stated that “pleural plaques do not indicate the existence of asbestosis any more than do asbestos bodies in the sputum . . . an index of past asbestos exposure.” Craighead et al6 observed for plaques on parietal and diaphragmatic pleura that “in recent years these lesions have been considered one of the pathologic and radiologic hallmarks of exposure.” An American thoracic society committee has labelled these as “benign pleural abnormalities associated with asbestos.”

In a contrasting view, Fridriksson et al14 have suggested recently that “since asbestos fibers must pass through the lungs to reach the pleural space, it is conceivable that persons with pleural plaques also may have lung parenchymal changes that are not detectable on the chest radiograph (subclinical asbestosis).”15 Becklake et al16 noted nearly two decades ago that “for any given grade of parenchymal disease function was somewhat more impaired when pleural thickening and/or calcification was present.”

Similarly, since 1968, at least 16 papers before this one5-10,17-26 have chronicled the pulmonary impairment associated with diffuse pleural thickening and plaques, or both, after occupational and environmental exposure to asbestos.27 Although the first of these18 found reduced FVC and reduced maximal voluntary ventilation, which is highly dependent upon FEV1, direct reductions in FEV1 and mid flow were recognised subsequently.19 The reported association between increased lung stiffness (decreased compliance), and reduced FEV1, and FVC is consistent with “bridging” between fibrotic loci around small airways.21-30

Two observations have suggested that with time, asbestos disease in the lung progresses to the visual threshold on radiographs. Firstly, asbestos cement workers identified with plaques only, showed an increased prevalence after four years coincident with greater decrements in FEV1 and FVC;22 secondly, development of parenchymal asbestosis was identified from the radiographs of 10-3% of dockyard workers with plaques 10 years after initial study.26 This implies that many asbestos exposed subjects with pleural plaques or thickening have pulmonary fibrosis, some visible radiographically and some not yet visible.

The pathogenesis of plaques remains obscure. The clearest proposal was made by Hillerdal27—namely that small asbestos fibres spread to the visceral pleura, penetrate the pleural space, and follow normal lymph flow from the pleural space to the parietal pleura. As they pass into the parietal pleura, they retain macrophages there which stimulate submesothelial fibroblasts. After several decades this results in visible pleural plaques. Recently, fine fibres of asbestos have been observed in pleural plaques using electron microscopy (R F Dodson, M G J Williams, C J Corn, A Brollo, and C C Bianchi, unpublished observations). This provides the first direct confirmation of Hillerdal’s hypothesis. Coincidently and inevitably, longer asbestos fibres are trapped in airways, and many shorter ones are phagocytosed by macrophages and produce peribronchiolar fibrosis, bridging, and finally diffuse fibrosis.28 The presence of irregular opacities, plaques, and diffuse pleural thickening on chest x ray films has produced a dichotomous classification of asbestosis as parenchymal or pleural. Review of the evidence, however, suggests that asbestosis in the human lung is a continuum.

11 Becklake MR, Ernst P. Asbestos exposure and airway responses.
Zitting Arzt 21


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