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 (FEV_{10} , FEF_{75-85} and FEV_{10}/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,¹⁻⁴ or are associated with impairment of function similar to that seen in pulmonary asbestosis.⁵⁻¹⁰ 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^{5 11 12} 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

University of Southern California School of Medicine, Environmental Sciences Laboratory, Los Angeles, California 90033, USA

K H Kilburn

Workers Disease Detection Services Inc, 441 West Allen Ave, Suite 114, San Dimas, California 91773

R H Warshaw

and wearing a nose clip. Otherwise the technique was as the ATS Snowbird recommendations.¹³ Care was taken to ensure full expiration of 10 seconds or more. The best spirometry tracing was digitised and measured for volumes and flows, which were corrected to body temperature.

Percentage of the predicted result was calculated for each measurement by reference to a Michigan comparison population specific for duration of cigarette smoking.¹⁴ Chest radiographs were obtained on standard (14 × 17 inch) films using a Picker portable x ray machine (KV 120–130 and suitable grid) and a Kodak 180 second processor. They were read "on the scene" in the presence of the worker for profusion of irregular opacities—that is, for pulmonary asbestosis and for type and extent of pleural plaques, diffuse thickening, and calcification using the International Labour Office (ILO) criteria for pneumoconiosis.¹⁵ Unsatisfactory x ray films were repeated until film quality was ILO 1. For this analysis men with pleural disease only were further selected for plaques on one or both diaphragms including calcifications, in the absence of other disease. Lung field areas were measured by planimetry to calculate TGV.¹⁶

All data were recorded in an optically coded format, machine read into a microcomputer (Atari 1040ST), and transferred to a Compaq computer for analysis using Stata statistical programs. The table gives measurements on pulmonary function for 21 non-smokers and 43 smokers expressed as percentage of the predicted result, compared with 94 normal men who were non-smokers and 82 current smokers from a stratified random population sample of Michigan whose pulmonary functions have been modelled using regression equations.¹⁴ Thus each

man's measurements were expressed as a percentage of the predicted result from the modelled population adjusted for height, age, and years of cigarette smoking. For comparison of group means by *t* test for unequal group size there were 167 referent men who were current smokers from the random population sample that comprised the 82 "normal" men plus 85 with one or more of the following: sputum production, dyspnoea, wheezing, angina pectoris, previously diagnosed lung disease, coronary heart disease, hypertension, rales, clubbing, and cyanosis. The same strategy was used for 119 non-smokers by adding 25 men with abnormalities to 94 "normals." The measurements of pulmonary function for these two comparison groups, 167 current smokers and 119 non-smokers were also expressed as a percentage of the predicted result for the modelled normal group of 188. The significance of differences between group means expressed as percentages of the predicted result for the non-smokers and current smokers with DPP and Michigan non-smokers and current smokers was determined using Student's *t* test.

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 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

Pulmonary expiratory flows and lung volumes as percentage of predicted in 64 men with diaphragmatic pleural plaques compared with referents

	Referents ¹⁵	Subjects with diaphragmatic pleural plaques	p Value
<i>Cigarette smokers</i>			
No	167	43	
FVC	95.8	93.5	0.4
FEV ₁	95.2	93.1	0.2
FEV ₁ /FVC × 100	77.4	72.3	0.0001
FEF _{25–75}	95.1	82.7	0.0013
FEF _{75–85}	106.8	83.2	0.0001
TGV	101.3	108.0	0.0001
RV/TGV × 100	34.0	46.0	0.0001
<i>Non-smokers</i>			
No	119	21	
FVC	99.0	96.0	0.3
FEV ₁	99.2	92.1	0.015
FEV ₁ /FVC × 100	80.0	76.5	0.018
FEF _{25–75}	100.1	92.1	0.4
FEF _{75–85}	102.1	72.3	0.0014
TGV	100.1	110.8	0.0009
RV/TGV × 100	30.3	46.8	0.0001

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 al*³ 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 al*⁵ 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)." Becklake *et al*⁶ 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 one^{5-10 17-26} have chronicled the pulmonary impairment associated with diffuse pleural thickening and plaques, or both, after occupational and environmental exposure to asbestos.^{5,8} 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.²⁷⁻³⁰

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;²⁵ 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. Coincidentally 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.³ 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.

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Accepted 19 March 1990

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