Findings from high resolution computed tomography of the lung and pleura of symptom free workers exposed to amosite who had normal chest radiographs and pulmonary function tests

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Abstract
The lungs of 50 symptom free workers exposed to amosite and with normal pulmonary function tests were examined by high resolution computed tomography (HRCT). Twenty five had normal standard chest radiographs whereas the other 25 had radiographs interpreted as near normal (International Labour Office profusion score <0.1 or suspected pleural plaques). In 13 of the workers the results of HRCT were negative; in 22 pleural plaques were found, in five there was only parenchymal involvement, and 10 had both pleural and parenchymal changes. The mean duration of exposure to amosite was significantly longer for the subjects with parenchymal signs than for those with normal parenchyma and for the workers with pleural plaques than for those with normal pleura and lung parenchyma. The prevalence of identified pleural and parenchymal abnormalities in the 50 workers was also significantly higher than in a reference group without exposure to asbestos. It is concluded that HRCT may detect initial lung and pleural involvement in symptom free workers exposed to amosite and the mean duration of exposure is longer for subjects with parenchymal or pleural involvement.

Methods
All the subjects of the study group worked in a factory producing naval furniture where one case of mesothelioma had been previously found by the sentinel health event method. In this factory a material containing about 40% amosite was used, from 1958 to 1980. This was especially in the carpentry department where panels were built consisting of asbestos insulation between two external layers of wood. The study group comprised 127 workers whose chest radiographs, performed according to ILO criteria, were previously judged as negative by outside readers. Three radiologists experienced in the reading of radiographs according to the ILO classification have re-examined the 127 standard chest radiographs.

Among the 127 workers we selected the subjects who fitted the following criteria: (1) documented occupational exposure to asbestos; (2) absence of any clinical symptomatology...
Individual health histories were also investigated: none of the workers had a history of pleurisy, empyema, haemorrhage, tuberculosis treated with pneumothorax, or other pulmonary diseases.

The interval between HRCT and standard chest radiograph varied from 0-2 to 19 months (mean interval 4-4 (3-8) months). The HRCT study was performed on a GE-9800 scanner. All patients were examined at suspended maximum inspiration, both in the supine position and prone when posteroinferior portions of the lungs showed obscuration dependent on gravity attenuation or any of the HRCT abnormalities associated with asbestosis were identified. HRCT sections 1-5 mm thick were made at 20 mm intervals from the aortic arch to the diaphragm. To minimise the noise 140 KVP and 170 mAs were used, with 2-5 seconds of acquisition time. The image was finally obtained through a reconstruction with a convolution filter of the bone detail algorithm. FeV1 was 24/30 cm. All images were photographed at the 500 HU window for pleura and mediastin and 1500 HU window for pulmonary parenchyma. HRCT scans were interpreted by a radiologist blinded to individual exposure data and to chest radiographic interpretation. Pleural alterations were quantified applying 1980 ILO criteria to the reading of CT scans. Parenchymal abnormalities were interpreted on the bases of published data and were considered diagnostic of asbestosis when present in a combination of findings (two or more).

HRCT findings have been related to the individual exposure data and compared with those of a reference group of 20 hospital patients (mean age 47-1(13-4), range 26-67 years; 19 men) who were given HRCT for suspected localised pulmonary pathology (in most of cases nodules cysts, or embolus) not confirmed by HRCT, without occupational or significant environmental exposure to asbestos.

Smoking histories were not different for the subjects exposed to asbestos with negative or positive chest radiographs and the control group (pack-years respectively 12-1(9-2), 13-6(8-4), and 14-8(9-7)).

Statistical analysis was by analysis of variance (ANOVA-Fisher PLSD), independent t test (two tailed), or contingency table analysis, as indicated. The results are expressed as means (SD). A statistically significant level was considered to be present at p <0-05.

The protocol of this study was approved by the University Ethics Committee for Human Studies.

**Results**

Among the 50 workers examined by HRCT, 22 showed pleural plaques, five exclusively parenchymal abnormalities, and 10 both pleural and parenchymal abnormalities; in the other 13 workers no pathological finding was shown.
The parenchymal abnormalities were: subpleural curvilinear lines (eight cases; fig 1); thickened interlobular (septal) lines (three cases; fig 2); hazy patches of increased attenuation (six cases); and thickened intralobular (core) lines (three cases). In four workers two or more of the described signs were found. No case of honeycombing was reported.

Thirty two workers had pleural plaques (fig 3) (23 of them bilateral). Only one worker showed diffuse pleural thickening (the same subject also had interstitial abnormalities). No one had benign exudative pleurisy. In nine subjects, plaques were calcified. Plaques located in the tendinous part of the diaphragm were present in 21 cases (one of these had exclusively diaphragmatic plaques).

Among the 25 subjects whose standard radiographs were confirmed "negative" by our radiologists, HRCT showed 11 cases of pleural plaques, two cases with both pleural and parenchymal involvement, and two cases with only a subpleural curvilinear shadow, which is not specific for asbestosis as an isolated finding. Among the workers for whom pleural plaques were suggested at standard chest radiographic reading (18 cases), HRCT confirmed these in 16 cases, in five of whom HRCT also showed parenchymal involvement; in two cases pleural plaques were not confirmed and no pathological finding emerged. HRCT confirmed parenchymal involvement for five of the six subjects whose radiographs showed parenchymal opacities with a profusion 0/1 and in two of these cases not shown as having pleural plaques; in one case no pathological finding was shown and in one case a standard radiograph and HRCT showed both pleural and parenchymal involvement.

Sensitivity, specificity, accuracy, and positive and negative predictive values of standard chest radiographs were calculated with respect to HRCT (artificially assuming it as gold standard) and resulted in, respectively, for pleural and parenchymal findings: sensitivity 89% and 40%; specificity 53% and 97%; accuracy 66% and 80%; negative predictive value 52% and 79%; and positive predictive value 89% and 86%.

In the control group (20 subjects) HRCT identified five cases with pleural plaques (only in one case bilaterally; all these were 1A on the ILO scale); parenchymal bands were found in one subject. Lung and pleural lesions detected by HRCT in the control group were significantly less than those found among the group exposed to amosite (continuity table analysis: p < 0.001; fig 4).

The mean duration of exposure of the whole group of workers exposed to amosite was 6.4 (5.5) (range: 0.2–21) years and the mean latency since the time of first exposure to the examination was 20.7 (5.0) years. In the different subgroups the mean duration of exposure (fig 5) was 2.3 (3.0) years for subjects with normal HRCT (group 1); mean latency 18.3 (5.2) years; 7.0 (5.5) years for the workers with pleural alterations (group 2); mean latency 21.1 (4.7) years; 5.2 (3.0) years.
years for those with exclusively parenchymal abnormalities (group 3); mean latency 20.8 (6.1) years; and 11.0 (5.2) years for those who presented both pleural and parenchymal involvement (group 4); mean latency 23.0 (4.0) years.

The duration of exposure to amosite for the workers of group 4 and group 2 was significantly longer than for the workers of group 1 (ANOVA Fisher PLSD: p < 0.005 and p < 0.05, respectively). Also, considering parenchymal involvement separately, the subjects with HRCT findings suggestive of pulmonary fibrosis (group 3 + group 4) had been exposed to amosite for a longer time than workers with normal parenchyma (group 1 + group 2); 9.1 years v 5.3 years (p < 0.05; t independent test).

Discussion

HRCT of the lung is probably the most sensitive current radiological means to detect early parenchymal and pleural asbestos related diseases, and has proved to be more sensitive than chest radiographs or conventional CT. Our data confirm that HRCT is very sensitive and suggest that the accuracy of standard chest radiographs is not high in symptom free workers even if expert readers are involved. The specificity of HRCT findings seems to be confirmed by the high prevalence of detected lesions among workers exposed to asbestos and by the proof that HRCT findings correlate well with pathological findings, even if it remains a controversial issue due to the limited number of correlative pathological studies. Our data from the symptom free amosite exposed workers in comparison with the controls suggest a probable relation between HRCT findings and exposure to asbestos. Pleural and parenchymal findings among controls may be due to causes other than exposure to asbestos or a possible occupational exposure to asbestos not known from individual health histories. The presence of low levels of asbestos fibres in the general environment also seems to be related to development of parenchymal or pleural abnormalities. Whereas exposure-response relations for the major asbestos related diseases have been considered demonstrable, the correlation between the early lung lesions related to asbestos as detected by HRCT and the levels and duration of exposure has actually not yet been proved. Staples et al. did not find a significant difference in the mean duration of exposure between a group of workers with normal or near normal HRCT for lung parenchymal findings and those with abnormal HRCT suggestive of asbestosis, although the mean exposure was higher for the subjects with pleural plaques compared with workers with normal HRCT. Al Jarad et al. also failed to find any significant correlation between lung findings from HRCT and asbestos exposure in patients with lung involvement. In our study duration of exposure to amosite has been shown to be higher for subjects with pleural or lung parenchymal involvement than for subjects with normal HRCT scans. These results indicate that the prevalence of parenchymal lesions shown by HRCT and the severity of lung involvement are dose related, by contrast with the previous findings. There are various explanations for the discrepancy. Our subjects were clinically symptom free whereas many of the subjects evaluated by Staples et al. presented with dyspnoea or abnormalities of pulmonary function and the patients evaluated by Al Jarad et al. had asbestosis. The mean age of the subjects in our study, their mean duration of exposure to asbestos, and the latency times since first exposure were also lower than in the previous studies; these data may explain why in our cohort only four cases of radiologically confirmed asbestosis were present. Furthermore our sample of workers had been exposed to the same type of asbestos fibre (amosite) in the same occupations, so the quality and severity of exposure at any moment was not much different from one subject to another, and the differences in the amount of exposure were almost exclusively due to differences in duration of exposure.

In conclusion our study suggests that HRCT can show pulmonary or pleural involvement in asbestos exposed workers before the presence of a clinical symptomatology and may allow the detection of asbestosis in some clinically symptom free workers. In fact in our study HRCT showed a combination of parenchymal abnormalities sufficient to be considered diagnostic for asbestosis in four symptom free subjects with normal pulmonary function tests and diffusing capacity (in a preclinical phase). Furthermore, 11 cases of pleural plaques and two cases with both pleural and parenchymal involvement were found by means of HRCT among the 25 workers with normal chest radiographs. The lung and pleural abnormalities detected by HRCT in our sample of symptom free workers seem to be related to asbestos exposure also in the subjects with negative or equivocal chest radiographs, as in most clinically evident asbestos cases. The relevance of isolated slight pleural or parenchymal HRCT findings in the clinically symptom free workers with normal pulmonary function tests is not yet clear and...
there is no evidence that isolated parenchymal or pleural findings may progress and produce clinical disability. We suggest a careful surveillance of these workers, however, and we propose to re-evaluate them after a period long enough to assess the progression of such abnormalities.


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