Ferruginous bodies and pulmonary fibrosis in dead low to moderately exposed asbestos cement workers: histological examination

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ABSTRACT Histological slides from the lungs of 89 dead asbestos cement workers have been examined with respect to ferruginous bodies and fibrosis. The results have been compared with individually matched controls with no known exposure to asbestos, and related to asbestos exposure, expressed as duration of exposure and cumulative asbestos dose, and smoking habits. The asbestos cement workers studied had been employed for on average 15 years, with a mean cumulative dose of 26 fibre-years per ml (f-y/ml). Clear dose-response relations between exposure (duration of exposure and cumulative asbestos dose) and level of ferruginous bodies were found. An association was evident already at a low cumulative dose (1-10 f-y/ml). Fibrosis was more common and more pronounced among the exposed workers than among controls. An association between ferruginous bodies and fibrosis was also found. Among the controls, but not among exposed workers, there was an association between smoking history and fibrosis.

In the first decades of the twentieth century it became evident that exposure to asbestos fibres could lead to diffuse pulmonary fibrosis, a condition termed asbestosis.[1] [2] Dose-response relations between exposure in different industrial settings and response expressed as clinical signs of interstitial lung disease, radiological changes, physiological changes, or mortality in pneumoconiosis have been established.[3] Information on this subject is, however, still insufficient, especially in the area of low exposure. The adverse effects of asbestos seen today reflect exposure decades earlier with dust concentrations usually far exceeding the levels of interest in current TLV discussions.

Some authors have argued that findings from other branches of the asbestos industry cannot be applied to the asbestos cement industry as the fibres are covered with calcium particles during processing.[4] As the asbestos cement industry is now the main consumer of the world asbestos production and is still expanding, adverse effects of exposure to asbestos cement are of considerable interest.

We have investigated the relations between asbestos dose and histological lung fibrosis and ferruginous bodies in low to moderately exposed asbestos cement workers. Smoking habits have also been studied, as smoking in itself may cause lung fibrosis[5] and might have a confounding effect on the fibrosis caused by asbestos.[6-10]

Material and methods

THE FACTORY

An asbestos cement plant in the south of Sweden produced sheets, shingles, ventilation pipes, and various hand moulded details between 1907 and 1977. The asbesos handled was mainly chrysotile (>90%). Crocidolite was used before 1966 in small amounts, usually <1% of the total asbestos used and never exceeding 3–4%. Amosite might have been used in small amounts in the 1950s. All types of asbestos were milled before mixing. The Portland cement used had a low silica content (below 0·1%). There was little change in formula or process over the history of the plant, except for changing from dry to wet milling in 1952. Systematic efforts to reduce the dust concentrations started in the late 1960s.

The work force reached a maximum in the mid 1960s with 450 employees. The turnover was low as the plant was located in a small community.

EXPOSURE

Dust measurements are available for the period 1956–77. Before 1969 only impinger or gravimetric determinations exist. The membrane filter method was introduced in 1969 and fully replaced the impinger method from 1971 together with a gravimetric method for determination of total dust. Some data exist from simultaneous samplings with the different methods. Extensive sampling was performed after 1975. The average dust exposure for different jobs and periods has been estimated in fibres per ml (f/ml) from data on dust concentrations, production, and dust control. The duration of specific tasks during the workday has been taken into account. Only millers, mixers, and workers performing sawing and polishing operations were continually exposed to more than 2 f/ml (table 1). Occasional exposure to high dust concentrations occurred during unloading and storing of asbestos bags; this has not been taken into account.

Conversion factors from million particles per cubic foot (mppcf) to f/ml are based on simultaneous samplings in this plant and in another asbestos cement factory.

EXPOSED WORKERS

In the total cohort of 3144 male and female blue collar workers employed for more than three months between 1907 and 1977, starting employment before 1 January 1976, there were 707 deaths until 1980 when this study started. In 396 cases a necropsy had been performed. For 89 of these the criteria for inclusion in this study were fulfilled—that is, a necropsy performed at the Department of Pathology, University Hospital, or the Institute for Forensic Medicine, Lund, and the availability of at least two blocks of lung tissue not containing tumours. The mean age of the 84 men and five women at death was 66 (range 35–91). On average 3·7 blocks of lung tissue were preserved.

CONTROL POPULATION

For each case, the next person of the same sex and age at death (within five years) in the necropsy files of the University Hospital of Lund was chosen as a control. Those who might have been exposed to agents causing pneumoconiosis (as from information about occupation in the medical record) were rejected and another control was chosen. For 46 controls the main occupation was either not known or was specified as labourer. Of the remainder, 21 were manual workers, including five construction workers, and 22 were white collar workers. Their mean age at death was 67 (37–93). On average 3·4 blocks of lung tissue were preserved.

Table 1   *Average airborne dust concentrations (fibres and total dust) for different job assignments and periods. Measured and estimated concentrations and sampling time is given*

	Job assignment				
Period and type of measurement	Milling	Mixing	Forming machine	Sawing	Grinding
1956:					
Gravimetric method*					
Total dust (mg/m³)	6·7	5·5	—	2·8	0·7
Impinger:					
Particles (mppcf)	15	29	8	24	47
Sampling time (h)	0·8	0·8	0·8	1·2	0·4
Fibres†	6·0	3·0	1·5	4·0	6·3
1965:					
Impinger:					
Particles (mppcf)	21	4	11	16	45
Sampling time (h)	0·3	0·03	0·2	0·1	0·1
Fibres†	5·0	2·0	1·2	2·8	5·5
1969:					
Impinger:					
Total dust (mg/m³)	3·3	—	0·5	2·5	—
Particles (mppcf)	11	3	2	9	9
Sampling time (h)	0·4	0·3	0·8	1·2	0·9
Membrane filter:					
Fibres (f/ml)	5·0	0·3	0·3	1·7	—
Sampling time (h)	26	2·2	7·1	0·5	—
1975:					
Membrane filter:					
Total dust (mg/m³)	4·5	5·0	2·3	4·5	4·0
Fibres (f/ml)	1·7	1·3	0·9	1·2	1·5
Sampling time (h)	29	13	12	28	10

*Stationary sampling.
†Estimated value.

SMOKING HABITS

A postal inquiry to the relatives was used to obtain information on smoking habits. The accumulated consumption of tobacco was calculated as pack-years (years smoking × daily consumption in terms of packs of cigarettes). Pipe tobacco and cigars were included (converting 1 g of tobacco to one cigarette). The average tobacco consumption among 81 exposed workers whose smoking habits could be established was 22 (0–116) pack-years; 19 were lifelong non-smokers. Among the 66 controls with known smoking habits the average consumption was 29 (0–125) pack-years; 17 were lifelong non-smokers. This difference in smoking habits is not significant. Smoking habits could be obtained for both individuals in 59 pairs. In 36 of the pairs both the exposed and control were smokers, in six pairs both were non-smokers, and in eight pairs only the exposed, and in nine only the control had ever smoked.

INDIVIDUAL DOSE ESTIMATES

For each case, data on various job assignments were collected from the company personnel records and were complemented with information from a former foreman in the factory. The cumulative dose was calculated as level of exposure × duration of each job held, and expressed as fibre-years (f/ml × years; f-y/ml). In 14 workers, all with short term employment for whom no details concerning job assignments were available, the mean level of exposure of all jobs for the appropriate period was assumed.

The exposed workers had been employed on average for 15 (0·25–47) years. The average latency from first exposure to death was 26 (1–63) years. The average cumulative asbestos dose was 26 (0·2–230) f-y/ml. The average intensity of exposure (cumulative dose divided by total duration of exposure) was 1·8 (0·1–7·5) f/ml.

HISTOLOGICAL EXAMINATION

All slides were examined without knowledge of identity, exposure, disease, or findings at necropsy.

Only "asbestos bodies" with an optically transparent core and a yellow brown iron protein coat were counted. In the text they are referred to as "ferruginous bodies," avoiding the term asbestos bodies as the nature of the core was not analysed.

Ferruginous bodies were studied in $25\,\mu$ unstained sections (about $1\,cm^2$) and scored 0–3, where score 0 refers to the absence of ferruginous bodies, score 1 denotes about 1–15, score 2 denotes 15–75, and score 3 denotes more than 75 ferruginous bodies.

To study the degree of fibrosis all sections were stained with haematoxylin and eosin, Van Gieson-elastica, and the Gordon Sweet reticulum stain. The severity of the fibrosis was graded[11]: 0 = None; 1 =

the lesions consist of a slight focal fibrosis around respiratory bronchioles; 2 = the lesions are confined to respiratory bronchioles of scattered acini. Fibrosis extends to alveolar ducts and atria as well as to the wall of adjacent air sacs; 3 = further increase and condensation of the peribronciolar fibrosis with early widespread interstitial fibrosis; and, 4 = few alveoli are recognisable in the widespread diffuse fibrosis; bronchioli are distorted. The different degrees of fibrosis are illustrated in the figure.

STATISTICAL METHODS

The material was primarily analysed taking the matching into account. That is, the unit of analysis was each exposed worker and control pair. The Wilcoxon matched pair signed rank test was thus used to test for the differences in levels of ferruginous bodies and fibrosis between the exposed and control subjects. To test for possible dose-response associations with asbestos exposure a chi-square test for trend applied to the proportion of pairs in which the exposed worker had more ferruginous bodies or more severe fibrosis. In dissolved pairs chi-square test, chi-square test for trend, and the non-parametric rank correlation coefficient, and Kendall's tau were used to test associations. "Statistically significant" refers to $p < 0.05$. All p values are two tailed, unless otherwise stated.

Results

CAUSES OF DEATH

In three exposed workers pulmonary fibrosis was stated as cause of death. There was no such diagnosis among the controls, among whom were seven cases with obstructive pulmonary disease.

When the final necropsy report, which may be considered as the best evidence available, was used, five deaths from pulmonary fibrosis among the exposed subjects were found and none among the controls. Pneumonia and pulmonary embolism were more common causes of death among the exposed workers than the controls. In the final necropsy reports these diagnoses are stated less frequently than on the death certificate, due to the recognition of a major underlying disease (table 2). Further, there were microscopic signs of pneumonia in 42 of the exposed subjects versus 36 of the controls (not in table). The latter difference is not significant.

As cases with tumour tissue in the pulmonary microscopic slides were excluded, no general conclusions can be drawn as to the frequency of malignancies in the material. According to the best available evidence, however, 25 exposed workers and 28 controls had tumours at other sites than are shown in the slides (table 2).
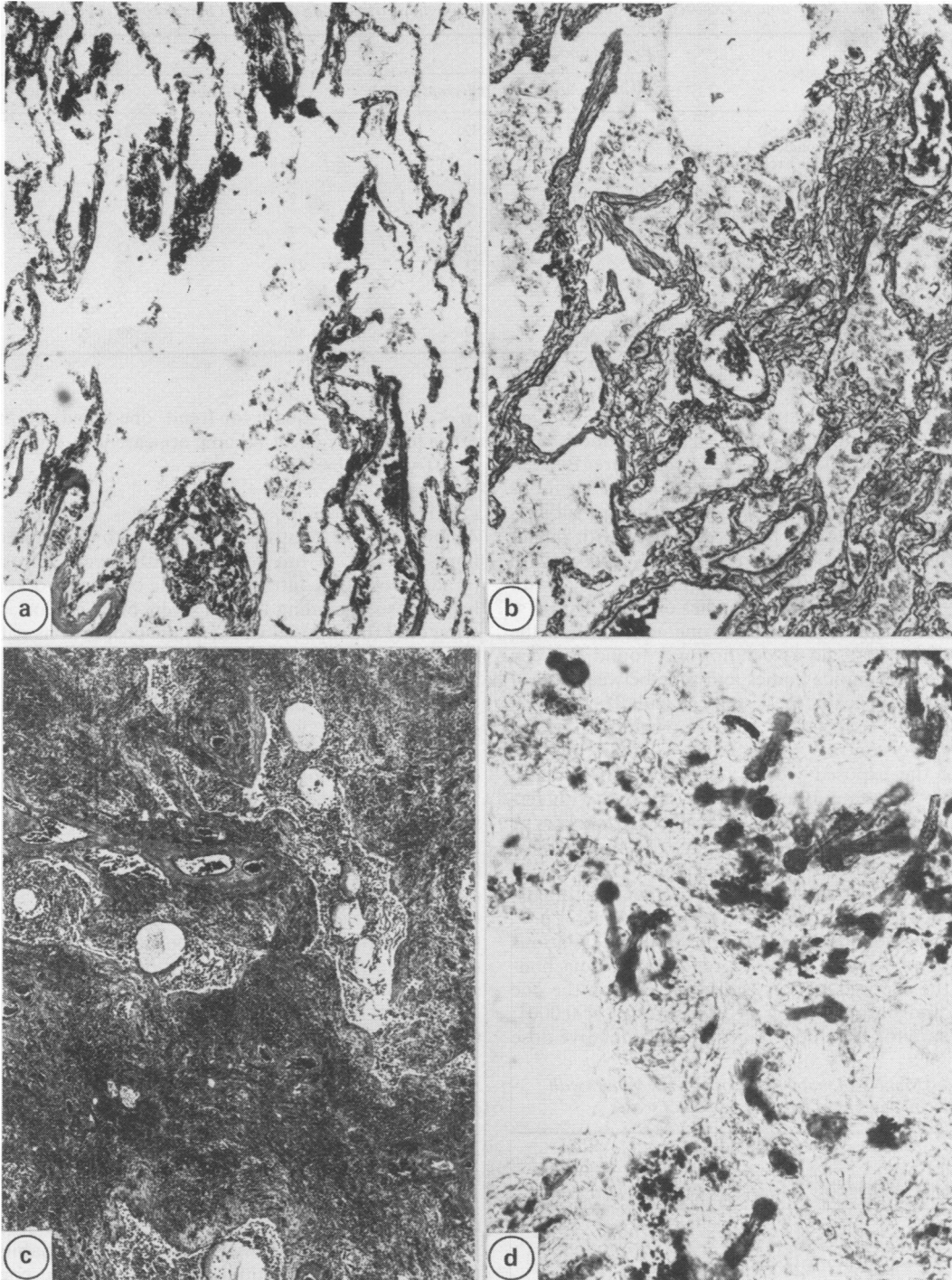
(a) Lesion grade 2. Slight extension of fibrosis to acini. Gordon Sweet reticulum stain × 60. (b) Lesion grade 3. Early widespread interstitial fibrosis. Gordon Sweet reticulum stain × 80. (c) Lesion grade 4. Massive fibrosis with architecture of lung totally destroyed. Gordon Sweet reticulum stain × 20. (d) Ferruginous bodies in a dense fibrotic area. There is much carbon pigment in lesion. This corresponds to ferruginous bodies grade 3. 25 μ unstained section × 300.

Table 2   *Causes of death among exposed subjects according to the official death certificate and to the necropsy report*

Causes of death	Exposed workers		Controls	
	Death certificate	Necropsy report	Death certificate	Necropsy report
Vascular disease (stroke included)	35	32	35	33
Renal disease (tumours excluded)	4	2	7	5
Pulmonary disease (tumours excluded):				
Pneumonia	10	6	4	3
Pulmonary embolism	5	1	2	—
Other pulmonary disease (obstructive				
and restrictive, including cor pulmonale)	5	7	7	6
Other diseases, except tumours	6	10	7	12
Carcinoma	16	21	21	22
Sarcoma	3	4	5	6
Trauma or intoxication	5	6	1	2
Total	89	89	89	89

FERRUGINOUS BODIES

Among the 89 controls, only 12 had ferruginous bodies (table 3) and all were of the lowest score. By contrast, 57 of the 89 exposed subjects had ferruginous bodies, 21 with score 2–3. The proportion of subjects with many ferruginous bodies increased with higher asbestos dose. Two per cent of those exposed with <10 f-y/ml, 29% with 11–40 f-y/ml, and 69% with >40 f-y/ml had ferruginous bodies of grade 2–3 (p < 0·0001, chi-square for trend, one tailed). For the exposed workers, no association was found between levels of ferruginous bodies and time between end of exposure and death (p = 0·28; Kendall). Age was significantly associated with ferruginous bodies among the controls (p = 0·03; Kendall) but not among the exposed workers (p = 0·17; Kendall). Tobacco consumption was not associated with ferruginous bodies among either the exposed workers or the controls (p = 0·26 and p = 0·34 respectively; Kendall).

Ferruginous bodies were more frequent among the exposed workers in all but seven pairs (table 3; p < 0·0001; Wilcoxon). Positive dose-response relations were found between higher score for ferruginous bodies in the exposed worker within the pair on the one hand, and both duration of exposure (p < 0·0001; chi-square for trend, one tailed) and cumulative dose

Table 3   *Number of matched exposed/control pairs with various combinations of ferruginous bodies scores*

Exposed worker's score	Control's score				
	0	1	2	3	Total
0	25	7	0	0	32
1	32	4	0	0	36
2	18	0	0	0	18
3	2	1	0	0	3
Total	77	12	0	0	89

(p < 0·0001; chi-square for trend, one tailed) on the other hand. The effect became appearent at doses of 1–10 f-y/ml (table 4).

FIBROSIS

Among the 89 controls were 56 with pulmonary fibrosis (table 5) but only six with severe fibrosis (grades 3–4). By contrast, 68 of the exposed workers had fibrosis, including 16 with severe fibrosis. Considering only the exposed workers, the proportions with fibrosis of grade 2 or worse were 40% with a cumulative dose <10 f-y/ml, 35% with 11–40 f-y/ml, and 62% with >40 f-y/ml (p = 0·07, chi-square for trend, one tailed). Age was significantly associated with fibrosis among the exposed workers (p = 0·04; Kendall) but not among the controls (p = 0·28; Kendall).

In a paired analysis, considering higher degree of fibrosis for the exposed worker within the pair, fibrosis was more pronounced among the exposed workers (table 5; p = 0·005; Wilcoxon). An association with cumulative asbestos dose was suggested but did not reach significance (table 6; p = 0·07; chi-square for trend, one tailed). Duration of exposure did not show a significant association (p = 0·30; chi-square for trend, one tailed).

RELATION BETWEEN FIBROSIS AND
FERRUGINOUS BODIES

Among the exposed workers there was a strong association between ferruginous body score and fibrosis grade (table 7; p = 0·005; Kendall). A similar relation was also found among the controls (p = 0·034; Kendall).

RELATION BETWEEN SMOKING AND FIBROSIS

Among the 67 controls with known smoking habits, there was an association between tobacco consumption and fibrosis grade (table 8; p = 0·048; Kendall, one tailed). Such an association was not evident

Table 4 *Number of matched exposed/control pairs in which the exposed worker has a lower/equal/higher (with per cent) score on ferruginous bodies as compared with his/her control, for various levels of cumulative asbestos dose, expressed as fibre-years (f-y/ml)*

| Asbestos dose of exposed worker (f-y/ml) | Total | Score for exposed subject compared with score for matched control | | |
		Lower	Equal	Higher
< 1	11	3	6	2 (18%)
1–10	31	4	12	15 (48%)
11–20	16	0	6	10 (63%)
21–30	9	0	2	7 (78%)
31–40	6	0	2	4 (67%)
> 40	16	0	1	15 (94%)
Total	89	7	29	53 (60%)

among the exposed workers (p = 0·35; Kendall, one tailed). When exposed workers with and without known smoking habits were compared, the fibrosis grade did not differ significantly (p = 0·68; chi-square). The same result was found for the controls (p = 0·59; chi-square).

Discussion

The necropsy rate in the cohort of asbestos cement workers from which the exposed workers originated was 60%, the corresponding figure for the general adult male population in the area being 54%. The necropsy rate was thus not appreciably raised among the asbestos cement workers and we have no reason to believe that they have been treated in any particular way as regards necropsy.

Although new slides were prepared for all cases, the technical quality of the tissue was sometimes low. In some cases there was autolysis, haemorrhage, or infarction. In addition, we usually do not know from which lobe of the lung the sample was taken, although we have reason to believe that most of the material was from the lower lobes. This may be important, as particle deposition as well as fibrosis is not uniform in the lung.[12]

Effects were seen at low cumulative asbestos doses. It is thus important to ensure that we do not system-

atically underestimate the levels of exposure. The estimation of early exposure included a conversion of workroom measurements from mppcf to f/ml, which is difficult.[13] We estimate the calculations of concentrations to be accurate within a factor of two. The dust monitoring data from the 1970s are in good agreement with the levels given in several other investigations.[14–17] We estimate the dust concentrations before the 1970s for most jobs to have been two to three times higher, and for the most dusty jobs, five to six times higher. The dust monitoring measurements with the impinger method, performed in 1957, although of short duration, are in good accordance with those from another Swedish asbestos cement industry,[15] and with some other data,[18] but lower than some reports.[15 17] The variations may be due to a real difference between factories. Also, if the duration of specific tasks during the workday has not been accounted for in the various studies, as we did, individual dose calculations might be overestimated.

Membrane filter techniques for estimation of air levels of asbestos fibres have changed during the years. Our data are based on the original methods and do not represent present recommendations for filter preparation and rules for fibre counting, which would give higher fibre counts.[19]

Information about the different work tasks used in the calculation of the individual cumulated dose was incomplete in some subjects. This tends to reduce the accuracy of the individual dose calculations, thus obscuring possible dose-response relations.

FERRUGINOUS BODIES
In this study a dose-response association between asbestos cement exposure, expressed as duration and cumulative dose, and ferruginous bodies score, was evident. A survey of ferruginous bodies with the light microscope (LM) in unstained undigested sections is a rough method for quantitative estimation of the content of asbestos fibres in the lungs. As to digestion, it has recently been shown that there is good correlation between ferruginous body count on undigested iron

Table 5 *Number of matched exposed/control pairs with various combinations of fibrosis grades*

| Exposed worker's grade | Control's grade | | | | | |
	0	1	2	3	4	Total
0	12	7	2	0	0	21
1	11	10	9	0	0	30
2	7	5	6	4	0	22
3	2	4	4	0	1	11
4	1	3	0	0	1	5
Total	33	29	21	4	2	89

Table 6   *Number of matched exposed/control pairs, in which the exposed worker has a lower/equal/higher (with per cent) degree of fibrosis compared with his/her control, for various levels of cumulative asbestos dose, expressed as fibre-years (f-y/ml)*

Asbestos dose of exposed worker (f-y/ml)	Total	Grade for exposed subject compared with grade for matched control		
		Lower	Equal	Higher
<1	11	4	4	3 (27%)
1–10	31	9	10	12 (39%)
11–20	16	7	4	5 (31%)
21–30	9	1	2	6 (67%)
31–40	6	0	3	3 (50%)
>40	16	2	6	8 (50%)
Total	89	23	29	37 (42%)

stained sections and with digestive techniques.[20] Also, ferruginous body counts with LM and scanning electron microscopy (EM) are well correlated in digested lung dissue.[10] Reliable measurements of fibre dust burden in lung tissue can, however, be obtained only with EM techniques.[21] Fibre counting and classification with transmission EM is now in progress on our specimens.

A quantitative association between asbestos exposure and ferruginous bodies has been shown in animals[22] but, to our knowledge, not in man. Several studies have shown, however, that asbestos workers generally have more ferruginous bodies than other workers, who in their turn have more ferruginous bodies than a general adult population.[23]

Asbestos fibres, especially chrysotile,[23] disappear from the lung with time. The exposed workers had been out of exposure for varying and often long periods before death. If ferruginous bodies disintegrate with time dose-response associations would be affected. The time passed since the end of exposure, however, was not associated with a diminishing score of ferruginous bodies. A probable explanation is that ferruginous bodies are formed mainly from amphibole fibres, which are relatively stable in the lung.

This is in agreement with findings in a general population,[23] from workers exposed to different types of asbestos fibres,[24] and in individuals with asbestos associated diseases.[10]

Among the controls, 13% had ferruginous bodies, which is less than reported in the general population living in the city of Malmö, where ferruginous bodies were found in 44% of the necropsies.[25] Malmö is a nearby, relatively large city with a high proportion of manual workers, including workers from a large shipyard. Our material originated mainly from a smaller town, without a shipyard, and from its rural surroundings. Earlier investigations have shown that urban dwellers have more ferruginous bodies than rural dwellers.[26 27] The Malmö material also showed a higher frequency of ferruginous bodies than most comparable urban materials.[26 28–30] Thus we find the lower figure in our study reasonable.

Age was associated with ferruginous bodies among controls. This may be due to an accumulation with time or to a higher exposure in the general population in earlier decades.

PULMONARY FIBROSIS
This finding was more common and more pro-

Table 7   *Number of exposed subjects and controls classified by grade of fibrosis and ferruginous bodies score*

Fibrosis grade	Exposure group	Ferruginous bodies score				
		0	1	2	3	All
0	Exposed subject	11	10	0	0	21
	Control	32	1	0	0	33
1	Exposed subject	10	16	3	1	30
	Control	24	5	0	0	29
2	Exposed subject	5	5	11	1	22
	Control	16	5	0	0	21
3	Exposed subject	4	4	3	0	11
	Control	3	1	0	0	4
4	Exposed subject	2	1	1	1	5
	Control	2	0	0	0	2
Total	Exposed	32	36	18	3	89
	Control	77	12	0	0	89

Table 8   *Number of exposed subjects and controls classified by grade of fibrosis and smoking habits*

Smoking habits (pack-years)	Exposure group	Fibrosis grade					
		0	1	2	3	4	All
0	Exposed	5	5	4	3	2	19
	Control	8	5	3	0	1	17
1–20	Exposed	7	9	5	4	0	25
	Control	8	7	2	0	0	17
21–40	Exposed	4	8	5	3	2	22
	Control	5	3	4	1	1	14
>40	Exposed	3	4	6	1	1	15
	Control	4	8	4	2	0	18
Unknown	Exposed	2	4	2	0	0	8
	Control	8	6	8	1	0	23
Total	Exposed	21	30	22	11	5	89
	Control	33	29	21	4	2	89

nounced in exposed workers than in controls and also an association between cumulative dose and degree of fibrosis was suggested, though not statistically significant.

The grading of microscopic fibrosis has some degree of uncertainty. A lack of precision, however, should rather dim than exaggerate any existing association with exposure.

The employees in the factory were exposed to Portland cement, which may contain silica. Nodular lesions in the necropsy material, however, suggesting lung fibrosis due to silicoses were not found.

The association of fibrosis with exposure was less strong than that between ferruginous bodies and exposure. This is reasonable, as the formation of ferruginous bodies around inhaled fibres is a rather specific reaction after exposure to asbestos, whereas lung fibrosis is a non-specific reaction caused by various noxious stimuli and may also be more host dependent. Our data is in accordance with a recent study of selected patients with varying occupational exposure to asbestos, in whom the histological grade of fibrosis was shown to be related to uncoated fibre count and total fibre count, using tissue digestive techniques and scanning EM.[10]

Living workers from the present asbestos cement factory, at examination by x ray computed tomography (unpublished observations) and extensive lung function tests (unpublished observations), display signs of increased lung density and reduced compliance. These findings also support a fibrosing effect of asbestos cement.

In previous dose-response studies relations between exposure to asbestos cement and asbestos related pulmonary disease have been expressed as clinical asbestosis,[17] radiological fibrosis,[9 31] and physiological changes.[31] In those studies the cumulative doses have been higher than in our workers. As the effects have usually not been separately analysed in the low dose area, it is not possible to draw any general conclu-

sions from these studies concerning the possible fibrosing effects of low exposure. Also, histological evaluation is probably a more sensitive method.

An association between cigarette smoking and microscopic lung fibrosis,[5] and increased lung density in x ray computed tomography,[32] has been noted. This is in agreement with our findings among the controls.

We found no association between smoking and either ferruginous bodies or fibrosis in exposed workers. This is in contrast with reports that, among insulators cigarette smokers had an increased risk of dying from asbestosis[21] and an association between histological grade of fibrosis and smoking in selected asbestos exposed patients.[10] Also, studies of lung function and x ray changes have indicated that smoking accentuates the fibrotic effect of asbestos,[6 8] including asbestos cement.[9 33−35] These findings, however, have been questioned.[36] The lack of association between smoking and fibrosis among the exposed workers in the present study does not, however, exclude that a small effect of smoking, similar to that among the controls, may be hidden by a stronger fibrosing effect of asbestos exposure, but a strong interaction between smoking and asbestos exposure is unlikely.

We found a strong association between ferruginous bodies and fibrosis in the exposed subjects and in the controls. This is in agreement with earlier studies of individuals with occupational exposure.[37 38] The present workers were mainly exposed to chrysotile but there was also a small exposure to amphiboles. Thus conclusions about the relative fibrogenic effects of different fibre types cannot be drawn from this study. The finding of an association between ferruginous bodies and fibrosis among the controls may be explained by the presence of asbestos exposure among some of the controls, construction workers, for example.

Pulmonary fibrosis was the cause of death accord-

ing to the death certificate in only three of the exposed workers. The clinical significance of the much more prevalent finding of microscopical fibrosis is unclear. It is, however, quite likely that some of the individuals with a fibrosis grade of 3-4 were respiratory disabled to some degree.

It is reasonable that the threshold limit value for asbestos should be low enough to ensure that histological pulmonary fibrosis is avoided.

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