Pleural Plaques and Cigarette Smoking in Asbestos Workers

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In a survey of 45 men aged 40 or over who had worked five years or more in an asbestos manufacturing plant, the prevalence of pleural plaques was studied with respect to age, duration of asbestos exposure, estimated cumulative asbestos dose, and smoking habit. Plaques were found in 38 to 53% of the men, depending on the interpretation of the chest film reader. Cigarette habit appeared to be the most important factor; the prevalence was lowest in nonsmokers, intermediate in current smokers, and particularly high in exsmokers. There was some confounding of this relationship by estimated cumulative asbestos dose but such confounding did not seem to be sufficient to explain fully the relationship between the prevalence of plaques and smoking habit. Both factors must be considered in studies of the risk of pleural plaques in asbestos workers.

In a previous report Weiss and Theodos[1] described the results of a 1975 chest x-ray survey in two asbestos products manufacturing plants. Plant A had used only chrysotile asbestos throughout its history while Plant B had used both chrysotile and amosite from 1950 to 1964 but only chrysotile before and after this period. The prevalences of both pulmonary fibrosis and pleural disease were higher in Plant B. Cigarette smoking was a factor in the prevalence of pulmonary fibrosis and perhaps also of pleural disease at Plant B.

Pleural thickening was found in only one of 10 nonsmokers and in 42% of the 38 current and exsmokers of cigarettes at Plant B. This difference was not quite statistically significant ($p = 0.074$ by Fisher's exact test), but it has stimulated further investigation of the problem by the authors. This paper analyzes the results of the 1977 and 1978 surveys with respect to the relationships between the prevalence of pleural plaques in men aged 40 or over and the factors of age, duration of asbestos exposure, estimated cumulative dose of asbestos, and cigarette habit.

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Method

A detailed description of the products and processes in Plant B was provided in the previous report,[1] a summary of which follows.

In 1935 this facility was manufacturing asbestos textiles, compressed sheet packing, paper, millboard, and molded thermal insulations. Textiles were made of chrysotile asbestos in a dry, dusty process; this operation was discontinued in 1951. Sheet packing was also made only of chrysotile and, because of milling the asbestos, the operation was dustier before the 1950s than it was in later years. Paper and millboard operations were very dusty prior to 1960, but after 1960 process improvements led to better conditions. Molded insulation was made of chrysotile from 1935 to 1950; thereafter, amosite, which had to be milled dry, was added to the chrysotile until manufacture of these products was discontinued in 1964. In 1948 the plant began to produce corrugated and monolithic asbestos cement boards made of chrysotile and portland cement.

Asbestos fiber counts were not made until 1972 but have been generally under 2/cm³ in recent years. Because of the lack of counts prior to 1972, the cumulative asbestos exposure (dose) for each employee in this study had to be estimated on a semiquantitative basis. A job index was devised at a meeting of the industrial hygienist (R.L.) with three foremen who had begun work at this plant between 1941 and 1947. Each job was rated as to degree of asbestos exposure on a scale of 1 to 3 (largest exposure). To take into account the change in conditions over time, job ratings were multiplied by three during the period prior to 1951, by two during the period 1951 through 1963, and by one from 1964 on. The employment record of each man was reviewed and an index of cumulative asbestos exposure was computed by multiplying the job rating, the period rating, and the number of years worked at each job during each period. The maximum index recorded in this group of men was 159.

Pleural plaques were noted only in men aged 40 or over. There were 69 such employees eligible for examination between 1977 and 1978, and 56 (81%) had 110 kv 36X 43 cm postero-anterior chest films during one or both of

Table 1. — Prevalence of Pleural Plaques by Reader, Age, Duration of Asbestos Exposure, Estimated Cumulative Dose of Asbestos, and Cigarette Habit in Workers Aged 40 or Over.

Characteristic	Distribution No.	Distribution % of Total	Prevalence of Plaques by Reader: W.W. No.	W.W. % of Group	W.W. Probability (Chi Square)	L.C. No.	L.C. % of Group	L.C. Probability (Chi Square)
Age — years								
40-54	20	44	9	45	>0.05	8	40	>0.05
55•	25	56	15	60		9	36	
Years exposed								
5-29	20	44	6	30	<0.05	5	25	>0.05
30•	25	56	18	72		12	48	
Cumulative dose index								
0-19	14	31	4	29	>0.05	2	14	>0.05
20-59	14	31	9	64		8	57	
60•	17	38	11	65		7	41	
Cigarette habit								
Nonsmoker	12	27	4	33	<0.025	2	17	<0.05
Current smoker	19	42	8	42		6	32	
Exsmoker	14	31	12	86		9	64	
Total	45	100	24	53		17	38	

these annual surveys. Eleven men who had worked for less than five years at this plant were eliminated to allow for a minimal latent period of five years, leaving 45 in the study. The chest films were read by two of the authors (W.W. and L.C.) independently without knowledge of the individual's age, work experience, or smoking habit. Pleural plaques were recorded as present when pleural thickening of irregular width was noted along the lateral chest wall, provided it spared the apex and the costophrenic angle, or on the dome of the diaphragm, with or without calcification.

A careful smoking history was recorded at each survey. For the purpose of this investigation, each employee was classified according to cigarette habit as a nonsmoker (had never smoked cigarettes), a current smoker, or an exsmoker (had stopped smoking one or more years ago).

The statistical significance of differences was determined by calculating exact probability by the binomial distribution or by estimating probability by the t test, the chi square test (with Yates' correction when there was only one degree of freedom), one-way analysis of variance, or significance limits for the fourfold table test based on the hypergeometric distribution.

Results

There was 31% disagreement between the two chest film readers on the presence of pleural plaques. In 11 (24%) of the 45 cases W.W. found plaques when L.C. did not and in 3 (7%) L.C. found them when W.W. did not. This difference was not quite statistically significant at the 0.05 level ($p = 0.0574$ using the binomial distribution for paired observations). The prevalence of plaques is presented for each reader separately.

Table 1 shows that the prevalence of plaques was 53% for W.W. and 38% for L.C. Age was not a factor. The data suggest that both duration of asbestos exposure and cumulative dose of asbestos were factors although, because of small numbers, three of the four comparisons did not reach statistical significance at the 0.05 level. However, cigarette habit was found to be an important factor, the prevalence of plaques being particularly high in exsmokers, and the differences were statistically significant for both readers. Only two men had calcified plaques (interpreted in both cases by L.C.).

One must consider the possibility that the relationship between pleural plaques and cigarette habit was confounded by the other factors investigated, particularly

Table 2. — Comparison of Cigarette Habit Groups by Age, Duration of Asbestos Exposure, and Estimated Cumulative Dose of Asbestos in Workers Aged 40 or Over.

Characteristic	Cigarette Habit: Nonsmokers N = 12	Current Smokers N = 19	Exsmokers N = 14	Probability
Age — years				
Mean	53.9	53.4	56.3	exsmokers vs. others:
S.D.	6.67	6.18	5.17	$t = 1.41$, $p > 0.05$
Years of exposure				
Mean	24.50	23.68	32.43	exsmokers vs. others:
S.D.	12.95	14.63	9.02	$t = 2.09$, $p < 0.05$
Cumulative dose index				
Mean	40.90	45.32	63.36	exsmokers vs. others:
S.D.	27.28	42.79	28.72	$t = 1.76$, $p > 0.05$
				ANOVA* for 3 groups: $F = 1.58$, $p > 0.05$

*One-way analysis of variance

degree and duration of asbestos exposure. Table 2 shows that the smoking groups were similar in age. With respect to duration of asbestos exposure, nonsmokers and current smokers were similar but exsmokers averaged eight years more of work at the plant, this difference being statistically significant. With respect to cumulative asbestos dose, the same pattern appeared: current smokers were similar to nonsmokers, but exsmokers had an average index which was 40 to 55% higher than the average index for the other two groups. Although these differences may be important, they are not statistically significant by two different methods of analysis.

When the men were distributed according to both cumulative dose of asbestos and cigarette habit, the prevalence of plaques read by W.W. varied with respect to both factors (Table 3). The data suggest that the prevalence of plaques is high in exsmokers at any asbestos dosage but that in nonsmokers and current smokers the prevalence increases with increasing asbestos dose. Unfortunately, cross-classification by the two factors results in cells with very small numbers. However, if the data in the two lower asbestos dose categories are combined, then plaques were found in 6 of 21 nonsmokers and current smokers compared with 6 of 7 exsmokers. This difference is statistically significant at the 0.05 level using significance limits for the fourfold table test based on the hypergeometrical distribution.* The findings were similar for plaques read by L.G. but the differences were not as clear-cut and were not statistically significant at the 0.05 level.

Discussion

Several investigators have noted an association between pleural thickening and smoking in workers exposed to asbestos. In a large survey of English naval dockyard workers exposed to chrysotile, amosite, and crocidolite, P. G. Harries et al[2] found pleural thickening in 2.7% of 5,552 nonsmokers, 4.9% of 12,798 smokers, and 6.4% of 4,990 exsmokers. The prevalence of pleural thickening tended to fall slightly with increasing cigarette dosage.

In recent published reports of the studies of these dockyard workers, Rossiter et al[3,4] have provided more details for segments of this population. In a sample of 1,200 men who were aged 50 to 59, pleural thickening was separated into diffuse disease and plaques.[3] Only the presence of plaques was related to the duration of exposure to asbestos and there was an excess of plaques in exsmokers (29.5%) compared with the prevalence in smokers (23.9%) and in nonsmokers (23.1%). The prevalence of pleural calcification was different: 8.8% among nonsmokers, 3.5% among smokers, and 6.1% among exsmokers. A nine-year (1966-1975) follow-up study of 253 dockyard workers[4] found increases in the prevalence of diffuse pleural thickening, almost entirely limited to those men who had stopped smoking after 1966, and of pleural plaques, with the greatest increase (from 10% to 23%) in smokers, but little change in the prevalence of calcified plaques.

Hillerdal[5] reported a study of pleural plaques in chest x-ray surveys of the general population in the Swedish county of Uppsala. Of 492 men with plaques, 354 were interviewed and it was found that 79% were or had been smokers. The expected frequency in men of the same age and occupation is 55%. In a survey of 197 Swedish asbestos workers, Hedenberg et al[6] found pleural plaques in 30% of 103 smokers and 19% of 94 nonsmokers.

Thus, there is general consistency between the reports from England and Sweden and the data reported in the present study, especially with respect to exsmokers in those studies in which these have been separated from current smokers. Unfortunately the studies cited from the literature have no information on the possible confounding of this relationship by degree of asbestos exposure. The data in this study suggest that there may be some confounding. While the association between the prevalence of plaques and smoking was somewhat stronger than that between plaques and cumulative asbestos dosage, it must be remembered that the estimates of dosage were crude. It is uncertain whether the finding of 40 to 55% greater asbestos exposure in exsmokers could account for a prevalence of plaques which was more than double that in the other groups. Conclusions are restrained by the small number of workers in this investigation. A clear-cut answer to the question as to whether the association between plaques and smoking is spurious will require a much larger research effort, preferably in a cohort study.

The hypothesis that smoking is a factor in the pathogenesis of asbestos-related pleural plaques is a plausible one despite the fact that the mechanism by which inhaled asbestos fibers produces fibrous plaques in the parietal pleura is unknown. Smoking is detrimental to various aspects of pulmonary function although the effect on the clearance of particulate matter is not clear.[7] A recent study by Cohen et al[8] shows, by the use of inhaled magnetic dust (magnetite), that long-term dust clearance is impaired in smokers: 50% retention compared to 10% in nonsmokers. It might well be that once smoking has damaged the clearance mechanisms, cessation of smoking could be more harmful in this type of defense than continued smoking because the short-term effect of cigarette smoking is to enhance deep bronchial clearance transiently in some people[9] and smokers may become dependent on this effect to maintain clearance. This

Table 3. — Prevalence of Pleural Plaques (Read by W.W.) by Estimated Cumulative Dose of Asbestos and Cigarette Habit in Men Aged 40 or Over.

Asbestos Dose and Cigarette Habit	No. of Men in Group	No. of Men with Plaques
Asbestos index under 20		
Nonsmoker	5	1
Current smoker	8	2
Exsmoker	1	1
Asbestos index 20-59		
Nonsmoker	3	1
Current smoker	5	2
Exsmoker	6	5
Asbestos index 60+		
Nonsmoker	4	2
Current smoker	6	5
Exsmoker	7	5
Total	45	24

* [illegible]

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could explain an increased frequency of pleural plaques in exsmokers because damaged clearance mechanisms unaided by continued smoking may lead to higher "effective" doses of asbestos in the tissues.

The clinical significance of a relationship between the prevalence of pleural plaques and smoking depends on the clinical significance of plaques. The immediate importance of these lesions is negligible but there is some suspicion that plaques may be indicators of an enhanced risk of lung cancer[10,11] and mesothelioma.[11]

With respect to lung cancer risk the evidence is equivocal. Kiviluoto et al[10] found 700 cases of calcified plaque in 6,000 adults during a mass chest x-ray survey in Tuusniemi commune, Finland, in 1962. The lung cancer incidence between 1962 and 1977 was almost identical to the incidence in controls without plaques in Maaninka commune. 13 and 14, respectively. It may be important to note that this study was limited to calcified plaques. In a case-control study of 69 lung cancer cases there was an elevated risk of lung cancer of 2.8 only when there was pulmonary fibrosis in addition to calcified plaques. Information on smoking habits was not provided.

Edge[11] has reported an increased incidence of lung cancer in 429 older British shipyard workers with pleural plaques unassociated with pulmonary fibrosis found between 1964 and 1971 who were compared with a matched control group of 429 men in another city where there was neither known asbestos exposure nor plaques. After excluding six men with lung cancer who had clinical evidence of tumor at the time observation was begun in the men with plaques, the relative risk was 3.25 (13 cases in the men with plaques compared to 4 in the controls, chi square with Yates' correction = 3.84, $p = 0.05$). However, this comparison is probably invalid because only 231 of the 429 men with plaques were discovered by routine chest films and the remaining 198 were found by clinic or hospital films whereas all 429 controls had routine films. Thus, there was undoubtedly some selection bias operating to increase the incidence of lung cancer in the men with plaques. Comparing only the groups that had routine films, six (2.6%) of 231 men with plaques and four (0.9%) of 429 controls developed lung cancer, a difference which is not statistically significant at the 0.05 level. Furthermore, half the lung cancer cases in the men with plaques were diagnosed in the first two years of follow-up and therefore these individuals presumably had their tumors at the time observation began. After exclusion of the early cases, the relative risk, as compared to the incidence of lung cancer in the general population, remained at 1.0 until after six years of follow-up it rose to 2.1 (6 cases compared to 2.8 expected), which also is not statistically significant at the 0.05 level. Most importantly, no smoking habit information was available for adjustment of the relative risk.

A similar problem indicating selection bias in the men with plaques operated with respect to the incidence of mesothelioma: most of the cases occurred early in the follow-up period and only two developed after six years of follow-up. However, mesothelioma is so rare in the general population that even two cases in the men with plaques is suspicious, especially since mesothelioma is not related to smoking.

Thus, at present the prognostic significance of pleural plaques with regard to the risk of lung cancer is doubtful. In the absence of smoking-habit data, no conclusions are warranted. If plaques are related to smoking as well as to asbestos exposure and if lung cancer is similarly related, then any association between plaques and lung cancer is likely to be spurious.

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