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Ann. occup. Hyg., Vol. 39, No. 3, pp. 363–374, 1995
Elsevier Science Ltd
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0003-4878/95 $9.50+0.00

0003-4878(95)00006-2

MALIGNANT MESOTHELIOMA AND DURATION OF ASBESTOS EXPOSURE: CORRELATION WITH TISSUE MINERAL FIBRE CONTENT

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(*Received in final form* 11 *January* 1995)

Abstract—Among 441 cases of malignant mesothelioma in the author's files, there were 324 for whom reliable information was available regarding the duration of exposure to asbestos. Included were 298 pleural and 26 peritoneal mesotheliomas. The mean duration of exposure to asbestos was 23±14 years for all cases, and was not different for the pleural and peritoneal groups. Lung tissue was available for analysis of mineral fibre content in 94 cases. Linear regression analysis showed a significant correlation between duration of exposure and asbestos bodies per gramme of wet lung as determined by light microscopy, and between duration of exposure and total uncoated fibres (5 μm or greater in length) as well as commercial amphibole fibres per gramme as determined by scanning electron microscopy ($P<0.05$). Individuals with direct exposures had on average higher asbestos contents than patients with indirect exposures. Furthermore, for each duration of exposure, shipyard workers had on average higher asbestos contents than non-shipyard workers ($P<0.05$). Mesotheliomas are associated with a wide range of durations of exposure to asbestos and pulmonary asbestos burdens, and there is a rough correlation between duration of exposure and pulmonary commercial amphibole content.

INTRODUCTION

The association between asbestos exposure and mesothelioma is undisputed and has been confirmed in numerous epidemiological studies (Roggli *et al.*, 1992a). Mesotheliomas may occur following relatively brief or low-level exposures to asbestos, and most patients lack the histologic features of asbestosis, which is generally associated with heavier exposures to asbestos (Roggli, 1992a). However, relatively few studies have examined the relationship between mesothelioma and the duration of exposure to asbestos. In this regard, nine studies including a total of 472 patients were identified, reporting ranges of exposure from a few days to more than 60 years, with median values of 3–35 years (Browne and Smither, 1983; Chahinian *et al.*, 1982; de Lajartre and de Lajartre, 1979; Lerner *et al.*, 1983; Ruffie *et al.*, 1989; Sluis-Cremer, 1991; Tuomi *et al.*, 1991; Vogelzang *et al.*, 1984; Warnock, 1989). In two of these studies, duration of exposure to asbestos was examined separately for pleural and peritoneal mesotheliomas: one found no difference in median exposure duration for pleural as compared to peritoneal cases (Browne and Smither, 1983), whereas one reported a longer median exposure duration for peritoneal (11 years) as compared to pleural (5 years) cases (Chahinian *et al.*, 1982).

There is also considerable uncertainty regarding how brief of an exposure to

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asbestos can result in subsequent development of mesothelioma. Chahinian *et al.* (1982) reported one case with an exposure duration of only a few days, and Gibbs *et al.* (1990) noted a gas mask manufacturer with only 10 days of exposure to crocidolite who subsequently died of mesothelioma. Browne and Smither (1983) in a study of 144 mesotheliomas with a history of asbestos exposure, noted that 6% were exposed for less than 3 months. In a study of asbestos-related diseases due to short-term exposures, Seidman *et al.* (1979) reported three cases of mesothelioma with durations of exposure ranging from 6 to 11 months. In seven other studies comprising a total of 275 cases of mesothelioma, there were no cases with a duration of exposure less than 3 months (de Lajartre and de Lajartre, 1979; Lerner *et al.*, 1983; Ruffie *et al.*, 1989; Sluis-Cremer, 1991; Tuomi *et al.*, 1991; Vogelzang *et al.*, 1984; Warnock, 1989).

Few studies have been reported in which the investigators attempted to correlate the pulmonary asbestos burdens with the duration of exposure to asbestos. In Table 1 of the study by Tuomi *et al.* (1991), the duration of asbestos exposure and fibre concentration per gramme of dry lung are reported for 15 mesothelioma patients. These authors found an increasing fibre burden with increasing probability of asbestos exposure by job category. However, among the eight cases with the longest durations of exposure, only five had fibre burdens that equalled or exceeded the median burden, and among the seven cases with the shorest durations, three cases had fibre burdens that equalled or exceeded the median value. Wagner *et al.* (1988) correlated lung fibre burdens to an exposure index based on relative intensity and duration of exposure to asbestos in a group of 36 east London factory workers with various asbestos-related diseases. The total fibre burden as well as the proportions of amosite and crocidolite tended to rise in those with the higher indices, whereas the proportion of chrysotile and non-asbestos mineral fibres tended to decrease.

In the present study, a database including more than 400 cases of malignant mesothelioma was examined for information regarding duration of exposure to asbestos. In 94 of these patients, information was also available regarding pulmonary asbestos burdens as well as duration of asbestos exposure so that correlations could be examined between these two variables. Observations from these comparisons and analyses form the basis for this report.

MATERIALS AND METHODS

Patient population

Among some 441 cases of malignant mesothelioma from the author's files, 324 (73%) were identified for which information was available regarding duration of exposure to asbestos. All cases were pathologically confirmed based on open or thoracoscopic biopsy, decortication, pneumonectomy or autopsy specimens using previously described criteria (Roggli *et al.*, 1992a). Information regarding type of employment with exposure to asbestos and duration of exposure to asbestos were obtained by direct patient interview. Age, sex and primary site of the mesothelioma (i.e. pleural or peritoneal) were also recorded in each instance.

Occupations were further categorized as direct vs indirect exposures, and as shipyard vs non-shipyard exposures. Direct exposures included individuals whose occupations involved direct handling of asbestos-containing materials, such as insulators, pipecoverers, pipefitters, boiler-workers, asbestos sprayers, asbestos

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sawers, asbestos cement workers, asbestos textile workers, other asbestos manufacturers and brake repair workers. Indirect exposures included occupations with asbestos exposures which occurred on a by-stander basis, that is someone who worked in proximity to an individual with direct exposure. Examples include construction workers, electricians, welders, sheet-metal workers, merchant marine seamen, power plant workers and shipyard workers other than insulators. Household contacts of asbestos workers were also classified as indirect exposures. Classification of cases as shipyard workers included the occupations of shipyard insulator, shipwright, joiner, welder, boiler-worker, sheet metal-worker, carpenter, painter and burner. Non-shipyard workers included any occupation with asbestos exposure outside of the shipyard environment. Merchant marine seamen were classified as non-shipyard workers, since exposures aboard ship were quite different from those in shipyards where construction and renovation were constantly taking place.

Tissue asbestos analysis

Formalin-fixed or paraffin-embedded peripheral lung parenchyma was available for analysis of tissue asbestos content in 94 of the 324 cases. The vast majority of these were autopsy cases where lung tissue was available for analysis, although a few were from surgically resected specimens. For the remaining 230 cases, only tumour tissue was available for review, or the amount of lung tissue sampled was insufficient for analysis. Lung tissue was processed for digestion using the sodium hypochlorite technique as previously described (Roggli *et al.*, 1992b). The residue was collected on 0.4 μm pore-size Nuclepore filters. For light microscopic (LM) analysis, the filter was mounted on a glass slide for asbestos body quantification. Filters were counted at a magnification of × 400, and only bodies with typical morphology and thin, translucent cores were counted as asbestos bodies (Roggli, 1992b). Results were reported as asbestos bodies per gramme of wet lung tissue (AB g^{-1}). The normal range for our laboratory is 0–20 AB g^{-1}, and the detection limit for a 0.3 g sample size is approximately 3 AB g^{-1}. For cases in which no asbestos bodies were detected in the sample, the value was recorded as less than the detection limit for that sample.

For scanning electron microscopic (SEM) analysis, the filter was mounted on a carbon stub with colloidal graphite, sputter-coated with gold or platinum, and examined in a JEOL scanning electron microscope at a screen magnification of × 1000. Fibres 5 μm or greater in length were counted using a protocol in which 100 consecutive fields or 200 fibres were counted, whichever came first. Fibres were defined as particles with an aspect ratio (length to width) of at least 3:1 and roughly parallel sides. The concentration of fibres for each case was calculated based on the fibre density (i.e. per mm^2) on the filter surface times the effective area of the filter, divided by the weight of the lung sample which was analysed. The results were reported as total uncoated fibres 5 μm or greater in length per gramme of wet lung (UF g^{-1}). The normal range for our laboratory is < 440–13000 UF g^{-1}) (median, 3100 UF g^{-1}), and the detection limit for a 0.3 g sample size is approximately 440 UF g^{-1}. Uncoated fibres were detected in every case which was analysed.

Fibre types were determined using a combination of fibre morphology assessed by SEM and elemental composition assessed by energy dispersive X-ray analysis (EDXA). Fibres were classified as asbestos or non-asbestos mineral fibres (NAMF) as previously described (Roggli *et al.*, 1992b). Asbestos fibres were further classified as amosite,

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crocidolite, tremolite, anthophyllite, actinolite or chrysotile. For purposes of analysis, amosite and crocidolite were grouped together as commercial amphiboles (AC), and tremolite, anthophyllite and actinolite were grouped together as non-commercial amphiboles (TAA). A total of between five and 30 fibres were analysed for each case (mean, 16 fibres per case). The proportion of each fibre type and the total uncoated fibre concentration were used to determine the tissue concentration of AC, TAA, chrysotile and NAMF for each case. For cases where no fibres of a particular fibre type were detected, the value was recorded as less than the detection limit for that fibre type for that case.

Statistical analysis

For all analyses involving fibre types, the log-transformation of the asbestos body or fibre concentration was used, since these values are log-normally distributed. For values that were below the detection limit, half of the detection limit was used for purposes of analysis. A small number of cases (two cases) had both shipyard and non-shipyard exposures. For these cases, the shipyard duration of exposure was used in the analysis of shipyard cases, and the non-shipyard duration was used in the analysis of non-shipyard cases. Exclusion of these cases from the analysis had no effect on the results. Durations of exposure were compared with asbestos body counts as well as fibre counts (total and by fibre type) using a linear regression algorithm. Differences for duration of exposure for pleural vs peritoneal cases and for different fibre types were compared using Fisher's exact test. Asbestos body counts, uncoated fibre concentrations and commercial amphibole burdens were compared between shipyard and non-shipyard workers and between direct and indirect exposures using student's t-test for the log-transformed values. P values were determined for each correlation coefficient (r), and associations were considered to be statistically significant for $P < 0.05$.

RESULTS

The median duration and range of asbestos exposures for the 324 cases in the present study are displayed in Table 1, along with data from 472 other cases from the literature. The mean duration of exposure for the 324 cases was 23 ± 14 years. The

Table 1. Malignant mesothelioma and duration of asbestos exposure in 796 cases

Reference	No. of cases	Duration of exposure*	Range
de Lajartre and de Lajartre (1979)	40	25–35 years	<15–55 years
Chahinian *et al.* (1982)	53	5 years (pleural) 11 years (peritoneal)	Few days–40+ years
Browne and Smither (1983)	144	10.5 years	1 month–50 years
Lerner *et al.* (1983)	11	ND	9–35 years
Vogelzang *et al.* (1984)	7	3 years	2–25+ years
Ruffie *et al.* (1989)	145	12 years	3 months–35+ years
Warnock (1989)	27	35 years	2–51 years
Sluis-Cremer (1991)	30	ND	3 months–16+ years
Tuomi *et al.* (1991)	15	21 years	7–39 years
Roggli (present study)	324	24 years (pleural) 28 years (peritoneal)	1 month–53 years

*Median values.
ND = not determined.

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mean durations for the pleural cases (23 ± 14 years) and for the peritoneal cases (24 ± 11 years) were not statistically different ($P > 0.05$). However, when the data for the pleural and peritoneal cases are displayed as a histogram (Fig. 1), it is of interest to note that 51 out of 298 pleural cases (17%) but only one out of 26 peritoneal cases (4%) had a duration of exposure of 5 years or less ($P = 0.056$ by Fisher's exact test).

Cases of mesothelioma from the present study for which the duration of exposure was less than 1 year are summarized in Table 2. Four such cases were identified among

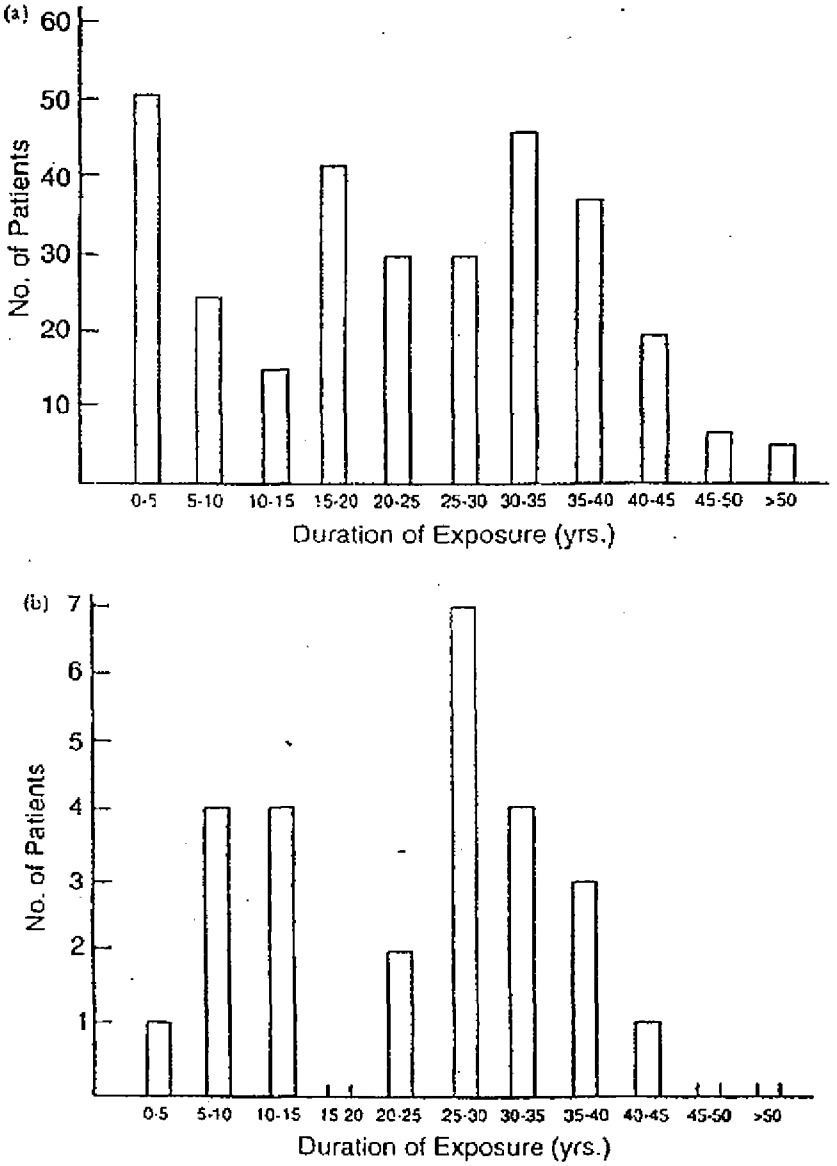

Fig. 1. (a) Histogram showing the distribution of durations of asbestos exposure for 298 patients with pleural mesothelioma. (b) Histogram showing a similar distribution for 26 patients with peritoneal mesothelioma

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Table 2. Demographic and exposure data in four cases of malignant pleural mesothelioma with less than 1 year exposure

Case No.	Age (years)/ sex	Histologic Dx.	Occupation	Exposure duration
1	65/M	Epithelial	Asbestos factory worker	7 months
2	48/M	Epithelial	Boilerman, U.S. Navy	6 months
3	39/M	Epithelial	U.S. Navy	6 months
4	49/M	Epithelial	Asbestos sprayer	1 month

the total of 324. All four were the epithelial variant of pleural mesothelioma, and all were men ranging in age from 39 to 65 years. Two were exposed to asbestos while serving in the U.S. Navy. The shortest duration (1 month) occurred in an individual who was an asbestos sprayer (Case 4). None of these individuals had any other identifiable exposure to asbestos. Tissue was not available for analysis in any of these four cases.

There were 94 cases for which tissue was available for asbestos analysis and information was available regarding the duration of exposure to asbestos. These included 85 men and nine women, with a mean age of 61 ± 10 years and a median age of 61 years (range: 31–87 years). There were 89 pleural and five peritoneal cases in this group. Asbestos body counts were performed by light microscopy in 93 out of 94 cases, and fibre type analysis by SEM was performed in 84 out of 94 cases. Linear regression analysis demonstrated a significant correlation between the numbers of asbestos bodies (AB g^{-1}) or commercial amphibole fibres (AC g^{-1}) per gramme of wet lung and the duration of exposure to asbestos ($r = 0.31$, $P < 0.01$, Fig. 2). A less strong correlation was noted between uncoated fibres (UF g^{-1}) per gramme of wet lung and duration of asbestos exposure ($r = 0.22$, $P < 0.05$). There was no significant correlation between age and Ab g^{-1} ($r = 0.12$, P = NS) or for any other parameter of pulmonary mineral fibre analysis.

The 94 mesothelioma cases were further divided into shipyard vs non-shipyard exposure categories and direct vs indirect exposure categories as described in the Materials and Methods section. The number of cases in each of these categories as well as their mean age and duration of exposure and median asbestos body, commercial amphibole and total uncoated fibre counts are given in Table 3. The median fibre counts for asbestos bodies, commercial amphiboles and total uncoated fibres are substantially greater for the individuals with direct exposures to asbestos as compared to those with indirect exposures ($P < 0.001$). Similarly, the median values for each of these fibre parameters are greater for shipyard as compared to non-shipyard workers ($P < 0.05$ for commercial amphibole and total uncoated fibre concentrations, $P = 0.09$ for asbestos bodies), even though the mean duration of exposure was 4 years less for the shipyard workers.

Linear regression analysis shows a significant correlation between AB g^{-1} or AC g^{-1} and duration of exposure to asbestos for each of the four exposure categories of shipyard, non-shipyard, direct and indirect exposures (Table 4), except that there was no significant correlation between direct exposures and AC g^{-1} ($P > 0.10$). For each duration of exposure, shipyard workers had higher asbestos body counts than did non-shipyard workers, and individuals with direct exposures had higher asbestos body

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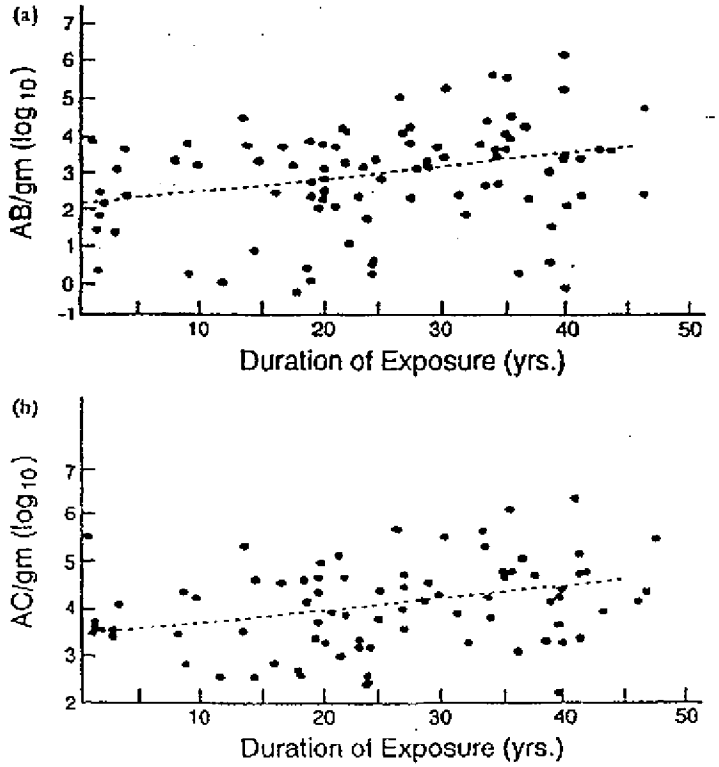

Fig. 2. (a) Scattergram showing the relationship between asbestos bodies per gramme of wet lung (AB g^{-1}) and duration of exposure to asbestos for 94 patients with malignant mesothelioma. Linear regresssion line is defined by $y=0.036\,x+2.05$ ($r=0.31$, $P<0.01$). (b) Similar scattergram for concentration of commercial amphiboles (AC g^{-1}) vs duration of exposure. Linear regression line is given by $y=0.025\,x+3.45$ ($r=0.31$, $P<0.01$).

Table 3. Demographic and mineral fibre content data on 94 cases of malignant mesothelioma by exposure group*

	Shipyard workers	Non-shipyard workers	Direct exposure	Indirect exposure
N	28	66	29	65
Age (years)	63 ± 7	60 ± 12	59 ± 8	62 ± 11
Duration (years)	22 ± 15	26 ± 11	26 ± 11	24 ± 12
AB g^{-1}	1670 (< 20–1 600 000)	1570 (1–322 000)	6450‡ (205–1 600 000)	390 (1–436 000)
UF g^{-1}	39 700† (4300–2 890 000)	25 300 (670–901 000)	67 000‡ (4520–2 890 000)	21 600 (670–1890)
AC g^{-1}	18 400† (< 1460–2 890 000)	8460 (122–781 000)	63 200‡ (1940–2 890 000)	5160 (122–1 890 000)

*Values shown are mean ± 1 SD for age and duration of exposure; median with range in parentheses for asbestos bodies (AB), uncoated fibres ≥ 5 μm in length (UF), and amosite or crocidolite fibres ≥ 5 μm in length (AC) per gramme of wet lung. Direct and indirect exposures defined in text.

†$P<0.05$ (student's *t*-test) as compared to non-shipyard workers.

‡$P<0.001$ (student's *t*-test) as compared to indirect exposure.

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Table 4. Regression lines for asbestos content vs duration of exposure by occupational category in 94 cases of malignant mesothelioma

	x	y	m	b	r	P
Shipyard workers ($N=28$)	Exposure duration (years)	$\log_{10}$ AB g^{-1}	0.047	2.24	0.52	<0.01
		$\log_{10}$ UF g^{-1}	0.014	4.46	0.29	NS
		$\log_{10}$ AC g^{-1}	0.026	3.84	0.40	0.05
Non-shipyard workers ($N=66$)	Exposure duration (years)	$\log_{10}$ AB g^{-1}	0.035	1.88	0.27	<0.05
		$\log_{10}$ UF g^{-1}	0.013	4.06	0.23	NS
		$\log_{10}$ AC g^{-1}	0.025	3.29	0.31	<0.05
Direct workers ($N=29$)	Exposure duration (years)	$\log_{10}$ AB g^{-1}	0.036	2.97	0.44	<0.05
		$\log_{10}$ UF g^{-1}	0.014	4.56	0.24	NS
		$\log_{10}$ AC g^{-1}	0.017	4.31	0.24	NS
Indirect exposures ($N=65$)	Exposure duration (years)	$\log_{10}$ UF g^{-1}	0.010	4.07	0.20	NS
		$\log_{10}$ AB g^{-1}	0.030	1.79	0.27	<0.05
		$\log_{10}$ AC g^{-1}	0.022	3.23	0.33	<0.05

Values represent the coefficients for the standard linear represssion equation $y=mx+b$, where m is the slope, b the intercept, r the correlation coefficient, and P the probability values for the null hypothesis.

AB = asbestos bodies, UF = uncoated fibres $\geq 5\,\mu m$ in length, AC = amosite and crocidolite fibres $>5\,\mu m$ in length, all per gramme of wet lung.

NS = not significant ($P>0.05$).

counts than did those with indirect exposures (Fig. 3, Table 4). Similar results were observed for pulmonary content of commercial amphiboles (Fig. 4, Table 4). There was no significant correlation between total uncoated fibres (UF g^{-1}) and any of these exposure categories (Table 4). Furthermore, there was no significant correlation between non-commercial amphibole, chrysotile or non-asbestos mineral fibre content and duration of exposure for any exposure category (data not shown).

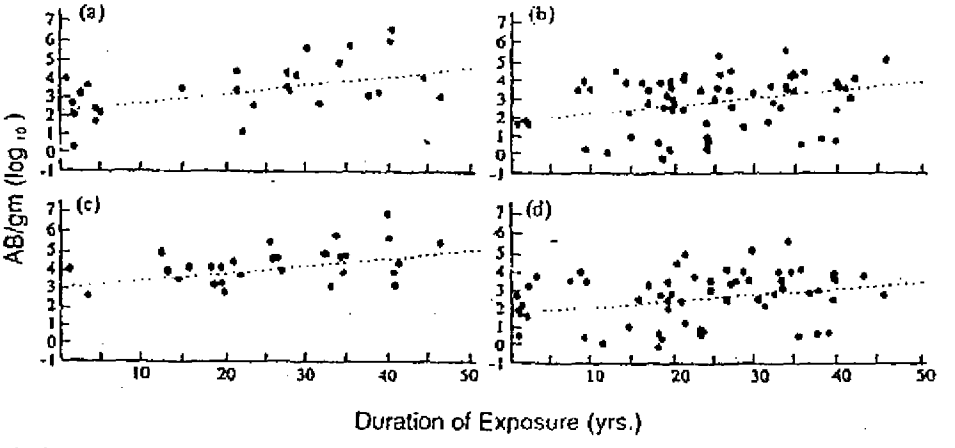
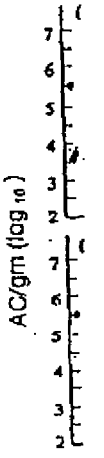


Fig. 3. (a) and (b) Scattergram showing relationship between asbestos bodies per gramme of wet lung (AB g^{-1}) and duration of asbestos exposure for shipyard [(a) $N=28$] and non-shipyard [(b) $N=65$] workers. (c) and (d) Similar scattergram showing AB g^{-1} vs duration of exposure for direct [(c) $N=29$] and indirect [(d) $N=64$] exposures to asbestos. Slope, intercept, correlation coefficient and P value for each regression line are given in Table 4.



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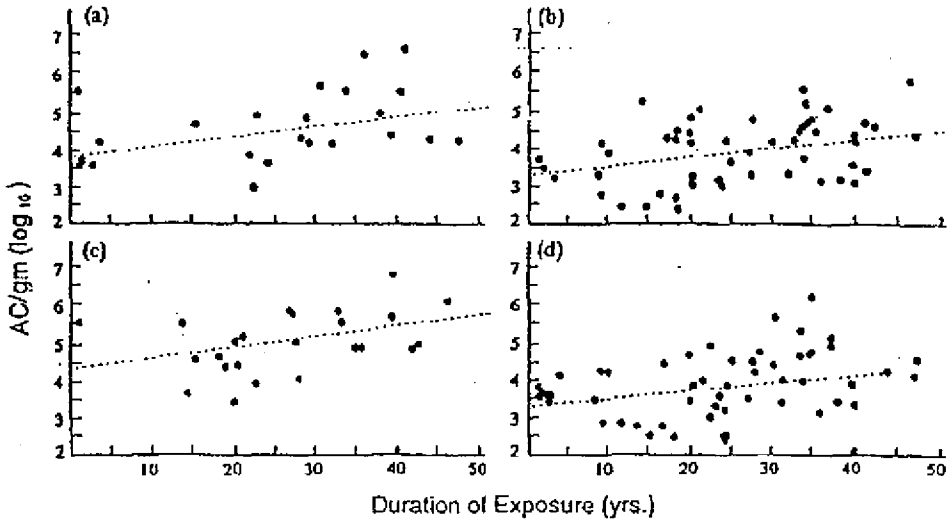

Fig. 4. (a) and (b) Scattergram showing relationship between commercial amphibole concentrations (AC g^{-1}) and duration of asbestos exposure for shipyard [(a) $N=23$] and non-shipyard [(b) $N=61$ workers]. (c) and (d) Similar scattergram showing AC g^{-1} vs duration of exposure for direct [(c) $N=26$] and indirect [(d) $N=58$] exposures to asbestos. Slope, intercept, correlation coefficient and P value for each regression line are given in Table 4.

DISCUSSION

The present study confirms the association of malignant mesothelioma with a wide range of durations of exposure to asbestos. The median duration of exposure among our 324 cases of 24 years is similar to that reported by some authors (de Lajartre and de Lajartre 1979; Tuomi *et al.*, 1991; Warnock, 1989) but substantially longer than the values reported by others (Browne and Smither, 1983; Chahinian *et al.*, 1982; Ruffie *et al.*, 1989; Vogelzang *et al.*, 1984) (Table 1). The differences in duration of exposure among these various studies could reflect differences in types of exposure (e.g. predominantly shipyard) or in types of fibre (e.g. crocidolite as opposed to amosite or chrysotile). The median duration of exposure could also be affected by the date when asbestos exposure first started for the group investigated and, hence, the maximum follow-up period. Shorter exposure durations might also reflect incomplete ascertainment of the various jobs in which a patient had some exposure to asbestos.

The mean duration of exposure was not statistically different for our 298 pleural cases as compared to the 26 peritoneal cases (23 ± 14 years as compared to 24 ± 11 years). This finding is similar to that of Browne and Smither (1983) but different from that of Chahinian *et al.* (1982). However, there was a longer median duration of exposure for peritoneal (28 years) as compared to pleural (24 years) cases (Table 1), and a substantially smaller percentage of peritoneal cases had less than 5 years of exposure to asbestos. These findings would indicate that although there is substantial overlap in exposure durations between pleural and peritoneal cases, the latter are associated with, on the average, somewhat longer durations (Chahinian *et al.*, 1982) or somewhat greater intensities (Browne and Smither, 1983) of exposure to asbestos.

Among the nine previously reported studies listed in Table 1, four (Browne and Smither, 1983; Chahinian *et al.*, 1982; Ruffie *et al.*, 1989; Sluis-Cremer, 1991) included

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patients with less than 1 year of exposure to asbestos. These four studies included 372 of the 472 cases included in these nine series. Mesotheliomas occurring after less than 1 year of exposure encompass a wide variety of occupations, including asbestos miners, gas mask manufacturers, shipyard workers, asbestos sprayer, asbestos factory worker and U.S. Navy servicemen. In addition to the present study, two other studies reported cases with less than 3 months of exposure (Browne and Smither, 1983; Chahinian *et al.*, 1982) (Table 1). Browne and Smither (1983) note that 6% of 144 cases had less than 3 months of exposure, whereas in the present study, only one out of 324 cases (0.3%) had exposures of less than 3 months ($P<0.001$ by Fisher's exact test). This difference may again be related to the relative potency of crocidolite asbestos as compared to amosite or chrysotile in the induction of mesotheliomas in man, or alternatively, to differences in intensity of exposure.

Previous studies have shown that patients with mesothelioma have considerably lower tissue asbestos burdens on average than patients with asbestosis, and that there is a rough correlation between tissue asbestos burden and exposure category (Roggli *et al.*, 1992b; Wagner *et al.*, 1988). The present study extends these observations by showing that there is a significant correlation between duration of exposure to asbestos and the pulmonary content of asbestos bodies and commercial amphibole fibres. Figures 2–4 indicate that there is too much individual variation for the regression lines listed in Table 4 to accurately predict asbestos burdens from duration of exposure for an individual case. Nonetheless, there is a sufficiently strong correlation to show that individuals with direct exposures, as one would expect, have on the average greater pulmonary asbestos burdens for the same duration of exposure as individuals with indirect or by-stander exposures. Similarly, shipyard workers have on the average greater pulmonary asbestos burdens for the same duration of exposure as non-shipyard workers. The latter observation is consistent with the heavy exposures known to have occurred in the shipyard industry in the past (Marr, 1964).

In contrast to the findings for asbestos bodies and commercial amphibole fibres, there was no association between non-commercial amphibole, chrysotile or non-asbestos mineral fibre concentrations, and duration of exposure. This is no doubt related to the fact that amphiboles tend to accumulate progressively in the lungs with continuing exposure, whereas chrysotile is broken down into smaller fibrils which tend to be removed from the lung. Although tremolite, anthophyllite and actinolite are also amphibole fibres, they are mainly important as contaminants (~1%) of chrysotile, and would therefore tend to be diluted in the lung at higher concentrations of amosite or crocidolite (Roggli and Brody, 1992). The good correlation between asbestos body counts and amphibole fibres 5 μm or greater in length has been well documented (Roggli *et al.*, 1992b). These findings also parallel the observations of McDonald *et al.* (1989) that mesothelioma risk can be accounted for by the tissue burden of long (> 8 μm) amphibole fibres, and that no additional information is provided by the concentrations of chrysotile, non-asbestos or short fibres in the lung. Wagner *et al.* (1988) and Churg and Vedal (1994) also reported little or no correlation between chrysotile, non-commercial amphiboles or non-asbestos mineral fibre burdens and disease.

A few additional comments are necessary regarding the limitations of the present study. Some of the variations in the data shown in Figs 2–4 are due to differences in intensity of exposure between individuals with the same duration of exposure.

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Information regarding intensity of exposure was not available in this study, although differences in intensity are clearly reflected in the analyses of direct vs indirect or shipyard vs non-shipyard exposures. Similarly, continuous vs intermittent exposure could result in differences in pulmonary asbestos burdens even though durations and intensities might be the same. Furthermore, some exposures such as brake repair workers were treated as direct exposures although such individuals are exposed to low levels of, and have low pulmonary burdens of, fibres 5 μm or greater in length (Roggli *et al.*, 1992b). Finally, there is some inherent inaccuracy in an individual's ability to remember information regarding exposures which occurred decades previously.

These limitations regarding exposure information suggest that the best approximation of an individual's exposure history is the actual burden of mineral fibres present in that person's lungs. However, as noted above, tissue mineral fibre analysis correlates poorly with chrysotile exposure, and there is substantial variation from one individual to another in the efficiency with which dust particles are removed from the lungs (Mastin *et al.*, 1986; Pratt and Kilburn, 1971). Furthermore, there is some site to site variation of mineral fibre content within the lung, although no consistent differences are found from one region to another (Roggli *et al.*, 1992b). Such regional differences could account for some of the variation noted in Figs 2–4.

In spite of the limitations noted above, the present study provides useful information regarding asbestos exposure, tissue asbestos burdens and the occurrence of malignant mesothelioma of the pleura and peritoneum. The findings confirm that mesotheliomas are associated with a wide range of durations of exposure to asbestos and pulmonary asbestos burdens, and show for the first time that there is a rough correlation between duration of exposure and pulmonary asbestos body and commercial amphibole fibre content in a large series of patients with mesothelioma.

Acknowledgements—The author would like to thank Greg Sanisa and Pauline Lyna for assistance with the statistical analyses, and Earl Linthicum for preparation of the illustrations.

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