Asbestos lung burden and asbestosis after occupational and environmental exposure in an asbestos cement manufacturing area: a necropsy study

Corrado Magnani, Franco Mollo, Luigi Paoletti, Donata Bellis, Paolo Bernardi, Piergiacomo Betta, Mario Botta, Mario Falchi, Cristiana Ivaldi, Mansueto Pavesi

Abstract

Objective—The largest Italian asbestos cement factory had been active in Casale Monferrato until 1986: in previous studies a substantial increase in the incidence of pleural mesothelioma was found among residents without occupational exposure to asbestos. To estimate exposure to asbestosis in the population, this study evaluated the presence of histological asbestosis and the lung burden of asbestos fibres (AFs) and asbestos bodies (ABs).

Methods—The study comprises the consecutive series of necropsies performed at the Hospital of Casale Monferrato between 1985 and 1988. A sample of lung parenchima was collected and stored for 48 out of 55 necropsies. The AF concentration was measured with a TEM electron microscope with x ray mineralogical analysis. The ABs were counted and fibrosis evaluated by optical microscopy. The nearest relative of each subject was interviewed on occupational and residential history. Mineralogical and histological analyses and interviews were conducted in 1993–4.

Results—Statistical analyses included 41 subjects with AF, AB count, and interview. Subjects without occupational exposure who ever lived in Casale Monferrato had an average concentration of 1500 AB/g dried weight (gdw); Seven of 18 presented with asbestosis or small airway lung disease (SAL). G2 asbestosis was diagnosed in two women with no occupational asbestos exposure. One of them had been teaching at a school close to the factory for 12 years. Ten subjects had experienced occupational asbestos exposure, seven in asbestos cement production: the Town Office reported the use of 15 000 metric tonnes of asbestos, 10% of which was crocidolite. Environmental asbestos pollution in Casale Monferrato also originated from the large use of asbestos cement products: the Town Office estimated in 1990 that asbestos cement roofs amounted to 500 000 m² in a town of about 40 000 inhabitants. The factory is about 1300 m from the centre of the town and 250 m from the closest residential areas. The town is downwind from the factory in respect to dominant winds.

Measurements of environmental asbestos exposure in the town of Casale Monferrato are limited in number and close in time, or subsequent to the cessation of asbestos cement production. Marconi et al. in 1984 reported average concentrations of asbestos fibres (AFs) longer than 5 µm of 11 AF/l close to the plant and 1 AF/l in the city area farthest away from it. A study conducted between March 1990 and July 1991 by the Local Health Authority in cooperation with the ISS measured in 12 sampling sites in the town annual averages below 1 AF/l (longer than 5 µm). This threshold was exceeded in 12% of samples (Internal report, Local Health Authority of Casale Monferrato). Chiappino et al. in 1991 found that the average concentration of AF (length >5µm and diameter >0.3 µm) was in the range 2.2–7.4 AF/l in residential areas of the city. In these studies the
Figure 1 Microphotograph of a preparation used for counting asbestos bodies.

A personal interview took place in 1994 with the nearest relative of subjects in the study to obtain information on: smoking habits, occupational history, residential history, and chest diseases. Occupational exposure in the asbestos cement industry was defined on the basis of both the interview and the nominal search in the rosters of the employees in the local asbestos cement industry. Occupational asbestos exposure in other activities was estimated on the basis of interview data. Among the occupations held by study subjects, those considered at definite or probable exposure were in the asbestos cement production (any job) and in the construction industry. No other asbestos related jobs were found in the study.

Both the interviews and the microscopical analyses were done blindly.

Fibre count and mineralogical analyses
Parenchyma samples, 40 to 200 mg of dehydrated tissue depending on the size of the original lung sample, were digested using hydrogen peroxide and sodium hypochlorite. The solution was filtered on cellulose ester filters (pore size 0.45 µm). The filters were dried,
One death from asbestosis.

Mann-Whitney non-parametric tests. Subclasses of exposure using Kruskall-Wallis or analyses of fibre burden.

It was impossible to perform repeated necroscopy sample was available for every subject. As only summarised by the arithmetic mean (SD). As only data on fibre and AB concentrations are summarised.

Asbestos fibres (total) (10^6 fibres/gdw):

<table>
<thead>
<tr>
<th>Fibrosis absent</th>
<th>2 19</th>
</tr>
</thead>
<tbody>
<tr>
<td>G1 asbestos</td>
<td>0</td>
</tr>
<tr>
<td>G2 asbestos</td>
<td>2</td>
</tr>
<tr>
<td>G3 asbestos</td>
<td>2</td>
</tr>
<tr>
<td>G4 asbestos</td>
<td>4</td>
</tr>
<tr>
<td>SAL</td>
<td>1</td>
</tr>
<tr>
<td>Other</td>
<td>0</td>
</tr>
</tbody>
</table>

Asbestos bodies (light microscope) (AB/gdw):

| <0.5            | 1 3 |
| 0.5–<1          | 0    |
| ≥1              | 1    |
| Arithmetic mean | 0.045 0.006 |
| SD              | 0.142 0.016 |

Frequency distributions were compared using the chi^2 test.

Results

Study subjects are described in table 1. Average age was 71 (SD 13.3) years (range 24–92). Seven subjects (17.1%) worked in asbestos cement production and six others (14.6%) lived with a relative or the spouse working in the asbestos cement industry.

Table 2 presents the concentration of AFs, dust, and ABs and frequency of asbestosis and SAL in the 41 subjects included in the statistical analyses, according to occupational asbestos exposure. Ten subjects reported occupational asbestos exposure (seven in the asbestos cement industry). The difference between the two groups (defined as “exposed” and “non-exposed”) was significant for AFs (p<0.005), crocidolite (p=0.02), and ABs (p=0.006) as well as for the frequency of asbestosis and SAL (p<0.005). Correlation between ABs and fibres was poor (ABs and total AFs: Spearman r=0.28 among all subjects and −0.01 among

The fibres and the mineral particles detected were identified by morphology, chemical composition (elements with atomic number>11), and crystalline structure. All fibres, independent of length, and all mineral particles were counted. Fibre and particle concentration is reported in 10^6/gdw.

**STATISTICAL ANALYSES**

Data on fibre and AB concentrations are summarised by the arithmetic mean (SD). As only one necroscopy sample was available for every subject it was impossible to perform repeated analyses of fibre burden.

Fibre concentration was compared over classes of exposure using Kruskall-Wallis or Mann-Whitney non-parametric tests. Subjects with no fibres or no ABs detected were included with the value of 0. This underestimates the value of the mean compared with the use of a fraction of the detection limit but does not affect the median and the statistical significance of the tests, which are based on ranks.
subjects with no occupational asbestos exposure; ABs and crocidolite: Spearman $r=0.26$ and 0.19 respectively). Concentration of mineral particles was similar in the two groups (subjects with occupational asbestos exposure: mean 14.50 (SD 2.76) × $10^6$ particles/gdw; subjects without exposure: mean 14.00 (SD 13.22) × $10^6$ particles/gdw.

No fibres were found for three subjects with occupational exposure (one in the asbestos cement industry and two in the construction industry) but in two of these subjects ABs were present.

Asbestosis was found in seven and SAL in one out of 10 subjects with occupational asbestos exposure and asbestosis was found in two and SAL in nine out of 31 subjects without occupational exposure.

Table 3 presents AF and AB concentrations according to both asbestosis and occupational asbestos exposure. In both groups (subjects with and without asbestosis or SAL) the concentration of AFs was higher among subjects with occupational asbestos exposure. Only two subjects with occupational asbestos exposure did not have asbestosis or SAL.

The total number of fibres detected in the study was 392 (83% in occupationally exposed subjects), with an average for the positive cases of 19 fibres/case (range from 2 in a subject without occupational asbestos exposure to over 100 for a subject with asbestosis). Only 4% of fibres were chrysotile, the remaining 96% amphibole. In subjects with occupational asbestos exposure the amphibole fibre burden was very much higher then the chrysotile burden (table 2) in accordance to the data reported in most studies on workers with exposure to mixed fibre types.

Figures 2 and 3 present the frequency distribution of amphibole fibre length (average 13.6 µm) and diameters (average 3.6 µm) separately in “exposed” and “non-exposed” groups. Eighty three per cent of fibres were in subjects with occupational asbestos exposure, who also had a higher proportion of long AFs. The average fibre length in subjects with occupational exposure was 16.3 whereas in subjects without occupational exposure it was 11.7 ($p<0.0001$). Diameter distribution was similar in the two groups (mean 0.36 and 0.40). The few chrysotile fibres showed an average length of 11.5 µm and an average diameter of 0.8 µm.

Table 4 presents the concentration of ABs among the 31 subjects with no occupational asbestos exposure, subdivided according to sex and residence (ever in life and irrespective of duration) in Casale Monferrato. In both sexes people who ever lived in Casale presented a higher AB count but the difference was not significant. Five subjects living in Casale and never resident elsewhere presented more than 1000 ABs, whereas AFs did not show remarkable differences according to residence.

Analyses of AB and AF concentrations after subdividing Casale Monferrato into smaller units and according to the distance of dwelling from the factory did not provide consistent results because of small numbers and are not presented.

Out of 18 subjects ever living in Casale Monferrato five had SAL and 2 G2-asbestosis, compared with four with SAL and none with asbestosis in the 13 subjects never living there. Both cases of asbestosis were women not occupationally exposed and never living with persons occupationally exposed (fig 4). Both had been in Casale Monferrato for over 50 years.

Table 3 Mean (SD) necropsy cases in the hospital at Casale Monferrato (1985–8)

<table>
<thead>
<tr>
<th></th>
<th>No lung fibrosis</th>
<th></th>
<th>G1-G4 asbestosis+SAL</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Occupational exposure to asbestos</td>
<td>p Value</td>
<td>Occupational exposure to asbestos</td>
<td>p Value</td>
</tr>
<tr>
<td>n</td>
<td>Yes</td>
<td>No</td>
<td>NS</td>
<td>No</td>
</tr>
<tr>
<td>Total asbestos fibres (10^6 fibres/gdw)</td>
<td>2</td>
<td>20</td>
<td>1.007 (1.424) 0.023 (0.034) NS</td>
<td>8</td>
</tr>
<tr>
<td>Chrysotile (million fibres/gdw)</td>
<td>0 (0)</td>
<td>0.05 (0.012) NS</td>
<td>0.0 (0)</td>
<td>0.006 (0.014) NS</td>
</tr>
<tr>
<td>Total amphiboles (10^6 fibres/gdw)</td>
<td>1.007 (1.424) 0.019 (0.032) NS</td>
<td>1.039 (1.277) 0.020 (0.023) 0.024</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Asbestos bodies (AB/gdw)</td>
<td>0 (0)</td>
<td>0.461 (0.007) NS</td>
<td>120.356 (120.362) 2.152 (2.635) 0.003</td>
<td></td>
</tr>
</tbody>
</table>
years; one was a school teacher who had been working for 12 years (1958–69) in a school close (250 m) to the asbestos cement factory; no information was available for the other. Both presented 800 AB/gdw.

Seven subjects died from lung cancer and five from mesothelioma. The mean AF concentration for cases of lung cancer was 0.50 (SD 1.25)×10^6 fibres/gdw, the mean concentration of crocidolite was 0.49 (SD 1.21)×10^6 fibres/gdw and, the mean concentration of ABs was 44.3 (SD 78.2)/gdw. Corresponding figures for mesothelioma cases were: 0.15 (SD 0.26) fibres/gdw for total AFs, 0.13 (SD 0.27)×10^6 fibres/gdw for crocidolite and 0.41 (SD 0.26) fibres/gdw for ABs. In cases of mesothelioma only amphibole fibres were detected. Two cases of lung cancer and one of mesothelioma had worked in asbestos cement production. The last had 2.8×10^6 fibres (only amphiboles) and 268 800 asbestos bodies. The lung fibre burdens in asbestosis cases were consistently greater than 10^6 fibres/gdw with a mean concentration of 2.4×10^6 fibres/gdw.

Discussion

The present study, albeit based on limited numbers, is unique as it includes the consecutive series of necropsies conducted in Casale Monferrato in the years immediately after the cessation of asbestos cement production. It is based on samples collected routinely for the archive of the pathology department and analysed separately. The use of these samples is a weakness as the collection was not optimal (only one sample a subject, taken from an unspecified part of the lung): the effect could be a reduction of the fibre count in some subjects and an increased variability. By contrast, the interval between tissue collection and the analyses does not affect the results as AFs are stable in formaldehyde fixed tissues and the interval is similar for all subjects. Occupational and residential histories were collected blindly. The concentration of mineral particles is similar in subjects with and without occupational exposure, which gives an indication of the absence of bias.

Limited evidence is available on the concentration of ABs and AFs in environmentally exposed populations. Published results show large variability, because of differences in case mix, presence of occupational exposure, intensity of exposure, and analytical methods. Moreover, in some instances environmental exposure is defined in only very general terms, such as “urban” and “rural”, whereas in the present study it is clearly defined in relation to a source of occupational and environmental asbestos exposure.

The present study shows consistent (not always significant) variations in the concentration of AFs and ABs in relation to both occupational asbestos exposure and residence in Casale Monferrato.

The concentration of 1000 AB/gdw or higher can be taken as a cut off point as it is considered indicative of occupational exposure to asbestos.19–23 This concentration was exceeded by eight out of 10 subjects with occupational exposure (six of seven persons employed in the asbestos cement factory), by five out of 18 of those non-occupationally exposed but living in Casale and by one of 13 of those non-occupationally exposed and never living in Casale. Mollo et al.30 and Andrion et al.27 showed a gradient in AF and AB concentration between controls and environmentally exposed subjects living in the asbestos mining areas of Quebec. There was a median concentration of 480 AB/gdw in Asbestos and 1880 AB/gdw in Thetford whereas controls presented 80 AB/gdw and subjects occupationally exposed 35 000 AB/gdw. Corresponding figures for total AFs were 0.57×10^6, 1.16×10^6, 0.26×10^6, and 24.6×10^6/gdw. Monsò et al.28 found ABs in nine out of 18 non-occupationally exposed subjects living in Barcelona (range 0 to 430 AB/gdw). Dufresne et al.29 measured ABs and AFs in the lung of residents in Asbestos never occupationally exposed and dying from diseases not related to asbestos: the average concentrations were 192 AB/gdw and 208×10^6 AF/gdw. Yamada et al.30 found in 108 Japanese women a significantly higher concentration of ABs and AFs among urban than rural dwellers, measured by optical microscopy.
Several studies have been conducted to use AF burden measured by electron microscopy for estimating occupational and environmental exposure, nevertheless the variation between laboratories is still large and makes the comparison of results from different laboratories uncertain. Roggli reviewed the published studies on AF burden in subjects not affected by asbestos related diseases: average concentrations ranged between $0.03\times10^6$ and $1.12\times10^6$ fibres/g dw. Chung, on the basis of these uncertainties, recommended the use of internal reference values in each laboratory but until now there is no generally accepted value of fibre concentration to distinguish between fibre burden of the "normal" population and of occupationally exposed subjects. Present results are therefore compared with findings in the ISS laboratory, obtained in the city of Rome among subjects without evidence of occupational exposure to asbestos. Asbestos fibres were found in the lungs in nine of 18 subjects who ever lived in Casale Monferrato at 14 of 85 in Rome (p<0.003). In addition, chrysotile fibres were present in 33% of positive subjects (those with AFs) in Casale and in 68% in Rome and corresponding values for amphiboles were 89% and 32%. Fibre concentration in Rome ranged between $2\times10^6$ and $3\times10^6$ fibres/g dw. A range of fibre length was 1–50 µm (mean 13.6 µm) in Casale and 1–8 µm (mean 3 µm) in Rome. Diameters were similar in the two studies. These differences are consistent with the likely substantial differences in the main source and the intensity of airborne asbestos exposure in the two cities. In Casale asbestos exposure is related mostly to asbestos cement production and to the use of asbestos cement products whereas in Rome it is related to vehicle circulation and only to a lesser extent to asbestos cement used in the building industry.

Concentration of chrysotile fibres in this study was low, even among occupationally exposed subjects. This finding corresponds with the results of studies on workers exposed to mixed fibres, and with a lower biopersistence of chrysotile compared with amphibole fibres.

Out of 31 subjects not engaged in occupations at probable asbestos exposure, two had histological signs of asbestosis and nine of SAL, which is considered likely indicative of asbestos exposure. No suggestion of occupational or domestic exposure was found for the two women with asbestosis. To our knowledge, this is a new finding, which indicates high levels of environmental asbestos exposure in the past. Asbestosis in relation to environmental exposure has been reported in Turkey and attributed to high environmental levels of tremolite. The two cases of non-occupational asbestosis had 800 AB/g dw, which is the average for women living in Casale and not occupationally exposed. In the interpretation of this value we must take into consideration that individual susceptibility plays a part in both the pathogenesis of asbestosis and the production of ABs. Dodson et al described lung asbestosis even without finding ABs in digested lungs. Moreover, chrysotile, which is fibrogenic but induces low production of ABs, accounts for 50%–85% of airborne AFs, (longer than 5 µm) in the general environment of Casale.

Conclusion

We found two cases of histological asbestosis, a high prevalence of SAL, and a high concentration of ABs among people with no occupational exposure who lived in Casale Monferrato, which confirms the high prevalence of environmental asbestos exposure that was experienced in the area in relation to asbestos cement production.

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doi: 10.1136/oem.55.12.840

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