ROENTGENOGRAPHIC LUNG CHANGES, ASBESTOSIS AND MORTALITY IN A BELGIAN ASBESTOS-CEMENT FACTORY

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The Eternit factory at Kapelle op de Bos employs about 2000 workers and 400 staff members and processes annually about 35,000 tons of chrysotile, 3000 tons of crocidolite, and 1000 tons of amosite for the manufacture of a variety of asbestos-cement building materials and pipes.

In the present study, findings of yearly roentgenographic examinations of the lung and the mortality of workers are related to the age of the individual and to the duration and level of dust exposure. We looked for possible effects of exposure to asbestos on the occurrence of pneumoconiosis, pleural changes and malignancies.

METHODS

Dust concentration

We considered the following five typical working areas, which are given in decreasing order of dustiness: area 4, which involves the handling of asbestos fibres, such as carrying asbestos bags, milling asbestos, preparing the asbestos-cement mixture; area 3, where asbestos-cement products are finished by sawing, drilling, filing, etc.; area 2, which is situated between the previous two and where the asbestos-cement sheets and pipes are moulded, pressed, dried, and lifted off the mould;

area 1, where very little dust exposure is expected, such as in offices; and area 0, which represents work outside the asbestos industry, with negligible dust levels.

Actual fibre counts obtained with the filter-membrane methods are available for 1970 through 1976; dust concentrations were much higher in previous years, but the actual values can only be estimated. Dust concentrations are believed to have followed a more or less logistic decay, with an inflection point at the year 1960, which is satisfied by the formula $c_y = c_0/(1 + 1.16^{y-1960})$, where c is concentration in fibres/ ml, y is a number (year) between 1928-1977, and c_0 is 0.4, 16, 24 or 100 fibres/ml for areas 1, 2, 3 or 4, respectively (i.e., roughly 10 times present-day levels).

Fibre-years

The degree of individual exposure to asbestos was expressed in fibres per ml times duration in years, or 'fibre-years'. Since employees may have worked consecutively in different areas, fibre-years for any one individual were calculated as $\Sigma\ (\text{fibres/ml})_{i,y}$, where i is the type of area (0, 1, 2, 3, 4) and y is the year.

Roentgenologic study

In 1975, 2650 employees were enlisted, of which 1973 (74.5%) had both a history taken and a chest roentgenogram made; they are distributed as follows: 1963 male workers (85.5% of those enlisted), 214 female workers (81.4%); 78 male (25.1%) and 2 female (1.8%) staff members. The yearly chest roentgenogram is compulsory for all workers, while the staff submit to this examination on a voluntary basis.

The roentgenologic findings were coded according to the extended system elaborated by the International Union Against Cancer. Irregular small opacities were graded according to the full 12-point scale of the UICC/Cincinnati (1970) Classification.

The pleural changes were classified as: (a) pleural adhesion; (b) blurred contour of heart and/or diaphragm; (c) pleural thickening; or (d) calcified pleural plaque. Three grades (1 = minimal, 2 = moderate, 3 = marked) were noted but were pooled for analysis because of the small number observed. Pleural adhesions are exudative sequelae, e.g., obliteration of the costophrenic angle. Pleural thickening comprises 'hyaline' plaques and probably a few cases of post-exudative diffuse thickening, as it is not always possible to distinguish these two on a routine chest roentgenogram. Also noted were changes suggestive of cancer, tuberculosis, sarcoidosis, heart disease, active or inactive tuberculosis and trauma (e.g., rib fractures, thoracotomy).

Diagnosis of asbestosis

The criteria for making the diagnosis of asbestosis were threefold: the presence of irregular small lung opacities with profusion of at least 1/0; and the presence of at least two of the following abnormalities: ill-defined outline of heart and/or diaphragm, clubbing of the fingertips, crackling rales audible over the lung bases, carbon monoxide transfer or vital capacity less than 76% of the predicted value. A decrease of vital capacity was disregarded if it could be attributed to some obvious restrictive lesion other than asbestosis or to obstructive lung disease. The mere presence of pleural plaques was not used as a criterion for asbestosis.

Asbestosis and mortality study

The population studied consisted only of male workers who, within the 15-year period 1963-1977, worked in the factory for at least 12 months. All causes of death were checked through family doctors and/or social workers who visited the relatives (Belgian authorities never release individual information from death certificates).

Expected mortalities by age group and by cause of death were calculated from the yearly mortality rates for Belgium, available in the tables of the World Health Organization for 1965 through 1975; data for other years were obtained through extrapolation.

RESULTS

Table 1 shows the number of chest roentgenograms with small lung opacities and with pleural changes, by group of exposure. We saw no small opacities with profusion greater than 2. We pooled all grades of pleural changes because the numbers were small; grade 3 was scored twice and only on account of calcified plaques.

We found 29 cases of asbestosis during the 15-year observation period (Table 5). Total mortality, by age and cause of death, is given in Table 6; and details of malignant neoplasms are given in Table 7. Among the cases of respiratory cancer there were three cancers of the upper airways, 17 cancers of the lung and one mesothelioma of the pleura.

Table 1. Number of roentgenographic lung changes found in 1958 employees examined in 1975

Fibre-years	Small opacities					Pleural changes			
	0/-	0/0	0/1	1	2	Adhesion 1, 2	Blurred contour 1, 2	Thickening 1, 2	Calcified plaque 1, 2, 3
0 - 49	128	886	46	2	0	36	0	15	4
50 - 99	3	225	29	2	0	15	0	7	7
100 - 199	5	302	35	9	0	34	3	23	6
200 - 399	5	184	40	11	1	30	2	16	6
400 - 799	0	22	6	2	1	7	1	5	0
800 -1599	1	11	1	1	0	3	0	1	0
Total	142	1630	157	27	2	125	6	67	23

DISCUSSION

Fibre-years

We realize that our estimates of dust concentrations prevailing in the past are only good guesses at best. Nevertheless, it is unlikely that they would be inaccurate by more than one order of magnitude, and, more importantly, the figures proposed have at least relative accuracy: the dustiness in areas where dry asbestos fibres are being handled is certainly greater than in other areas, and the dustiness was certainly higher during the first 30 years than during the last 15 years of the factory's existence.

Roentgenographic changes

We excluded 15 cases from the study, either because of a history of sarcoidosis or of exposure to silica dust which would lead to interpretation of roentgenographic changes as being due solely to asbestos exposure. The profusion of small lung opacities and of benign pleural changes correlate strongly with fibre-years, as well as with age. We therefore examined, by age group, the linear trend in proportions (i.e., number with changes per number X-rayed, by fibre-years groups). The trends are significant for small lung opacities grades 1 and 2 (Table 2) and grade 0/1 (not shown, $P = 0.001$); the trend is also significant for pleural adhesion (Table 3), and for pleural thickening (Table 4); the trend is not significant for calcified plaques (not shown).

To rule out the effect on our analysis of post-inflammatory pleural changes unrelated to asbestos exposure, we reexamined the given trends in proportion after eliminating 175 cases with evidence of old or recent

Table 2. Prevalence (%) of s-t-u lung opacities grades 1 and 2

Fibre-years[a]	Age group (yrs)				Total
	15-34	35-44	45-54	55-65	
0 - 49	0	1.1	0	0	0.2
50 - 99	0	0	1.1	2.9	0.8
100 - 199	0	0	2.5	7.5	2.6
200 - 399	0	4.5	2.2	9.8	5.0
400 - 799	0	0	5.9	15.4	9.7
800 - 1599	0	0	33.3	0	7.1
Total %	0	0.7	1.7	5.3	1.5

[a] Median taken as the score

Linear trend with pooled regression coefficients: P = 0.001

Table 3. Prevalence (%) of pleural adhesions

Fibre-years[a]	Age group (yrs)				Total
	15-34	35-44	45-54	55-65	
0 - 49	1.2	3.2	6.7	11.7	3.4
50 - 99	0	4.2	6.4	14.3	5.8
100 - 199	0	3.3	12.3	14.9	9.7
200 - 399	0	4.5	11.7	15.9	12.4
400 - 799	0	0	17.6	30.8	22.6
800 - 1599	0	0	33.3	22.2	21.4
Total %	1.1	3.5	9.8	15.0	6.4

[a] Median taken as the score

Linear trend with pooled regression coefficients: P = 0.002

Table 4. Prevalence (%) of pleural thickening

Fibre-years[a]	Age group (yrs)				Total
	15-34	35-44	45-54	55-65	
0 - 49	0	0.5	3.3	8.5	1.4
50 - 99	0	0	6.4	2.9	2.7
100 - 199	0	2.5	8.0	10.4	6.6
200 - 399	0	0	9.5	3.7	6.6
400 - 799	0	0	17.6	15.4	16.1
800 - 1599	0	0	33.3	11.1	7.1
Total %	0	0.9	7.1	7.3	3.4

[a] Median taken as the score

Linear trend with pooled regression coefficients: P = 0.01

chest trauma (e.g., rib fracture), tuberculosis (e.g., hilar calcification), or empyema. This did not alter the conclusions (for pleural adhesion, P = 0.008; for pleural plaques, P = 0.005).

Asbestosis

The number of cases with diagnosed asbestosis increases highly significantly with the degree of exposure, expressed in fibre-years (Table 5). We observed no case of asbestosis for an exposure below 100, and only one case in the range 100-200 fibre-years. Two workers who had never handled free asbestos fibres (area 4) developed asbestosis, but their degree of exposure (starting in 1930) had nevertheless been high: 435 and 350 fibre-years, respectively (on account of work in area 3). The present study thus indicates that the handling of asbestos-cement is less dangerous than the handling of free asbestos fibres; however, since less dust is generated by the former, we cannot conclude from the present data whether asbestos-cement dust is less fibrogenic *per se* than free asbestos.

Mortality

Total mortality was not significantly different from that which would be expected in a Belgian population of matched age and sex (Table 8). There is, however, a significant excess mortality due to external causes. There is also an excess mortality, not really significant, due to non-malignant respiratory disease, which probably must be attributed to the seven deaths due to asbestosis (Table 6).

Table 5. Incidence of asbestosis from 1963 to 1977

Fibre-years[a]	Man-years	New cases No.	New cases %
0 - 49	11,340	0	0
50 - 99	4094	0	0
100 - 199	5791	1	0.02
200 - 399	6629	7	0.11
400 - 799	1179	8	0.68
800 - 1599	307	10	3.26
1600 - 3200	26	3	11.54
Total	29,366	29	0.1

[a] Median taken as the score

Linear trend in proportions: $P < 10^{-6}$

Table 6. Deaths observed in male workers by age and by cause of death, 1963-1977

Age group (yrs)	Man-years	External cause	Malignant cause	Non-malignant cause: Cerebro-cardio-vascular	Respiratory	Gastro-intestinal	Other	Unknown or poorly specified cause	Total deaths
15 - 24	3463	3							3
25 - 34	5142	7	1	1	1				10
35 - 44	6261	8	3	6			1		18
45 - 54	9340	13	11	16	5	6	3	4	58
55 - 65	5160	12	33	37	14	5	4	7	112
Total	29,366	43	48	60	20[a]	11	8	11	201
Expected		29.0	55.4	77.8	15.9	9.0	9.2	16.7	213
P		0.01[b]	NS	NS	0.06[c]	0.10[c]	NS	0.04[c]	NS

[a] Include asbestosis in 7 cases

[b] In the standard normal approximation of the binomial distribution

[c] In a Poisson distribution with the expected number as the mean

NS - not significant

The mortality due to all malignant neoplasms does not exceed expectation (Table 7), but there is a significant excess of deaths due to, and only to, gastrointestinal cancer (Table 8). A similar excess of gastrointestinal cancer, and not of respiratory cancer, was found by Van de Voorde et al. (1967) for workers employed in this same factory.

Table 7. Deaths due to malignant neoplasms observed in male workers, by age and site (29,366 man-years)

Age group (yrs)	Respiratory	Gastrointestinal	Nervous	Lymphoid & haematopoietic	Other	Not specified	Total
15 - 24							
25 - 34				1			1
35 - 44	2						2
45 - 54	6	3		1		1	11
55 - 65	14[a]	14	4		2		34
Total	22	17	4	2	2	1	48
Expected	22.3	11.8	2.1	3.9	2.4	12.9	55.4
P[b]	NS	0.04	0.10	NS	NS		

[a] Includes one case of pleural mesothelioma

[b] In a Poisson distribution, with the expected number as the mean

NS - not significant

Table 8. Deaths of male workers due to respiratory and gastrointestinal cancer, by exposure group

Fibre-years[a]	Man-years	Respiratory cancer		Gastrointestinal cancer	
	1963-1977	Observed	Expected[b]	Observed	Expected[b]
0 - 49	11,340	6	5.16	4	2.76
50 - 99	4094	3	2.43	1	1.32
100 - 199	5791	5	4.60	1	2.46
200 - 399	6629	4	7.47	7	3.93
400 - 799	1179	1	1.95	2	1.00
800 - 1599	307	2	0.57	2	0.29
1600 - 3200	26	1[c]	0.17	0	0.04
Total	29,366	22	22.35	17	11.80
Linear trend in proportion		P = 0.22		P = 0.16	

[a] Median taken as the score

[b] Adjusted for age distribution within fibre-years groups

[c] Pleural mesothelioma

Table 9. Distribution by exposure group of cancer cases and of matched internal controls (4 per case)

Fibre-years[a]	Respiratory cancer			Gastrointestinal cancer		
	Cases	Controls	Cases/Total	Cases	Controls	Cases/Total
0 - 49	6	20	0.23	4	16	0.20
50 - 99	3	17	0.15	1	5	0.17
100 - 199	5	7	0.42	1	14	0.07
200 - 399	4	32	0.11	7	20	0.26
400 - 799	1	8	0.11	2	8	0.20
800 - 1599	2	4	0.33	2	5	0.29
1600 - 3200	1[b]	0	1.00			
Total	22	88		17	68	
Linear trend in proportions	P = 0.11			P = 0.23		

[a] Median taken as the score
[b] Pleural mesothelioma

Either this excess is due to asbestos exposure, or the workers studied differ from the general Belgian population. An argument against an effect of asbestos exposure is that we found no significant relationship between excess of gastrointestinal cancer and fibre-years (Table 8).

The validity of comparing the mortality in a population of enlisted workers with national statistics might be questionable. To eliminate the so-called 'healthy worker effect' we made comparisons with internal case-controls; the principles of the method were described by Liddell et al. (1977). In the present analysis, for each male worker who died of respiratory or gastrointestinal cancer, we selected four controls, at random, out of the group of all male workers alive at least one year after the case worker had expired, and matched for age ± 1 year and for date of enlistment ± 1 year. We compared the distribution of the cases and the controls with respect to dust exposure in fibre-years, which could differ only in the fibres/ml and not in the years: there was no significant difference (Table 9). This means that dust exposure did not significantly affect mortality due to respiratory cancer (even though the one case of mesothelioma is almost certainly related to heavy exposure and is included in the analysis).

CONCLUSIONS

The following conclusions were drawn with regard to the workers in the asbestos-cement factory that we investigated:

(1) there is a strong dose-response relationship for asbestosis; no case was observed for an exposure of less than 100 fibre-years;

(2) there is a dose-response relationship for s-t-u small lung opacities, pleural adhesions and pleural thickening visible on a roentgenogram;

(3) general mortality is not in excess of the national expected figures, but there is an excess of accidental deaths;

(4) the mortality due to malignant tumours is not in excess of the expected figures;

(5) there is no excess mortality due to respiratory cancer;

(6) there is an excess mortality due to gastrointestinal cancer, which shows no dose-response relationship when compared with the expected figures or with internal case-controls.

SUMMARY

Annual chest radiographs, work history and mortality of 1,973 workers in an asbestos-cement factory were correlated with age and with duration and level of dust exposure. Degree of radiographic lung change was significantly related to fibre-years of exposure in the case of small lung opacities, pleural adhesions and pleural thickening. For 29 cases of asbestosis diagnosed between 1963 and 1977, a highly significant dose-response relationship was found. In comparison with national mortality rates, there was an excess of deaths due to cancer of the gastrointestinal tract, although there was no relationship to fibre-years.

RESUME

Les auteurs ont mis en corrélation les radiographies thoraciques annuelles, les antécédents professionnels et la mortalité de 1 973 travailleurs d'une usine d'amiante-ciment avec l'âge de ces sujets et la durée et le niveau de leur exposition aux poussières. Le degré de lésion pulmonaire radiographique s'est avéré lié de manière significative aux années-fibre d'exposition dans le cas des petites opacités pulmonaires, des adhésions pleurales et de l'épaississement pleural. Pour 29 cas d'asbestose diagnostiqués entre 1963 et 1977, une relation dose-réponse très nette a été observée. Comparativement aux taux nationaux de mortalité, on notait un excédent de décès par cancer des voies digestives, mais sans relation avec les années-fibre.

REFERENCES

Liddell, F.D.K., McDonald, J.C. & Thomas, D.C. (1977) Methods of cohort analysis: appraisal by application to asbestos mining. *J. R. stat. Soc., Ser. A, 140*, 469-491

UICC/Cincinnati (1970) Classification of the radiographic appearances of pneumoconioses. *Chest, 58*, 57-67

Van de Voorde, H., Meulepas, E., Gyselen, A. & Koppen, O. (1967) Doodsoorzaken bij de bevolking woonachtig rond en bij de arbeiders werkzaam in een asbestverwerkende nijverheid in het noorden van Brabant. *Acta tuberc. pneumol. Belg., 58*, 924-942

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Proceedings of a Symposium organized by IARC, l'Institut National de la Santé et de la Recherche Médicale (National Institute of Health and Medical Research), and the MRC Pneumoconiosis Unit, Penarth, UK, held at the International Agency for Research on Cancer, Lyon, France
25–27 September 1979

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INSERM Symposia Series Volume 92

INTERNATIONAL AGENCY FOR RESEARCH ON CANCER
LYON
1980