Table 4 *Male deaths 20 years after first employment, by cause, in relation to duration of service*

| Cause of death* | Duration of gross service (y) | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | <1 | | 1–<5 | | 5–<20 | | ≥20 | | Complete cohort | |
| | O | SMR | O | SMR | O | SMR | O | SMR | O | SMR |
| All causes | 246 | 129·9 | 189 | 104·0 | 130 | 104·8 | 238 | 97·2 | 803 | 108·5 |
| Malignant neoplasms | 60 | 144·9 | 50 | 125·7 | 29 | 114·0 | 63 | 118·3 | 202 | 126·5 |
| Respiratory | 24 | 180·0 | 19 | 149·4 | 9 | 122·6 | 21 | 133·4 | 73 | 148·7 |
| Digestive | 17 | 132·9 | 16 | 128·3 | 5 | 60·6 | 21 | 116·9 | 59 | 114·4 |
| Other | 19 | 120·4 | 25 | 164·9 | 15 | 190·4 | 21 | 107·2 | 70 | 115·9 |
| Heart disease | 99 | 125·3 | 79 | 104·9 | 44 | 83·7 | 100 | 93·1 | 322 | 102·5 |
| Respiratory tuberculosis | 0 | | 0 | | 0 | — | 4 | 283·3 | 4 | 145·9 |
| Other respiratory | 13 | 196·3 | 8 | 126·2 | 4 | 85·2 | 8 | 92·2 | 33 | |
| Pneumoconiosis | (6) | | (3) | | (1) | | (2) | | (12) | |
| Cerebrovascular | 18 | 137·6 | 14 | 108·4 | 15 | 142·7 | 20 | 102·4 | 67 | 119·6 |
| Accidents | 11 | 121·1 | 5 | 69·2 | 5 | 101·7 | 7 | 68·6 | 28 | 89·1 |
| Other known | 37 | 123·5 | 24 | 90·4 | 29 | 147·1 | 35 | 87·9 | 125 | 107·7 |

*As in table 1, except that ICD codes 160–64 are here grouped under "respiratory" malignant neoplasms and the "other respiratory" category includes only bronchitis, pneumonia, and pneumoconiosis (ICD 490–502, 523–4)

Table 5 gives SMRs by total accumulated dust exposure. The same lack of any clear or systemic exposure-effect pattern is present. The SMR for respiratory cancer for men in the 2 highest dust groups combined (125.8) was higher than for the 2 intermediate dust groups combined (103.3) but still substantially below that for the lowest exposure category (167.4). A similar pattern of relative risk was obtained from the Mantel-Haenszel analysis (Table 6), which showed an increasing risk only if the minimal exposure group is ignored.

Table 5 *Male deaths 20 years after first employment, by cause, in relation to dust exposure (mpcf y)*

| | Accumulated dust exposure (mpcf y) | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | <10 | | 10–<20 | | 20–<40 | | 40–<80 | | ≥80 | |
| | O | SMR | O | SMR | O | SMR | O | SMR | O | SMR |
| All causes | 546 | 113·8 | 89 | 92·3 | 71 | 96·6 | 62 | 110·2 | 35 | 103·1 |
| Malignant neoplasms | 134 | 128·1 | 22 | 109·6 | 19 | 120·1 | 19 | 153·9 | 8 | 117·9 |
| Respiratory | 55 | 167·4 | 6 | 101·7 | 5 | 105·4 | 6 | 162·8 | 1 | 55·22 |
| Digestive | 34 | 102·6 | 9 | 135·1 | 8 | 153·4 | 5 | 120·2 | 3 | 126·6 |
| Other | 45 | 114·0 | 7 | 89·5 | 6 | 101·0 | 8 | 176·6 | 4 | 150·4 |
| Heart disease | 60 | 101·9 | 14 | 83·8 | 13 | 76·6 | 18 | 106·4 | 13 | 93·0 |
| Respiratory tuberculosis | 2 | 123·6 | 0 | — | 0 | — | 0 | — | 2 | 1112·9 |
| Other respiratory | 21 | 125·1 | 5 | 135·6 | 2 | 74·4 | 2 | 109·0 | 3 | 230·8 |
| Pneumoconiosis | (9) | | (1) | | (1) | | (1) | | (0) | |
| Cerebrovascular | 43 | 122·9 | 8 | 101·7 | 7 | 118·4 | 5 | 117·1 | 4 | 135·4 |
| Accidents | 22 | 101·0 | 3 | 86·5 | 0 | — | 2 | 86·3 | 1 | 94·2 |
| Other known | 83 | 109·5 | 15 | 102·9 | 15 | 128·5 | 10 | 112·2 | 2 | 43·4 |

The more detailed analysis for respiratory cancer in Table 8 shows that the same pattern is shared by men in the lowest accumulated dust category regardless of duration of employment.

Table 8 *Male deaths from respiratory cancer 20 years after first employment in relation to duration of service and dust exposure*

| Duration of service (y) | Dust exposure (mpcf y) | | | | | |
|---|---|---|---|---|---|---|
| | <10 | | 10–<40 | | ≥40 | |
| | O | SMR | O | SMR | O | SMR |
| <1 | 24 | 180·0 | 0 | — | 0 | — |
| 1–<5 | 17 | 166·3 | 2 | 83·2 | 0 | — |
| ≥5 | 14 | 150·0 | 9 | 109·9 | 7 | 125·4 |

Table 6 *Relative risks of respiratory cancer by dust exposure from (1) Mantel-Haenszel analysis and (2) SMRs*

| | mpcf y | | | | | Chi-square | |
|---|---|---|---|---|---|---|---|
| | <10 | 10-<20 | 20-<40 | 40-<80 | ≥80 | Difference | Linearity |
| Mantel-Haenszel | | | | | | | |
| Observed | 54 | 4 | 5 | 6 | 1 | | |
| Expected | 51·1 | 8·7 | 4·6 | 4·1 | 1·5 | | |
| Relative risk | 1 | 0·40 | 0·91 | 1·40 | 1·13 | 4·50 | 0·00 |
| From SMRs. | | | | | | | |
| Relative risk | 1 | 0·59 | 0·64 | 0·98 | 0·31 | | |

The other respiratory group of diseases that included pneumoconiosis also showed little indication of an exposure response. Six of the 12 whose deaths were from pneumoconiosis (ICD 523) had worked in the plant for less than a year and only 3 of the other 12 had a total dust exposures index of 10 mppcf-yrs. or more. Table 7 shows details from death certificates given ICD code 523. In no case was asbestosis mentioned but anthracosilicosis or silicosis were given as the cause of death in all but 2 cases. It was further noted that all 12 had either been born or had died in the coal mining area of Pennsylvania.

Table 7 *Deaths attributed to pneumoconiosis (ICD 523)*

| Case No | Employment | | | Birth place | Death | | Certified cause |
|---|---|---|---|---|---|---|---|
| | Age at start (y) | Duration | Total dust (mpcf y) | | Age (y) | Place | |
| 1 | 36 | 2 months | 0·1 | Sandy Run, Pa | 64 | Freeland, Pa | Anthracosilicosis |
| 2 | 26 | 6 months | 0·2 | Taylor, Pa | 57 | Taylor, Pa | Silicosis and emphysema |
| 3 | 35 | 2 months | 0·1 | Wilkes-Barre, Pa | 57 | Wilkes-Barre, Pa | Anthracosilicosis |
| 4 | 29 | 5 months | 0·2 | Wilmington, De | 58 | Wilkes-Barre, Pa | 3° anthracosilicosis |
| 5 | 38 | 10 months | 0·7 | Pennsylvania | 68 | Wilkes-Barre, Pa | Anthracosilicosis |
| 6 | 22 | 3 months | 0·1 | Wyoming, Pa | 53 | Wyoming, Pa | Anthracosilicosis |
| 7 | 50 | 1 y 10 m | 2·0 | Mexico | 79 | Windber, Pa | Coal workers pneumoconiosis |
| 8 | 47 | 3 years | 6·8 | Scranton, Pa | 75 | Scranton, Pa | Anthracosilicosis |
| 9 | 35 | 3 years | 17·4 | Nanticoke, Pa | 58 | Nanticoke, Pa | Silicosis |
| 10 | 51 | 20 years | 8·3 | Scranton, Pa | 72 | Bridgeport, Ct | Pulmonary silicosis |
| 11 | 40 | 16 years | 21·8 | Nanticoke, Pa | 68 | Bridgeport, Ct | Pneumoconiosis |
| 12 | 31 | 30 years | 51·4 | Nanticoke, Pa | 62 | Bridgeport, Ct | Pneumoconiosis |

## CONCLUSION

The authors concluded that if it is accepted that the high mortality from all causes (including respiratory cancer) in men employed for less than 1 year was probably due to some form of selection, then the results suggest that the adverse health effects of employment in this chrysotile friction products plant were small.

6. Workers[73] in an asbestos textile factory, which were exposed to dust levels higher than current standards permit, were divided into 5 cohorts on the basis of duration and period of work in scheduled areas (Table 1).

Table 1 *Number of workers in each exposure cohort*

| Cohort | Sex | Years in scheduled areas | Years in scheduled areas before 1933 | Number | Person-years observation |
|---|---|---|---|---|---|
| 1 | Male | 20 or more | 10 or more | 69 | 1686 |
| 2 | Male | 20 or more | Less than 10 | 74 | 1397 |
| 3 | Male | 20 or more | None | 263 | 3848 |
| 4 | Male | 10-19 | None | 679* | 7264 |
| 5 | Female | 10 or more | None | 284 | 4388 |
| Total | | | | 1186 | 16972 |

*Including the 263 men in cohort 3 before they had completed 20 years in scheduled areas.

The number of deaths in each group attributed to lung cancer (includes mesothelioma), other cancers, respiratory diseases and other causes are compared in Table 2 with the number expected, which is calculated from national death rates by 5-year age-groups.

Table 2 *Number of deaths observed and expected, by exposure cohort and cause*

| Cause of death† | Cohort | Observed deaths‡ | Expected deaths | Ratio observed/expected | Probability of observed number or more |
|---|---|---|---|---|---|
| Lung cancer and pleural mesothelioma (162, 163 and 228) | 1 | 13 (2) | 1·49 | 10·1 | <0·001 |
| | 2 | 10 (3) | 3·05 | 3·3 | 0·001 |
| | 3 | 9 (2) | 5·36 | 1·6 | 0·111 |
| | 4 | 24 (2) | 12·02 | 1·9 | 0·020 |
| | 5 | 3 (1) | 0·92 | 3·3 | 0·066 |
| Other cancers (140-239) | 1 | 8 | 4·14 | 1·9 | 0·260 |
| | 2 | 3 | 4·29 | 0·7 | 0·891 |
| | 3 | 6 | 6·61 | 0·9 | 0·647 |
| | 4 | 11 | 17·78 | 0·6 | 0·966 |
| | 5 | 6 | 7·63 | 0·8 | 0·772 |
| Respiratory disease (460-519) | 1 | 14 | 3·86 | 3·6 | <0·001 |
| | 2 | 7 | 4·32 | 1·6 | 0·147 |
| | 3 | 8 | 5·93 | 1·3 | 0·266 |
| | 4 | 23 | 17·28 | 1·3 | 0·108 |
| | 5 | 4 | 1·81 | 2·2 | 0·110 |
| Other causes | 1 | 27 | 18·29 | 1·5 | 0·033 |
| | 2 | 23 | 17·89 | 1·3 | 0·139 |
| | 3 | 36 | 26·37 | 1·4 | 0·047 |
| | 4 | 69* | 75·06 | 0·9 | 0·773 |
| | 5 | 11 | 13·34 | 0·8 | 0·776 |
| All causes | 1 | 64 | 27·78 | 2·3 | <0·001 |
| | 2 | 43 | 28·55 | 1·5 | 0·012 |
| | 3 | 59 | 44·67 | 1·3 | 0·023 |
| | 4 | 127 | 122·94 | 1·0 | 0·369 |
| | 5 | 24 | 23·70 | 1·0 | 0·503 |

†Coded according to the eighth revision of the *International Classification of Diseases* (World Health Organization, 1967).
‡Deaths due to pleural mesothelioma are included in the observed number for lung cancer and also given separately in parentheses.
*Includes one man in which a pleural mesothelioma was a contributory cause of death.

Lung cancer mortality in the area of the factory was lower than the national average among men (SMR = 87) and similar for women (SMR = 104) in 1959-63.

Workers first exposed before 1933 (cohorts 1 and 2) suffered a marked excess of lung cancer and respiratory disease, particularly those with 10 or more years' exposure prior to 1933. There is also some excess mortality from lung cancer and mesothelioma (36 observed, 19.3 expected; p 0.001) and respiratory disease (35 observed, 25 expected; p = 0.03) in those who entered after 1933 (cohorts 3, 4 and 5 combined), although the excess is very much less than in the first 2 cohorts. There were 16 deaths attributable to gastrointestinal cancers compared with 15.70 expected. No excess for any of these rubics approached statistical significance in any cohort, and no peritoneal mesothelioma was reported. In order to

distinguish between exposures of 1933 and after 1950, observed and expected deaths for those first exposed between 1933 and 1950, and those first exposed later were determined (Table 3). There is clear evidence of some excess of lung cancer and respiratory deaths among those first exposed between 1933 and 1950, although very much less than in cohorts 1 and 2. There have been few deaths among those first exposed after 1950, but there still appears to be an excess of deaths from lung cancer 15 or more years after first exposure (5 observed, 1.86 expected; p = 0.04)).

Table 3 *Number of deaths observed and expected, by date of first exposure*

| Cohort | Cause | Observed deaths† | Expected deaths | Ratio observed/expected | Probability of observed number or more |
|---|---|---|---|---|---|
| Men and women first exposed 1933-1950 (n = 646) | Lung cancer | 30 (5) | 16·10 | 1·9 | 0·001 |
| | Other cancers | 20 | 27·68 | 0·7 | 0·901 |
| | Respiratory | 33 | 21·91 | 1·5 | 0·035 |
| | Other causes | 109* | 97·96 | 1·1 | 0·308 |
| Men and women first exposed 1951 or later (n = 347) | Lung cancer | 6 (0) | 3·20 | 1·9 | 0·165 |
| | Other cancers | 3 | 5·02 | 0·6 | 0·677 |
| | Respiratory | 2 | 3·11 | 0·6 | 0·817 |
| | Other causes | 13 | 17·01 | 0·8 | 0·810 |

†Deaths due to pleural mesotheliomas are included in the observed number for lung cancer and also given separately in parentheses.
*Includes one case in which a pleural mesothelioma was a contributory cause of death.

This is shown in Table 4, in which deaths from lung cancer including pleural mesotheliomas in these groups are distributed according to the time since first exposure; the relative risk increases progressively with time since first exposure in both groups.

Table 4 *Observed and expected deaths from lung cancer by date of first exposure and time since first exposure*

| Cohort | Period since first entering scheduled area (years) | Observed deaths† | Expected deaths | Ratio observed/expected | Probability of observed number or more |
|---|---|---|---|---|---|
| Men and women first exposed 1933-1950 (n = 646) | 10-14 | 1 (0) | 1·65 | 1·6 | 0·353 |
| | 15-19 | 4 (0) | 3·60 | 1·1 | 0·355 |
| | 20 and over | 25 (5) | 11·16 | 2·1 | 0·028 |
| | Total | 30 (5) | 16·10 | 1·9 | 0·002 |
| Men and women first exposed 1951 or later (n = 347) | 10-14 | 1 | 1·26 | 0·7 | 0·721 |
| | 15-19 | 3 | 1·26 | 2·5 | 0·120 |
| | 20 and over | 2 | 0·53 | 3·8 | 0·038 |
| | Total | 6 (0) | 3·20 | 1·9 | 0·165 |

†Deaths from pleural mesotheliomas are included in the observed number for lung cancer and also given separately in parentheses.

The 6 workers first exposed after 1950 who died of lung cancer were all smokers; five worked in areas where dust levels were high in 1951 and one may have had previous exposure from another job. No mesotheliomas have occurred in this group although in view of the long latency period none would be expected yet. Asbestosis was found in 3 of the 6 cases. The numbers are too small for the magnitude of the excess of lung cancer in those first employed after 1950 to be estimated with any precision. Dust levels associated with various processes are shown in Table 5.

Table 5 Dust levels accompanying different textile processes, 1953-1974

| Department | Process | Yearly mean dust levels | | | | |
|---|---|---|---|---|---|---|
| | | Casella thermal precipitator (particles per cc) | | Lang running thermal precipitator or millipore membranes (fibres per cc) | | |
| | | 1953 | 1960 | 1961 | 1968 | 1974 |
| Fibreroom | Mixing | 500 | — | — | — | — |
| | Opening | 440 | | now totally enclosed | | |
| | Bag filling | — | 110 | 5 | 4 | 2 |
| | Maintenance lagging | — | 120 | 4 | 5 | 3 |
| Carding | Fine cards | 280 | 280 | 6 | 6 | 3 |
| | Medium cards | 810 | 400 | 8 | 8 | 3 |
| | Coarse cards | 1140 | 420 | 7 | 8 | 4 |
| | Electrical silver cards | 490 | 260 | 5 | 2 | 2 |
| Spinning | Fine spinning | 170 | 110 | 4 | 3 | 1 |
| | Roving frames | 510 | 150 | 5 | 6 | 3 |
| | Intermediate frames | 530 | 160 | 5 | 6 | 4 |
| Weaving | Beaming | 190 | 220 | 8 | 4 | <1 |
| | Pirn winding | 350 | 130 | 3 | 3 | <1 |
| | Cloth weaving | 180 | 140 | 3 | 2 | <1 |
| | Lining weaving | 130 | 110 | 2 | 1 | <1 |
| Finishing | Finishing | 140 | 80 | 4 | 4 | 3 |

CONCLUSIONS:

Results for Groups 1 and 2 were similar to that of Doll (1955)[101] and Knox, et al. (1968)[102], in that there was a 10-fold increase in risk of lung cancer in Group 1 and a three-fold increase for Group 2.

There was approximately a 2-fold increase in lung cancer for Group 3 and no increase for cancer of other sites. A 2-fold increase in lung cancer was seen in Group 4 and a 3-fold increase in Group 5. No increase in gastrointestinal cancer was observed for all groups combined.

7. In a study[84] of asbestos textile factory workers, excess lung cancer mortality has been reported. Observed and expected deaths due to lung cancer, other cancers, respiratory disease and other causes are shown in Table 1, together with death rates for asbestosis and mesothelioma. In men first exposed before 1951 (cohort 1), there were 22 deaths due to lung cancer compared with 13.85 expected ($P^1$ 0.05) 20 or more years after first exposure; while in later employees (cohort 2) there were 8 compared with 1.62 expected (P 0.0[redacted] If it were assumed that all men not known to have died or emi[redacted]ed were alive on the follow-up date, 31 December 1978, these observed/expected ratios would become 22/14.12 (cohort 1; P 0.05) and 8/1.75 (cohort 2; P 0.001), respectively.

[1]All significant levels are one-sided.

Table 1: Mortality experience of 679 male asbestos textile workers

| Year first employed | Period since first exposure (years) | Man-years | Lung cancer O | Lung cancer E | Pleural mesothelioma O | Pleural mesothelioma rate x 10³ | Other cancers O | Other cancers E | Asbestosis O | Asbestosis rate x 10³ | Other respiratory disease O | Other respiratory disease E | [illegible] | [illegible] |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| [illegible] | 10- | 1033 | 2 | 1.20 | 0 | 0.0 | 1 | 2.41 | 0 | 0.0 | 1 | [illegible] | 2 | 1.92 |
| 1950 | 15- | 1460 | 4 | 2.38 | 0 | 0.0 | 2 | 4.16 | 2 | 1.1 | 3 | [illegible] | 7 | 6.71 |
| n = 401 | 20- | 1760 | 3 | 3.97 | 1 | 0.6 | 6 | 5.16 | 2 | 1.1 | 1 | - | 29 | 21.2 |
| | 25- | 1496 | 10 | 4.58 | 2 | 1.3 | 6 | 5.38 | 2 | 1.3 | 9 | [illegible] | 24 | 21.2 |
| | 30- | 537 | 8 | 3.14 | 2 | 3.4 | 5 | 4.21 | 2 | 3.4 | 4 | [illegible] | 7 | [illegible] |
| | 35- | 507 | 1 | 2.20 | 2 | 3.9 | 4 | 2.93 | 2 | 3.9 | 5 | [illegible] | - | - |
| | Total | 6093 | 28 | 18.63 | 7 | - | 24 | 25.07 | 10 | - | 26 | 24.73 | [illegible] | 1 |
| 1951 or later | 10- | 1123 | 1 | 1.30 | 0 | 0.0 | 0 | 1.62 | 0 | 0.0 | 1 | [illegible] | 6 | [illegible] |
| | 15- | 1022 | 3 | 1.74 | 0 | 0.0 | 3 | 2.16 | 0 | 0.0 | 2 | [illegible] | - | - |
| n = 205 | 20- | 546 | 7 | 1.31 | 0 | 0.0 | 2 | 1.64 | 0 | 0.0 | 0 | [illegible] | 3 | - |
| | [illegible] | 46 | 1 | 0.31 | 0 | 0.0 | 0 | 0.37 | 0 | 0.0 | 0 | [illegible] | - | - |
| | Total | 2737 | 12 | 4.65 | 0 | - | 5 | 5.80 | 0 | - | 3 | [illegible] | - | [illegible] |

The excess mortality 20 or more years after first exposure due to nonmalignant respiratory disease in men first employed before 1951 (28 observed, 18.63 expected; P 0.01) was largely accounted for by deaths specifically attributed to asbestosis. The observed incidence of mesothelioma rose steadily from 0.0006 per annum at 20-25 years after first employment to 0.004 per annum beyond 35 years among pre-1951 employees. The absence of deaths due to asbestosis or mesothelioma in later employees may be due to their relatively short period of follow-up rather than to a substantial reduction in risk. Applying the incidence rates for asbestosis and mesothelioma observed in cohort 1 in successive five-year periods to the corresponding man-years of observation of cohort 2, only 1.9 deaths due to asbestosis and 0.4 due to mesothelioma would so far have been expected, and it has been reported that 10 men in cohort 2 have already been certified as having asbestosis (Berry et al., 1979)[103]. There is no evidence of excess mortality due to any other cause of death: 14 deaths (12.60 expected) were attributed to gastrointestinal cancers (ICD nos. 151-154) in the two cohorts, including 6 (5.38 expected) 25 or more years after first exposure; and no peritoneal mesotheliomas have occurred.

Exposure data are shown in Table 2.

Table 2. Previous and revised estimates of mean dust levels in fibres/ml (weighted by the number of men at each level) in selected years

| | 1936 | 1941 | 1946 | 1951 | 1956 | 1961 | 1966 | 1971 | 1976 |
|---|---|---|---|---|---|---|---|---|---|
| Previous estimates corresponding to early fibre counts (Peto et al., 1977) | 13.3 | 14.5 | 13.2 | 10.8 | 5.3 | 5.2 | 5.4 | 3.4 | - |
| Revised estimates corresponding to modern counting of static samples[a] | No measurements prior to 1951 | | | 32.4 | 23.9 | 12.2 | 12.7 | [illegible] | [illegible] |

[a] These estimates are based on preliminary data on 126 men first employed between 1951 and 1955, and should be regarded as provisional.

The authors stated that the average dust levels were in the region of 30 f/ml in 1951 and remained high until about 1974. It was further stated that levels prior to 1951 were probably not much higher than this:

The cumulative exposures of the eight men first exposed in 1951 and who later died of lung cancer 20 or more years after first exposure are compared with those of unaffected controls (Table 3). The analysis is based on cumulative exposure up to the end of 1971, and the control group consisted of 42 men born between 1901 and 1914 who entered the factory between 1951 and 1955. The eight lung cancer cases all entered the factory before 1956 and died in 1972 or later; all but one, who was born in 1925, were within the age range of the controls, and all were cigarette smokers. There is no evidence that their exposures were anomalously heavy, although this may merely reflect the inevitable inaccuracy of individual exposure estimates.

Table 3. Estimated exposures of men first exposed between 1951 and 1955

| | Cumulative exposure (fibres/ml-years) to December 1971 | | | | | | |
|---|---|---|---|---|---|---|---|
| | 0- | 100- | 150- | 200- | 300- | 400+ | Total |
| Men dying from lung cancer over 20 years after first exposure | 1 | 1 | 0 | 4 | 1 | 1 | 8 |
| Other men born 1901-1914 | 2 | 4 | 4 | 14 | 9 | 9 | 42 |

The observed relative risk for lung cancer 20 or more years after first exposure in post-1950 employees was 4.9 (8 observed, 1.62 expected; 95% confidence limits, 2.1-9.7). This is significantly higher (P = 0.01) than that observed in men entering between 1933 and 1950 (22 observed, 13.85 expected); but, as the majority of pre-1951 employees in this study were still employed in 1951, it seems likely that this apparently marked increase in risk is largely due to chance. The eventual relative risk for lung cancer among men with estimated cumulative exposures of about 200-300 fibres/ml-years (the order of magnitude of the average exposures of men first employed in 1951 or later (Table 3)) is therefore probably between 2 and 3. This is in reasonably close agreement with an earlier analysis (Peto, 1978)[109], which was based on the assumption that the relative risk would be about 2 in men who had suffered cumulative exposures of about 200 fibres/ml-years and indicated that lifelong exposure to 2 fibres/ml might eventually cause lung cancer in about 4% of men.

CONCLUSION:

The risk of lung cancer 20 years after exposure in post-1950 workers was 4.9 (8 obs. vs. 1.6 exp.), which is significantly higher than in workers initially exposed in 1933-1950 (20 obs. vs. 13.8 exp.). A relative risk of 2 to 3 for lung cancer among men with cumulative exposures of 200-300 (fibers/cm$^3$)(yrs.) was estimated. No clear-cut gradient in risk of lung cancer was associated with increased exposure, suggesting that exposure estimates may be imprecise.

8. Chrysotile textile workers (South Carolina)[85] were studied to investigate the risk of exposure to this asbestos-type mineral.

The mortality and exposure data were analyzed in two ways. The first followed the orthodox man-years life table approach of Hill[104] and others, whereby standardized mortality ratios (SMRs) are derived from comparison of observed numbers of deaths with numbers expected from mortality rates in a standard population. In this case age-, sex-, race (colour)-, and year-specific rates for South Carolina were used. The second approach, essentially internal and case-control in type, followed the Mantel-Haenszel (or log rank) procedure,[105] yielding relative risks from entirely intracohort comparisons. In calculating SMRs a "lag time" of 10 years before death (or end of 1977) was imposed in determining exposure, and only deaths 20 years or more from first employment were included. In the Mantel-Haenszel analysis the same exclusions were applied, controls being selected from all other members of the cohort of the same sex and colour (black or white) who met the following criteria: (1) alive at death of case, (2) same year of birth, if in or after 1900, or within five years if before 1900, (3) within five years of date of first employment, before or after 1938. The statistical significance of differences between observed and expected numbers in this analysis and for departures from linearity were calculated as $X^2$ values by the method of Peto and Pike.[106] Lines were fitted to exposure-response results by Liddell using the method of Hanley and Liddell (to be published).

Estimates of dust concentration in millions of particles per cubic foot (mppcf) and duration of exposure in years were established for each worker. Tables 2 and 3 give exposure estimates.

Table 2 *Estimated average prevailing dust concentrations (mpcf) in main departments, 1930–70*

| | 1930 | 1940 | 1950 | 1960 | 1970 |
|---|---|---|---|---|---|
| Preparation | 3·5 • | 2·0 • | 1·0 • | 0·8 |
| Carding | 3·1 • | 1·5 • | 1·2 • | 0·9 |
| Spinning | 3·5 •· | 2·0 • | 1·6 |
| Winding | 2·8 • | 1·7 • | 1·1 |
| Twisting | 6·1 • | 4·0 • | 1·1 |
| Weaving | 2·1 • | 1·5 | • 1·2 |
| Finishing and inspection | 1·4 | • 1·0 • | 0·8 • | 0·5 |

*Apparent improvement usually associated with technical change

Table 3 *Age at start, duration of employment, and dust exposure (men only)*

| | *Length of gross service (years)* | | | | |
|---|---|---|---|---|---|
| | *<1* | *1, <5* | *5, <20* | *≥20* | *Total* |
| No | 950 | 574 | 421 | 465 | 2410* |
| Average age at start (years) | 25·6 | 25·9 | 26·5 | 25·2 | 25·77 |
| Gross service (years) | 0·39 | 2·43 | 10·50 | 31·86 | 8·71 |
| Net service (years) | 0·37 | 1·81 | 7·55 | 29·51 | 7·59 |
| Average dust concentration (mpcf) | 2·11 | 1·86 | 1·67 | 1·23 | 1·80 |

*Excluding five whose employment histories were incomplete

Mortality of the males of known age shown by age and cause is presented in Table 1.

Table 1 *Male deaths by age and certified cause*

| *Cause of death (ICD code)* | *Age at death* | | | *Total* |
|---|---|---|---|---|
| | *<45* | *45–64* | *≥65* | |
| All causes | 178 | 502 | 177 | 857 |
| Malignant neoplasms: | | | | |
| Lung (162–164) | 1 | 47 | 18 | 66 |
| Oesophagus and stomach (150–151) | 0 | 13 | 2 | 15 |
| Colon and rectum (152–154) | 2 | 3 | 4 | 9 |
| Other abdominal (155–159) | 0 | 10 | 2 | 12 |
| Larynx (161) | 0 | 2 | 1 | 3 |
| Other (140–48, 160, 165–205) | 6 | 23 | 12 | 41 |
| Heart disease (400–443) | 38 | 189 | 70 | 297 |
| Respiratory tuberculosis (001–008) | 8 | 4 | 2 | 14 |
| Other respiratory (470–522; 525–527) | 10 | 27 | 11 | 48 |
| Pneumoconiosis (523–4) | 2 | 12 | 7 | 21 |
| Cerebrovascular (330–334) | 5 | 30 | 21 | 56 |
| Accidents (800–999) | 67 | 42 | 3 | 112 |
| Other known causes | 24 | 89 | 19 | 132 |
| Causes not known | 15 | 11 | 5 | 31 |

Table 4 summarizes the mortality experience based on the modified life table analysis. Overall, the SMR (all causes) is 27% above expectation and perhaps twice that in men employed 5 years or more.

Table 4 *Male deaths 20 years after first employment, by cause, in relation to duration of service*

| *Cause of death** | *Length of gross service (years)* | | | | | | | | *Complete cohort* | |
|---|---|---|---|---|---|---|---|---|---|---|
| | *<1* | | *1 <5* | | *5, <20* | | *≥20* | | | |
| | *O* | *SMR* | *O* | *SMR* | *O* | *SMR* | *O* | *SMR* | *O* | *SMR* |
| All causes | 159 | 107·4 | 113 | 122·7 | 120 | 156·1 | 178 | 136·7 | 570 | 127·4 |
| Malignant neoplasms. | | | | | | | | | | |
| Respiratory | 8 | 78·2 | 10 | 163·9 | 15 | 304·1 | 26 | 317·3 | 59 | 199·5 |
| Abdominal | 6 | 107·9 | 5 | 146·4 | 7 | 240·3 | 8 | 151·4 | 26 | 151·7 |
| Other | 12 | 130·2 | 7 | 124·9 | 9 | 195·9 | 7 | 146·2 | 35 | 127·5 |
| Heart disease | 69 | 108·9 | 34 | 87·6 | 45 | 141·7 | 70 | 120·8 | 218 | 113·7 |
| Respiratory tuberculosis | 1 | 231·8 | 1 | 347·8 | 1 | 307·9 | 1 | 131·5 | 4 | 222·8 |
| Other respiratory | 3 | 53·3 | 3 | 85·6 | 2 | 78·3 | 27 | 557·5 | 35 | 207·3 |
| Pneumoconiosis | (0) | — | (0) | — | (0) | — | (20) | — | (20) | — |
| Cerebrovascular | 9 | 83·0 | 14 | 193·0 | 6 | 107·3 | 9 | 76·2 | 38 | 107·2 |
| Accidents | 18 | 121·2 | 8 | 89·7 | 5 | 75·8 | 9 | 85·0 | 40 | 97·0 |
| Other known | 30 | 116·9 | 28 | 175·5 | 23 | 177·7 | 21 | 92·3 | 102 | 132·4 |
| Not known | 3 | | 3 | | 7 | | 0 | | 13 | |

*As in table 1 except that ICD codes 160–164 are here grouped under "respiratory" malignant neoplasms and the "other respiratory" category includes only bronchitis, pneumonia, and pneumoconiosis (ICD 490–502, 523–4)

As there is (a) a 7% excess of deaths even in men employed less than one year, unexplained by any asbestos related cause of death, and (b) a 32% overall excess in deaths of "other known causes," the SMRs are probably somewhat inflated, mortality in South Carolina having presumably provided an imperfect basis for comparison. Much of the excess, however, is clearly attributable to respiratory cancer, pneumoconiosis, and gastrointestinal cancers. Table 5 shows the cohort mortality, related to dust exposure. There is a steady gradient from 115.5 to 264.4 for mortality (all causes) and a much steeper slope for respiratory cancer and also for selected other respiratory diseases (which include pneumoconiosis). No clear trend is apparent in the other diagnostic categories.

Table 5 *Male deaths 20 years after first employment, by cause, in relation to dust exposure (mpcf.y) accumulated to 10 years before death*

| *Cause of death** | *Dust exposure (mpcf.y)* | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | *<10* | | *10 <20* | | *20 <40* | | *40 <80* | | *≥80* | |
| | *0* | *SMR* | *0* | *SMR* | *0* | *SMR* | *0* | *SMR* | *0* | *SMR* |
| All causes | 376 | 115·5 | 55 | 125·5 | 63 | 156·9 | 43 | 170·8 | 33 | 264·4 |
| Malignant neoplasms: | | | | | | | | | | |
| Respiratory | 31 | 143·1 | 5 | 182·7 | 8 | 304·2 | 7 | 419·5 | 8 | 1031·9 |
| Abdominal | 14 | 114·9 | 4 | 231·6 | 4 | 247·0 | 4 | 383·6 | 0 | — |
| Other | 28 | 140·0 | 3 | 109·2 | 1 | 44·9 | 0 | — | 3 | 383·5 |
| Heart disease | 143 | 103·5 | 28 | 143·6 | 29 | 166·6 | 10 | 88·6 | 8 | 149·9 |
| Respiratory tuberculosis | 3 | 264·4 | 0 | — | 0 | — | 1 | 634·4 | 0 | — |
| Other respiratory: | 8 | 65·9 | 2 | 119·5 | 6 | 421·7 | 13 | 1407·8 | 6 | 1296·0 |
| Pneumoconiosis | (0) | — | (0) | — | (3) | — | (9) | — | (8) | — |
| Cerebrovascular | 29 | 115·3 | 2 | 50·0 | 4 | 124·4 | 2 | 93·4 | 1 | 99·8 |
| Accidents | 31 | 99·2 | 2 | 54·1 | 5 | 152·9 | 1 | 49·4 | 1 | 120·0 |
| Other known | 79 | 140·4 | 9 | 116·9 | 4 | 630 | 5 | 111·5 | 5 | 263·3 |
| Not known | 10 | | 0 | | 2 | | 0 | | 1 | |

Table 6 shows the results of the posteriori Mantel-Haenszel analysis for certain diagnostic groups only. The number of deaths included in this analysis falls short of those used in tables 4 and 5--for example, 490 compared with 570 from all causes; in the remainder no matching control could be found. There is clear confirmation of a statistically significant linear trend in lung cancer, pneumoconiosis, and deaths (all causes) but no convincing association for the abdominal cancers.

One death ascribed to mesothelioma was found--a man born in 1907 who died in 1967. He was first employed at the plant in 1925, worked as a mule spinner from 1933 to 1955 and as an oven helper until he left in 1965. The tumour was stated to be peritoneal but there was no necropsy.

Table 6 — Dust exposure in male deaths from selected causes and controls (Mantel-Haenszel analysis)

| | Dust exposure (mpcf) accumulated up to 10 years before death of case | | | | | Chi square | |
|---|---|---|---|---|---|---|---|
| Linearity | <10 | 10-19 | 20-39 | 40-79 | ≥80 | Difference | Linearity |
| Pneumoconiosis (ICD 523) | | | | | | | |
| Deaths | 0 | 0 | 3 | 10 | 4 | 17.36 | 10.80 |
| Expected | 3.1 | 2.2 | 3.8 | 4.1 | 3.7 | | |
| Relative risk | — | — | — | — | — | | |
| Lung cancer (ICD 162-4) | | | | | | | |
| Deaths | 25 | 3 | 8 | 7 | 6 | 24.08 | 20.43 |
| Expected | 32.4 | 5.4 | 5.3 | 3.7 | 2.2 | | |
| Relative risk | 1 | 0.98 | 2.95 | 4.32 | 15.00 | | |
| Abdominal cancer (ICD 150-9) | | | | | | | |
| Deaths | 13 | 4 | 2 | 4 | 0 | 4.06 | 2.53 |
| Expected | 15.5 | 2.9 | 2.5 | 2.1 | 0 | | |
| Relative risk | 1 | 1.64 | 1.30 | 7.63 | — | | |
| All causes | | | | | | | |
| Deaths | 331 | 45 | 53 | 37 | 24 | 14.42 | 10.63 |
| Expected | 348.0 | 46.2 | 48.5 | 32.4 | 15.0 | | |
| Relative risk | 1 | 1.05 | 1.43 | 1.51 | 2.17 | | |

This study shows that the relationship of lung cancer mortality to accumulated dust exposure is virtually linear.

The pattern of mortality in this cohort of chrysotile textile workers is similar to that reported for Quebec chrysotile miners and millers, particularly those employed at Thetford Mines.[57] Overall, the SMRs for the factory workers are somewhat higher than for the miners (perhaps due in part to questions of comparability with the reference populations). There is the same scarcity of deaths attributed to mesothelioma and, in both cohorts, the relationship of lung cancer mortality to accumulated dust exposure is virtually linear. It is only when actual levels of exposure are examined that the astonishing difference between the experience of these two chrysotile-exposed cohorts is seen. This is illustrated in Fig. 1 where, to facilitate comparison, the SMRs in both cohorts are based on exposure accumulated to age 45.[57] In fact, the slope of the exposure-response line for lung cancer in the textile workers is 50 times more steep than that observed in miners and millers. This confirms almost exactly the findings of Dement et al.[61] in their similar cohort from the same plant; the agreement is very close (see Fig. 2). The data shown in this graph are based on mortality for white men only, 15 years or more from first employment and therefore differ somewhat from the figures in Table 5.

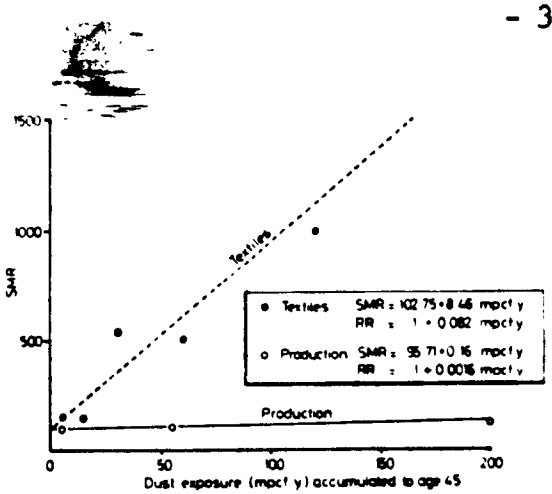



Fig 1 *Respiratory cancer SMRs in relation to dust exposure accumulated to age 45 in chrysotile production and textile manufacture*

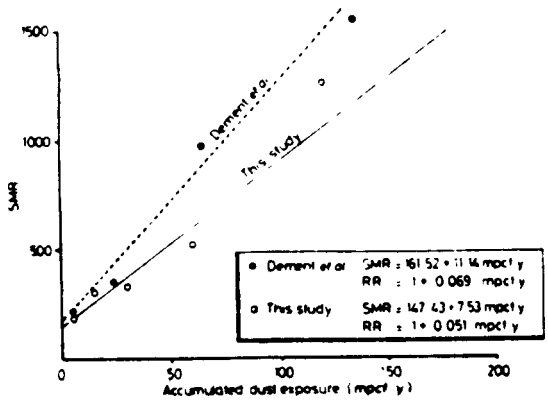



Fig 2 *Respiratory cancer SMRs in white men 15 years or more from first employment in relation to accumulated dust exposure. Comparison of this study and that of Dement et al*[9]

CONCLUSION:

Various reasons were discussed to determine whether the differences observed were due to errors in exposure estimates, etc. Assuming errors, the difference remains at least 10 fold.

9. Another cohort[86] of chrysotile asbestos factory (textile) workers in a Pennsylvania plant was studied, which included those employed during 1938-1959 for at least one month. Crocidolite and amosite were used at this plant also. Exposure data are shown in Tables 2 and 3.

Table 2 *Estimated average prevailing dust concentrations (MPCF) in main departments 1930–70*

| | 1930 | 1940 | 1950 | 1960 | 1970 |
|---|---|---|---|---|---|
| Textile | | | | | |
| Preparation | 15·0 * 14·6 | * 3·5 | * 2·0 | * | * 1·5 |
| Carding | 12·0 * 9·3 | * 3·2 | *2·0 * | 1·6 | |
| Spinning | 7·0 | * 2·5 | * 1·8 | * | 1·5 |
| Twisting | 7·2 | * 4·0 | * 1·8 | *0·5 * | 1·1 |
| Winding | 3·0 | * 1·5 | * | 0·8 | |
| Cloth weaving | 7·9 *3·4 | * | 0·9 | | |
| Tape weaving | 7·3 *3·1 | * | 1·4 | * | 1·2 |
| Felted tape | 2·0 | * 1·0 | * 0·5 | | |
| Rope | 4·0 | * 2·5 | * 1·2 | * | 0·5 |
| Friction: | | | | | |
| Woven brakes | 2·0 | 1·5 | 1·0 | 0·7 | |
| Extruded brakes | 2·0 | 1·5 | 1·0 | 0·8 | |
| Dry [illegible] | 10·0 | 6·0 | 4·0 | 3·8 | |
| Cloth | 2·0 | 1·5 | 1·5 | 1·5 | |
| Brake finishing | 2·0 | 1·5 | 1·0 | 0·7 | |
| Sanding and finishing | 2·0 | 1·5 | 1·0 | 0·7 | |
| Finishing and shipping | 0·5 | | 0·2 | 0·2 | |
| Packings, gaskets | 1·3 | 1·3 | 0·6 | 0·7 | |
| Maintenance, etc | 0·5 | 0·5 | 0·2 | 0·2 | |

*Asterisks shown against textile processes indicate approximate date of improvements usually associated with technical change. Figures for friction and other departments are estimates for each decade

Table 3 *Age at start, duration of employment, and dust exposure (male only)*

| | *Length of gross service* | | | | |
|---|---|---|---|---|---|
| | *<1* | *1, <5* | *5, <20* | *≥20* | *Total* |
| No | 1248 | 906 | 855 | 1013 | 4022* |
| Average age at start (years) | 28·80 | 29·30 | 30·77 | 27·22 | 28·92 |
| Gross service (years) | 0·40 | 2·39 | 11·01 | 30·63 | 10·71 |
| Net service (years) | 0·38 | 1·87 | 8·06 | 27·51 | 9·18 |
| Average dust concentration (mpcf) | 2·60 | 2·40 | 2·73 | 1·58 | 2·32 |

*Excluding two whose employment histories were incomplete.

Mortality was analyzed as in #8 above, using Pennsylvania death rates for reference. Mortality data by age and certified cause are presented in Table 1.

Table 1 *Male deaths by age and certified cause*

| *Cause of death (ICD code)* | *Age at death* | | | *Total* |
|---|---|---|---|---|
| | *<45* | *45–64* | *≥65* | |
| All causes | 191 | 667 | 534 | 1392 |
| Malignant neoplasms. | | | | |
| Lung* (162–164) | 3 | 49 | 18 | 70 |
| Oesophagus and stomach (150–151) | 1 | 7 | 6 | 14 |
| Colon and rectum (152–154) | 2 | 21 | 12 | 35 |
| Other abdominal* (155–159) | 3 | 16 | 5 | 24 |
| Larynx (161) | 0 | 0 | 0 | 0 |
| Other* (140–148, 160, 165–205) | 16 | 57 | 40 | 113 |
| Heart disease (400–443) | 43 | 285 | 245 | 573 |
| Respiratory tuberculous (001–008)* | 5 | 4 | 2 | 11 |
| Other respiratory (470–522, 525–527) | 6 | 17 | 25 | 48 |
| Pneumoconiosis (523–524) | 2 | 48 | 24 | 74 |
| Cerebrovascular (330–334) | 3 | 33 | 44 | 80 |
| Accidents (800–999) | 74 | 44 | 20 | 138 |
| Other known causes* | 23 | 73 | 80 | 176 |
| Cause not known | 10 | 13 | 13 | 36 |

*In 13 cases in these categories, mesothelioma was given as the cause of death, in one death ascribed to asbestosis, mesothelioma was also mentioned.

The SMR for all causes of death was 109.0. Those employed for less than 1 year had a SMR of 87.2, and those who had worked 20 or more years, 127.2. (Table 4)

Table 4 *Male deaths 20 years after first employment, by cause, in relation to length of service*

| *Cause of death** | *Length of gross service years* | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | *<1* | | *1, <5* | | *5, <20* | | *≥20* | | *Complete cohort* | |
| | *O* | *SMR* | *O* | *SMR* | *O* | *SMR* | *O* | *SMR* | *O* | *SMR* |
| All causes | 171 | 87·2 | 154 | 106·2 | 187 | 104·5 | 383 | 127·2 | 895 | 109·0 |
| Malignant neoplasms | | | | | | | | | | |
| Respiratory | 9 | 69·6 | 3 | 32·9 | 14 | 128·8 | 27 | 158·9 | 53 | 105·0 |
| Abdominal | 8 | 72·9 | 11 | 133·7 | 11 | 105·9 | 24 | 131·3 | 54 | 112·7 |
| Other | 19 | 132·4 | 16 | 152·0 | 15 | 118·5 | 32 | 155·3 | 82 | 141·1 |
| Heart disease | 77 | 92·7 | 77 | 125·1 | 78 | 100·2 | 153 | 115·7 | 385 | 108·5 |
| Respiratory tuberculosis | 0 | - | 1 | 133·4 | 0 | — | 2 | 67·3 | 3 | 51·7 |
| Other respiratory | 4 | 54·2 | 2 | 38·1 | 11 | 161·0 | 50 | 442·4 | 67 | 215·0 |
| Pneumoconiosis | (2) | — | (1) | — | (10) | — | (46) | — | (59) | — |
| Cerebrovascular | 7 | 54·9 | 10 | 106·5 | 10 | 77·7 | 20 | 87·6 | 47 | 81·2 |
| Accidents | 13 | 117·5 | 15 | 181·1 | 8 | 87·2 | 9 | 60·1 | 45 | 103·5 |
| Other known | 30 | 75·2 | 15 | 52·4 | 37 | 103·0 | 62 | 103·1 | 144 | 87·2 |
| Not known | 4 | | 4 | | 3 | | 4 | | 15 | |

*As Table 1 except that ICD codes 160–164 are here grouped under "respiratory" malignnt neoplasms and the "other respiratory" category includes only bronchitis, pneumonia, and pneumoconiosis (ICD 490–502, 523–4)

Malignant neoplasms, heart disease, and "other respiratory" disease were mainly responsible for the higher SMR in these long term workers. The other respiratory category included bronchitis and pneumonia (ICD 470-502) and pneumoconiosis (ICD 523-4) and was chosen for study because expected figures for pneumoconiosis alone were not available. Table 5 shows SMRs by cause and by accumulated dust exposure. The SMR for all causes rose steadily from 93.1 for

men with an exposure at under 10 mpcf.y to 215.2 in the highest category ( 80 mpcf.y). Respiratory, abdominal, and other malignant diseases and the non-malignant other respiratory group all contributed to this rising trend. On 14 death certificates a diagnosis of mesothelioma was specified: 10 were pleural tumours and four peritoneal. These deaths occurred in the period 1960-75. One (in 1960) was 16 years after first employment; the remaining 13 occurred 25-53 years after first employment. Two of the deaths from mesothelioma had been given the ICD code 199 (malignant neoplasms of other and unspecified sites); another 30 deaths 15 or more years after first employment were given the code 199. Seventeen of these 30 deaths occurred before 1965, the year after which most of the deaths from mesothelioma occurred. The diagnosis given in many of these cases was consistent with an unrecognized peritoneal mesothelioma.

Table 5 *Male deaths 20 years after first employment, by cause, in relation to dust exposure (mpcf.y) accumulated 10-20 years before death*

| *Cause of death* (See table 4)* | *Dust exposure (mpcf.y)* | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | *<10* | | *10 < 20* | | *20 < 40* | | *40 < 80* | | *≥80* | |
| | *0* | *SMR* | *0* | *SMR* | *0* | *SMR* | *0* | *SMR* | *0* | *SMR* |
| All causes | 470 | 93·1 | 86 | 82·1 | 130 | 125·6 | 105 | 174·9 | 104 | 215·2 |
| Malignant neoplasms | | | | | | | | | | |
| Respiratory | 21 | 66·9 | 5 | 83·6 | 10 | 156·0 | 6 | 160·0 | 11 | 416·1 |
| Abdominal | 26 | 90·2 | 8 | 130·5 | 5 | 79·7 | 8 | 218·8 | 7 | 237·2 |
| Other | 47 | 130·4 | 5 | 68·5 | 11 | 148·6 | 7 | 164·7 | 12 | 372·8 |
| Heart disease | 221 | 102·7 | 41 | 89·2 | 60 | 130·6 | 34 | 130·5 | 29 | 108·5 |
| Respiratory tuberculosis | 1 | 34·3 | 0 | — | — | — | 1 | 169·7 | 1 | 163·6 |
| Other respiratory | 8 | 43·6 | 5 | 122·0 | 10 | 263·0 | 14 | 623·3 | 30 | 1689·2 |
| Pneumoconiosis | (4) | — | (1) | — | (9) | — | (9) | — | (36) | — |
| Cerebrovascular | 27 | 78·3 | 1 | 13·3 | 10 | 133·5 | 8 | 187·2 | 1 | 29·3 |
| Accidents | 33 | 120·1 | 3 | 56·2 | 1 | 18·6 | 6 | 193·9 | 2 | 91·0 |
| Other known | 74 | 73·3 | 17 | 80·0 | 23 | 109·7 | 21 | 172·2 | 9 | 97·8 |
| Not known | 12 | | 1 | | 0 | | 0 | | 2 | |

The Mantel-Haenszel (log rank) analysis[105] (table 6) bore out the exposure-response relationships observed in Table 5. There is a small shortfall (5% overall) between the numbers of cases used in this analysis and in the man-years analyses presented in Tables 4 and 5. The deficiency is explained by failure to find matching controls for every selected case.

Table 6 *Dust exposure in male deaths from selected causes and controls (Mantel-Haenszel analysis*)*

| | *Dust exposure (mpcf.y) accumulated up to 10 years before death of case* | | | | | *Chi square Difference* | *Linearity* |
|---|---|---|---|---|---|---|---|
| | *<10* | *10 < 20* | *20 < 40* | *40 < 80* | *≥80* | | |
| **Pneumoconiosis (ICD 523)** | | | | | | | |
| Deaths | 3 | 4 | 10 | 11 | 28 | 39·56 | 39·17 |
| Expected | 14·6 | 8·1 | 10·9 | 8·1 | 14·3 | | |
| Relative risk | 1 | 4·04 | 13·72 | 14·93 | 37·90 | | |
| **Lung cancer (ICD 162–4)** | | | | | | | |
| Deaths | 20 | 4 | 10 | 6 | 11 | 5·77 | 4·98 |
| Expected | 24·4 | 5·2 | 8·0 | 5·6 | 7·7 | | |
| Relative risk | 1 | 0·83 | 1·54 | 2·90 | 6·82 | | |
| **Abdominal cancer (ICD 150–9):** | | | | | | | |
| Deaths | 26 | 8 | 5 | 8 | 7 | 3·22 | 1·09 |
| Expected | 28·8 | 6·8 | 7·0 | 5·3 | 6·1 | | |
| Relative risk | 1 | 1·15 | 0·66 | 2·45 | 2·85 | | |
| **All causes** | | | | | | | |
| Deaths | 451 | 81 | 121 | 100 | 99 | 34·66 | 26·12 |
| Expected | 476·6 | 104·5 | 118·6 | 80·4 | 72·0 | | |
| Relative risk | 1 | 0·82 | 1·20 | 1·6 | 2·12 | | |

The present cohort in the Pennsylvania plant was constituted in exactly the same way as that in the South Carolina chrysotile textile plant described elsewhere.[85]

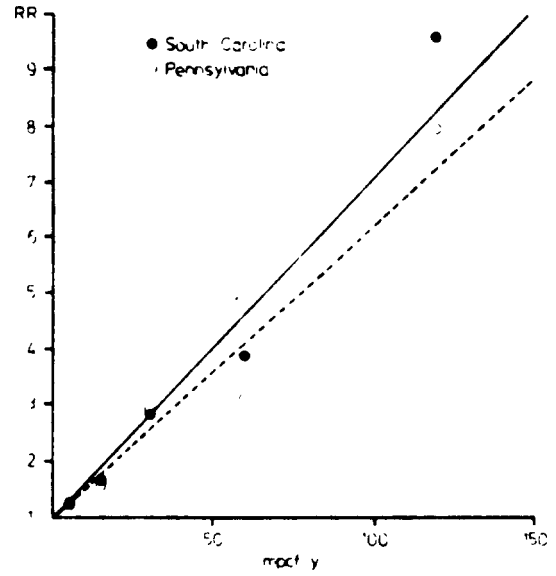
The Pennsylvania cohort was exposed to a somewhat higher average dust concentration: 2.32 mpcf compared with 1.80 mpcf in South Carolina. The mortality pattern in Pennsylvania resembled that in South Carolina in showing a rising SMR with increasing dust exposure for all causes of death, for respiratory cancer, and for pneumoconiosis. For respiratory cancer, however, the SMR for the lowest exposure group (less than 10 mpcf.y) was 115.5 in South Carolina but only 69.9 in Pennsylvania. By contrast with South Carolina, where the SMRs tended to be above 100 for causes unrelated to asbestos, and for all causes in very short-term employees,[85] the opposite was true in Pennsylvania. It seems likely that in both cohorts lack of comparability with the relevant state populations may be the explanation. Having regard for this possibility, the use of relative risks is perhaps more appropriate than SMRs for comparing the respiratory cancer mortality of the two cohorts. Table 7 shows that the relative risks of death from all causes, respiratory cancer, and pneumoconiosis in the two plants were extraordinarily similar. In both cohorts the relationships of respiratory cancer to exposure were essentially linear (figure) with slopes that were nearly identical (South Carolina, RR = 1 + 0.059 mpcf.y; Pennsylvania, RR = 1 + 0.051 mpcf.y).

Table 7 *Relative risks based on SMRs by cumulative exposure in two plants*

| | mpcf.y | | | | |
|---|---|---|---|---|---|
| | *<10* | *10 < 20* | *20 < 40* | *40 < 80* | *≥80* |
| All causes: | | | | | |
| South Carolina plant | 1·0 | 1·09 | 1·36 | 1·48 | 2·29 |
| Pennsylvania plant | 1·0 | 0·88 | 1·35 | 1·88 | 2·31 |
| Respiratory cancer | | | | | |
| South Carolina plant | 1·0 | 1·28 | 2·13 | 2·93 | 7·21 |
| | *(1·32)* | *(1·68)* | *(2·80)* | *(3·86)* | *(9·49)* |
| Pennsylvania plant | 1·0 | 1·25 | 2·33 | 2·39 | 6·22 |
| | *(1·26)* | *(1·58)* | *(2·94)* | *(3·03)* | *(7·87)* |
| Bronchitis, pneumonia, and pneumoconiosis. | | | | | |
| South Carolina plant | 1·0 | 1·81 | 6·40 | 21·36 | 19·67 |
| Pennsylvania plant | 1·0 | 2·79 | 6·03 | 14·29 | 38·74 |

Figures in italics are relative risks calculated from SMRs at zero exposure derived from fitted line.

Similar proportions of all deaths in the two cohorts were from malignant disease (17% in South Carolina and 18% in Pennsylvania), but the types of malignancy differed. In South Carolina respiratory cancer accounted for 47%, abdominal 25%, and other types 28% whereas in the Pennsylvania plant the corresponding proportions were reversed, 27%, 29%, and 44%. Moreover, in South Carolina no systemic relationship with exposure was seen for abdominal or other types of malignant disease whereas in Pennsylvania there was evidence of such a relationship.




*Relative risk of respiratory cancer and accumulated dust exposure in two mainly textile plants (Lines fitted by LDK Liddell using the methods of Hanley and Liddell.)*

[redacted]creased risk of mesothelioma in the Pennsylvania plant (14 cases in 1392 male deaths (1%) compared with one case in 867 (0.1%) in South Carolina) raises the question of whether the abdominal and more particularly other types of cancer included undiagnosed cases of mesothelioma. There is some support for this idea in the substantial number coded to ICD 199 (malignant disease of other and unspecified sites) and the fact that 17 of these deaths occurred before 1964 when malignant mesothelioma started to become more generally recognized. Once again there is evidence in this study of the special risk of mesothelioma associated with exposure to even quite small proportions of amphibole, in this case predominantly amosite.

## CONCLUSION

The very similar exposure-response relationships for respiratory cancer and asbestosis observed in this and the South Carolina plant support the previous conclusion that the risks of these diseases in chrysotile production (mining and milling) and in textile manufacture are quite different. In the third plant studied, a friction materials plant in Connecticut, there was little or no excess risk of respiratory cancer or asbestosis.[85] This was also true in a friction materials plant in the United Kingdom.[66] Possible reasons for the striking epidemiological differences--fibre size distributions in particular--have been discussed elsewhere.[85, 107]

10. Mortality was studied[70] among asbestos-cement workers who had been hired prior to 1960 and who had been employed for a minimum of 9 years.

Table 1 gives the mortality rates for each of the three exposure groups of production workers, for the interval 20-33 years from first exposure.

Table 1 *Mortality rates in the interval 20–33 years from first exposure and estimated dust exposure of three groups of workers (number of deaths in parentheses)*

| [redacted] | *Exposure group* | | | |
|---|---|---|---|---|
| | *Group A* | *Group B* | *Group C* | *Ontario men†* |
| | *Rates (per 1000 man-years)** | | | |
| Mesothelioma | 1·9 (1) | 4·9 (2) | 11·9 (6) | — |
| Lung cancer | 13·6 (5) | 26·1 (7) | 11·9 (6) | 1·6 |
| Gastrointestinal cancer | 0 (0) | 2·5 (1) | 6·0 (3) | 0·6 |
| All malignancies | 17·3 (7) | 35·9 (11) | 31·8 (16) | 4·7 |
| Mesothelioma crude rates | 2·5 (1) | 4·6 (2) | 11·9 (6) | — |
| Estimated exposure range (f-y ml) | 8–69 | 69–121 | 122–420 | |
| Estimated mean exposure (f-y ml) | 44 | 92 | 180 | |
| Standard deviation | 19·4 | 15·8 | 57 | |

*Standardised to age distribution of group C
†Based on Ontario vital statistics 1970–4

The mean exposure levels (in f-y/ml) were: Group A-44; Group B-92; and Group C-180.

The mortality observed among the employees was compared with the mortality predicted from Ontario population rates (Table 2). To increase the man-years of observation in each cell, the second group, listed as P + M in the table combines the experience of the production and maintenance employees, all of whom were exposed to asbestos.

Table 2 *Mortality among the factory workers compared with the population of Ontario*

| *Cause* | *Group* | *Years since first exposure* | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | *15–19* | | | *20–24* | | | *25–33* | | | *Total: 20–33* | | |
| | | *Obs* | *Exp* | *O/E* | *Obs* | *Exp* | *O/E* | *Obs* | *Exp* | *O/E* | *Obs* | *Exp* | *O/E* |
| All causes | P | 8 | 8·9 | 1 | 16 | 11·8 | 1·4 | 34 | 11 6 | 2 9 | 50 | 23 4 | 2 1 |
| | P + M | 11 | 11·9 | 1 | 22 | 15·5 | 1 4 | 39 | 15 1 | 2 6 | 61 | 30·6 | 2·0 |
| | C | 7 | 5·0 | 1·4 | 7 | 5·9 | 1·2 | 7 | 7 4 | 1 | 14 | 13·3 | 1 |
| All malignancies ICD. 140–209 | P | 2 | 1·9 | 1 | 9 | 2·8 | 3·2 | 20 | 2 9 | 6 9 | 29 | 5 7 | 5 |
| | P + M | 2 | 2 5 | 1 | 11 | 3 7 | 3·0 | 23 | 3·7 | 6 2 | 34 | 7 4 | 4 |
| | C | 3 | 1·1 | 2 7 | 3 | 1·4 | 2·1 | 1 | 1 8 | 1 | 4 | 3 2 | 1 |
| Lung cancer ICD 162 | P | 1 | 0·6 | 1 | 6 | 1 0 | 6·0 | 11 | 1 0 | 11·0 | 17 | 2 0 | 8·5 |
| | P + M | 1 | 0·8 | 1 | 7 | 1 2 | 5·8 | 12 | 1 3 | 9 2 | 19 | 2 5 | 7 6 |
| | C | 0 | 0·3 | 0 | 0 | 0·5 | 0 | 1 | 0·6 | 1 | 1 | 1 1 | 1 |
| Mesothelioma ICD 163, 158, 228 | P | 1 | - | - | 2 | - | - | 4 | - | - | 6 | - | - |
| Gastrointestinal cancer ICD. 150–154 | P | 0 | 0·5 | 0 | 1 | 0 7 | 1 | 2 | 0·7 | 2 9 | 3 | 1 4 | 2 1 |
| | P + M | 0 | 0·7 | 0 | 1 | 0·9 | 1 | 3 | 0·9 | 3 3 | 4 | 1·8 | 2 2 |
| | C | 1 | 0 3 | 1 | 1 | 0 3 | 1 | 0 | 0·4 | 0 | 1 | 0·7 | 1 |
| Non-malignant respiratory disease ICD. 460–519 | P | 1 | 0·4 | 1 | 1 | 0·7 | 1 | 3 | 0 8 | 3 8 | 4 | 1 5 | 2·7 |
| | P + M | 1 | 0·6 | 1 | 3 | 0·9 | 3 3 | 4 | 1 0 | 4·0 | 7 | 1 9 | 3 7 |
| | C | 0 | 0·3 | 0 | 0 | 0·4 | 0 | 1 | 0 5 | 1 | 1 | 0·9 | 1 |
| Ischaemic heart disease ICD 410–414 | P | 4 | 3·9 | 1 | 2 | 4 7 | 0 4 | 5 | 4 6 | 1 | 7 | 9·3 | 0·8 |
| | P + M | 7 | 4·9 | 1 4 | 3 | 6·2 | 0 5 | 6 | 6·0 | 1 | 9 | 12 2 | 0·7 |
| | C | 3 | 2·1 | 1 | 1 | 2·4 | 0·4 | 2 | 2 9 | 1 | 3 | 5 3 | 0·6 |

P = Production workers M = Maintenance workers C = Unexposed workers

There were 10 deaths from malignant mesothelioma (5 pleural, 5 peritoneal) among the 58 deaths occurring in the production workers--a proportional mortality of 17% (table 3). In addition, one of the maintenance workers died of a pleural mesothelioma. All of these men had been exposed to both chrysotile and crocidolite in the pipe plant. The mean age at death of these 10 men was 51 years and none was over 60 (table 4).

Table 3 *Mortality rates from mesothelioma and lung cancer among the production workers (based on best evidence)*

| *Time since first exposure (years)* | | *Age* | | | | |
|---|---|---|---|---|---|---|
| | | *35–44* | *45–54* | *55–64* | *65–75* | *75 or more* |
| Mesothelioma | No of cases | 2 | 5 | 3 | 0 | 0 |
| 15–33 | Man-years | 413 | 865 | 694 | 244 | 21·5 |
| | Rate (per 1000 man-years) | 4·8 | 5·8 | 4·3 | 0 | 0 |
| 20–33 | No of cases | 1 | 5 | 3 | 0 | 0 |
| | Man-years | 124 | 493 | 485 | 213 | 21·5 |
| | Rate (per 1000 man-years) | 8·0 | 10·1 | 6·2 | 0 | 0 |
| Lung cancer | No of cases | 0 | 0 | 13 | 6 | 1 |
| 15–33 | Man-years | 413 | 865 | 694 | 244 | 21·5 |
| | Rate (per 1000 man-years) | 0 | 0 | 18·7 | 24·6 | 46·5 |
| 20–33 | No of cases | 0 | 0 | 11 | 6 | 1 |
| | Man-years | 124 | 493 | 485 | 213 | 21·5 |
| | Rate (per 1000 man-years) | 0 | 0 | 22·7 | 28·2 | 46·5 |
| | Ontario rates (based on vital statistics 1970–4) (per 1000 man-years) | 0·1 | 0·5 | 1·7 | 3·5 | 3·8 |

The mortality rates for mesothelioma among the production workers are displayed in table 3 as a function of age. Table 5 gives the crude incidence rates for mesothelioma among all the asbestos-exposed employees, as related to the time interval since first exposure. Peto et al.[55] have suggested that the incidence of mesothelioma follows a power function relationship with time. The data are consistent with this suggestion, with an exponent value of between three and four.

There were 20 deaths from lung cancer among the 58 deaths in the production workers--a proportional mortality of 34%. Pathological information about 17 of these 20 cases indicates four were adenocarcinomas, eight were squamous, four were small cell undifferentiated, and one was a large cell undifferentiated tumor. As a group, these men were first exposed to asbestos in this plant at an older age, and they died later in life than the men dying of mesothelioma (table 4).

Table 4 *Some characteristics of the cases of mesothelioma and lung cancer (Classified according to best evidence)*

| | *Mean* | *Range* | *Standard deviation* |
|---|---|---|---|
| Mesothelioma (n = 10) | | | |
| Age at first exposure | 25 | 19–32 | 4·3 |
| Age at death | 51 | 42–57 | 5·4 |
| Latency (years) | 25 | 17–30 | 3·8 |
| Lung cancers (n = 20) | | | |
| Age at first exposure | 39 | 31–52 | 6·4 |
| Age at death | 64 | 55–78 | 5·9 |
| Latency (years)* | 25 | 17–29 | 3·6 |

*Latency is the interval from first exposure to death

Table 5 *Incidence rates of mesothelioma among the production and maintenance workers exposed to asbestos*

| | *Time since first exposure (years)* | | | |
|---|---|---|---|---|
| | *15–19* | *20–24* | *25–29* | *30–34* |
| No of cases | 1 | 4 | 5 | 1 |
| Man-years of risk | 1182 | 1061 | 555 | 104 |
| Incidence rate (per 1000 man-years) | 0·8 | 3·7 | 9·0 | 9·6 |

## CONCLUSION

Workers at this asbestos-cement factory exposed to historical dust conditions have experienced increased mortality rates from respiratory and malignant diseases. The lung cancer mortality rates

did not increase steadily with increasing estimates of cumulative exposure; in fact, the men in Group C experienced the lowest cancer rates of all. This may have been due to the small numbers involved, to differences in smoking habits, etc. Rates of death from mesothelioma were related to the magnitude of the cumulative exposure.

The cumulative exposure among production workers was estimated (to within a factor or 3 to 5) to have been about 100 f-y/ml, and the SMR for the period after 20 years was 850. The authors concluded that the lung cancer rates, at a cumulative exposure of 100-f-y/ml, may be raised several-fold.

11. Table 1 presents observed deaths and standardized mortality ratios (SMRs) for selected causes of death for the cohort[67] of production and maintenance-service workers (1075 men) for the intervals 1941-69 and 1970-3, which correspond to the original follow-up and the update periods, and for the total follow-up period 1941-73. For the period 1941-73, this cohort had an overall mortality rate 20.4% higher than that of all United States white males. This excess is due almost entirely to cancer and diseases of the respiratory system. For cancer, the greatest excess is in cancer of the respiratory system but with some excess also in cancer of the digestive system and all other cancers. For respiratory disease, the excess is due entirely to pneumoconiosis and pulmonary fibrosis, 19 cases of which were due to asbestosis (ISC 523.2). The pattern of deaths was similar during both of the follow-up periods, although overall mortality and cancer rates were somewhat higher during 1970-3. The increase in overall mortality for 1970-3 was primarily due to a large increase in death rates for stroke. Whether this increase is in any way related to occupational exposures is unknown.

TABLE 1

OBSERVED DEATHS AND SMRS FOR SELECTED CAUSES OF DEATH BY PERIOD OF FOLLOW-UP, 1075 MEN RETIRING FROM A UNITED STATES ASBESTOS COMPANY 1941-67 AND FOLLOWED THROUGH 1973

| | 1941-73 | | 1941-69 | | 1970-3 | |
|---|---|---|---|---|---|---|
| Cause of Death | Observed Deaths | SMR | Observed Deaths | SMR | Observed Deaths | SMR |
| All causes | 781 | 120 4 | 616 | 115 8 | 165 | 141 6 |
| Cancer (140-205) | 173 | 159 0 | 138 | 154.5 | 35 | 179 5 |
| Digestive (150-159) | 55 | 137 8 | 46 | 136.1 | 9 | 147 5 |
| Respiratory (162 163) | 63 | 270 4 | 49 | 270 7 | 14 | 269 2 |
| All other cancers | 55 | 120 6 | 43 | 115.0 | 12 | 146.3 |
| Stroke (330-334) | 74 | 96 4 | 48 | 76.7 | 26 | 183 1 |
| Heart disease (400-443) | 321 | 106 5 | 269 | 108.4 | 52 | 97 7 |
| Respiratory disease (470-527) | 68 | 173 0 | 54 | 178.2 | 14 | 155 6 |
| Pneumoconiosis and pulmonary fibrosis (523 525) | 31 | - | 25 | — | 6 | — |
| Asbestosis (523 2) | 19 | - | 16 | — | 3 | — |
| All other causes | 113 | 92 5 | 96 | 94.6 | 17 | 82.5 |
| Death certificates not located | 32 | - | 11 | — | 21 | — |

[redacted]

Estimates of exposure were based on midget impinger counts expressed in million particles per cubic foot (mppcf). Five classifications were used. These were:

no exposure (0), less than 5 mppcf (2.5), 5-10 mppcf (7.5), 10-30 mppcf (20.0), 30-50 mppcf (40.0), 50 or more mppcf (62.5).

To compute cumulative dust exposure for each man, the dust level at each job and time period was multiplied by years at that job and summed across all jobs during his working lifetime. This total cumulative exposure can be thought of as mppcf-years.

TABLE 2

OBSERVED DEATHS AND SMRs FOR RESPIRATORY CANCER BY TOTAL DUST EXPOSURE AND PERIOD OF FOLLOW-UP, 1075 MEN RETIRING 1941-67 AND FOLLOWED THROUGH 1973

| Total Dust Exposure (mppcf-years) | Number of Men | Mean Exposure (mppcf-years) | 1941-73 | | 1941-69 | | 1970-73 | |
|---|---|---|---|---|---|---|---|---|
| | | | Deaths | SMR | Deaths | SMR | Deaths | SMR |
| Under 125 | 437 | 62 | 19 | 197.9 | 15 | 200.0 | 4 | 198.5 |
| 125-249 | 224 | 182 | 9 | 180.0 | 8 | 200.0 | 1 | 100.0 |
| 250-499 | 265 | 352 | 19 | 327.6 | 13 | 309.5 | 6 | 375.0 |
| 500-749 | 105 | 606 | 9 | 450.0 | 8 | 470.6 | 1 | 333.3 |
| 750+ | 44 | 976 | 7 | 777.8 | 5 | 714.3 | 2 | 1000.0 |

Table 2 shows the relationship between total dose expressed as mppcf-years and mortality from respiratory cancer. For each dose interval, actual means are shown. These data, plotted on arithemetic paper, are also shown in Figure 1.*

[redacted]

*The relationship shown is not simply the result of time and the consequent fulfilling of latent period requirements. As noted in a previous paper, the dose rate makes an important contribution.[110]

There were 5 mesothelioma deaths observed in this cohort, of which 3 occurred during 1970-1973.

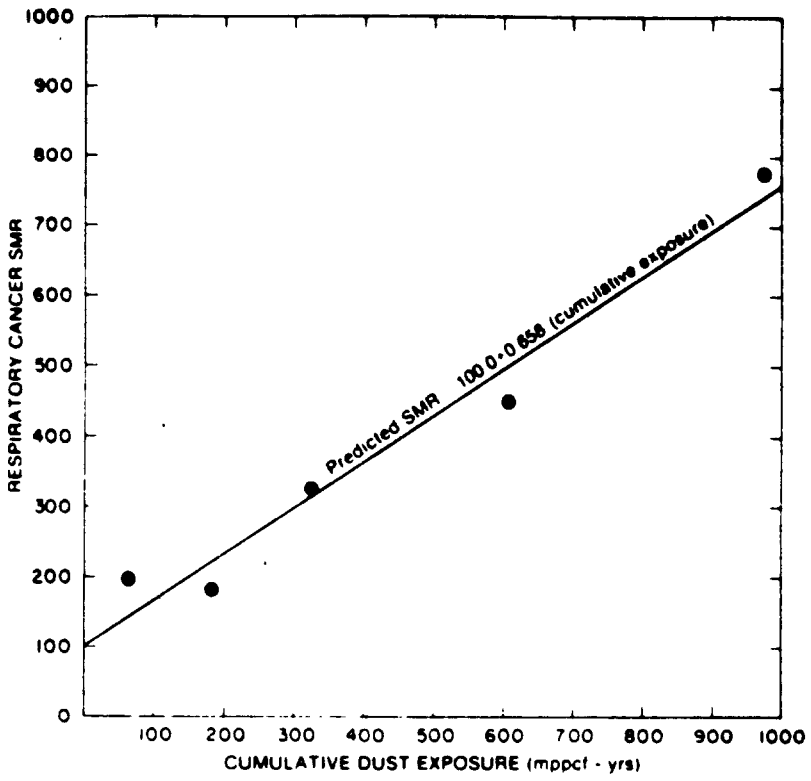



FIGURE 1 Total asbestos dust exposure and respiratory cancer mortality.

In an earlier report, it was speculated that the mathematical form of the dose-response relationship was the cumulative normal. The theoretical basis for this conjecture was the response curve in bioassay experiments. Schneiderman[108] has fitted a different curve to these data, while Peto[109] believes it is best described by a simple linear relationship. It does appear that omitting the Canadian data and adding 4 more years of follow-up change the relationship and make a linear relationship more likely. By use of the five data points from Table 1, this relationship can be expressed by the equation: predicted SMR - 100.0 + 0.658 (cumulative exposure).

The correlation between cumulative exposure and respiratory cancer SMR is 0.982. This prediction line is superimposed in Figure 1.

## CONCLUSION

Respiratory cancer risk increased as the quantitative exposure level increased. The SMR for the lowest level was 2.0; for the highest level, 7.8.

The effects of asbestos exposure with respect to lung cancer risk continued well past the termination of exposure.

The study population of retirees are "survivors," and mortality experience may not reflect actual risks associated with asbestos exposure. Most likely, risks were underestimated.

12. Mortality of asbestos factory workers exposed to crocidolite, chrysotile, and/or amosite in the production of textiles or insulation materials has been reported.[64] The levels of exposure were reported as follows:

    (1) before 1945 the dust levels in certain jobs were said to average 20 fibers/ml or higher;

    (2) jobs classified as "low-moderate" were probably 5-10 f/ml;

    (3) in non-production jobs and some departments the levels were below 5 f/ml;

    (4) after 1955, many areas were probably above 2 f/ml.

    Laggers were considered separately.

    The male cohort consisted of 4600 men and 922 women. There have been 775 deaths among the male workers. An analysis of the 545 deaths that occurred among workers, excluding laggers, who had been followed for 10 years or longer is presented in Table 1. Asbestos-related disease is rarely if ever manifest in those dying within 10 years of first exposure. In the Tables, the deaths from mesothelial tumors are given in parentheses but are included in the total number of observed deaths in any particular diagnostic category.

TABLE 1

MORTALITY EXPERIENCES OF MALE FACTORY WORKERS

| | Exposure Category | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | Low to Moderate | | | | Severe | | | |
| | <2 Years (884) | | >2 Years (554) | | <2 Years (937) | | >2 Years (512) | |
| Cause of Death | Observed | Expected | Observed | Expected | Observed | Expected | Observed | Expected |
| All causes | 118(4) | 118 0 | 89 (7) | 95 3 | 162*(16) | 122.2 | 176*(19) | 102.5 |
| Cancers of lung and pleura (ICD 162, 163) | 17(3) | 11.01 | 16†(1) | 9.0 | 31*(6) | 12.8 | 56*(7) | 10.4 |
| Gastrointestinal cancer (ICD 150-158) | 10 | 9 0 | 9 (4) | 7 3 | 20‡(6) | 9 5 | 19‡(8) | 8.2 |
| Other cancers | 6 | 7.4 | 8 (1) | 5.8 | 16‡(3) | 7 9 | 16*(4) | 6.3 |
| Chronic respiratory disease | 19 | 17 5 | 16 | 14 7 | 20 (1) | 17.6 | 28‡ | 15 9 |

*p <0.001
†p <0.05
‡p <0.01.

There were 46 deaths from mesothelial tumors, 19 pleural and 27 peritoneal. All have been validated by histologic examination. Nearly all of the pleural tumors were identified among the intrathoracic tumors (carcinoma of the lung and pleura, ICD 162, 163). The peritoneal tumors were included with gastrointestinal tumors if certified as a peritoneal mesothelioma (ICD 158) or if confused with carcinoma of the bowel or pancreas. They were included with "other cancers" if certified as carcinomatosis (ICD 199) or as sarcoma or other tumors. Two deaths from mesothelial tumors were identified among causes of death not shown in the Tables. There were, apart from pleural mesothelioma, 103 deaths from carcinoma of the lung, which remains the most common tumor of asbestos workers.

Statistically significant excess mortality from chronic respiratory disease is seen only among those with long and severe exposure. Asbestosis was given as the cause of death in 13 instances but as the underlying cause of death in 34 of the deaths from lung cancer and in 27 of the deaths from either pleural or peritoneal mesothelioma. In four instances, coronary thrombosis was the actual cause of death. In the majority of the above cases, exposure had been long and severe.

Table 2 shows the mortality experiences of the laggers. The majority of these men were first employed after 1955. It is the custom, however, for laggers to work on contract for various employers, and some may have had previous exposure, so the authors are not entirely sure of their durations of exposure. Only approximately 2% of the entire group has been followed for 30 years or longer, but to date their experience is not dissimilar from that of other severely exposed male workers.

TABLE 2

LAGGERS AND MATES (1368 MALES)

| | Observed | Expected |
|---|---|---|
| All causes | 83*(10) | 57.2 |
| Cancers of lung and pleura (ICD 162,163) | 25*(4) | 5.6 |
| Gastrointestinal cancer (ICD 150-158) | 8 (5) | 4.3 |
| Other cancers | 8 | 4.1 |
| Chronic respiratory disease | 12 | 7.4 |

*$p < 0.001$.

Mortality experience was also examined according to the length of follow-up, and an analysis of the standardized mortality ratios (SMRs) for cancers of the lung and pleura is presented in Table 3. In general, the SMR increases with increased length of follow-up and with increasing exposure, but for those with long exposure, the SMRs are higher in the group with follow-ups between 20 and 30 years. Only 20% of these workers have been followed up for 30 years or

longer, and currently about half of the deaths from mesothelial tumors occurred between 20 and 30 years after their first

TABLE 3

CANCERS OF THE LUNG AND PLEURA IN MALES (SMRs)

| Length of Follow-up (years) | Low to Moderate Exposure | | Severe Exposure | |
|---|---|---|---|---|
| | < 2 Years | >2 Years | < 2 Years | >2 Years |
| 10-20 | 104 | 112 | 255 | 463 |
| 20-30 | 159 | 261 | 218 | 675 |
| 30+ | 278 | 184 | 265 | 446 |

employment. However, as has been demonstrated previously,[111] the number of deaths from mesothelial tumors will continue to rise for some time.

In Table 4, a finer subdivision of job categories and of periods of employment in the factory are presented. It is noteworthy that in categories 1 and 2, ground workers, canteen workers, and production workers with very little and short exposures to dust, the SMR was 176, and there were three deaths from mesothelial tumors. Up to 1955, the estimated level of asbestos in the air was 2-5 fibers/ml.

TABLE 4

CANCERS OF LUNG AND PLEURA (SMRs)

| Exposure Category | Duration of Exposure | | |
|---|---|---|---|
| | >2 Years | 2-5 Years | 5 or More Years |
| Low to moderate | | | |
| 1, 2 | 176 | 0 | 216 |
| 3 | 126 | 351 | 152 |
| Severe | | | |
| 4 | 247 | 227 | 714 |
| 5 | 238 | 236 | 567 |

However, looking at the death rates for mesothelial tumors graded by exposure category (Table 5), it is found that the rates reveal a very definite relationship to length and severity of exposure.

TABLE 5

MESOTHELIOMA DEATH RATES

| Exposure Category and Duration (years) | Pleura | Peritoneum | S years | Rate per 100,000 S years |
|---|---|---|---|---|
| Males | | | | |
| Low to moderate | | | | |
| <2 | 3 | 1 | 12,031 | 33 |
| >2 | 3 | 4 | 7,500 | 93 |
| Severe | | | | |
| <2 | 6 | 10 | 15,428 | 104 |
| >2 | 7 | 12 | 7,827 | 243 |
| Laggers | | | | |
| <2 | 3 | 2 | 7,893 | 63 |
| >2 | 1 | 4 | 2,690 | 186 |
| Females | | | | |
| Low to moderate | 1 | 0 | 2,066 | 48 |
| Severe | | | | |
| <2 | 8 | 5 | 9,538 | 136 |
| >2 | 4 | 3 | 4,388 | 360 |

Over 400 women were employed in the traditionally female jobs of carding, spinning, and doubling; 100 were employed in mattress making. Crocidolite was used heavily in textile departments, exposure was generally estimated to be very high, and women were also employed in other production departments, as well as in offices, canteens, and other low-exposure departments. The same pattern of analyses has been adopted, and Table 6 shows the observed versus the expected mortality in the general population, for groups with 10 years or more of followup.

TABLE 6

MORTALITY EXPERIENCES OF FEMALE FACTORY WORKERS

| | Exposure Category | | | | | |
|---|---|---|---|---|---|---|
| | | | Severe | | | |
| | Low to Moderate (98) | | <2 Years (396) | | >2 Years (199) | |
| Cause of Death | Observed | Expected | Observed | Expected | Observed | Expected |
| All causes | 34*(1) | 22.0 | 88†(13) | 65 6 | 78‡(7) | 30 4 |
| Cancers of lung and pleura (ICD 162.163) | 3*(1) | 0.5 | 15‡(7) | 1.9 | 21‡(4) | 0.8 |
| Gastrointestinal cancer (ICD 150–158) | 3 | 1.9 | 14†(4) | 5.7 | 9†(2) | 2.6 |
| Other cancers | 4 | 3 2 | 16 (2) | 11.9 | 16‡(1) | 5.3 |
| Chronic respiratory disease | 3 | 2.3 | 6 | 6 8 | 10† | 3.2 |

*p < 0.05
†p < 0.01.
‡p < 0.001

In the low-moderate exposure group, there was one death from a mesothelial-pleural tumor. In all, there were 13 pleural-mesothelial tumors identified and eight peritoneal tumors, approximately the same proportion of all deaths (10%) as among the males. Among the severely exposed women with long exposures, there was a greater excess of lung cancer than among males with similar exposure. Also, apart from peritoneal mesotheliomas, there was an excess of deaths from gastrointestinal tumors and other cancers. Cancers of the ovary, uterus, and breast were analyzed separately. In the group of severely exposed women with long periods of employment, statistically significant excesses of cancer of the breast (obs., 6; exp., 2.1; p 0.05) and ovary (obs., 3; exp., 0.74; p 0.05) were noted. Not too much reliance can be placed on a single set of figures from one comparatively small cohort of women, and other factors related to marital status and parity that may operate in industrially employed women may be of importance. As in the males, the mesothelioma death rate (Table 5) relates clearly to the degree and length of exposure.

## CONCLUSION

In the male cohort, SMR of 5.4 for lung cancer was observed in the severely exposed workers ( 20 f/cc) with 2 years of exposure (54/10.4) and 2.4 for those in the low to moderately exposed group (5-10 fibers/cc) (31/12.8). Risk increased with duration of follow-up and severity of exposure. Nineteen pleural and 27 peritoneal mesotheliomas were observed.

In the female cohort, the SMR of 6.0 (3/0.5) for lung cancer was observed in low to moderately exposed group; 7.9 (15/1.9) and 26.3 (21/0.8) in the severely exposed groups with 2 years and 2 years of employment, respectively. An apparent excess of breast (6/2.1) and ovarian (3/0.7) cancer was observed in the severely exposed group. Thirteen pleural and 7 peritoneal mesotheliomas were observed.

13. The experience of insulation workers in the U.S. has been reported by Selikoff, et al.[74] With regard to exposure data, reconstruction of work situations and extrapolation to the past suggests that these workers would have been exposed to dust levels of 4-12 fibers/ml (as time weighted averages). While there might have been periods of little or no exposure, there could also have been times of peak exposures much higher than the calculated averages.

TABLE 2

EXPECTED AND OBSERVED DEATHS AMONG 623 ASBESTOS INSULATION WORKERS NEW YORK-NEW JERSEY, 20 OR MORE YEARS AFTER ONSET OF WORK JANUARY 1, 1943-DECEMBER 31, 1962 (8545 Man-years of Observation)

| Underlying Cause of Death | Expected* | Observed |
|---|---|---|
| Total deaths-all causes | 195 4 | 253 |
| Total cancer-all sites | 32.1 | 95 |
| Cancer of lung | 6 0 | 42 |
| Pleural mesothelioma | † | 3 |
| Peritoneal mesothelioma | † | 4 |
| Cancer of esophagus, stomach, colon-rectum | 9 7 | 29 |
| Cancer of larynx, pharynx, buccal cavity | 1 7 | 2 |
| Cancer of kidney | 0.7 | 0 |
| All other cancer | 14 0 | 15 |
| Noninfectious pulmonary diseases, total | 4.0 | 14 |
| Asbestosis | † | 12 |
| All other causes | 159 3 | 144 |

*Expected deaths are based upon white male age-specific U.S. death rates of the U.S. National Center for Health Statistics, 1949-1962. Rates for specific causes of death for 1943-1948 were extrapolated from rates for 1949-1955.

†Rates are not available, but these have been rare causes of death in the general population.

Table 2 shows the mortality rates for workers with 20 + years of exposure followed to 1962. The authors point out that while deaths related to asbestos exposure seen in insulation workers may sometimes occur in less than 20 years from first exposure (lung cancer, asbestosis, and occasionally, mesothelioma), these are not common and, therefore, data on experience beyond the 20-year point was thought to more clearly define the influence of exposure. Observation of survivors was extended to 1976 (Table 3). The same overall pattern of causes of death continued, although distribution of deaths by cause changed somewhat, reflecting a number of epidemiological influences. Thus, pleural and peritoneal mesothelioma, which tend to occur somewhat later than bronchogenic

carcinoma, became proportionately more common. This change also reflects the smaller proportions of older men who ever smoked cigarettes, and also a "survivor effect." Since the smokers in the original group had increased mortality risk (especially from lung cancer and cardiovascular disease) there would likely have been comparatively fewer of these and still fewer who continued smoking at least the same amount, among the cohort survivors, as the years went by. Except as influenced by other factors associated with advancing lapsed time since onset of exposure, this would make for fewer deaths of lung cancer, with more men at risk of dying of other asbestos-associated disease.

TABLE 3

EXPECTED AND OBSERVED DEATHS AMONG 632 NEW YORK-NEW JERSEY ASBESTOS INSULATION WORKERS JANUARY 1, 1943–DECEMBER 31, 1976 (13,925 Man-years of Observation)

| Underlying Cause of Death | Expected* | Observed |
|---|---|---|
| Total deaths, all causes | 328.9 | 478 |
| Total cancer, all sites | 57.0 | 210 |
| Cancer of lung | 13.3 | 93 |
| Pleural mesothelioma | † | 11 |
| Peritoneal mesothelioma | † | 27 |
| Cancer of esophagus | 1 4 | 1 |
| Cancer of stomach | 5.4 | 19 |
| Cancer of colon-rectum | 8.3 | 23 |
| Cancer of larynx, pharynx, buccal cavity | 2.8 | 6 |
| Cancer of kidney | 1 3 | 2 |
| All other cancer | 24.5 | 28 |
| Noninfectious pulmonary diseases, total | 9.3 | 45 |
| Asbestosis | † | 41 |
| All other causes | 262.6 | 223 |

*Expected deaths are based upon white male age-specific U.S. death rates of the U.S National Center for Health Statistics, 1949-1976. Rates for specific cause of death for 1943–1948 were extrapolated from rates for 1949-1955.

†Rates are not available, but these have been rare causes of death in the general population.

Lung cancer remained the most important cause of excess deaths, with 93 observed, 13.3 expected. Gastrointestinal cancer was also increased as seen in the original report (43 observed, 15.1 expected). Seventy-six percent of the original cohort enrolled in 1943 had died by 1976.

Variations in distribution of deaths by cause over time are shown in Table 4.

TABLE 4

EXPECTED AND OBSERVED DEATHS AMONG 632 NEW YORK-NEW JERSEY ASBESTOS INSULATION WORKERS JANUARY 1, 1943-DECEMBER 31, 1976

| Number of Men Attaining Category<br>Man-years of Observation | Less than 20 Years<br>325<br>1970 | | 20-34 Years<br>561<br>6263 | | 35 or More Years<br>498<br>5692 | |
|---|---|---|---|---|---|---|
| Underlying Cause of Death | Expected* | Observed | Expected* | Observed | Expected | Observed |
| Total deaths, all causes | 9.0 | 9 | 80.4 | 119 | 239.5 | 358 |
| Total cancer, all sites | 1.1 | 2 | 13.5 | 53 | 42.4 | 155 |
| Cancer of lung | 0.2 | 0 | 3.0 | 26 | 10.1 | 67 |
| Pleural mesothelioma | † | 0 | † | 4 | † | 7 |
| Peritoneal mesothelioma | † | 0 | † | 3 | † | 24 |
| Cancer of esophagus | 0.02 | 0 | 0.4 | 0 | 1.0 | 1 |
| Cancer of stomach | 0.1 | 0 | 1.5 | 6 | 3.8 | 13 |
| Cancer of colon-rectum | 0.2 | 0 | 1.9 | 7 | 6.2 | 16 |
| Cancer of larynx, pharynx, buccal cavity | 0.05 | 2 | 0.8 | 2 | 1.9 | 2 |
| Cancer of kidney | 0.03 | 0 | 0.4 | 0 | 0.9 | 2 |
| All other cancer | 0.5 | 0 | 5.5 | 5 | 18.5 | 23 |
| Noninfectious pulmonary diseases, total | 0.1 | 0 | 1.6 | 4 | 7.6 | 41 |
| Asbestosis | † | 0 | † | 3 | † | 38 |
| All other causes | 7.8 | 7 | 65.3 | 62 | 189.5 | 154 |

*Expected deaths are based upon white male age-specific U.S. death rates of the U.S. National Center for Health Statistics, 1949-1976. Rates for specific causes of death for 1943-1948 were extrapolated from rates for 1949-1955.

†Rates are not available, but these have been rare causes of death in the general population.

The experience of workers exposed after 1943 (reflecting postwar "cleaner" conditions) has also been reported. In the 15,520 man-years of observation during the less than 20-year period (Table 6), there was no unusual mortality experience. Altogether there were fewer deaths than expected, and there was no increase in cancer deaths.

TABLE 6

EXPECTED AND OBSERVED DEATHS AMONG 833 NEW YORK-NEW JERSEY ASBESTOS INSULATION WORKERS FIRST EMPLOYED JANUARY 1, 1943-DECEMBER 31, 1962, AND OBSERVED FROM FIRST EMPLOYMENT-DECEMBER 31, 1976
(Duration from Onset of Employment)

| Number of Men Attaining Category<br>Man-years of Observation | Less than 20 Years<br>833<br>15,520 | | 20-34 Years<br>523<br>3281 | |
|---|---|---|---|---|
| Underlying Cause of Death | Expected* | Observed | Expected* | Observed |
| Total deaths, all causes | 39.8 | 23 | 24.8 | 39 |
| Total cancer, all sites | 5.1 | 5 | 5.0 | 15 |
| Cancer of lung | 1.1 | 2 | 1.8 | 8 |
| Pleural mesothelioma | † | 0 | † | 2 |
| Peritoneal mesothelioma | † | 0 | † | 1 |
| Cancer of esophagus, stomach, colon-rectum | 0.7 | 1 | 0.8 | 2 |
| Cancer of larynx, pharynx, buccal cavity | 0.2 | 1 | 0.3 | 1 |
| Cancer of kidney | 0.1 | 0 | 0.1 | 1 |
| All other cancer | 3.0 | 1 | 2.0 | 0 |
| Noninfectious pulmonary diseases, total | 0.5 | 0 | 0.6 | 7 |
| Asbestosis | † | 0 | † | 6 |
| All other causes | 34.2 | 18 | 19.2 | 17 |

*Expected deaths are based upon white male age-specific U.S. death rates of the U.S. National Center for Health Statistics, 1949-1976. Rates for specific causes of death for 1943-1948 were extrapolated from rates for 1949-1955.

†Rates are not available, but these have been rare causes of death in the general population.

In the 3281 man-years of observation 20-34 years from onset of exposure, there were 3 times as many cancer deaths as expected, primarily due to lung cancer.

CONCLUSION

No dose-response inference is possible because of the lack of exposure data.

14. Observations on 17,800 asbestos insulation workers in the U.S. and Canada followed from 1967 to 1976 is discussed below.[64] During the decade of observation 2271 deaths occurred (Table 12), whereas only 1658.9 deaths were expected. The excess deaths were primarily the result of an increased number of instances of cancer at several sites.

TABLE 12

DEATHS AMONG 17,800 ASBESTOS INSULATION WORKERS IN THE UNITED STATES AND CANADA JANUARY 1, 1967 DECEMBER 31, 1976

NUMBER OF MEN 17,800

MAN-YEARS OF OBSERVATION 166,853

| Underlying Cause of Death | Expected* | Observed (BE) | Observed (DC) | Ratio o/e (BE) | Ratio o/e (DC) |
|---|---|---|---|---|---|
| Total deaths, all causes | 1658 9 | 2271 | 2271 | 1.37 | 1 37 |
| Total cancer, all sites | 319 7 | 995 | 922 | 3.11 | 2 88 |
| Cancer of lung | 105.6 | 486 | 429 | 4.60 | 4 06 |
| Pleural mesothelioma | † | 63 | 25 | — | — |
| Peritoneal mesothelioma | † | 112 | 24 | — | — |
| Mesothelioma, n.o.s. | † | 0 | 55 | — | — |
| Cancer of esophagus | 7.1 | 18 | 18 | 2.53 | 2.53 |
| Cancer of stomach | 14 2 | 22 | 18 | 1.54 | 1.26 |
| Cancer of colon-rectum | 38 1 | 59 | 58 | 1.55 | 1 52 |
| Cancer of larynx | 4.7 | 11 | 9 | 2.34 | 1 91 |
| Cancer of pharynx, buccal | 10.1 | 21 | 16 | 2.08 | 1 59 |
| Cancer of kidney | 8.1 | 19 | 18 | 2.36 | 2.23 |
| All other cancer | 131.8 | 184 | 252 | 1.40 | 1.91 |
| Nonmalignant pulmonary diseases, total | 59 0 | 212 | 188 | 3.59 | 3 19 |
| Asbestosis | † | 168 | 78 | — | — |
| All other causes | 1280 2 | 1064 | 1161 | 0 83 | 0 91 |

*Expected deaths are based upon white male age-specific U.S death rates of the U.S. National Center for Health Statistics, 1967-1976.

†Rates are not available, but these have been rare causes of death in the general population

(BE): Best evidence. Number of deaths categorized after review of best available information (autopsy, surgical, clinical).

(DC). Number of deaths as recorded from death certificate information only.

Apart from lung cancer, mesothelioma, gastrointestinal cancer, cancer of the larynx, pharynx and oral cavity and cancer of the kidney, there was still an excess of cancer of other sites, with 184 observed, 131.8 expected (Table 13).

TABLE 13

DEATHS AMONG 17,800 ASBESTOS INSULATION WORKERS IN THE UNITED STATES AND CANADA JANUARY 1, 1967-DECEMBER 31, 1976
NUMBER OF MEN 17,800
MAN-YEARS OF OBSERVATION 166,853

| Underlying Cause of Death | Expected* | Observed (BE) | Observed (DC) | Ratio o/e (BE) | Ratio o/e (DC) |
|---|---|---|---|---|---|
| Total deaths, all causes | 1658.9 | 2271 | 2271 | 1.37 | 1.37 |
| Cancer, all sites | 319.7 | 995 | 922 | 3.11 | 2.88 |
| Deaths of less common malignant neoplasms | | | | | |
| Pancreas | 17.5 | 23 | 49 | 1.32 | 2.81 |
| Liver, biliary passages | 7.2 | 5 | 19 | 0.70 | 2.65 |
| Bladder | 9.1 | 9 | 7 | 0.99 | 0.77 |
| Testes | 1.9 | 2 | 1 | — | — |
| Prostate | 20.4 | 30 | 28 | 1.47 | 1.37 |
| Leukemias | 13.1 | 15 | 15 | 1.15 | 1.15 |
| Lymphomas | 20.1 | 19 | 16 | 0.95 | 0.80 |
| Skin | 6.6 | 12 | 8 | 1.82 | 1.22 |
| Brain | 10.4 | 14 | 17 | 1.35 | 1.63 |

*Expected deaths are based upon white male age-specific U.S. death rates of the U.S. National Center for Health Statistics, 1967-1976.

(BE): Best evidence. Number of deaths categorized after review of best available information (autopsy, surgical, clinical).

(DC): Number of deaths as recorded from death certificate information only.

From a purely statistical point of view, in view of the increased incidence of cancer of several sites among asbestos insulation workers, it was expected that a proportion of these men would suffer multiple cancers simultaneously, even beyond the tendency of such findings to be made among individuals with cancer, in general.[12] Again, this would not be reflected in tabulations of causes of death by single underlying cause, as is the usual practice. Analysis demonstrated one hundred malignant neoplasms present but not causing death (Table 14). Sometimes these additional neoplasms were

TABLE 14

MORTALITY EXPERIENCE AMONG 17,800 ASBESTOS INSULATION WORKERS IN THE UNITED STATES AND CANADA 1967-1976 OBSERVATIONS IN 2271 CONSECUTIVE DEATHS

| Malignant Neoplasms Present, but not Causing Death* Site | Number |
|---|---|
| Lung | 24 |
| Pleural mesothelioma | 2 |
| Peritoneal mesothelioma | 1 |
| Esophagus | 0 |
| Stomach | 1 |
| Colon | 19 |
| Oropharynx | 3 |
| Larynx | 5 |
| Kidney | 3 |
| Other | 42† |
| | 100‡ |

*Twenty-one of these neoplasms were mentioned on the death certificate (but were not categorized as underlying cause of death).

†Including leukemia 5, lymphoma 3, bladder 5, prostate 13, thyroid, etc.

‡In 92 individuals; total includes multiple cancers in eight cases.

mentioned on the death certificate but as an "other significant condition," not in the section on the underlying cause of death. Forty were present among the 1064 cases where death was due to causes other than cancer or asbestosis (Table 15). Among the 168 deaths of asbestosis, cancer was also present in 7, 6 of these being bronchogenic carcinoma. Analysis of the circumstances leading to death, however, indicated that the underlying cause was asbestotic pulmonary insufficiency, and that the lung cancers were present but with no decisive influence at the time of death. Nineteen other cancers were present among the 486 deaths of lung cancer and 10 other cancers accompanied the 175 deaths of mesothelioma. There were 9 "incidental" neoplasms among the 99 deaths of gastrointestinal cancer. Although experiences are so far limited, it may not be wholly unexpected that there were proportionately more incidental neoplasms accompanying deaths of colon-rectum cancer, compared to those of lung cancer (8.5% vs. 3.9%). One may speculate that this could be due to the longer

TABLE 15

MORTALITY EXPERIENCE AMONG 17,800 ASBESTOS INSULATION WORKERS IN THE UNITED STATES AND CANADA 1967-1976: OBSERVATIONS IN 2271 CONSECUTIVE DEATHS NUMBER OF INCIDENTAL MALIGNANT NEOPLASMS (NOT CAUSING DEATH) IN RELATION TO UNDERLYING CAUSE OF DEATH AS ESTABLISHED BY BEST EVIDENCE (BE)

| Underlying Cause of Death | Number of Deaths of Underlying Cause | Incidental Malignant Neoplasms | |
|---|---|---|---|
| | | No. of Deaths | Total Cancers |
| Cancer all sites | 995 | 45 | 50 |
| Cancer of lung | 486 | 17 | 19 |
| Pleural mesothelioma | 63 | 4 | 4 |
| Peritoneal mesothelioma | 112 | 5 | 6 |
| Cancer of esophagus | 18 | 1 | 1 |
| Cancer of stomach | 22 | 3 | 3 |
| Cancer of colon-rectum | 59 | 5 | 5 |
| Cancer of larynx | 11 | 0 | 0 |
| Cancer of pharynx, buccal cavity | 21 | 2 | 3 |
| Cancer of kidney | 19 | 0 | 0 |
| All other cancers | 184 | 8 | 9 |
| Noninfectious pulmonary diseases, total | 212 | 10 | 10* |
| Asbestosis | 168 | 7 | 7* |
| All other causes | 1064 | 37 | 40 |
| Total | 2271 | 92 | 100 |

*Six of these were lung cancer.

clinical course of many patients with colon-rectum cancer, compared to lung cancer, with greater opportunity, simply in terms of time, to develop additional disease.

Multiple cancers were present, overall, in 2.1% of deaths among these asbestos insulation workers (48 of 2271). It is perhaps to be expected that this was more likely to be the case among those for whom cancer was the primary cause of death (4.5%), while only 3 of the 1276 other deaths had this finding.

It is now well appreciated that most asbestos associated disease is first seen after considerable periods from onset of exposure in both occupational and environmental circumstances. This is true both for the presence and extent of parenchymal fibrosis and pleural fibrosis and/or calcification,[3,13] and for asbestos-associated neoplasms.[14]

Some limited excess disease was observed in less than 20 years from onset of exposure (Table 16). Among 12,683 men with such experience, covering 89,462 man-years of observation, the number of cancer deaths was about doubled, with 42.6 deaths expected and 83 observed. There were no excess deaths of gastrointestinal cancer and only 5 deaths of mesothelioma, with these in the 15-19 years from onset category. Age, year and sex specific mortality data of the U.S. National Cancer for Health Statistics indicated that 11.9 deaths of lung cancer were to be expected. Thirty-six occurred. There were 8 deaths from asbestosis.

TABLE 16

DEATHS AMONG 17,800 ASBESTOS INSULATION WORKERS IN THE UNITED STATES AND CANADA JANUARY 1, 1967–DECEMBER 31, 1976. ANALYSIS BY DURATION FROM ONSET OF EMPLOYMENT

| | Before 20 Years from Onset | | | | | 20 or More Years from Onset | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| Total Men | 12,683 | | | | | 12,851 | | | | |
| Man-years of Observation | 89,462 | | | | | 77,391 | | | | |
| | | Observed | | Ratio o/e | | | Observed | | Ratio o/e | |
| Underlying Cause of Death | Expected* | (BE) | (DC) | (BE) | (DC) | Expected* | (BE) | (DC) | (BE) | (DC) |
| Total deaths, all causes | 282.9 | 325 | 325 | 1.15 | 1.15 | 1376.0 | 1946 | 1946 | 1.41 | 1.41 |
| Cancer, all sites | 42.6 | 83 | 77 | 1.95 | 1.81 | 277.1 | 912 | 845 | 3.29 | 3.05 |
| Cancer of lung | 11.9 | 36 | 32 | 3.03 | 2.69 | 93.7 | 450 | 397 | 4.80 | 4.24 |
| Pleural mesothelioma | † | 2 | 2 | — | — | † | 61 | 23 | — | — |
| Peritoneal mesothelioma | † | 3 | 0 | — | — | † | 109 | 24 | — | — |
| Mesothelioma, n.o.s. | † | 0 | 1 | — | — | † | 0 | 54 | — | — |
| Cancer of esophagus | 0.6 | 1 | 1 | — | — | 6.5 | 17 | 17 | 2.64 | 2.64 |
| Cancer of stomach | 1.5 | 1 | 0 | — | — | 12.7 | 21 | 18 | 1.65 | 1.42 |
| Cancer of colon-rectum | 4.1 | 4 | 4 | — | — | 34.0 | 55 | 54 | 1.62 | 1.59 |
| Cancer of larynx | 0.4 | 2 | 2 | — | — | 4.3 | 9 | 7 | 2.09 | 1.63 |
| Cancer of pharynx, buccal | 1.3 | 3 | 2 | — | — | 8.8 | 18 | 14 | 2.05 | 1.59 |
| Cancer of kidney | 1.1 | 3 | 3 | — | — | 7.0 | 16 | 15 | 2.29 | 2.14 |
| All other cancer | 21.7 | 28 | 30 | 1.29 | 1.38 | 110.1 | 156 | 222 | 1.42 | 2.02 |
| Noninfectious pulmonary diseases, total | 5.2 | 8 | 11 | 1.54 | 2.12 | 53.8 | 204 | 177 | 3.78 | 3.28 |
| Asbestosis | † | 8 | 2 | — | — | † | 160 | 76 | — | — |
| All other causes | 235.1 | 234 | 237 | 1.00 | 1.01 | 1045.1 | 830 | 924 | 0.79 | 0.88 |

*Expected deaths are based upon white male age-specific U.S. death rates of the U.S. National Center for Health Statistics, 1967–1976.
†Rates are not available, but these have been rare causes of death in the general population.
(BE): Best evidence. Number of deaths categorized after review of best available information (autopsy, surgical, clinical).
(DC): Number of deaths as recorded from death certificate information only.

On the other hand, extensive disease was seen among the 12,051 men who had reached 20 or more years from onset during the decade of study. Here, 1376.0 deaths were anticipated; 1946 occurred. There were 160 deaths of asbestosis and 912 of cancer. It was at this time that bronchogenic carcinoma made its heaviest contribution, with 93.7 such deaths expected and 450 observed. One hundred and seventy deaths of mesothelioma were then seen and the increase in gastrointestinal cancer found. Table 17 depicts these data in some detail, in five-year periods from onset of employment. Lung cancer data are given as both expected and observed numbers of death. This practice cannot be followed for mesothelioma, where expected deaths cannot be computed for the general population. Instead, both the number of deaths of pleural and peritoneal mesothelioma, as well as the number of deaths of these causes per thousand persons years at risk are provided. The latter does not take into account variations in achieved age, but this may have less influence than achieved duration from onset of employment. It will be seen that very major increases in numbers of deaths of lung cancer are first seen at 15-24 years from onset of work, with continued further increases. The extraordinary increase in deaths of mesothelioma, both of the pleura and the peritoneum, is not observed until somewhat later, reaching 2.78 deaths per thousand person-years at risk for pleural mesothelioma at 35-39 years from onset of work, and 5.47 deaths of peritoneal mesothelioma per thousand person-years at 45 + years from onset.

TABLE 17

DEATHS AMONG 17,800 ASBESTOS INSULATION WORKERS IN UNITED STATES AND CANADA, JANUARY 1, 1967-DECEMBER 31, 1976
ANALYSIS BY DURATION FROM ONSET OF EMPLOYMENT

| Duration from Onset (Years) | Number of Men | Person-years of Observation | Lung Cancer | | | | | Pleural Mesothelioma | | | Peritoneal Mesothelioma | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | Observed | | Ratio o/e | | Number | | No./1000 Person-years | Number | | No./1000 Person-years |
| | | | Exp.* | (BE) | (DC) | (BE) | (DC) | (BE) | (DC) | (BE) | (BE) | (DC) | (BE) |
| -10 | 8,190 | 26,393 | 0.7 | 0 | 0 | — | — | 0 | 0 | 0 | 0 | 0 | 0 |
| 10-14 | 9,083 | 29,003 | 2.7 | 7 | 5 | 2.55 | 1.82 | 0 | 0 | 0 | 0 | 0 | 0 |
| 15-19 | 9,948 | 34,066 | 8.5 | 29 | 27 | 3.40 | 3.17 | 2 | 2 | 0.06 | 3 | 0 | 0.09 |
| 20-24 | 8,887 | 31,268 | 17.0 | 59 | 57 | 3.48 | 3.36 | 6 | 4 | 0.19 | 3 | 2 | 0.10 |
| 25-29 | 6,596 | 20,657 | 21.0 | 105 | 96 | 5.00 | 4.58 | 13 | 5 | 0.63 | 19 | 3 | 0.92 |
| 30-34 | 3,547 | 11,598 | 18.4 | 112 | 103 | 6.08 | 5.59 | 9 | 3 | 0.78 | 23 | 6 | 1.98 |
| 35-39 | 2,020 | 5,403 | 11.5 | 65 | 57 | 5.68 | 4.96 | 15 | 4 | 2.78 | 19 | 5 | 3.52 |
| 40-44 | 1,108 | 3,160 | 8.1 | 40 | 131 | 4.93 | 3.82 | 4 | 3 | 1.27 | 16 | 3 | 5.06 |
| 45 + | 1,448 | 5,305 | 17.8 | 69 | 53 | 3.89 | 2.98 | 14 | 4 | 2.64 | 29 | 5 | 5.47 |

*Expected deaths are based upon white male age-specific U.S. death rates of the U.S. National Center for Health Statistics, 1967-1976. Smoking habits not taken into account.

(BE): Best evidence. Number of deaths categorized after review of best available information (autopsy, surgical, clinical).

(DC): Number of deaths as recorded from death certificate information only.

In another reflection of the clinical concerns among these workers, Table 18 indicates that approximately one-third of all deaths were due to lung cancer at 30-34 years from onset, while mesothelioma accounted for 13% of all deaths at 35-39 years.

Altogether, lung cancer was responsible for 21% of all deaths observed in this cohort and mesothelioma for 8%.

TABLE 18

DEATHS AMONG 17,800 ASBESTOS INSULATION WORKERS IN THE UNITED STATES AND CANADA, JANUARY 1, 1967 DECEMBER 31, 1976.
ANALYSIS BY DURATION FROM ONSET OF EMPLOYMENT

| Years from Onset of Employment | Total Deaths | Percent of All Deaths | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | Lung Cancer | | Mesothelioma | | | | | |
| | | | | Pleural | | Peritoneal | | Total | |
| | | (BE) | (DC) | (BE) | (DC) | (BE) | (DC) | (BE) | (DC) |
| <10 | 51 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 10-14 | 85 | 8 2 | 5.9 | 0 | 0 | 0 | 0 | 0 | 0 |
| 15-19 | 189 | 15.3 | 14.3 | 1.1 | 1.1 | 1.6 | 0 | 2.7 | 1.6 |
| 20-24 | 320 | 18.4 | 17.8 | 1.9 | 1.3 | 0 9 | 0.6 | 2.8 | 2.5 |
| 25-29 | 388 | 27.1 | 24.7 | 3 4 | 1 3 | 4.9 | 0.8 | 8.3 | 5.2 |
| 30-34 | 340 | 32.9 | 30.3 | 2 7 | 0.9 | 6.8 | 1.8 | 9.4 | 6.5 |
| 35-39 | 253 | 25.7 | 22.5 | 5 9 | 1.6 | 7 5 | 2.0 | 13.4 | 7.9 |
| 40-44 | 203 | 19.7 | 15.3 | 2.0 | 1.5 | 7 9 | 1.5 | 9.9 | 6.4 |
| 45+ | 442 | 15.6 | 12.0 | 3.2 | 0.9 | 6.6 | 1.1 | 9.7 | 4.1 |
| Total | 2271 | 21.4 | 18.9 | 2.8 | 1 1 | 4 9 | 1.1 | 7.7 | 4.6 |

*Total includes mesotheliomas not specified as either pleural or peritoneal.
(BE). Best evidence Number of death categorized after review of best available information (autopsy, surgical, clinical).
(DC) Number of deaths as recorded from death certificate information only.

## CONCLUSION

The study results indicate a high increase in risk of lung cancer associated with asbestos exposure, but the lack of exposure data makes it difficult to show a dose-response relationship.

15. Asbestos cement building materials plant workers have been studied[87] to determine the risk of respiratory malignancy in relation to duration, degree, and fiber type of exposure to asbestos. Subjects were classified into 5 total dust categories for which mean length of follow-up and mean age at initial exposure are comparable. (Table 1)

TABLE 1

COHORT BY FOLLOW-UP WITHIN EXPOSURE CATEGORIES

| Total Dust within 20 Yr of Initial Exposure (mppcf-yr*) | No | Mean Follow-Up (yr.) | Mean Age at Initial Exposure (yr) |
|---|---|---|---|
| ≤ 10 | 3,037 | 28.7 | 27.8 |
| 11-50 | 1,303 | 27.3 | 27.4 |
| 51-100 | 383 | 28.1 | 27.6 |
| 101-200 | 344 | 27.3 | 27.7 |
| > 200 | 878 | 28.7 | 28.0 |

*Million particles per cubic foot-yr.

Using the standard man-yr approach, expected numbers of deaths for each exposure category were calculated on the basis of race-age-cause-specific rates for both the U.S. and Louisianna male populations for 1950, 1960, and 1970.

Cause-specific standard mortality ratios, SMR (100 x observed number of deaths/expected number), were obtained for various causes for each of the 5 exposure categories (Table 2). SMR for all causes combined remain generally low, but increase slightly with degree of exposure: 60, 64, 75, 80, and 94. SMR for respiratory system neoplasms remain low for the 3 lowest exposure groups, but exceed 100 in the 2 highest categories: 77, 70, 26, 290, and 226. The very low SMR in the middle dust category is probably a chance occurrence; with only 3.8 respiratory neoplasm deaths expected, the probability (assuming a Poisson distribution) of observing one or fewer is 0.11.

TABLE 2

STANDARD MORTALITY RATIOS BY CAUSE WITHIN EXPOSURE CATEGORIES

| | Total Dust Within 20 Yr of Initial Exposure (mppcf-yr*) | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | < 10 (n = 2,037) | | 11-60 (n = 1,303) | | 61-100 (n = 363) | | 101-200 (n = 344) | | > 200 (n = 578) | |
| Cause of Death | O/E† | SMR‡ | O/E | SMR | O/E | SMR | O/E | SMR | O/E | SMR |
| All causes | 269/433.7 | 60 | 141/218.9 | 64 | 56/75.1 | 75 | 42/52.2 | 80 | 103/110.1 | 94 |
| All malignant neoplasms (140-209) | 54/77.3 | 70 | 27/37.1 | 73 | 7/12.9 | 54 | 14/9.6 | 147 | 19/19.6 | 91 |
| Digestive system (150-159) | 10/24.6 | 41 | 10/11.9 | 84 | 3/4.2 | 71 | 0/3.0 | - | 2/6.4 | 31 |
| Respiratory system (160-163) | 19/24.7 | 77 | 8/11.4 | 70 | 1/3.8 | 26 | 8/3.1 | 290§ | 14/6.2 | 226§ |
| Other (residual) | 25/28.0 | 89 | 9/13.8 | 65 | 3/4.9 | 61 | 6/3.4 | 147 | 2/7.2 | 28 |
| Major cardiovascular diseases (390-448) | 129/215.7 | 60 | 78/113.9 | 68 | 33/46.1 | 82 | 14/26.5 | 53 | 61/57.4 | 106 |
| All other causes | 76/140.7 | 54 | 26/47.8 | 54 | 12/16.2 | 74 | 6/11.6 | 78 | 20/23.8 | 84 |

* Millions of particles per cubic foot-yr

† Ratio of observed to expected deaths.

‡ Standard mortality ratio

§ $P < 0.01$ (number of observed deaths compared to the number expected, assuming a Poisson distribution).

In the 3 lowest exposure categories, the SMR for over-all mortality and respiratory neoplasms are comparable, as demonstrated graphically (figure 1) by the extensive overlap of their respective 95 per cent confidence intervals (based on a Poisson distribution). On the contrary, there was no overlap in either of the 2 highest exposure groups. Assuming no association between trace and cause of death, the close agreement of the over-all and respiratory malignancy SMR in the low exposure groups is additional evidence that, although some underestimation might have occurred because of those lost to view, there are no excess respiratory neoplasms in these categories.

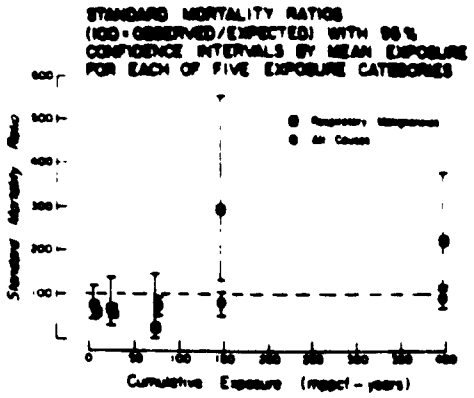



Fig 1 Standard mortality ratios with 95 per cent confidence intervals by mean exposure for each of 5 exposure categories.

No excess mortality occurred in any exposure group for any cause other than respiratory neoplasms.

The analysis was also performed with the number of deaths expected on the basis of Louisiana death rates. Because lung cancer rates are higher in Louisiana than in most states, the expected numbers of respiratory neoplasms are greater than with the U.S. rates, thus resulting in lower SMR. The patterns observed for the 5 exposure categories were the same as with the U.S. rates; over-all mortality SMR were 56, 64, 71, 73, and 83; respiratory neoplasm SMR were 64, 59, 23, 225, and 187. As with U.S. rates, no excess mortality other than for respiratory neoplasms were observed.

Two pleural mesotheliomas were diagnosed in the total study population: one person was employed for 10 months (with known exposure only to chrysotile), the other for 14 yr (with most of his employment in the pipe plant, which resulted in exposure to both chrysotile and crocidolite). Because these men died 18 and 19 yr after initial employment, respectively, neither fulfilled the cohort criterion of a minimum of 20 yr of follow-up and therefore are not included in this analysis. It was considered possible that this tumor was underdiagnosed in this population.

The results of Newhouse[112] suggest that the latent period for the development of asbestos-related neoplasms may be less than 20 yr, as with the 2 mesotheliomas found here. Using Newhouse's methodology, the effect of latency on the mortality experience of this population was assessed by performing the analysis by 5-yr periods after initial employment. In each analysis, persons with follow-up of less than the prescribed minimum are excluded; an individual person's exposure is calculated at the start of the particular time period. Because each period is only 5 yr in length, it was necessary to condense the original 5 exposure categories into three, although the expected numbers of deaths remain very small.

Results for the 2 lowest exposure categories (representing the original 3 lowest groups) indicate no discernible pattern for respiratory neoplasm SMR as time since initial exposure increases; those for the highest exposure category exhibit an increasing trend as long as 30 yr. since initial exposure (Table 3).

TABLE 3

RESPIRATORY MALIGNANCY STANDARD MORTALITY RATIOS BY 5-YR FOLLOW-UP AND TOTAL DUST AT START OF PERIOD

| Yr since Initial Exposure | No. | Total Dust at Start of 5-Yr Period (mppcf-yr) | | | | | |
|---|---|---|---|---|---|---|---|
| | | < 10 | | 10–100 | | > 100 | |
| | | O/E | SMR | O/E | SMR | O/E | SMR |
| 10–15 | 6,328 | 7/4.4 | 159 | 1/2.4 | 42 | 1/1.3 | 77 |
| 15–20 | 6,144 | 8/8.5 | 94 | 5/4.3 | 116 | 3/2.4 | 126 |
| 20–25 | 5,648 | 10/12.1 | 83 | 8/6.4 | 78 | 6/3.9 | 154 |
| 25–30 | 4,387 | 6/10.1 | 59 | 3/5.4 | 56 | 7/3.0 | 233* |
| 30–35 | 1,220 | 3/1.8 | 167 | 1/2.2 | 45 | 5/1.5 | 333* |
| > 35 | 313 | 0/0.6 | 0 | 0/1.0 | 0 | 4/1.3 | 308* |

For definitions of abbreviations, see table 2.

*P < 0.05 (number of deaths observed compared to number of deaths expected, assuming a Poisson distribution).

To compare the preceding results with those which would have been obtained with a different study design[115], an alternate method of analysis was performed for this cohort (men with at least 20 yr of follow-up) by considering 4 control subjects for each case of lung cancer. These control subjects were selected at random from among men in the cohort who were born in the same year as the cancer patient, were of the same race, had survived at least into the year following that in which the patient died, and if they subsequently died, did not die of a malignancy.

The mean total dust exposure (accumulated within 20 yr. after initial employment) was 164.1 mppcf-yr. for the cancer patients and 77.8 for the control subjects. A 2-way analysis of variance (the matched sets acting as a blocking factor), with Scheffe's multiple comparisons, found that there were no differences among the exposure means of the 4 sequences of control subjects, but that the mean dust exposure for the patients was significantly greater than that of the control subjects (P  0.005).

The distributions of the cancer patients and the control subjects by total exposure to dust are presented in Table 4. The odds ratio, an estimate of relative risk, was calculated for each category relative to the lowest degree of exposure.

TABLE 4

LUNG CANCER CASES AND MATCHED CONTROLS (4 PER CASE): TOTAL DUST EXPOSURE AND ODDS RATIOS

| Total Dust within 20 Yr of Initial Exposure (mppcf-yr*) | No. Cases | No. Controls | Odds Ratio† (Relative to Lowest Category) |
|---|---|---|---|
| < 10 | 17 | 87 | 1.00 |
| 10-99 | 7 | 36 | 1.14 |
| 99-199 | 1 | 11 | 0.52 |
| 199-299 | 8 | 16 | 2.06‡ |
| > 299 | 14 | 29 | 2.78‡ |
| Total | 47§ | 188 | |

* Million particles per cubic foot-yr.

† Usual estimate of relative risk.

‡ $P < 0.05$, based on a $\chi^2$ (1) distribution.

§ The total of 51 respiratory malignancy deaths in table 2 resulted from random allocation of deaths without certificates.

The over-all pattern of the odds ratio is similar to that of the respiratory malignancy SMR: the risk in the second exposure category is comparable to that in the lowest, an unexplained dip occurs in the third category (doubtless the same chance occurrence), and a significantly greater risk is observed at the 2 highest exposure categories.

Because information had already been collected on the entire cohort, the case-control approach, using only a subset of the population, does not make full use of the data available. Moreover, although this alternate approach provides estimation of the risk for each exposure category relative to the lowest category, no assessment of the risk experienced in the lowest category is possible. Despite these limitations, the observed pattern of risk across exposure categories was similar to that obtained with man-yr., prospective design, and analysis.

The preceding analysis was based on cumulative dust exposure, which has 2 components: (1) duration of exposure, and (2) average dust concentration. To assess the contribution of each, the population was divided into 9 duration-by-average-concentration categories. For these groups, the mean values of each variable within a fixed category were comparable across the categories of the other, and mean follow-up times were homogeneous (Table 5).

TABLE 5

COHORT BY DURATION AND CONCENTRATION OF EXPOSURE

| Average Dust Concentration (mppcf)* | Duration of Employment (yr) | | |
|---|---|---|---|
| | ≤ 2 | 2–10 | > 10 |
| ≤ 5 | n = 1,223 | n = 204 | n = 168 |
| | 4.6† | 4.2 | 3.2 |
| | 0.5‡ | 4.7 | 21.6 |
| | 28.8§ | 27.5 | 28.3 |
| 5–20 | n = 1,691 | n = 361 | n = 888 |
| | 17.9 | 13.6 | 12.9 |
| | 0.5 | 4.6 | 21.7 |
| | 27.9 | 28.2 | 27.6 |
| > 20 | n = 764 | n = 288 | n = 174 |
| | 34.6 | 29.4 | 26.7 |
| | 0.7 | 4.4 | 22.8 |
| | 27.1 | 28.7 | 28.7 |

*Million particles per cubic foot.
†Mean average dust concentration (mppcf).
‡Mean length of employment (yr).
§Mean length of follow-up (yr).

The SMR for respiratory malignancy for these groups (Table 6) generally indicate increasing risk with duration of employment, which is concentration dependent, and increasing risk with average concentration, which is duration dependent. These results are consistent with others,[88] which indicate that it is not sufficient to equate total exposure with either duration or average concentration; each constitutes an important component of risk, and each exhibits degrees with no apparent excess hazard.

TABLE 6

STANDARD MORTALITY RATIOS FOR RESPIRATORY MALIGNANCY BY DURATION OF EMPLOYMENT AND AVERAGE DUST CONCENTRATION

| Average Dust Concentration (mppcf)* | Duration of Employment (yr) | | | |
|---|---|---|---|---|
| | ≤ 2 | 2–10 | > 10 | All Durations |
| ≤ 5 | 7/10.0† | 2/3.2 | 1/1.0 | 10/14.1 |
| | 70 | 61 | 98 | 71 |
| 5–20 | 12/17.1 | 1/2.8 | 12/6.2 | 25/26.1 |
| | 70 | 36 | 231‡ | 169 |
| > 20 | 5/5.3 | 2/2.5 | 7/2.2 | 19/10.0 |
| | 94 | 120 | 318‡ | 189 |
| All dust concentrations | 24/32.4 | 5/7.5 | 20/9.3 | |
| | 74 | 69 | 216‡ | |

*Million particles per cubic foot.
†Ratio of observed deaths to expected deaths.
‡P < 0.01 (based on a Poisson distribution).

In assessing the possible influence of fiber type exposure on risk of respiratory malignancy, workers with exposure to chrysotile only (n = 4,201) were compared with 2 groups of workers exposed to crocidolite: those with steady employment in the pipe plant (n = 1,004) and those with intermittent exposure to crocidolite through occasional maintenance work in that area (n = 235). Persons with exposure to amosite (n = 205) were excluded from this analysis. All follow-up times were similar, and total fiber exposures were comparable among the fiber type groups within each category of exposure (Table 7).

TABLE 7

COHORT BY TYPE AND LEVEL OF FIBER EXPOSURE*

| Exposure | Total Fiber Exposure within 20 Yr of Initial Employment (mppcf-mos†) | | |
|---|---|---|---|
| | < 20 | 20–200 | > 200 |
| No crocidolite exposure | n = 2,503<br>6.0‡<br>26.9§ | n = 1,337<br>64.0<br>28.2 | n = 361<br>665.6<br>29.8 |
| Intermittent exposure to crocidolite in pipe plant | n = 44<br>6.2<br>26.4 | n = 86<br>69.7<br>27.3 | n = 105<br>663.6<br>30.6 |
| Steady employment in pipe plant with crocidolite exposure | n = 221<br>10.5<br>26.6 | n = 363<br>77.0<br>26.9 | n = 420<br>668.2<br>27.2 |

*Subjects with exposure to amosite are excluded (n = 205).
†Millions of particles per cubic foot-months.
‡Mean total fiber exposure (mppcf-mos).
§Mean length of follow-up (yr).

The pattern that emerges from the SMR (Table 8) suggests that the addition of crocidolite to chrysotile enhances the risk for respiratory malignancy, particularly for those workers exposed intermittently in maintenance jobs. The exposure history of this latter group is characterized by exposure to high concentrations of dust for short periods of time.

TABLE 8

STANDARD MORTALITY RATIOS FOR RESPIRATORY MALIGNANCY BY FIBER TYPE

| | Total Fiber Exposure within 20 Yr of Initial Employment (mppcf-mos*) | | | |
|---|---|---|---|---|
| | < 20 | 20–200 | > 200 | Total |
| No crocidolite exposure | 12/21.4<br>56 | 10/13.0<br>77 | 8/4.4<br>182 | 30/38.8<br>77 |
| Intermittent exposure to crocidolite in pipe plant | 2/0.2<br>1,000† | 0/0.7<br>0 | 5/1.4<br>357† | 7/2.3<br>304† |
| Steady employment in pipe plant with crocidolite exposure | 1/1.0<br>100 | 1/1.9<br>53 | 7/2.9<br>241† | 9/5.8<br>155 |

*Million particles per cubic foot months.
†$P < 0.05$

CONCLUSION

The risk increased more steeply with increased quantitative exposure than with increased duration of employment. Excess mortality for lung cancer was observed only for groups with moderate and high cumulative exposure (SMR 2.9 and 2.3).

There was no detectable excess risk of lung cancer in persons employed for less than 2 years or with low exposure. The risk appears high for two subgroups exposed to crocidolite, but only in the high exposure group ( 200 mppcf-yr.). There was no increased risk observed for gastrointestinal cancer in any subgroup.

There were 2 pleural mesotheliomas observed (one employed less than 1 year and one for 14 years).

There was no increased risk of respiratory cancer for exposures below 10 mppcf-yrs.

There was a low (75%) tracing rate.

16. In a study of female asbestos workers[35], compared with national rates there was an excess overall mortality among those who worked in jobs with low to moderate exposure (Table 2), which was partly accounted for by deaths from cancer.

Table 2

Mortality of Women with Low to Moderate Asbestos Exposure

| Registered cause of death | All periods of employment (126 women) | |
|---|---|---|
| | Obs. | Exp. |
| All causes | 29[1] | 18.1 |
| Cancer of lung and pleura | 2[1] | 0.3 |
| Other cancer | 8 | 4.4 |
| Respiratory disease excluding cancer | 2 | 2.2 |
| Other disease | 17 | 11.2 |

[1] $P < 0.05$

In the group with severe exposure who had worked for less than two years (Table 3), there was an excess of cancer of the lung and pleura.

Table 3

Mortality of Women with Severe Exposure

| Registered cause of death | Duration of employment: Less than 2 yrs (557 women) Obs. | Exp. | More than 2 yrs (239 women) Obs. | Exp. |
|---|---|---|---|---|
| All causes | 55 | 49.9 | 56[3] | 24.5 |
| Cancer of lung and pleura | 6[3] | 1.0 | 14[3] | 0.5 |
| Other cancer | 16 | 12.4 | 17[8] | 6.1 |
| Respiratory disease excluding cancer | 10 | 7.4 | 11[2] | 3.6 |
| Other disease | 23 | 29.1 | 14 | 14.3 |

[2] P 0.01
[3] P 0.001

However, the most marked increased mortality was in those with severe exposure who had worked for more than two years in the asbestos factory; in this group there were excess deaths from cancer of the lung and pleura, from other cancers, and from respiratory diseases. Three deaths registered as cancer of the pleura were identified as pleural mesotheliol tumors; in all there were 11 mesotheliomas, six of pleural and five of peritoneal origin.

In this study the results were assessed by comparing the number of observed deaths with the number of expected deaths.[36] The "expected" deaths were calculated by the "man-years" method, multiplying years of risk by death rates. Excess mortality has been tested by treating the observed number of deaths as a Poisson variable with expectation equal to the man-years expected number of deaths. Mortality as a function of length of time from first exposure is shown in Table 5.

Table 5

Mortality by Length of Follow-Up since First Exposure

| Registered cause of death | Years since first exposure: Less than 10 (922 women) | | 10 to 20 (692 women) | | More than 20 (655 women) | |
|---|---|---|---|---|---|---|
| | Obs. | Exp. | Obs. | Exp. | Obs. | Exp. |
| All causes | 25 | 23.7 | 36[1] | 29.3 | 79[3] | 39.4 |
| Cancer of lung and pleura | 0 | 0.2 | 3[1] | 0.6 | 19[3] | 1.1 |
| Other cancer | 5 | 4.2 | 10 | 7.8 | 26[3] | 10.8 |
| Respiratory disease excluding cancer | 9 | 6.1 | 5 | 3.4 | 9[1] | 3.7 |
| Other disease | 11 | 13.2 | 18 | 17.5 | 25 | 23.8 |

[1] $P < 0.05$
[3] $P < 0.001$

There were four deaths in all registered as cancer of the ovary; three of these occurred among women with severe and long exposure and, compared with the expected number of 0.6 in this particular group, this was a significant finding ($p=0.0025$). The histological review suggested that at least two of the other deaths in the group that were registered as carcinomatosis were due to this cause. The possibility that ovarian cancer may be caused by exposure to certain hydrous magnesium silicates such as talc and asbestos has been raised by several researchers. Strong evidence of a link was found by Graham and Graham,[36] who injected mice, hamsters, guinea pigs, and Dutch rabbits with tremolite asbestos. The mice and hamsters showed no lesions, presumably because of a protective layer of peritoneum surrounding their ovaries, which is absent in the guinea pig and rabbit. Both of these latter species developed an atypical papillary pattern of ovarian epithelial hyperplasia, which the authors suggested was similar to early ovarian epithelial tumors in women. Additionally, birefringent bodies were observed in sections of six out of twelve ovarian tumors, and none of nine normal controls. These bodies were thought to be asbestos (but were not examined).

APPENDIX II

1. Mesothelioma in Pet Dogs Associated with Exposure of Their Owners to Asbestos. Glickman, L.T., Domanski, L.M., Maguire, T.G., Dubielzig, R.R., and Churg, A. Environ. Res., 32, 305-313 (1983)

This paper describes the findings of an epidemiological study of pet dogs and the incidence of mesothelioma and asbestos exposure. Eighteen histologically-confirmed canine mesotheliomas were diagnosed at the Veterinary Hospital of the University of Pennsylvania (VHUP), Philadelphia, from April 1977 to December 1981. An asbestos-related occupation or hobby of a household member and use of flea repellents on the dog were significantly associated with mesotheliomas. In addition, there was a trend indicating an increased risk of mesotheliomas with an urban residence. Lung tissue from three dogs with squamous cell carcinoma of the lung had higher levels of chrysotile asbestos fibers than lung tissue from control dogs. The VHUP is a major veterinary referral center for the Northeast and Middle-Atlantic regions of the U.S. Each year there are approximately 17,000 admissions and visits to the VHUP and an additional 6000 submissions of biopsy specimens to the Pathology Department (could not ascertain whether these numbers refer to all animals or to dogs only).

A cancer and noncancer control patient were selected from hospital records and matched to each mesothelioma case by age and date of diagnosis (± 1 year), sex, and breed. Excluded from the noncancer control group were dogs with any respiratory disease or suspected malignancy. Dogs with respiratory cancer were excluded from the cancer control group.

Because controls had been matched on age, sex, and breed, these characteristics for the cases were first compared to the entire canine hospital population. The odds ratio (OR), an estimate of the relative risk of disease for each category, was determined using the Mantel-Haenszel procedure.[1] Age was controlled in sex comparisons, and sex was controled in age comparisons. Odds ratios for other risk factors were determined for matched pairs using the cancer and non-cancer groups separately.[2] The control groups were then combined and odds ratios calculated for matched triplets. Using a 95% confidence interval, the null hypothesis of an odds ratio equal to one was tested with computer programs developed by Rothman and Boice.[3] Characteristics of the patients with mesothelioma and the source of asbestos exposure of their owners are listed in Table I. The distribution of mesothelioma by site was six (33%) peritoneal, five (28%) pleural, five (28%) both peritoneal and pleural, and two (11%) pericardial.

The mean age (± 1 SD) of the mesothelioma dogs was 8.0 ± 1.9 years; 17 (94%) were male and 15 (83%) were purebreeds. When compared to the entire canine hospital population, males had a relative risk for

TABLE 1

CHARACTERISTICS OF 18 CANINE PATIENTS DIAGNOSED WITH MESOTHELIOMA AT

| Patient | Breed | Sex | Age at diagnosis (years) | Year of diagnosis | Site of meso-thelioma[a] |
|---|---|---|---|---|---|
| 1 | Mixed | M | 12 | 1978 | P |
| 2 | German Shepherd | M | 7 | 1978 | P |
| 3 | German Shepherd | M | 9 | 1978 | P |
| 4 | Doberman Pinscher | M | 8 | 1978 | P&Pl |
| 5 | Irish Setter | F-S[b] | 8 | 1979 | Pe |
| 6 | Bouvier des Flandres | M | 8 | 1979 | P |
| 7. | Mixed[c] | M | 10 | 1979 | P&Pl |
| 8 | Bouvier des Flandres | M | 8 | 1979 | Pl |
| 9 | German Shepherd | M | 7 | 1979 | P&Pl |
| 10 | Boston Terrier | M | [illegible] | 1979 | P&Pl |
| 11 | Irish Setter | M | [illegible] | 1980 | Pl |
| 12 | German Shepherd | M | 10 | 1981 | P&Pl |
| 13 | Bernese Mtn. Dog | M | [illegible] | 1977 | Pl |
| 14 | Old Eng. Sheepdog | M | 6 | 1981 | Pe |
| 15 | German Shepherd | M | 8 | 1981 | P |
| 16 | German Short Hair Pointer | M | 11 | 1981 | Pl |
| 17 | Mixed | M | 8 | 1981 | Pl |
| 18 | German Shepherd | M | 6 | 1981 | P |

[a] P = peritoneal, Pl = pleural, Pe = pericardial

[b] Female-spayed

[c] Not included in case-control analysis. Unable to contact owner for interview

VHUP BETWEEN 1977 AND 1981, AND THEIR EXPOSURE TO ASBESTOS

| Type of asbestos exposure | | |
|---|---|---|
| Owner occupation (O) hobby (H) | Household neighborhood | Other possible |
| Auto body repair (O) | Extensive home remodeling | None |
| Auto mechanic (H) | Change of heating system | None |
| Truck repair (O) adjacent to shipyard | None | Accompanied owner to job adjacent to shipyard |
| None | None | None |
| Plumbing, heating sheet rock spackling (H) | Cement factory | None |
| None | None | Flea powder |
| — | — | — |
| None | None | None |
| Sheet rock spackling at shipyard (O) | Demolition and construction site | Flea powder |
| None | None | None |
| None | Home insulation, construction site | Flea powder |
| Pipefitting at shipyard (O) | None | Flea powder |
| None | None | None |
| None | Demolition & construction sites | None |
| Auto mechanic (O) | Home insulation | None |
| — | — | — |
| Oil burner and furnace installation (O) | None | Flea powder |
| Auto body and used parts supply (O) | None | Accompanied owner to work |

TABLE 2

MATCHED PAIR ANALYSIS OF RISK FACTORS FOR CANINE MESOTHELIOMA

| Risk factor | Noncancer controls | | | Cancer controls | | |
|---|---|---|---|---|---|---|
| | Odds ratio | No. D.P.[a] | Confidence limits (95%) | Odds ratio | No. D.P.[a] | Confidence limits (95%) |
| Domestic and owner occupational exposures | | | | | | |
| Home remodeling or construction | 0.3 | 8 | 0.1–1.2 | 0.4 | 10 | 0.1–1.6 |
| Addition of home insulation | 0.5 | 6 | 0.1–2.6 | 0.8 | 7 | 0.2–3.3 |
| Home in vicinity of asbestos-related industry | 2.0 | 6 | 0.4–10.6 | 0.8 | 7 | 0.2–3.3 |
| Occupation or hobby asbestos related | 8.0 | 9 | 1.4–10.6 | 2.3 | 10 | 0.6–8.7 |
| Urban (vs rural) residence of dog | | | | | | |
| First residence | ∞[b] | 5 | — | 1.5 | 9 | 0.4–5.3 |
| Longest residence | 4.0 | 5 | 0.5–30.3 | 1.2 | 11 | 0.4–3.9 |
| Residence at diagnosis | 2.0 | 6 | 0.5–10.6 | 1.0 | 10 | — |
| Management of dog | | | | | | |
| Source: stray vs all other | 2.0 | 3 | 0.2–21.0 | ∞[c] | 4 | — |
| Time outside: >50% vs <50% | 5.0 | 6 | 0.7–34.5 | 2.5 | 7 | 0.5–12.2 |
| Supervision: allowed to roam vs confined | 2.0 | 9 | 0.5–7.8 | 3.0 | 8 | 0.7–13.8 |
| Pesticides used on dog | | | | | | |
| Flea powder | 5.0 | 6 | 0.7–34.5 | 1.7 | 8 | 0.4–6.9 |
| Flea spray | 3.0 | 4 | 0.4–25.8 | 1.5 | 10 | 0.4–5.3 |
| Flea dip | 2.5 | 7 | 0.5–12.2 | 1.5 | 10 | 0.4–5.3 |
| Flea collar | 1.3 | 7 | 0.3–5.9 | 1.0 | 6 | — |
| Any pesticide | 11.0 | 5 | 1.5–82.1 | 5.0 | 6 | 0.7–35.5 |

[a] Number of Discordant Pairs

[b] Not able to calculate. The cases were all strays while the controls were of known origin

[c] Not able to calculate. The cases all had an urban residence while the controls had a rural residence

TABLE 3

ASBESTOS FIBER CONTENTS IN LUNG TISSUE OF DOGS

| Patient | Category | Age at Diagnosis (Years) | Fiber type (No. g dry wt.) | |
|---|---|---|---|---|
| | | | Chrysotile | Amphibole |
| | Mesothelioma | | | |
| 12 | | 10 | 3,100,000 | 0 |
| 14 | | 6 | 7,200,000 | 3,300,000 |
| 18 | | 6 | 22,000,000 | 760,000 |
| | Lung Cancer | | | |
| A | Squamous cell carcinoma | 12 | 8,200,000 | 4,800,000 |
| B | Bronchial alveolar carcinoma | 13 | 280,000 | 280,000 |
| C | Bronchial–alveolar carcinoma | 8 | 69,000 | 0 |
| | Controls[a] | | | |
| D | | 5 | 325,000 | 81,000 |
| E | | 9 | 700,000 | 0 |
| F | | 6 | 300,000 | 200,000 |
| G | | 6 | 2,900,000 | 720,000 |
| H | | 8 | 1,100,000 | 0 |
| I | | 8 | 0 | 340,000 |

[a] Non-respiratory disease and noncancer

mesothelioma of 16.6 ($CL_{95\%}$ 6.4-97.3). When dogs 1 to 4 years of age were assigned a relative risk of 1.0 the greatest risk was observed in dogs 5 to 9 years of age (OR = 16.9, $CL_{95\%}$ 3.4-84.3). The risk for purebreed dogs when compared to dogs of mixed breeding was 1.7 but this difference was not statistically significant ($CL_{95\%}$ 0.51-5.9). The relative risk for individual purebreeds represented by more than one dog with mesothelioma was Bouvier des Flandres (OR = 124.3, $CL_{95\%}$ 62.6-246.7), Irish Setter (OR = 5.3, $CL_{95\%}$ 1.4-9.6), and German Shepherd (OR = 3.3, $CL_{95\%}$ 1.3-8.2).

The cancer and noncancer control patients represented a wide variety of diseases and conditions; not more than two dogs had the same diagnosis. Owners of 16 of the 18 mesothelioma patients were contacted and interviewed. The OR for suspected risk factors for canine mesothelioma are shown in Table 2. The findings were similar when mesothelioma patients were compared to either the cancer or noncancer control group. However, for 11 of the 14 risk factors studied, a stronger association with mesothelioma was noted in the analysis using the noncancer controls. Exposure of the owner to asbestos at work or through a hobby was found to be significantly associated with mesothelioma in the analysis using noncancer controls, (OR = 8.0, $CL_{95\%}$ 1.4-45.9); when cancer controls were used the odds ratio was 2.3, but was not significant ($CL_{95}$ 0.6-8.7). The relative risk for mesothelioma with both control groups combined was 3.5 ($CL_{95\%}$ 1.1-11.0).

Information on the use of pesticides and insect repellents was obtained because talc may be contaminated with asbestos and other mineral fibers.[4] The relative risk for all forms of pesticides was elevated and was significant when any pesticide use was considered in comparison to noncancer controls (OR=11.0, $CL_{95\%}$ 1.5-82.1). The risk associated with any pesticide use when the control groups were combined was also significant (OR= 7.6, $CL_{95\%}$ 1.2-49.0). Preliminary microscopic observations of seven commercially available pet flea powders and sprays revealed large amounts of quartz, silicates, and silica, and small amounts of antigonite, a fiber closely related to chrysotile asbestos. While asbestos fibers were not specifically identified, exposure of humans to other mineral fibers has been associated with pulmonary disease (e.g., silicosis). Results of the lung tissue fiber analysis are presented in Table 3. The three dogs with mesothelioma had the highest levels of chrysotile fibers. The amphibole consisted of tremolite and actinolite, except in the case of control dog 1, where it was commercial amphibole in the form of amosite and crocidolite. The authors stated that the tremolite and actinolite were probably contaminants of the chrysotile.

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2. An Animal Model for Inhalation Exposure to Talc; performed by Wagner, J.C., Berry, G., Hill, R.J., and Skidmore, J.W., In: Dust and Disease, ed. Lemen, R. and Dement, M.J., Pathotox. Publ. Inc., pp. 389-392 (1979)

Methods: Ninety-six male and 96 female (barrier protected caesarian derived; Wistar strain) 6-8 week old rats were randomly allocated to one of the following groups:

(a) talc - Italian 00000 grade (92% talc mineral, 3% chlorite and 1% carbonate minerals; quartz was found in the powder at 0.5-1.0% level); no asbestos minerals of either tremolite or chrysotile varieties were detected;

(b) super fine chrysotile asbestos (SFA chrysotile);

(c) controls - no exposure to either material.

The animals were housed four to a cage except when in inhalation chambers (in a separate room) when there were 6 to a cage. Rats were fed on a proprietary brand of autoclaved cubes and water ad libitum; home cages were supplied with filtered air. There were sacrifices ten days after the end of each exposure period and at one year. The remaining animals were allowed to live until they died or appeared to be distressed. A full necropsy examination was carried out on all animals.

The dust clouds were generated for 7½ hours a day, 5 days a week. After 6 months' exposure half of the rats were removed and transferred to ordinary cages and were replaced by another 24 animals per dust. These rats were in turn removed and replaced after 3 months' exposure, and all exposure ceased after another 3 months (48 rats were exposed for 3 months, 24 for 6 months, and 24 for 12 months). The dosage was calculated as the product of concentration and time. The mean respirable dust concentration was 10.8 $mg/m^3$ for each dust and the cumulative doses, i.e., the product of concentration and time, were approximately 4100, 8200, and 16400 $mg/m^3$ hrs. for the 3-, 6-, and 12-month exposures.

Results: Survival data were not presented. The amount of dust in the lungs was determined for the sacrificed rats. For talc, the mean amounts of dust in the lungs were 2.8, 4.5, and 12.3 mg per rat at the end of exposures of 3, 6, and 12 months, respectively. In contrast, the amount of SFA crysotile was close to the detection limit of the method and was estimated as only 0.6 mg/rat after 12 months' exposure.

An assessment was made of the severity of fibrosis in the lungs of rats sacrificed at the end of exposure and one year later (see Table 1 below).

**TABLE 1.** Inhalation Experiment - Mean Fibrosis at End of Exposure and One Year Later (Number of Rats)

| Material | Time | Length of exposure 3 months | 6 months | 12 months |
|---|---|---|---|---|
| Italian talc | End of exposure | 2.2 (8) | 2.7 (6) | 3.4 (6) |
| | 1 year later | 2.4 (8) | 3.4 (4) | 4.6 (4) |
| SFA chrysotile | End of exposure | 2.8 (8) | 3.0 (6) | 3.2 (6) |
| | 1 year later | 2.2 (8) | 3.2 (4) | 4.2 (4) |
| Controls | End of exposure | 1.8 (8) | 1.9 (6) | 1.3 (6) |
| | 1 year later | 1.6 (8) | 1.5 (3) | 1.9 (3) |

The main features are that both Italian talc and SFA chrysotile produced fibrosis to a similar extent, and that there was some evidence of progression after exposure was discontinued in the longer exposed animals.

The number of rats with lung tumors are shown in Table 2. One adenoma occurred in the control group, two adenomata were observed in the rats exposed to talc, and 13 lung tumors, including one mesothelioma and 3 adenocarcinomata were observed in the SFA chrysotile group.

**TABLE 2.** Inhalation Experiment - Lung Tumors

| Material | Exposure | Number at risk[1] | Number of lung tumors: Adenomas | Adenomatosis | Adenocarcinomas | Mesotheliomas |
|---|---|---|---|---|---|---|
| Italian Talc | 3 months | 39 | 0 | 0 | 0 | 0 |
| | 6 months | 18 | 0 | 0 | 0 | 0 |
| | 12 months | 24 | 2 | 0 | 0 | 0 |
| SFA Chrysotile | 3 months | 40 | 0 | 0 | 0 | 1 |
| | 6 months | 18 | 1 | 2 | 1 | 0 |
| | 12 months | 22 | 3 | 3 | 2 | 0 |
| Controls | | 71 | 1 | 0 | 0 | 0 |

[1]Number surviving at least 300 days from start of exposure

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| Study No. | Type of Activity | Fiber Type | Exposure (how measured*) | No. in Cohort | Total Deaths (O/E) SMR | No. mesothel-iomas | Lung Cancer Obs exp. SMR | Slope | Gastrointestinal Cancer obs exp SMR RR | Time since first exposure | Duration of Exposure | Type of Control | Analysis method |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 57 | mining | chrysotile | mppcf<br>low: 2.5-4.2<br>medium: 4.3-9.4<br>high: 14.4-23.6<br>very high: 46.8-82.6<br>(1) | 10,939(M)<br>440(F) | 4463(M)<br>(1.06)<br>84(f)<br>(0.9) | 10(M)<br>1(F) | 230 184 1.25 | 0.14 mppcf-yr | 276 272.4 1.01 | 20+ years | At least one month | Quebec population | a,b |
| 81 | mining | chrysotile | 10-36 f/ml<br>(8) | 544 | 178<br>(1.11) | 1 | 28 11.1 2.5 | mppcf-yr<br>0.30 | 10 9.5 1.05 | 20 yrs | 20 yrs | Canadian death rates | |
| ● | mining | chrysotile | Cumulative exposure<br><100 f/y<br>≥100 f/y<br>(2,3) | 952 | 332<br>(1.55)<br>20 yrs<br>(207)<br>20 yrs<br>(137) | 1 | 11 10.4 106<br>20 yrs:<br>1 1.7 59<br>20 yrs:<br>10 8.7 115 | 0.17<br>f/ml-yr | 19 19.3 98<br>20 yrs:<br>4 4.8 83<br>20 yrs:<br>15 14.5 103 | 20 yrs<br>20 yrs | At least 30 days | National death rate (Italian) | a,c |
| 65 | friction materi-als | chrysotile chrocido-lite | Cumulative exposure (f-y/ml) (6)<br>0-9<br>10-49<br>50-99<br>100-356 | 13,460 | M 1339<br>(0.9)<br>F 299<br>(0.9) | 8<br>2 | M<br>51 139.5 1.09<br>F<br>8 11.3 0.71 | f/ml-yrs<br>0.06 | 103 107 0.96<br>29 27 1.1 | | At least 10 yrs | National rates in U.K. | a,d |
| 83 | friction materi-als | chrysolite | mppcf (1)<br>yrs level<br><1 2.28<br>1>5 2.06<br>5>20 1.56<br>≥20 1.06<br>Total 1.84 | 3641 | 1267 | 0 | 73 148.7 | 0.16 | 59 114.4 | 20 yrs | At least 1 month | Connect-icut rates | e,f |
| 73 | textile | chrysolite crocido-lite | 1951- 10.8 f/cc<br>1972 - 2.9 f/cc<br>(2,3) | 822<br>(M)<br>284<br>(F) | 293<br>(1.3)<br>24<br>(1.0) | 9<br>1 | 51 23.8 2.1<br>F<br>3 0.9 3.3 | | 16 15.7 1.02 | from 10 to greater than 20 yrs | At least 10 yrs | National death rates | |
| ● | | | | | | | | | | | | | |

| Study No. | Type of Activity | Fiber Type | Exposure (how measured*) | No. in Cohort | Total deaths (O/E) | No. mesothel-iomas | Lung Cancer | | | Slope | Gastrointestinal Cancer | | | | Time since first exposure | Duration of Exposure | Type of Control | Analysis method |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | | Obs | Exp | SMR | RR | | | | |
| | cement products | chrysotile crocido-lite | f-yr/ml (mean) (1) A - 44 B - 92 C - 180 | 328 | 125 | 11 | 37 | 5.6 | 6.6 | f/ml-yr 4.82 | 8 | 5.4 | 1.48 | | 20-33 yrs | at least 9 yrs | Ontario death rates | a |
| 70 | | | P=production workers 18 yr-112.5f-yr/ml M=maintenance workers C=unexposed workers | 186 | 58 (1.7) | 10 | 20 | 3.3 | 6.1 | K-0.067 | 4 | 2.5 | 1.6 | | | 18 yrs | | |
| 67 | general manufac-turing | chrysotile crocidolite amosite | mppcf (1) cumulative dust exposure <125 (62) 125-249 (182) 250-499 (352) 500-749 (606) 750 + (976) | 1075 | 781 (1.2) | 5 | 19<br>9<br>19<br>9<br>7<br>63 | 197.9<br>180.0<br>327.6<br>450.0<br>777.8<br>270.0 | | 0.658 mppcf-yr | 55 | 39.9 | 1.4 | | retired workers | Ave. 25 yrs (3-51) | US male population | g |
| 64 | general manufac-turing (tex-tiles insula-tion materials) | chrysotile crocidolite amosite | f/ml 2 5 5-10 ≥20 | 4600 (M) 922 (f) | 545 (1.24) 200 (1.69) | 46<br>21 | 103<br>27 | 43.2<br>3.2 | 2.4<br>8.4 | | 40<br>20 | 34<br>10.2 | 118<br>196 | | from 10-30 yrs | variable | national death rates of U.K. | |
| 74 | insula-tors | chrysotile crocidolite amosite | (6) 4-12 f/ml | 632 | 478 | 38 | 93 | 13.3 | 699 | | 43 | 15.1 | 285 | | 20+yrs | | U.S. death | |

| Study No. | Type of Activity | Fiber Type | Exposure (how measured*) | No. in Cohort | Total deaths (O/E) | No. mesothel-iomas | Lung Cancer | Slope | Gastrointestinal Cancer Obs | Exp | SMR | RR | Time since first exposure | Duration of Exposure | Type of Control | Analysis method |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 74 | insula-tors | chrysotile amosite | 4-12 f/ml (6) | 17,800 | 2271 (1.4) | 175 | 429 105.6 4.60 | EPA .0107 1.01 (f/m/yr) | 94 | 59.4 | 1.67 | | under 20 yrs over 20 years | | U.S. death rates | |
| 88 | general manuf. | chrysotile crocidolite amosite | mppcf <125 125-249 250-400 500-749 750+ | 1348 | 754 (115) | not reported | 58 21.7 267.3 | | 53 | 41.8 | 126.8 | | 20 yrs | ave. 25 yrs | urban popula-tion US males | |
| 87 | cement products | chrysotile crocidolite | total dust w/in 20 yrs initial exposure mppcf-yr (1) <10 11-50 51-100 101-200 >200 | 5645 | 601 (0.7) | 2 | <10 19 24.7 .77<br>11-50 8 11.4 .70<br>51-100 1 3.8 .26<br>101-200 9 3.1 2.90<br>>200 14 6.2 2.26<br>Total 51 49.2 1.0 | mppcf-yr .44 | 10<br>10<br>3<br>0<br>2<br>Total 25 | 24.6<br>11.9<br>4.2<br>3<br>6.4<br>50.1 | .41<br>.84<br>.71<br>-<br>.31<br>0.5 | | >20 yrs | - | US and Louisiana death rates | (a) |

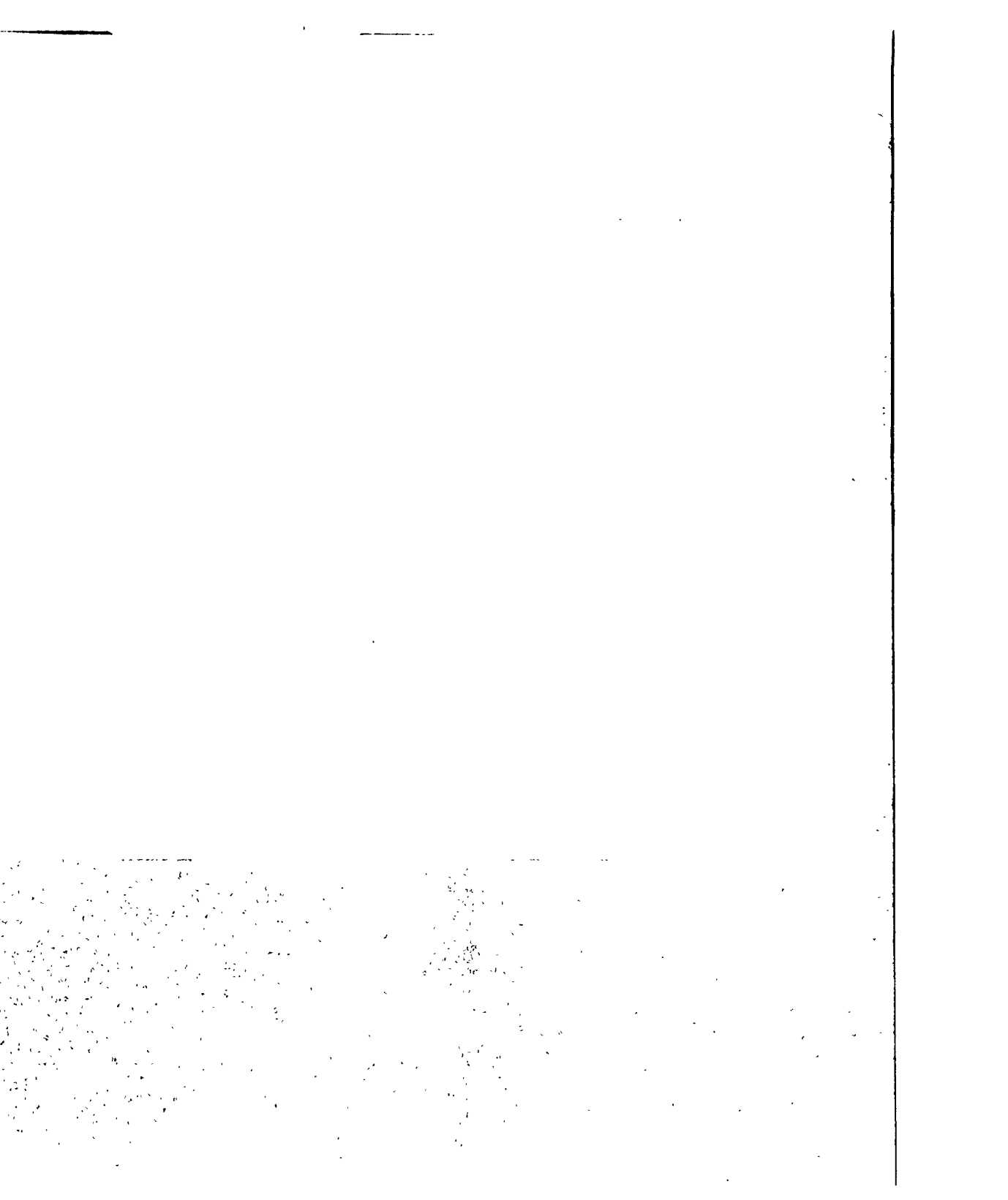
| Study No. | Type of Activity | Fiber Type | Exposure (how measured*) | No. in Cohort | Total deaths (O/E) | No. mesothel-iomas | Lung Cancer | Slope | Gastrointestinal Cancer Obs Exp SMR RR | Time since first exposure | Duration of Exposure | Type of Control | Analysis method |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 84 | Textile | chrysotile crocidolite | cumulative exposure(1,5) (f/ml-yrs) 100-400+ 30f/ml (ave.) | 679 | 201 | 7 | 28 18.6 1.5<br>12 4.65 2.6 | f/ml-yr 1.0 | 14 12.6 1.1 | 10-30 yrs<br>10-25 yrs | at least 10 yrs | national death rates | |
| 85 | Textile | chrysotile crocidolite | mppcf (ave. dust conc.) yrs / level: <1 2.11; 1,<5 1.86; 5,<20 1.67; ≥20 1.23; Total (1) 1.8 | 2410 | 857 (1.27) | 1 | 66 (not given)<br>59 199.5 | 8.2<br>mpcf.y 0.059 | 36 (not given)<br>26 151.7 | at least 10 yrs<br>20 yrs | at least one month | S.Carolina rates | e,f |
| 86 | Textile | chrysotile amosite crocido-lite | mppcf (ave. dust conc.) yrs / level: <1 2.60; 1,<5 2.40; 5,<20 2.73; ≥20 1.58; Total (1) 2.32 | 4022 | 1392 (SMR= 109) | 14 | 70<br>53 105 | mpcf.y 0.051 | 73<br>54 112.7 | 20 yrs | at least 1 month | Penna. rates | e,f |

Analysis method used

(a) man-years method-case
(b) case-Lea-multiple controls analysis
(c) McDonald & Liddell
(d) case-control - Liddell
(e) Mantel-Haenszel log-rank method
(f) man-yrs life table method - Hill
(g) modified lifetable method - Enterline

Exposure measurement procedure

(1) midget impinger
(2) membrane filter collection
(3) phase contrast microscopy
(4) thermal precipitator
(5) static membrane filter
(6) simulated conditions
(7) actual conditions
(8) NIOSH methods
(9)
(10) not stated



# 7
# Risk Assessment

Exposure, laboratory, and epidemiological data provided earlier in this report are used in this chapter to make quantitative and qualitative (or comparative) assessments of risks from exposure to asbestiform fibers. To place the discussion in context, the chapter begins with a brief general discussion of risk assessment and a few special considerations concerning asbestos and related fibrous materials.

Various difficulties often limit the accuracy and precision with which risk to human health can be estimated. Nevertheless, when the data base is good, the risk estimates can be sufficiently informative to aid policy judgments. Some of the factors that enhance the usefulness of the data include dose-response information based on several accurately known exposure levels; knowledge of physiologic and metabolic factors that affect exposure of body tissues; an understanding of the mechanism by which the substance results in toxicity; knowledge of the extent to which experimental systems mimic the human response; and an understanding of the properties of a complex and variable substance that account for its toxicity.

Many of these issues apply in the assessment of risk from asbestiform fibers, which have varying physical and chemical properties. Some members of the class, the commonly used naturally occurring forms of asbestos, have been clearly shown to cause fibrosis of the lung and pleura as well as cancer of the lung, mesothelium, and possibly the gastrointestinal tract in humans. Some occupational data on other fibers are also available, and considerable numbers of experimental studies have been conducted. It is reasonable from a biological viewpoint to use data from occupational studies to derive estimates of risk from nonoccupational exposure. However, differences in route of exposure, type and characteristics of fiber, exposure levels, and time patterns must be considered. Moreover, because working populations are generally healthier than the public at large, the latter may contain a higher proportion of more susceptible individuals.

## THE PROCESS OF RISK ASSESSMENT

The principles guiding the assessment of health risks from environmental substances were recently reviewed by a committee of the

National Research Council (1983). These principles are summarized here to provide a framework for assessing the health risks from exposure to asbestiform fibers.

The numerous terms used to describe different aspects of risk assessment include "hazard assessment," "hazard identification," "risk assessment," "qualitative risk assessment," "dose-response assessment," "comparative risk assessment," "quantitative risk assessment," and "risk characterization." The use of these terms has not been standardized.

Three concepts are generally incorporated into the risk assessment process. First is the identification of the kinds of harmful health effects, e.g., anemia, birth defects, or cancer, that can result from sufficient exposure to a substance. Second is the dose-response curve for a particular effect, i.e., the severity of damage and/or the percentage of people or animals likely to be at various exposure levels. Third is the number of people in a particular population, e.g., residents of the United States or workers in a particular industry, likely to be harmed under past, present, or projected levels and conditions of exposure.

In this report, the committee has used "risk assessment" as a broad term encompassing all three of these concepts. "Hazard identification" refers to the first concept, "dose-response" curves or relationships are used in discussions of particular sets of data, and "quantitative risk assessment" refers to the estimates of risk to humans derived by mathematical extrapolations from these data. "Population risk estimates" describe the expected frequency or incidence of a harmful effect in a specific group of humans under defined conditions of exposure.

The amount and complexity of information needed increase as we progress from hazard identification to dose-response assessment to population risk estimation, although each step builds on the preceding one. Hazard identification characterizes the nature of toxic effects that a substance is capable of causing in laboratory animals or humans. Dose-response curves based on experimental or epidemiological observations define the frequency and sometimes the severity of these toxic effects at several levels of exposure.

The dose-response information is used in quantitative risk estimation. Through mathematical modeling and application of known biological principles, attempts are often made to estimate risk for dose levels, exposure conditions, or species other than those for which dose-response data have been obtained. For example, quantitative risk assessments often rely on dose-response data from studies of laboratory animals exposed to relatively high exposure levels in order to estimate the risk to humans exposed to lower levels. Assumptions and uncertainties involved in the application of quantitative risk assessment to cancer induction have been discussed extensively (Food

Safety Council, 1980; International Regulatory Liaison Group, 1979; Office of Technology Assessment, 1981). Population risk estimates bring together quantitative risk estimates and data on exposure of a specific group of humans to identify their risk under actual or anticipated exposure conditions.

The most relevant information for categorizing the hazard or the dose-response for humans is derived from studies of exposed humans. Unfortunately, evidence from this source is often unavailable or inconclusive at times when decisions about acceptable exposure must be made. Humans are exposed to so many different substances through food, medicines, air, water, household materials, and occupational environments that sorting out the causes of harmful effects on health is often difficult. Perhaps of most importance is the fact that evidence of human health hazards from substances introduced into our environment cannot be obtained directly from observations in humans until people have been harmed.

For these reasons, evidence from laboratory animals or from other biological test systems is often used as an alternative or as a supplement to data on humans. A substantial body of evidence has demonstrated the utility of these experimental systems (Doull et al., 1980; National Research Council, 1977; Richmond et al., 1981). A variety of mathematical models have been developed for using data at high doses, usually only available from studies in animals, to estimate risks for humans at low doses (Armitage, 1982; Cornfield et al., 1978; Crump et al., 1976; Fishbein, 1980; Food Safety Council, 1980; Krewski and Van Ryzin, 1981; Van Ryzin, 1980). Because there are extensive data on the effects of asbestos and some other fibers in humans, the quantitative risk assessments in this chapter are based exclusively on data from epidemiological studies in humans, whereas the comparative risk assessments also take into consideration data from laboratory studies.

Every scientific study or technique has some lower limit to its sensitivity. A sensitive method in analytical chemistry may be capable of detecting a few molecules of a particular chemical among a billion other kinds of molecules but incapable of detecting a few among a trillion. The sensitivity of an animal test for toxicity is limited by many factors, such as the number of animals that it is practical to study, the subtlety of the effect of interest, the occurrence of similar effects in animals not exposed to the material under test, and limitations on the amounts of material that can be administered and on the methods used to administer them.

Other difficulties limit the power of epidemiological studies. For example, it is often difficult to select appropriate control groups, estimate exposure, or detect health effects from the exposures of concern, especially if the exposures are much lower than those that occur among occupational groups.

Several kinds of information are useful for estimating risks at low exposure levels on the basis of observations at higher exposures. These include the shape of the dose-response curve in the range of exposures studied, knowledge of the mechanism by which the type of toxic effect occurs, and information on dose-related changes in the uptake, distribution, chemical or physical modification, and excretion of the substance, i.e., pharmacokinetics.

Substances vary markedly both in the quantity required to produce a toxic effect and in the rapidity with which the incidence of toxic effects decreases with decreasing dose, i.e., the shape of the dose-response curve. In an experiment covering a sufficiently wide range of exposure levels, it is possible to find some levels that are toxic and some lower levels at which no toxicity is observed. The highest dose at which no toxicity is seen is often called the "no-observed-effect level," or NOEL (Klaassen and Doull, 1980). However, any experiment will have some limit in its sensitivity to small effects, and the true no-effect-level, if any, may be below the NOEL in a particular experiment.

The fundamental assumption underlying the NOEL safety factor approach is that some minimal level of a toxic substance is required to cause damage and that the substance is not toxic below that level. The NOEL type of experiment is used to find that level.

The maximum dose at which no toxicity would occur is called the "threshold" for that substance. However, several mathematical models for quantitative estimation of cancer risk assume that there is no threshold; risk diminishes with decreasing dose, but some risk is assumed to remain as long as there is any exposure.

The determination of which of these two assumptions is correct will probably depend on the nature of the toxic effect. Thus, understanding the mechanism of toxicity can provide guidance in setting acceptable exposure levels. For a substance that exerts its toxic effect by inactivating an enzyme present in abundance in each cell, it is reasonable to assume that a threshold would exist. Inactivation of a few molecules of the enzyme is unlikely to damage the cell. On the other hand, a chemical that is mutagenic or carcinogenic because it damages some critical site on a DNA molecule that starts the carcinogenic process can reasonably be assumed not to have a threshold. The likelihood that a critical site would be damaged would decrease with decreasing dose, but the possibility that this damage could occur remains at any exposure above zero.

For many effects, the severity of the toxic effect, as well as the probability that it will occur, also decreases with dose. For example, a dose that damages a high proportion of cells in the liver may be lethal; one that damages a moderate number may cause severe illness but not death; a small dose that causes damage to a few cells may not lead

to any clinical symptoms. The error in assuming a threshold if none truly existed would generally not be expected to lead to serious cases of disease in this situation.

By contrast, the severity of cancer and of mutations is not related to the dose of the substance causing them. Low dose exposure to x-rays or cigarette smoke causes fewer cancers than does high dose exposure, but the resulting cancers are just as lethal. Thus, although there may be some substances that show a threshold for cancer induction (Hoel et al., 1983), an error in assuming a threshold when none really exists would severely harm those persons who got the disease despite a low exposure.

Accurate documentation of exposure is important for determining the dose-response curves for toxicity in animals or humans and also for estimating population risks. Errors in the estimation of exposure will lead to errors in defining the dose-response curve and in making quantitative risk estimates for individuals or specific populations. The amount of a toxic substance or its active metabolite that reaches the body site that is susceptible to its effect is the exposure that accounts for toxicity, but such measures are almost never available (Hoel et al., 1983). Other measurements, such as amounts in the blood, amounts entering the body, or concentrations in the air or water of a community, are often useful surrogates, but as noted earlier in this report, they are also often unavailable.

The sensitivity of the exposed population is another consideration in the risk estimation process. Some individuals may be more sensitive than others to specific environmental insults because of nutritional deficiencies, genetic predisposition, and for children, small body size, developmental immaturity, and increased metabolic and respiratory rates (Calabrese, 1978, 1980).

With their rapid metabolic rate, children consume proportionately more food and inhale greater volumes of air than an adult for a given body weight. Thus, they would also consume or inhale proportionately more of any contaminants that are present (Babich and Davis, 1981). Human infants do not have mature hepatic detoxification systems until they reach 2 to 3 months of age (Pelkonen et al., 1973; Rane and Ackerman, 1972). Serum immunoglobulin does not attain adult levels until children are 10 to 12 years old (Calabrese, 1978). Studies in animals have also demonstrated a greater sensitivity among the young after exposure to chemicals by a variety of routes (Goldenthal, 1971). Children's lungs may also be especially sensitive to environmental pollutants. Tager et al. (1983) have observed measurable differences in lung function between children of smoking mothers and children whose mothers did not smoke.

Population risk estimation is based on all the preceding steps. First, the exposure of the study population must be known. Heterogeneity of the population with respect to level of exposure or sensitivity to the toxic material should also be considered in the calculations. Exposure, dose-response curves, distribution of sensitivity factors, and the size of the population are then used to estimate the number of people likely to suffer toxic effects from the substance of interest. If the material causes more than one type of toxic effect, each effect requires separate calculations.

Ideally, calculation of risk is an objective, scientific activity devoid of policy judgments. The latter are made separately when deciding the acceptable level of exposure. However, policy decisions can seldom be divorced completely from the process of risk assessment. The reason for this lies in the uncertainty of many of the scientific judgments required. For example, if one experimental species is more susceptible to the toxicity of a material than another and data on humans are unavailable, which species should be used for estimating human risk? Which mathematical model should be applied to the data? These and many other questions of judgment were discussed in the recent National Research Council (1983) report.

In the following sections, the committee has used epidemiological data, mostly from occupational settings, to develop a quantitative model of the relationship between fiber dose and carcinogenic response for a generalized "asbestos" exposure resulting in either lung cancer or mesothelioma. That dose-response relationship is then applied to a hypothetical, but reasonable, exposure level to show potential population risk levels in populations of arbitrary size. In the final section, the committee assesses risks for other types of fibers and, in some cases, for other diseases by qualitative comparisons with the base case of a generalized asbestos exposure.

## QUANTITATIVE RISK ASSESSMENT

In the previous chapters, the committee extensively reviewed information on the health effects of asbestos and other asbestiform fibers. In preparing this section, it also reviewed several risk assessments for asbestos in the open literature and in government documents. On the basis of its evaluation of the quality and coverage of the information and the assessment techniques, the committee decided that a quantitative assessment of the risks for mesothelioma and lung cancer from nonoccupational exposures to asbestos would be meaningful. It also concluded that the information base was insufficient for useful quantitative assessments for other fiber types and diseases, but that in some cases a qualitative, comparative assessment was feasible and useful. These decisions do not mean that the asbestos assessment is without major uncertainties nor does it mean that the comparative assessments are of poor quality. In both cases, the objective is to

present information useful for evaluating the health risks of asbestiform fibers in nonoccupational settings.

First, an overview of mathematical models for carcinogenic risk assessment is presented to provide a context for the assessments for lung cancer and mesothelioma, which are of principal interest. Next, there is a review of several assessments for asbestos that were based on such models. Finally, these assessments and the committee's own analyses are applied to the information presented in earlier chapters to produce quantitative risk estimates for nonoccupational exposures to asbestos in ambient air.

## Mathematical Model for Carcinogenic Risk Estimate

As explained earlier, it is not necessary to use data on asbestos exposure from animal experiments to estimate risks for humans, but it is necessary to extrapolate from the health effects observed at high occupational levels of exposure to much lower nonoccupational exposures. Occupational epidemiology makes it possible to describe the probability of dying from a particular type of cancer as a function of age at first exposure, level and duration of exposure, and current age. Mathematical extrapolation models based on the multistage theory of carcinogenesis make it possible to estimate the probability of dying from that type of cancer for different ages at first exposure, different (lower) exposure levels, and different (often longer) duration of exposure, also as a function of current age. By considering the cumulative probability throughout a lifetime, the "lifetime risk" of cancer mortality can be computed.

At any age, an individual faces some probability of reaching an end point that is related to cancer in the next year, for example, dying of lung cancer. Suppose that at a given age, a, the probability is given by p(a,d), where d is the dose of the carcinogen--in this case, asbestos. When d = 0, p(a,0) is the probability of the end point for unexposed people. If t is some age of interest, then the cumulative probability P(t,d) of reaching the end point before that age is given by the sum of the annual probabilities up to that age:

$$P(t,d) = \text{the sum of } p(a,d) \text{ over all ages, } a, \leq t. \qquad (1)$$

Reaching the end point by time t is analogous to the "failure time" for a generalized system that is no longer effective after time t. General mathematical analysis can be used to show that the probability of failure as a function of time can be written as follows:

$$P(t,d) = 1 - e^{-I(t,d)}, \qquad (2)$$

where $I(t,d)$ represents the cumulative incidence function (or cumulative hazard function) of occurrence of the observable failure prior to time t.

Armitage and Doll (1961), Peto et al. (1982), Kalbfleisch and Prentice (1980), Hartley and Sielken (1977), Hartley et al. (1981), and Kalbfleisch et al. (1983) have applied this model to carcinogenesis. If the cumulative incidence I(t,d) is small, then equation (2) may be simplified to

$$P(t,d) \doteq I(t,d), \tag{3}$$

where $\doteq$ means approximately.

In carcinogenic risk assessment, attention is usually focussed on the cumulative incidence function I(t,d) rather than on the probability function P(t,d). The Armitage-Doll (1961) multistage theory of carcinogenesis suggests that I(t,d) can be written as a product of two terms--g(d), depending only on dose, and h(t), depending only on time. That is,

$$I(t,d) = g(d)\, h(t). \tag{4}$$

If there are k dose-dependent stages in the process of carcinogenesis and the rate of transformation from one stage to the next is assumed to be a linear function of dose, the function g(d) would be a polynomial of degree k in the dose. The function h(t) depends only on time. This model and its generalization and justification have been discussed by Crump et al. (1976), Hartley et al. (1981), and Kalbfleisch et al. (1983).

To determine the values of the constants in the polynomial g(d) and the functional form for h(t), the cumulative incidence function must be fitted to data--preferably to data based on observations in human populations. The multistage model described above has been fitted successfully to many sets of cancer data, including data on asbestos, and appears at present to be a generally adequate model for assessing cancer risk. Fitting equation (4) to data involves estimating the constants in the model for some suitably determined function h(t). This model has been applied to both mesothelioma and lung cancer data on asbestos-exposed workers. The form of h(t) and the values of the constants from those studies will be discussed in the next section. The function g(d)--and thus the cumulative excess incidence function I(t,d)--can be approximated as a linear function of dose in the low-dose range that equals 0 when d = 0. This relationship can be used for extrapolating from high to low doses and has the following form:

$$I(t,d) = cdh(t). \tag{5}$$

This form assumes that there is at least one dose-dependent stage of cancer development. The argument for a linear (with respect to dose) approximation for low-dose exposures has been justified on the basis that the exposure dose d is added to a background level (Hoel, 1980; Peto, 1978). This assumption may not always be justified in application

(see Cornfield et al., 1978 and Van Ryzin, 1981), but it should lead to an appropriate upper bound for the committee's risk assessments for asbestos. Furthermore, and more importantly, ruling out a linear dose term for asbestos exposure does not seem justified by the data now available (Nicholson, 1983; Peto, 1982; Schneiderman et al., 1981). Thus, the model adopted for risk assessment in the next three sections of this chapter is based on the cancer mortality incidence calculated by equation (5).

## PUBLISHED RISK ASSESSMENTS

This section reviews some published risk assessments for lung cancer and mesothelioma. These assessments helped the committee select a functional form for h(t) for the two diseases and to establish the value of the constant c in equation (5).

### Lung Cancer Risk from Nonoccupational Environmental Exposures

The following summary of risk assessments for lung cancer from asbestos exposures is based on data on exposure of worker populations. These data suggest that the function I(t,d) in equation (5) becomes

$$I(t,d) = c^{*}T_{0}dI_{0}(t), \qquad (6)$$

where $T_0$ is the duration of exposure to asbestos at dose d, $I_0(t)$ is the cumulative mortality incidence for lung cancer up to age t for those who have not been exposed to asbestos, and c* is a constant that depends on the cohort under study, but not on dose or age. As used in equation (6) and in the remainder of this section, d is the concentration of fibers in the workplace air, usually measured in fibers/$cm^3$. Although d is referred to as dose, some authors would call it dose rate and would refer to the product $T_0d$ as (cumulative) dose. Equation (6), derived by Peto (1982), is consistent with his earlier studies of chrysotile workers (Peto, 1978). This equation is also supported by four studies reviewed by Nicholson (1983), who noted that the relative risk of lung cancer deaths for asbestos workers compared to a similar population was linearly related to the accumulated dose years, i.e., fibers/$cm^3$ x years, or (fibers/$cm^3$)yr.

In equation (6), the underlying incidence rate $I_0(t)$ is considerably different for smokers and nonsmokers of each sex. Therefore, the risks for each of these groups must be assessed separately. Another consequence of equation (6) is that the relative risk of lung cancer due to asbestos exposure does not depend on age at first exposure.

Thus, lifelong risk of lung cancer resulting from exposure to asbestos can be calculated quite simply by using equation (6). As an example, consider the following calculation given by Peto (1982).

Consider the effect of 10 years of exposure at 1 fiber/cm$^3$. If we assume that the relative risk for lung cancer among insulation workers increased approximately fourfold [Hammond et al. (1979) reported 4.2 for nonsmokers and 3.9 for smokers] and that this risk is based on a cumulative dose of 600 fibers/cm$^3$ (20 years at 30 fibers/cm$^3$), then 10 years of exposure to 1 fiber/cm$^3$ will increase the relative risk by 4.0 x 10/600 = 0.067. Since approximately 15% of lifelong smokers die of lung cancer, this mortality rate will increase to 0.15 x 1.067 x 100, or 16%. Thus, the difference (1%) is the excess due to asbestos as predicted by the equation. Since only 0.5% of nonsmokers die of lung cancer, this would become 0.533% (0.005 x 1.067 x 100) for an added risk of 0.033% due to asbestos exposure.

## Mesothelioma Risk from Nonoccupational Environmental Exposures

The committee reviewed two estimations of mesothelioma risk, one by Peto and his colleagues (Peto, 1982; Peto et al., 1982) and the other by Nicholson (1983). These analyses and their consequences are summarized in this section.

Using the data of Selikoff et al. (1979) on mortality among 17,800 members of the International Association of Heat and Frost Insulators and Asbestos Workers, Peto et al. (1982) showed that the mortality rate from mesothelioma in these workers was dependent on the time since first exposure, but did not depend on the age at first exposure. From this finding, and the application of the multistage theory of carcinogenesis through equation (5), the cumulative incidence function becomes:

$$I(t,d) = cd(t - t_0)^k, \qquad (7)$$

where $t - t_0$ represents time since first exposure at age $t_0$. For any group of workers exposed at the same dose level d, the product cd = b is a constant depending on the type of asbestos exposure. Equation (7) suggests that the risk for mesothelioma is primarily dependent on the time since first exposure ($t - t_0$). This same phenomenon was noted by Schneiderman et al. (1981) and Nicholson (1983). Fitting equation (7) with b = cd to the data of Selikoff et al. (1979) for men up to age 80 by the method of maximum likelihood estimation resulted in an estimate of k = 3.2 with a standard error of $\pm$ 0.36 and b = 4.37 x $10^{-8}$. Using this calculation, Peto et al. (1982) estimated the lifelong mesothelioma risk for this worker group to be 15%, 7%, and 3% for age at first exposures of 20, 30, and 40 years, respectively. These figures have been adjusted for other competing causes of death.

Using equation (7) with k = 3.2, Peto and colleagues determined that b x $10^8$ ranges in value from 2.94 to 5.15 for four other sets of data (see Table 7-1). Using k = 3.5, Peto (1982) computed a lifetime mesothelioma rate of 1 in 100,000 children exposed from age 12 to age 18

TABLE 7-1. Mesothelioma Death Rates in Various Studies and Predictions of Risk[a]

| Study Population and Reference | Relative Risk ($b \times 10^8$) | Corresponding Lifetime Risk (%)[b] by Age at First Exposure (yrs) | | |
|---|---|---|---|---|
| | | 20 | 30 | 40 |
| North American insulation workers (mixed exposure) Selikoff et al., 1979 | 4.37 | 15 | 7 | 3 |
| Factory workers (mixed exposure) Newhouse and Berry, 1976 | 4.95 | 17 | 8 | 3 |
| Chrysotile textile factory workers Peto, 1980b | 2.94 | 10 | 5 | 2 |
| Australian crocidolite miners Hobbs et al., 1980 | 5.15 | 17 | 8 | 3 |
| U.S. amosite factory workers Seidman et al., 1979 | 4.91 | 17 | 8 | 3 |

[a]Adapted from Peto et al. (1982). The death rate at time $t - t_0$ since first exposure at age $t_0$ is proportional to b, obtained by fitting equation (7) with $k = 3.2$.

[b]The calculation of "lifetime risk," i.e., the percentage of similarly exposed men who would die of mesothelioma before age 80, is based on an actuarial calculation using 1977 U.S. rates for white males for all causes of death other than mesothelioma inflated by a factor of 1.26, the observed relative risk among insulation workers (Selikoff et al., 1979).

(i.e., 6 years of school age), assuming the fiber level was 0.003 fiber/cm$^3$ (1/1,000 of the exposure of the insulation workers).

A second risk assessment was done by Nicholson (1983), who criticized the Peto et al. (1982) analysis for fitting equation (7) to only those men who died of mesothelioma up to age 80. By including all insulation workers, he estimated k to be 5.0.

## QUANTITATIVE RISK ASSESSMENT FOR NONOCCUPATIONAL ENVIRONMENTAL EXPOSURES

As a starting point for assessing the risk from nonoccupational environmental exposure to asbestiform fibers, the committee adopted equation (6) as representing the cumulative mortality up to age t, which is appropriate for lung cancer induced by a continuous exposure of $T_0$ years at dose level d in fibers/cm$^3$. This model implies that any given total dose before time t would have the same effect on the relative risk at time t, regardless of the time at which exposure started or its duration. The model thus ignores a minimum latency period, which might cause the model to overestimate effects, but also ignores the difference between exposures at earlier and later ages, which might cause the model to underestimate effects.

Equation (7) was assumed to be a reasonable representation of the cumulative mortality from mesothelioma up to age t for continuous exposure to asbestos at dose level d in fibers/cm$^3$ from age $t_0$ until age t. In this case, latency is implicitly included in the dependence on $(t-t_0)$, because k is greater than 1, but no minimum latency is assumed. These assumptions are supported by the work of Peto (1982), Peto et al. (1982), Nicholson (1983), and Schneiderman et al. (1981), who extensively reviewed the basis for these assumptions by examining the models and their consistency for several observed worker cohorts exposed to ambient concentrations of asbestos fibers. These authors have suggested that asbestos acts as a late-stage carcinogen in producing lung cancer but acts at earlier stages in the development of mesothelioma. Using these models, the committee developed lifetime estimates of risk for lung cancer and mesothelioma mortality from continuous nonoccupational exposures to 0.0004 fibers/cm$^3$ and for 0.002 fibers/cm$^3$.

For lung cancer, the committee assessed the risk for four exposure subgroups: male smokers, female smokers, male nonsmokers, and female nonsmokers. For mesothelioma, only one calculation was made, since equation (7) and the supporting data in the papers cited above suggest that mesothelioma mortality does not depend on sex or smoking history, but does depend strongly on age at first exposure.

### Lifetime Risk Estimates for Lung Cancer and Mesothelioma

Table 7-2 summarizes lifetime risk estimates for lung cancer and mesothelioma for nonoccupational environmental exposures to 0.0004 fibers/cm$^3$ (a median level) and 0.002 fibers/cm$^3$ (a high level). It is assumed this exposure is continuous from birth through a lifetime of 73 years, an approximate average lifetime in the United States. Thus, in equations (6) and (7), t = 73 years and d = 0.0004 or 0.002. In equation (6), $T_0$ = 73 and in equation (7), $t_0$ = 0 to account for continuous exposure. Because equations (6) and (7) are linear in the dose unit d, one can immediately obtain from Table 7-2 lifetime risks at other continuous (from birth) environmental exposures by multiplying by the appropriate dose factor. For example, lifetime risk estimates at 0.02 fibers/cm$^3$ are 10 times higher than the estimates at 0.002 fibers/cm$^3$.

TABLE 7-2. Estimated Individual Lifetime Risks from a Continuous Exposure to Asbestos at 0.0004 Fibers/$cm^3$ (a Median Dose) or 0.002 Fibers/$cm^3$ (a High Dose)[a]

| Disease | Exposure Group | Estimated Individual Lifetime Risk x $10^6$ Median Exposure (0.0004 fibers/$cm^3$) | Estimated Individual Lifetime Risk x $10^6$ High Exposure (0.002 fibers/$cm^3$) |
|---|---|---|---|
| Lung cancer[b] | Male smoker | 64 (0 to 290)[c] | 320 (0 to 1,500) |
| Lung cancer | Female smoker | 23 (0 to 110) | 120 (0 to 530) |
| Lung cancer | Male nonsmoker | 6 (0 to 22) | 29 (0 to 130) |
| Lung cancer | Female nonsmoker | 3 (0 to 13) | 15 (0 to 66) |
| Mesothelioma | All | 9 (0 to 350) | 46 (0 to 1,700) |

[a]Lifetime assumed to be 73 years; exposure occurs from birth. Lung cancer risks are calculated with $c^* = 1.02$ or an excess risk of 2% per (fiber/$cm^3$)yr, estimated from nine studies with varied results. Mesothelioma risks are calculated with $c = 2.53 \times 10^{-8}$ and $k = 3.2$, estimated from five studies with varied results. See also explanations in text.

[b]Sex differences for lung cancer risk are due to differences in lung cancer background rates associated with smoking patterns, occupational exposures, and other factors.

[c]Range of estimates. The lower limit of 0 is always possible if linear extrapolation overestimates risk. See also text below.

The estimates in Table 7-2 were based on the following five considerations:

- Exposure levels. A mix of indoor and outdoor measured exposure levels was used to select the median value of 0.0004 fibers/$cm^3$ and the high value of 0.002 fibers/$cm^3$ as the reference levels.

- Use of the linear model. The models used by the committee all assume low-dose linearity and, as such, produce higher estimates of risk at low doses than would be obtained with other models. However, because the occupational data do not rule out low-dose linearity, the committee believes that these estimates do not unduly overstate the risks.

- Count-mass conversion. The conversion of ambient fiber mass measurements to an equivalent number of fibers was based on measurements

of mass and numbers of fibers in the workplace. The committee realized, however, that the number of fibers in ambient air would be much greater because these fibers tend to be smaller than those in the workplace (see Chapter 4). Depending on the toxicity of small fibers, the risks could be greater or less than those calculated in this chapter. If the presence of long fibers is necessary for a toxic response, risks would be lower.

- Model dependence. The results of the mesothelioma model depend very heavily on the value of k. This accounts for the large range of estimates for mesothelioma. It is assumed that this dependence on k among workers holds for the entire population throughout a lifetime. If the dependence is not as strong (i.e., a lower k value), the lower end of the range would apply. If this dependence is as strong (i.e., a higher k value), the upper bound may be more appropriate.

- Childhood exposure. The models used for extrapolation for both lung cancer and mesothelioma are based on the assumption that a unit dose of exposure (measured as fibers/$cm^3$ > 5 $\mu$m long) in early life is equivalent in its intrinsic carcinogenic potential to a unit dose in later life. If children are more biologically sensitive than the worker group, the risk per unit dose would be increased. Results from studies of exposure to other materials indicate that children are often more sensitive than adults to a given dose, even when expressed as dose/body weight.

The risk estimates and ranges shown in Table 7-2 are those the committee considers most reasonable. Because of the uncertain value of k and the sensitivity of equation (7) to its value, the range of estimates is much larger for mesothelioma than for lung cancer. Two conclusions can be drawn from the estimates in Table 7-2:

- For nonsmokers, the lifetime risk for mesothelioma from nonoccupational environmental exposure to asbestos is higher than for lung cancer. For smokers, however, the risks of lung cancer are substantially higher than for mesothelioma, because of the multiplicative interaction of smoking and asbestos exposures.

- Individual lifetime risk estimates for lung cancer from nonoccupational environmental exposures to 0.0004 fibers/$cm^3$ are much lower than the risks observed for smoking.

The basis for the calculations in Table 7-2 is discussed in detail in the following two subsections.

Calculation of the Lung Cancer Risk Estimates in Table 7-2. Calculating lifetime risk estimates from equation (6) involves the notion of relative risk up to time t, designated here as RR. From equation (6), the RR for lung cancer by age t can be shown as follows:

$$\frac{I(t,d)}{I_0(t)} \qquad (8)$$

$$= \frac{\text{cumulative lung cancer mortality by age t at dose d}}{\text{baseline cumulative lung cancer mortality by age t}}$$

$$= c^*(T_0 d),$$

where $(T_0 d)$ = total dose-years for the exposed group and $c^*$ is a constant that depends on the cohort.

For a given study showing an increased relative risk for lung cancer,

$$c^* = (1 + P/100), \qquad (9)$$

where P is the percentage increase in lung cancer risk per unit dose [% per (fibers/cm$^3$)yr]. Schneiderman et al. (1981) presented the values of P for nine different worker cohorts. The results are summarized in Table 7-3.

Values for P in Table 7-3 range from 0.06 (Study 8) to 9.1 (Study 1). The higher value establishes the upper end of the range given in Table 7-2. The zero value for the lower end of the range indicates that the low-dose linear approximation in equation (5) may overstate risk.

The median value for P in the studies shown in Table 7-3 is P = 1.1 (Study 7). This value, rounded upward to 2, was used in obtaining the estimates for lifetime lung cancer risk in Table 7-2. To calculate these estimates, it was necessary to know only the baseline absolute risks for the appropriate subpopulations. The baseline cumulative incidence rates of lung cancer for the four subgroups in Table 7-2 have been estimated by Schneiderman et al. (1981) as follows: male smokers = 0.11; female smokers = 0.04; male nonsmokers = 0.01; and female nonsmokers = 0.005.

Thus, using 2% as a value for P, the lifetime risk of lung cancer for a male smoker is

$$(0.11)(1 + P/100) = (0.11)(1 + 0.02) = 0.1122. \qquad (10)$$

The increased lifetime risk attributable to asbestos exposure at 1 fiber/cm$^3$ for 1 year is 0.0022, i.e., 0.1122 - 0.1100. At the ambient exposure of 0.0004 fibers/cm$^3$ assumed in Table 7-2 and for a 73-year lifetime exposure, the increased lifetime risk of lung cancer is $6.42 \times 10^{-5}$, i.e., 0.0022 x 0.0004 x 73. Rounding to two significant figures gives the estimate in Table 7-2 for male smokers. The other calculations in that table were derived in a similar fashion.

When describing the use of the percentages given in Table 7-3, Schneiderman et al. (1981) commented that the low percentage increases in risk in Studies 3, 6, 8, and 9 probably resulted from several factors. In Study 3, for example, the subjects were retirees older than 65.

TABLE 7-3. Estimated Increase in Lung Cancer Risk per Unit of Exposure to Asbestos[a]

| Study No. | Occupation of Worker Cohort | Asbestos Type | Percent Increase in Lung Cancer Risk per (fibers/cm$^3$)yr | Reference |
|---|---|---|---|---|
| 1 | Insulation manufacturing | Amosite | 9.1 | Seidman et al., 1979 |
| 2 | Asbestos product manufacturing | Crocidolite, chrysotile, and amosite | 1.3 males<br>8.4 females | Newhouse and Berry, 1979 |
| 3 | Asbestos manufacturing | Amosite and chrysotile; some crocidolite | 0.3 | Henderson and Enterline, 1979 |
| 4 | Asbestos product manufacturing | Chrysotile; some amosite and crocidolite | 1.1 | Nicholson et al., 1979 |
| 5 | Textile production | Chrysotile | 5.3 | Dement et al., 1982 |
| 6 | Textile production | Chrysotile | 0.07 early employees[b]<br>0.8 later employees[b] | Peto, 1980 |
| 7 | Insulation manufacturing | Chrysotile and amosite | 1.7 | Selikoff et al., 1979 |
| 8 | Mining and milling | Chrysotile | 0.06 | McDonald and Liddell, 1979 |
| 9 | Mining and milling | Chrysotile | 0.15 | Nicholson et al., 1979 |

[a]Adapted from Table 4 in Schneiderman et al., 1981.
[b]Early employees began work before or during 1950. Later employees began work after 1950.

Schneiderman et al. stated that the investigators may thus have missed asbestos-related deaths occurring at earlier ages. In Study 6, the disease rates for workers employed earlier were lower than those employed later who were followed for shorter periods. The discrepancy has diminished as more data have accumulated. The subjects in Studies 8 and 9 were mining and milling workers whose exposure patterns were quite different from environmental ambient air exposures. There is also some evidence that many lung cancer cases were missed in Studies 8 and 9 because of competing causes of death at earlier ages. Thus, Schneiderman et al. (1981) concluded that the range from 1.1 (Study 4) to 9.1 (Study 1) is the most representative of true values. The value of P = 2 used in the calculations in Table 7-2 falls near the bottom of this range, but is within a factor of 5 of the top of the range. If we use P = 5, which is the middle of the range, the lung cancer risk estimates in Table 7-2 would be multiplied by a factor of 2.5.

Calculation of Mesothelioma Risk Estimates. To calculate the lifetime risk with equation (7), the numbers c and k must be determined. Then the lifetime risk L at d = 0.0004 fibers/cm$^3$, assuming t = 73 and $t_0$ = 0 (continuous exposure from birth to age 73), is

$$L = c(0.0004)(73)^k. \qquad (11)$$

To apply this equation, c and k must be estimated from epidemiological studies of occupational exposures to asbestos. Each study must be stratified by duration of exposure $(t-t_0)$ to estimate these parameters. Most of the following analysis is similar to that of Peto et al. (1982).

First, let us consider the choice of k. As noted earlier, when Peto et al. (1982) fitted equation (7) to the data of Selikoff et al. (1979), they obtained the equation $I(t,d) = b(t - t_0)^{3.2}$, with b = 4.37 and k = 3.2 $\pm$ 0.36 (standard error). In equation (11), therefore, we initially use k = 3.2. Modifications using different values for k will give the range of estimates for d = 0.0004 fibers/cm$^3$ in Table 7-2. For d = 0.002 fibers/cm$^3$, we replace 0.0004 with 0.002 in equation (11). With k = 3.2, Peto et al. (1982) also fitted four other data sets to obtain four values of b in the equation $I(t,d) = b(t - t_0)^{3.2}$. The value of b is specific to each worker cohort and depends on three numbers: d (the average fiber/cm$^3$ exposure), $\ell$ (the average length of exposure), and $t - t_0$ (the average time since first exposure). These values are given in Table 7-4. In addition, Table 7-4 contains the estimates of c that are appropriate for equation (7), based on the corresponding estimate of b given by Peto et al. (1982). When exposure is not continuous from time of first exposure ($t_0$) to the age of observation (t) for these studies, the relationship between b and c changes from c = b/d to

$$\frac{4.56\ b/d}{1 - [1 - \ell/(t-t_0)]^{3.2}}. \qquad (12)$$

TABLE 7-4. Estimated Constants for Equations (11) and (12) for Five Studies

| Study | b x $10^8$ | d[a] | $\ell$[a] | t - $t_0$ [a] | c x $10^8$ |
|---|---|---|---|---|---|
| Selikoff et al., 1979 | 4.37 | 15 | 15 | 24 | 1.39 |
| Newhouse and Berry, 1976 | 4.95 | 12.5 | 6 | 31.5 | 3.67 |
| Peto, 1980a,b | 2.94 | 16.5 | 14 | 22.5 | 0.85 |
| Hobbs et al., 1980 | 5.15 | NA[b] | NA | NA | NA |
| Seidman et al., 1979 | 4.91 | 35 | 1 | 35 | 7.22 |

[a]Estimated from data given in Tables 4 and 10 of Schneiderman et al. (1981), using estimated median values. The product d$\ell$ from columns 3 and 4 above is the estimated cumulative exposure in (fiber/$cm^3$)yr of their Table 10.
[b]NA = not available.

The factor 4.56 adjusts from occupational exposures at about 1,920 hours per year to environmental exposures at 8,760 hours per year. Appendix G provides the mathematical basis for equation (12). Table 7-4 gives the values of the constants for each study in which Peto et al. (1982) estimated b.

To obtain the estimates for mesothelioma at the dose of 0.0004 fibers/$cm^3$ in Table 7-2, equation (11) is used with values for c from Table 7-4 and k = 3.2. In Table 7-2 the lifetime risk for mesothelioma at d = 0.0004 fibers/$cm^3$ is 9 per million. This is calculated from equation (11) with c = 2.53 x $10^{-8}$, the median of the range of the c values in Table 7-4, and k = 3.2. The highest value of the range in Table 7-2 at d = 0.0004 uses equation (11) with c = 7.22 x $10^{-8}$, the upper value of c in Table 7-4, and k = 3.8, obtained from 3.2 + 1.65 x 0.36. The selection of 3.8 as the value for k is based on an approximate upper 95% confidence limit for the estimate of k. The lower limit is taken as 0, which is always a possible lower limit, especially if the low-dose linear assumption in equation (5) overestimates the individual lifetime risk.

Peto (1982) recommended using a k value of 3.5 for risk assessment purposes. As an example, he estimated that the risk of mesothelioma for children exposed for a 6-year period (ages 12 to 18) at 0.003 fibers/cm$^3$ would be one in 100,000. Nicholson reviewed additional data, including data on older workers up to age 80, and determined that a k value would be 5. Schneiderman et al. (1981) used k = 3.0. For this study, the committee used a value of 3.2. Although neither existing data nor biological theory can provide very much guidance on the value of k, its value is very important in projecting the lifetime risks of mesothelioma from asbestos exposures. Table 7-5 shows how lifetime risk varies from the value of 9 per million for several values of k. Also shown are risk estimates for other values of c. The reader can easily calculate the results for other values of exposure.

Other authors have also estimated the risks of mesotheliomas. Enterline (1983) derived a lifetime risk of 100 per million by using current reported rates of mesothelioma, an assumption about the relative contributions of nonoccupational and occupational asbestos exposures, and other factors. This estimate clearly relates to past exposure to varying levels of asbestos. Schneiderman et al. (1981) estimated lifetime risks for mesothelioma to be between 800 and 5,000 per million for a cumulative exposure of 1 (fiber/cm$^3$)yr. These estimates correspond to lifetime risks of 23 to 150 per million for 0.0004 fibers/cm$^3$ for 73 years. As mentioned above, these investigators effectively assumed k = 3, but their equivalent c was higher than that used for the corresponding estimates in Tables 7-2 and 7-5.

TABLE 7-5. Sensitivity of Estimates for Lifetime Risks[a] of Mesothelioma to Values of k and c

| | Lifetime Risk Estimates x $10^6$, Using k Values from Various Studies | | | | | | |
|---|---|---|---|---|---|---|---|
| | This Study (low) | Schneiderman et al., 1981 | This Study (middle) | Peto et al., 1982 (middle) | This Study (high) | Peto et al., 1982 (high) | Nicholson, 1983 |
| c \ k | 2.6 | 3.0 | 3.2 | 3.5 | 3.8 | 4.0 | 5.0 |
| 0.85 x $10^{-8}$ | 0.2 | 1.3 | 3 | 11 | 41 | 97 | 7,000 |
| 2.53 x $10^{-8}$ | 0.7 | 4 | 9 | 34 | 120 | 290 | 21,000 |
| 7.22 x $10^{-8}$ | 2 | 11 | 26 | 96 | 350 | 820 | 60,000 |

[a]All estimates are derived from equation (11), $L = c(0.0004)(73)^k$, where $L$ = lifetime risk at a continuous exposure to 0.0004 fibers/cm$^3$ for a lifetime of 73 years.

Note: This table demonstrates that the risk estimates are extremely sensitive to changes in the value of k.

The Use of 0.0004 Fibers/$cm^3$ and 0.002 Fibers/$cm^3$ as the Median and High Nonoccupational Environmental Exposure Levels. The lifetime risk estimates given in Table 7-2 are based on an assumed continuous environmental ambient exposure equivalent to either 0.0004 or 0.002 fibers longer than 5 μm per $cm^3$ of air breathed. The committee believes that 0.0004 fibers/$cm^3$ is a reasonable assumption for a median population exposure level and that 0.002 fibers/$cm^3$ is a reasonable high exposure level (considering only exposures from breathing ambient air continuously). These assumptions are discussed below. The effects of noncontinuous high exposures are discussed later in this chapter.

Table 7-6 summarizes some environmental asbestos sampling data provided by Nicholson (1983). To convert from mass measurements ($ng/m^3$) of airborne exposures to fiber counts (fibers/$cm^3$), the committee used the conversion factor of 30 $\mu g/m^3$ for 1 fiber/$cm^3$. (See Chapter 4 of this report, Schneiderman et al., 1981, and Consumer Product Safety Commission, 1983 for further explanation.)

The dose-response data used in the committee's risk estimate were taken from measurements of exposures in the workplace, where the fibers tend to be longer than those in ambient environments not close to major sources of asbestos. As discussed in Chapter 4, there would typically be approximately 2,000 fibers per nanogram in workplace air; in remote areas, however, there would be approximately 70,000 ambient fibers in a nanogram. To convert mass in the workplace to ambient air, the committee used the number of fibers longer than 5 μm that would be found in the workplace when the workplace mass equaled the remote ambient fiber mass. The dose estimate in numbers of fibers would be approximately 35 times greater (70,000/2,000) if the actual sizes of fibers in ambient air were considered. If we assume that all fibers are equally potent, then the risk estimates would be correspondingly higher. On the other hand, fiber size apparently affects fiber potency, but the appropriate adjustment factors for fiber size are not known.

Table 7-6 indicates that median concentrations in outdoor air have ranged from 0.00002 to 0.00075 fibers/$cm^3$ in several studies (sample sets 1 to 8); their median is approximately 0.00007 fibers/$cm^3$. The observed median inside rooms without asbestos is 0.00054 (sample set 9). In rooms with asbestos surfaces, the median is 0.0006 fibers/$cm^3$ (range of medians for sample sets 10 through 14, 0.00006 to 0.00405 fibers/$cm^3$). If these three medians are weighted by assuming persons spend approximately one-fourth of their time outdoors, five-eighths of their time indoors in uncontaminated rooms, and one-eighth of their time in asbestos-contaminated rooms, a reasonable estimate for a median population exposure is 0.0004 fibers/$cm^3$.

The committee also used 0.002 fibers/$cm^3$ for a high value of continuous exposure in its calculations for Table 7-2. This value was obtained by using the median of the 90th percentiles in Table 7-6 for each exposure subcategory. For outdoor air, the median is 0.0003

TABLE 7-6. Summary of Environmental Asbestos Exposure Samples[a]

| Sample Sets | No. of Samples | Measured Concentration (ng/m$^3$) | | Equivalent Concentration (fibers/cm$^3$)[b] | | Reference |
|---|---|---|---|---|---|---|
| | | Median | 90th Percentile | Median | 90th Percentile | |
| 1. Paris air | 161 | 0.7 | 3.2 | 0.00002 | 0.00011 | Sebastien et al., 1980 |
| 2. Paris (outdoor control) | 19 | 0.7 | 5.2 | 0.00002 | 0.00017 | Sebastien et al., 1980 |
| 3. Outdoor control samples, for U.S. schools | 31 | 0.9 | 9.8 | 0.00003 | 0.00033 | Constant et al., 1982 |
| 4. Air of 48 U.S. cities | 187 | 1.6 | 6.8 | 0.00005 | 0.00023 | Nicholson, 1971 |
| 5. Air of U.S. cities | 127 | 2.3 | 7.8 | 0.00008 | 0.00026 | U.S. Environmental Protection Agency, 1974 |
| 6. Air of five U.S. cities (outdoor control sample) | 34 | 6.7 | 31.9 | 0.00022 | 0.00106 | Nicholson et al., 1975, 1976 |
| 7. New York City air | 22 | 13.7 | 42.9 | 0.00046 | 0.00143 | Nicholson et al., 1971 |
| 8. Air 0.5 mile (0.8 km) from asbestos spraying | 17 | 22.5 | 82.6 | 0.00075 | 0.00275 | Nicholson et al., 1971 |
| 9. Air in U.S. schoolrooms without asbestos | 31 | 16.3 | 72.7 | 0.00054 | 0.00242 | Constant et al., 1982 |
| 10. Air in Paris buildings with asbestos surfaces | 135 | 1.8 | 32.2 | 0.00006 | 0.00107 | Sebastien et al., 1980 |
| 11. Air in U.S. buildings with cementitious asbestos | 28 | 7.9 | 19.1 | 0.00026 | 0.00064 | Nicholson et al., 1975, 1976 |
| 12. Air in U.S. buildings with friable asbestos | 54 | 19.2 | 96.2 | 0.00064 | 0.00321 | Nicholson et al., 1975, 1976 |
| 13. Air in U.S. schoolrooms with asbestos surfaces | 54 | 62.5 | 550 | 0.00208 | 0.01833 | Constant et al., 1982 |
| 14. Air in U.S. schools with damaged asbestos surfacing materials | 27 | 121.5 | 465 | 0.00405 | 0.01550 | Nicholson et al., 1978 |

[a]Adapted from Nicholson, 1983.
[b]Based on conversion factor of 30 μg/m$^3$ = 1 fiber/cm$^3$.

fibers/cm$^3$; for indoor uncontaminated air, it is 0.002 fibers/cm$^3$; and for indoor asbestos-contaminated air, it is 0.003 fibers/cm$^3$. The same distribution of occupancy over time was used to arrive at the 0.002 fibers/cm$^3$ figure for a high exposure level.

## Risk Assessments for Special Subpopulations

Table 7-2 shows lifetime risk estimates for people who are exposed throughout their lives to levels of either 0.0004 or 0.002 fibers/cm$^3$ in ambient air. The predominant risk is from mesothelioma, but lung cancers also contribute to the risk, especially for male smokers. For exposure patterns that are different from those assumed, lifetime risks could be higher or lower. The following are three illustrations of how lifetime risks could be derived for such special populations.

Children Exposed in Asbestos-Contaminated Schools. The committee estimated the risk for persons exposed from birth to age 73 years to environmental levels of 0.002 fibers/cm$^3$ (as assumed in Table 7-2) plus an additional risk from a 10-year exposure (from ages 6 to 16) in an asbestos-contaminated schoolroom for 6 hours daily, 200 days per year, to 0.02 fibers/cm$^3$ (550 ng/m$^3$, the 90th percentile in Table 7-6). The equivalent continuous daily 10-year exposure is approximately 0.003 fibers/cm$^3$, i.e., 0.02 x (200 x 6)/(365 x 24). Using equation (6), the lifetime risk of lung cancer for a male who eventually becomes a smoker is 0.003 x 10 x 0.0022, or 66 in a million. This risk represents an approximately 20% addition to his ambient lifetime risk of 320 in a million (0.002 x 73 x 0.0022), for a total of about 390 in a million. For such an individual, the schoolroom exposure adds relatively more to the risk of mesothelioma, as shown below. Using equations (G4) and (G5) in Appendix G for the lifetime mesothelioma risk, L, at t = 73 for an exposure of $\ell$ = 10 years starting at age $t_0$ = 6 at the dose level d, this risk can be calculated from the formula:

$$L = cd\{1-[1-\ell/(t-t_0)]^k\}(t-t_0)^k,$$

with d = 0.003, $\ell$ = 10, $t - t_0 = 73 - 6 = 67$, and k = 3.2. This lifetime mesothelioma risk becomes

$$L = c(0.003)\{1-[1-(10/67)]^{3.2}\}(67)^{3.2} = 845c.$$

If c is the median value of Table 7-4 (i.e., $c = 2.53 \times 10^{-8}$), the estimated lifetime mesothelioma risk, L, from the 10-year exposure is $21 \times 10^{-6}$.

This risk is then added to the background risk of $46 \times 10^{-6}$ in Table 7-2, giving a lifetime mesothelioma risk for this subpopulation of $67 \times 10^{-6}$. If a million people had received such a pattern of exposures, about 67 might be expected to die of mesothelioma. In this example, the contribution to total risk from the schoolrooms is less than that of the lifetime exposure to the lower concentrations of asbestos estimated for the ambient air. However, if the value for k in Equation (7) were higher than 3.2, the significance of the schoolroom exposures

would increase because of the stronger dependence on time since first exposure. For example, if k = 3.8, the highest value used in Table 7-2, the lifetime mesothelioma risk would be $910 \times 10^{-6}$. If k were less than 3.2, the corresponding lifetime risk for mesothelioma would be less than $67 \times 10^{-6}$. These calculations show that childhood exposures to asbestiform fibers might contribute noticeable lifetime mesothelioma risks to those so exposed.

A Female Nonsmoker in a Relatively Asbestos-Free Environment. An example of a person in a low-risk group is a female nonsmoker exposed to an average level of 0.0001 fibers/cm$^3$. This exposure level would not be too unlikely for a person exposed primarily to rural indoor and outdoor air, since 0.00002 fibers/cm$^3$ is the lowest median value for all the outdoor city readings in Table 7-6. Then, the calculations in Table 7-2 would lead to a mesothelioma lifetime risk of $2.25 \times 10^{-6}$ ($9 \times 10^{-6}$ divided by 4) plus a lung cancer lifetime risk of $0.73 \times 10^{-6}$. The lifetime individual risk for such a person would be $3 \times 10^{-6}$ for both types of cancer.

A Male Smoker Living in an Area Contaminated with High Levels of Asbestos Who is Also Exposed to High Indoor Concentrations. As an example of a high-risk person, consider an urban male smoker exposed to 0.003 fibers/cm$^3$ for one-half the time and 0.018 fibers/cm$^3$ for the other half. This pattern is based on the assumption that the subject spends one-half of his time in indoor environments with a high asbestos concentration (see sample sets 13 and 14 of Table 7-6) and one-half either in highly contaminated outdoor environments (see sample sets 7 and 8 of Table 7-6) or in indoor environments at the high end of the distribution for rooms that are normally not contaminated with asbestos (see sample set 9 of Table 7-6). Thus, his continuous average exposure would be approximately 0.01 fibers/cm$^3$, i.e., 0.5(0.003) + 0.5(0.018). Therefore, multiplying the second column of Table 7-2 by a factor of 5 (0.01 = 5 x 0.002) would give the individual lifetime risks for such a person as $1.8 \times 10^{-3}$ for the two forms of cancer taken together ($230 \times 10^{-6}$ for mesothelioma and $1{,}600 \times 10^{-6}$ for lung cancer). This lifetime risk is the additional incurred risk attributable to the nonoccupational environmental exposure to asbestos and does not include the risk incurred by the smoking itself. The portion of the additional risk attributable to lung cancer is considerably higher than it would be for a nonsmoker experiencing identical asbestos exposures.

## COMPARATIVE RISK ASSESSMENT

### Methods

The goal of comparative risk assessments is to determine whether the fiber exposure in question presents risks--in terms of total number and severity of effects per year in the United States--that are about the same, considerably more, or considerably less than those assessed