

## Recent Trends in Mesothelioma Incidence in the United States

Robert Spirtas, DrPH, Gilbert W. Beebe, PhD, Roger R. Connelly, MS, William E. Wright, MD, MS, John M. Peters, MD, ScD, Russell P. Sherwin, MD, Brian E. Henderson, MD, Alice Stark, DrPH, Beatrice M. Kovasznay, MD, PhD, J.N.P. Davies, DSc, MD, ChB, F.R.C. Path, Nicholas J. Vianna, MD, MSPH, Robert J. Keehn, MS, Louis G. Ortega, MD, Liselotte Hochholzer, MD, and J.C. Wagner, MD, FRC Path

Mesothelioma incidence rates based on data from population-based cancer registries in New York State (exclusive of New York City), Los Angeles County, California, and the SEER Program of the National Cancer Institute were analyzed for trends, using original cancer registry diagnoses. Results indicate a significant increase in incidence during 1973-80 for pleural mesothelioma among white males older than 55 at time of diagnosis but not for other age-race-sex-site subgroups. A histopathologic review of New York State and Los Angeles County cases by two independent pathologists, expert in the diagnosis of mesothelioma, lowered the overall estimates but a significant upward trend remained. The observed trend does not appear to be related to changes in diagnostic practice. The results of a five-member panel of expert pathologists will be published in a separate methodology paper.

**Key words:** mesothelioma, trends, incidence, pathology, bias

### INTRODUCTION

There has been a great deal of interest in mesothelioma because of its well-known association with asbestos exposure, first noted in the 1950's and well documented by Wagner et al [1960]. Unfortunately, mesothelioma is difficult to diagnose. Further, it has not had a unique code in the International Classification of Disease and Causes of Death. For these reasons incidence data have been preferred to mortality data in investigating the occurrence of mesothelioma and its variation with time,

National Cancer Institute (R.S., G.W.B., R.R.C.).  
University of Southern California, Los Angeles (W.E.W., J.M.P., R.P.S., B.E.H.).  
New York State Health Department, Albany, NY (A.S., B.M.K., J.N.P.D., N.J.V.).  
National Research Council, Washington, DC (R.J.K.).  
Veterans Administration, Washington, DC (L.G.O.).  
Armed Forces Institute of Pathology, Washington, DC (L.H.).  
MRC Pneumoconiosis Unit, Penarth, Wales, U.K. (J.C.W.).  
Address reprint requests to Robert Spirtas, DrPH, National Cancer Institute, Landow Building, Room 4C-16, Bethesda, MD 20892.  
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place, and demographic characteristics [Bruckman et al, 1977; Ahlmark and Malker, 1981; Mowe, 1981; Teta et al, 1983; Armstrong et al, 1984; Andersson and Olsen, 1985]. The cancer registries of the National Cancer Institute's Surveillance, Epidemiology and End Results (SEER) program [Hinds, 1978; Walker et al, 1983; Devesa et al, 1984], and those in New York State (NYS) [Vianna et al, 1981] and Los Angeles County (LAC) [Peto et al, 1981; Wright et al, 1984] have been important sources of mesothelioma incidence data. Many reports have provided evidence of an increasing trend over time, especially among males, but others have not. A major issue concerns the possibility that the apparent trend may rest largely on greater recognition of the disease in recent years. The purpose of the present study is to update and expand the data-base for estimating incidence levels and trends and to evaluate some potential sources of bias.

An increasing trend in the incidence of mesothelioma, especially among males, has been reported in Connecticut [Bruckman et al, 1977], Norway [Mowe, 1981], Southern Sweden [Ahlmark and Malker, 1981], Western Australia [Armstrong et al, 1984], British Columbia [Churg, 1985], and Denmark [Andersson and Olsen, 1985]. Vianna et al [1981] did not find a significantly increasing trend in incidence using information from the tumor registry for New York State (excluding New York City). Evidence of an upward trend in incidence has also been reported by Wright et al [1984] for Los Angeles County. In the latter study, however, the upward trend disappeared after reclassification of cases following review of histopathology by an expert pathologist, suggesting the possibility that population-based data in cancer registries may over-report occurrence of mesothelioma.

From estimates of past exposures and employment patterns in asbestos-using industries, Nicholson et al [1982] projected an increasing trend in U.S. mortality from about 1,500 in 1980 to a peak of 3,000 around the year 2000. Gardner et al [1982] reported an increase in mortality among males from malignant neoplasms of the pleura in England and Wales during 1968-78. Using U.S. national mortality data, Archer and Rom [1983] could find no evidence of an upward trend in death rates between two time-periods, 1958-1967 and 1968-1977, intervals during which causes of death were coded to ICD-7 and ICDA-8, respectively.

## MATERIALS AND METHODS

### Case Selection

Mesothelioma incident cases were identified from cancer registries in Los Angeles County (1972-80), New York State (exclusive of New York City) (1973-80), and the SEER program (1973-80). The Los Angeles County Cancer Registry cases were obtained by the University of Southern California, Los Angeles County Cancer Surveillance Program, a comprehensive population-based cancer registry. For Los Angeles County, cancer cases are identified by review of all hospital pathology records and death certificates of residents and information is abstracted for the registry. The New York State Cancer Registry cases were obtained by the New York State Health Department, Bureau of Cancer Epidemiology, from its population-based registry covering the entire state of New York. Only cases that occurred outside of New York City were included in this study. All cancer cases diagnosed in New York State are reported to the Cancer Registry by physicians, hospitals, laboratories, and other medical facilities. In addition, periodic inspection of death certificate files

identifies additional cases not reported otherwise. SEER cases are provided to the National Cancer Institute through contracts with medically-oriented nonprofit organizations. Data are abstracted in a standard fashion from local hospitals and other medical facilities, private pathology laboratories and radiotherapy units, as well as from death certificates.

Cases were selected having the ICDO (1976) morphology code 905 (mesothelial neoplasms) and topography codes 163 (pleura) and 158 (peritoneum, excluding retroperitoneum). In addition, only malignant cases (tumor activity code 3) were included. The SEER areas used in this study were restricted to those judged to have data adequate for trend analysis, i.e., the states of Connecticut, Hawaii, Iowa, New Mexico, and Utah and the metropolitan areas of Atlanta, Detroit, San Francisco, and Seattle. These nine registries include approximately ten percent of the U.S. population. Other population-based registries exist which collect information on mesothelioma. However, these data were not available for the current study.

### Pathology Review

Histopathology slides and brief clinical summaries of the cases from LAC and NYS were subjected to a two-stage review, the first by an expert local pathologist at each respective registry, the second by two independent referee pathologists (JCW, LH) who are members of the European and U.S. Mesothelioma Review Panels, respectively. The clinical summaries included information on age, sex, clinical presentation, and gross pathology but did not include information on occupation or exposure. The results of the second pathology review were used to determine whether there was any evidence that U.S. pathologists generally were changing their diagnostic criteria over the 1973-80 period.

All available cases were reviewed jointly by the two referee pathologists and a consensus opinion was reached. A five-category degree-of-certainty assessment [Kannerstein et al, 1979] was used to record the diagnosis of mesothelioma by both the review pathologists and the local expert pathologists: cases were classified as definite, probable, possible, unlikely, or definitely not mesothelioma, according to standard criteria [Selikoff, 1981]. However, the pathologists were given no information regarding the exposure histories of the cases. Some cases had insufficient material to be classified. Although it was sometimes possible for the local expert pathologists to request tissue and prepare new histopathology slides, they usually had only the slides provided by the originating hospital or pathologist. To simplify the analysis we considered all cases classified by the referee pathologist as definite, probable, or possible to be correctly diagnosed as mesothelioma and all cases classified as unlikely or definitely not mesothelioma to be misdiagnosed. Since there were very few cases classified as possible (7%), their inclusion as correctly diagnosed should not have had a substantial effect on the results. The detailed results and analysis of the two pathology reviews, including an evaluation of areas of agreement and disagreement among the five study pathologists, will be provided in another report.

### Statistical Methods

Incidence rates were standardized to the 1970 U.S. population by the direct method for 10-year age intervals (for persons aged 15 years and older) and for each site according to sex and race. Persons classified as white (Hispanic) and white (non-Hispanic) were grouped together as whites. All other race categories were recorded

as nonwhite. Since the SEER cases had not been subjected to an expert pathology review, and since pathology material was not available for all LAC and NYS cases, the incidence rates calculated for this report are based on data from the source registries' files prior to the two-stage pathology review described in the previous section. Trends in age-adjusted rates were evaluated by fitting a log-linear regression model to the annual data by the method of least squares. The model was of the form  $\ln(y) = a + b(x - \bar{x})$ , where  $y$  = age-adjusted annual rate per million persons and  $x$  = calendar year. This model, which assumes that the percent change in rates is constant over time, has been previously used for the study of short-term cancer trends [Norwegian Cancer Registry, 1982]. The null hypothesis that the regression coefficient  $b$  is zero was evaluated by a  $t$ -test. The annual percentage change in rates was estimated by  $100(e^b - 1)$  and the geometric mean of the annual rates was estimated by  $e^a$  where  $a$  and  $b$  were estimated from the regression model.

## RESULTS

### Trend

Age-adjusted incidence rates for mesothelioma among residents of LAC, NYS, and SEER areas, based on raw data (prior to any pathology review) from the respective registries are shown in Table 1. The rates for all three data sources are generally higher for males than for females. The rates for pleural mesothelioma are higher than those for peritoneal mesothelioma for each sex. LAC (for which 1972 data are included) exhibits a slightly lower incidence for white and nonwhite male pleural mesotheliomas than the combined SEER areas. NYS exhibits a significantly lower incidence than SEER, consistent with the generally less industrialized nature of the New York State area or other differences between urban and rural areas that may be related to mesothelioma. Differences in local pathologists' approach to the diagnosis or in completeness of reporting may also account for some of the differences in incidence.

TABLE 1. Age-Adjusted Mesothelioma Incidence Rates by Study Area, Site, Race, and Sex

|          | Rate (n) <sup>f</sup>           |                         |                             |                         |                     |                         |
|----------|---------------------------------|-------------------------|-----------------------------|-------------------------|---------------------|-------------------------|
|          | Los Angeles County <sup>a</sup> |                         | New York State <sup>b</sup> |                         | SEER <sup>c</sup>   |                         |
|          | Pleura <sup>d</sup>             | Peritoneum <sup>e</sup> | Pleura <sup>d</sup>         | Peritoneum <sup>e</sup> | Pleura <sup>d</sup> | Peritoneum <sup>e</sup> |
| Males    |                                 |                         |                             |                         |                     |                         |
| White    | 11.3 (182)                      | 0.6 (11)                | 7.1 (191)                   | 1.0 (27)                | 13.3 (584)          | 1.7 (77)                |
| Nonwhite | 5.9 (15)                        | 0 (0)                   | 0 (0)                       | 1.8 (2)                 | 7.1 (46)            | 0.4 (3)                 |
| Females  |                                 |                         |                             |                         |                     |                         |
| White    | 1.7 (36)                        | 0.3 (6)                 | 1.7 (58)                    | 1.0 (32)                | 2.5 (138)           | 1.1 (63)                |
| Nonwhite | 1.6 (4)                         | 0.3 (1)                 | 1.1 (2)                     | 0 (0)                   | 2.4 (16)            | 0.8 (6)                 |

<sup>a</sup>Source: Los Angeles County Cancer Surveillance Program, University of Southern California (1972-80).

<sup>b</sup>Source: New York State Cancer Registry (1973-80), excluding New York City.

<sup>c</sup>Source: Registries in SEER Program, NCI (1973-80), excluding Puerto Rico.

<sup>d</sup>ICDO (1976) Morphology Code 905, Topography Code 163.

<sup>e</sup>ICDO (1976) Morphology Code 905, Topography Codes 158.8, 158.9.

<sup>f</sup>Rate per million persons age 15 and older per year, standardized to the 1970 U.S. population. (n), total number diagnosed as mesothelioma (before two-stage pathology review in LAC and NYS).

Figure 1 shows the trends in age-adjusted pleural mesothelioma incidence rates over time from 1973 to 1980 for white males living in the LAC, NYS, and SEER areas, respectively. The increasing trends over time for white males were similar in each study area. A separate analysis of the individual SEER registries revealed an increase in trend for pleural mesothelioma among white males in all but one registry [Connelly et al. submitted for publication].

Table II shows the age-adjusted mean annual rates and annual percentage changes for pleural mesothelioma among white males in LAC, NYS, and SEER as estimated by the log-linear model. The trend over the years 1973-80 was highly significant ( $p < .01$ ) in each of the three data sets for white males. There were insufficient data to measure trends in annual incidence for nonwhites, for peritoneal mesotheliomas in LAC and NYS, or for white females in LAC.

Analysis of age-specific incidence rates for pleural mesothelioma among white males (Table III) showed an increasing trend among older persons during the recent past. The SEER data showed significant increases only among white males above age 65. For NYS the increase began at age 55. The only significant increase for LAC was in the 65-74 age group. An evaluation of LAC and NYS trends by histologic subgroups was inconclusive because of the lack of sufficient numbers of cases. It was only for all histologic subtypes combined that the trend was significant.

#### Pathology Review

Of the 567 pleural and peritoneal cases collected in LAC and NYS, slides were obtained for 428 (75%). Of these, 405 (95%) were judged to be adequate for the

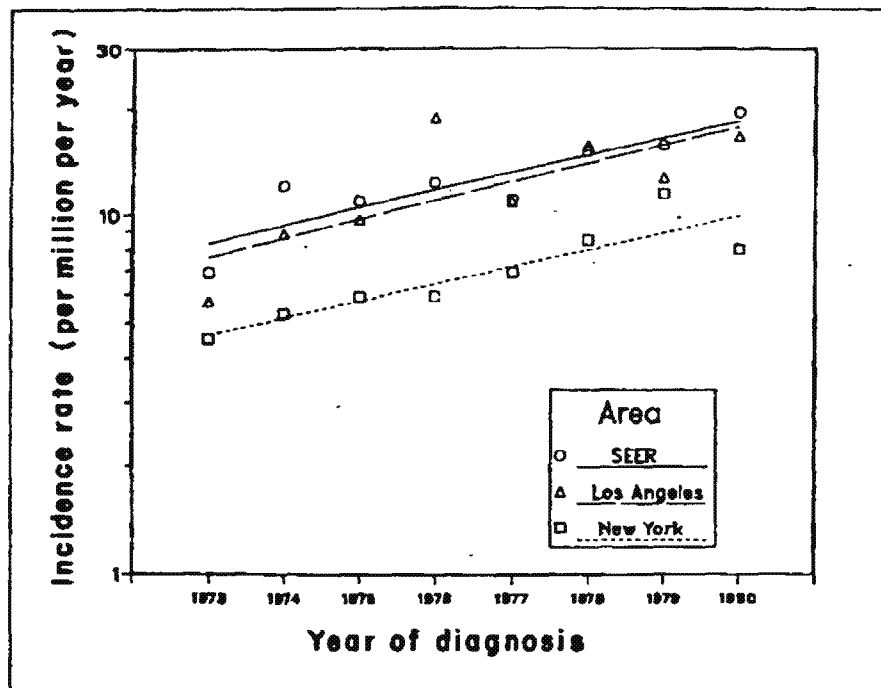


Fig. 1. Trend in age-adjusted pleural mesothelioma incidence rates among white males by study area, 1973-80.

TABLE II. Regression Estimates of Age-Adjusted Pleural Mesothelioma Incidence Rates Among Whites by Study Area, 1973-80

| Study area                      | Males       |                        |                            | Females     |                        |                            |
|---------------------------------|-------------|------------------------|----------------------------|-------------|------------------------|----------------------------|
|                                 | Total cases | Mean rate <sup>d</sup> | Percentage change (annual) | Total cases | Mean rate <sup>d</sup> | Percentage change (annual) |
| Los Angeles County <sup>a</sup> | 176         | 11.6                   | 12.9*                      | 33          | 1.5                    | ns                         |
| New York State <sup>b</sup>     | 191         | 6.8                    | 11.5*                      | 58          | 1.6                    | -0.5                       |
| SEER <sup>c</sup>               | 584         | 12.4                   | 12.1*                      | 138         | 2.4                    | 0.9                        |

<sup>a</sup>Source: Los Angeles County Cancer Surveillance Program, University of Southern California.<sup>b</sup>Source: New York State Cancer Registry, excluding N.Y.C.<sup>c</sup>Source: SEER Program, NCI, excluding Puerto Rico.<sup>d</sup>Rate per million persons age 15 and older per year, standardized to the 1970 U.S. population.

\*p &lt; .01.

ns. Insufficient data to estimate change over time.

TABLE III. Age-Specific Pleural Mesothelioma Incidence Rates Among White Males by Study Area and Time Period

| Age (yrs) | Rate (n) <sup>d</sup>           |            |                             |             |                   |               |
|-----------|---------------------------------|------------|-----------------------------|-------------|-------------------|---------------|
|           | Los Angeles County <sup>a</sup> |            | New York State <sup>b</sup> |             | SEER <sup>c</sup> |               |
|           | 1973-76                         | 1977-80    | 1973-76                     | 1977-80     | 1973-76           | 1977-80       |
| 15-24     | — (0)                           | — (0)      | 0.3 (1)                     | — (0)       | — (0)             | 0.2 (1)       |
| 25-34     | 0.6 (1)                         | — (0)      | — (0)                       | 0.7 (2)     | 1.2 (6)           | 0.2 (1)       |
| 35-44     | 3.3 (5)                         | 0.7 (1)    | 1.9 (4)                     | 1.9 (4)     | 2.6 (9)           | 1.5 (6)       |
| 45-54     | 8.1 (12)                        | 9.7 (14)   | 6.0 (14)                    | 4.6 (10)    | 11.2 (41)         | 13.8 (51)     |
| 55-64     | 21.5 (23)                       | 20.3 (21)  | 11.1 (21)                   | 22.0** (43) | 22.1 (65)         | 28.2 (93)     |
| 65-74     | 40.2 (23)                       | 65.1* (36) | 20.3 (22)                   | 32.8* (38)  | 37.9 (65)         | 66.9*** (132) |
| 75+       | 50.8 (16)                       | 79.2 (24)  | 17.6 (10)                   | 36.4* (22)  | 41.3 (40)         | 68.5** (74)   |

<sup>a</sup>Source: Los Angeles County Cancer Surveillance Program, University of Southern California.<sup>b</sup>Source: New York State Cancer Registry, excluding N.Y.C.<sup>c</sup>Source: Registries in SEER Program, NCI, excluding Puerto Rico.<sup>d</sup>Rate per million persons age 15 and older per year. (n), total number diagnosed as mesothelioma (before two-stage pathology review in LAC and NYS).

Statistically significant difference in age-specific rates between 1973-76 and 1977-80 by one-sided Z-test.

\*p &lt; .05.

\*\*p &lt; .01.

\*\*\*p &lt; .001.

second review panel (at least one biopsy or autopsy section excluding needle biopsies). In the second review of pathology material from LAC and NYS cases (conducted by LH and JCW), the overall level of confirmation was 64% (261/405), which is in the upper range of the 26-75% acceptance rate reported in the mesothelioma literature [Owen, 1965; Greenberg and Lloyd-Davies, 1974; Zielhuis et al, 1975; Bignon et al, 1979; Planteydt, 1979; McDonald and McDonald, 1980; Nicholson, 1983; Wright et al, 1984]. The five pathologists involved in the current study (JNPD, LH, LGO, RPS, JCW) varied in their level of confirmation. One panel expert (RPS) independently reviewed the LAC mesotheliomas and reported only a 29% confirmation rate [Wright et al, 1984]. This issue will be addressed in a subsequent paper on the two levels of diagnostic review.

Table IV contains the results of a logistic regression analysis of the fraction of confirmed cases (from the second review) among potential cases (from source regis-

TABLE IV. Logistic Regression Analysis Pathology Confirmation Rate, Second Review

| Source              | DF | Chi-square | Prob   |
|---------------------|----|------------|--------|
| Intercept           | 1  | 16.34      | 0.0001 |
| Date of review      | 1  | 35.61      | 0.0001 |
| Sex                 | 1  | 15.20      | 0.0001 |
| Registry            | 1  | 8.72       | 0.0031 |
| Age                 | 1  | 8.31       | 0.0039 |
| Histologic category | 2  | 10.88      | 0.0043 |
| Tumor site          | 1  | 0.67       | 0.4125 |
| Tumor site*sex      | 1  | 8.02       | 0.0046 |
| Year of diagnosis   | 1  | 2.14       | 0.1435 |

Sources: Los Angeles County Cancer Surveillance Program, University of Southern California (1972-80) and New York State Cancer Registry (1973-80), excluding N.Y.C.

tries) for LAC and NYS. The purpose of this analysis was to measure the effect of change over time in false positive diagnoses, after adjustment for other factors. In order for the trend in false positive diagnoses to have artifactually been a factor in the observed increase in mesothelioma incidence, the confirmation rate would necessarily have to decrease over time. On the contrary, empirical evidence from the current study implied that the confirmation rate increased over time, i.e., there was a higher percent of true positive diagnoses in more recent years. However, after adjustment for other variables in the model, year of diagnosis had a nonsignificant effect on the confirmation rate.

The following variables significantly affected the confirmation rate: date of review, histologic category, registry, age, and tumor site. In addition, there was an interaction between tumor site and sex. The second pathology review was held in two sessions, October 1983 and May 1984; a greater percent of cases was positively confirmed during the October 1983 session. Tumors were histologically classified as epithelial, biphasic, or mesenchymal. The histologic subgroup having the highest confirmation rate was the mesenchymal, followed by biphasic and epithelial. A greater percent of LAC cases was confirmed than NYS cases. Older cases had a higher confirmation rate than younger cases.

Because of the statistical interaction between tumor site and sex, it is necessary to consider these factors together. Male cases generally had a higher confirmation rate than female. In addition, for female peritoneal cases, the expert pathologists determined that the majority (22/30) were misdiagnosed (usually determined to be female genital cancers). The pattern of confirmation rates by tumor site and sex is shown in Table V.

## DISCUSSION

The trend analyses for pleural mesothelioma among white males during 1973-80 in LAC, NYS, and SEER indicate average annual increases of 13%, 12%, and 12%, respectively. These significant upward trends are, however, limited to older white males. None of the trends for pleural mesothelioma among white females was statistically significant. The current study is consistent with results showing higher

TABLE V. Percent Confirmation by Referee Pathologists: Second Pathology Review by Tumor Site, Sex, and Study Area (Combined Races)

| Sex    | Percentage (n)   |                  |                  |                  |
|--------|------------------|------------------|------------------|------------------|
|        | Pleura           |                  | Peritoneum       |                  |
|        | LAC <sup>a</sup> | NYS <sup>b</sup> | LAC <sup>a</sup> | NYS <sup>b</sup> |
| Male   | 75.6 (135)       | 61.9 (134)       | 100.0 (10)       | 66.7 (21)        |
| Female | 62.5 (32)        | 55.8 (43)        | 0 (7)            | 34.8 (23)        |

<sup>a</sup>Source: Los Angeles County Cancer Surveillance Program, University of Southern California (1972-80).

<sup>b</sup>Source: New York State Cancer Registry (1973-80), excluding N.Y.C.

%, Percent of total with confirmed diagnosis (1, 2, or 3 on International scale).

n, Total number reviewed in each category.

rates for pleural mesothelioma than for peritoneal mesothelioma [McDonald and McDonald, 1977; Ahlmark and Malker, 1981; Vianna et al, 1981; Teta et al, 1983; Armstrong et al, 1984; Wright et al, 1984; Andersson and Olsen, 1985]. However, two cohort studies of heavily exposed asbestos workers [Selikoff et al, 1979; Newhouse and Berry, 1979] showed greater excess risk for peritoneal mesothelioma.

The use of original registry diagnoses to measure trend is comparable to the approach used by Bruckman et al [1977], Mowe [1981], Vianna et al [1981], Armstrong et al [1984], Andersson and Olsen [1985], and Connelly et al [submitted for publication]. However, Wright et al [1984] and Churg [1985] have based their analyses on diagnoses reclassified on the basis of pathology reviews. For a disease which is difficult to diagnose, such as mesothelioma, it is reasonable to try to exclude false diagnoses from analysis. However, in trying to measure trends in disease incidence, it is also important to consider false negative diagnoses. Since we could not measure false negatives for the current study, and since there were cases having inadequate pathology material for review, we chose the original cancer registry diagnosis (prior to any pathology review) for measuring incidence in Tables I-III. This approach also allowed direct comparison with the SEER data. The effect of using rates based upon the second pathology review in the present study lowers the overall incidence estimates but still results in significant increases over time for older white male pleural cases in LAC and NYS.

Walker et al [1983] have suggested that SEER data overestimate mesothelioma incidence in the U.S. because of the disproportionate number of shipbuilding areas in the SEER regions. In a rejoinder to their article, Nicholson [1983] argued that, since the SEER registries omitted many large urban areas where asbestos was used in construction and industrial processes, it was inappropriate for Walker et al [1983] to correct for overrepresentation of shipbuilding areas. In addition, Nicholson [1983] noted a site-specific difference in diagnostic accuracy. An expert pathology review of 175 putative cases indicated agreement on 96.8% of 63 pleural cases and disagreement on 37.5% of 112 cases originally diagnosed as mesothelioma of the peritoneum.

In an attempt to address questions regarding the representativeness of SEER data, Connelly et al [submitted for publication] compared mortality rates from SEER areas with comparable National Center for Health Statistics data from the total U.S. for the years 1973-83. In general, the agreement seemed to be quite close. However, for white male pleural cancer (ICDA-8 = 163.0) the SEER mortality rate per million persons per year was higher than the rate for the entire U.S. (3.1 vs 2.5, respectively)

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after direct age-adjustment to the 1970 U.S. standard. This difference was statistically significant ( $p < 0.01$ ). Thus it does appear that the SEER data may well overestimate the national incidence: it does seem, however, that the SEER data may correctly reflect the changing incidence of mesothelioma.

Another approach seems reasonable for those who wish to estimate the U.S. incidence of mesothelioma. It should be possible to use SEER incidence data and U.S. mortality data in a stratified fashion. One could initially stratify the U.S. according to geographical differences in mortality rates for white male pleural cancer. Next, one would utilize incidence data from appropriately chosen population-based cancer registries to arrive at estimated incidence for each stratum. Finally, one would weight the within-stratum estimates by the appropriate multiplier to arrive at a national estimate. Any projections of the national trend in mesothelioma incidence should consider differences in sex, age, tumor site, race, and geographic area.

Could changes in local diagnostic practices have caused the increasing trend? With no true increase over time, a time-dependent increase in percent of false positive diagnoses, or decrease in false negative diagnoses, could create an apparent increasing trend over time. The sex-, tumor-site-, and age-specificity of the observed increase in two independent cancer registries argues against any appreciable change in diagnostic practice over time. Furthermore, although it was impossible to measure change in false negative diagnoses, the diagnostic reviews of the pathologists did not suggest any important change in false positive diagnoses over time. The only effort to measure false negatives of which we are aware is the study of Teta et al [1983], in which the authors suggest that the number of false negative diagnoses of mesothelioma (diagnosed as primary lung cancer) in the 1970's is approximately one case per thousand cases of lung cancer. However, false negative diagnoses may be classified as diseases other than lung cancer [Connelly et al, submitted for publication].

The observed increase in pleural mesothelioma among white males over 55 years of age is consistent with a cohort effect due to environmental or occupational exposure 25 to 40 years ago. Becklake [1976] has documented the great increase in world-wide asbestos usage which began around 1940. The latent period for mesothelioma due to asbestos exposure is felt to be quite long [Selikoff and Lee, 1978] and Davies [1984] has concluded that, at a minimum, it is 12 years. Thus, the current incidence rates are probably influenced by exposures during and just after World War II. Improvements in worker protection are more difficult to quantify over time, but the passage of the Occupational Safety and Health Act of 1970 may have resulted in improved workplace conditions.

It is difficult to predict future trends in mesothelioma incidence. However, the current levels of incidence are clearly of substantial enough magnitude to justify greater scientific as well as public health and economic concern.

The data collected from LAC and NYS will be pooled with data collected from Veterans Administration Medical Centers as part of a collaborative study that will provide a more detailed analysis of the results of the pathology review, as well as address questions regarding mesothelioma etiology.

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## REFERENCES

- Ahlmark A, Malker H (1981) Potential for epidemiological studies in occupational medicine. *Ann Occup Hyg* 24:159-162.
- Andersson M, Olsen JH (1985) Trend and distribution of mesothelioma in Denmark. *Br J Cancer* 51:699-705.
- Archer VE, Rom WN (1983) Trends in mortality of diffuse malignant mesothelioma of pleura. *Lancet* (July 9):112-113.
- Armstrong BK, Musk AW, Baker JE, Hunt JM, Newall CC, Henzell HR, Blunsdon BS, Clarke-Hundley MD, Woodward SD, Hobbs MST (1984) Epidemiology of malignant mesothelioma in Western Australia. *Med J Aust* 141:86-88.
- Becklake MR (1976) Asbestos-related diseases of the lung and other organs: Their epidemiology and implications for clinical practice. *Am Rev Respir Dis* 114:187-227.
- Bignon J, Sébastien P, Dimenya L, Payan H (1979) French mesothelioma register. *Ann NY Acad Sci* 330:455-466.
- Bruckman L, Rubino RS, Christine B (1977) Asbestos and mesothelioma incidence in Connecticut. *J Air Poll Contr Assoc* 27:121-126.
- Churg A (1985) Malignant mesothelioma in British Columbia in 1982. *Cancer* 55:672-674.
- Connelly RR, Spirtas R, Myers MH, Percy C, Fraumeni JF, Jr. (submitted for publication) Demographic patterns for mesothelioma in the United States. *J Nat Cancer Inst*.
- Davies D (1984) Are all mesotheliomas due to asbestos? *Br Med J* 289:1164-1165.
- Devesa SS, Horn JW, Connelly RR (1984) Trends in lung cancer incidence and mortality in the United States. In Mizell M, Correa P (Eds): "Lung Cancer: Causes and Prevention." Deerfield Beach, Florida: Verlag Chemie Int.
- Gardner MJ, Acheson ED, Winter PD (1982) Mortality from mesothelioma of the pleura during 1968-78 in England and Wales. *Br J Cancer* 46:81-88.
- Greenberg J, Lloyd-Davies TA (1974) Mesothelioma register 1967-8. *Br J Ind Med* 31:91-104.
- Hinds MW (1978) Mesothelioma in the United States: Incidence in the 1970's. *J Occup Med* 20:469-471.
- Kannerstein M, Churg J, McGaughey WTE (1979) Functions of mesothelioma panels. *Ann NY Acad Sci* 330:433-439.
- McDonald JC, McDonald AD (1979) Epidemiology of mesothelioma from estimated incidence. *Prev Med* 6:426-446.
- McDonald AD, McDonald JC (1980) Malignant mesothelioma in North America. *Cancer* 46:1650-56.
- Mowe G (1981) The trend in the incidence of malignant mesothelioma in Norway (1970-1979). *Proceedings of the International Symposium on the Prevention of Occupational Cancer*. Helsinki, 21-24 April 1981. Occupational Safety and Health Series No. 46, ILO, Geneva.
- Newhouse ML, Berry G (1979) Patterns of mortality in asbestos factory workers in London. *Ann NY Acad Sci* 330:53-60.
- Nicholson WJ (1983) Comments on "Projections of Asbestos-Related Disease, 1980-2000." A.M. Walker, unpublished Laboratory Report, Environmental Sciences Laboratory, Mt. Sinai School of Medicine, New York.
- Nicholson WJ, Perkel G, Selikoff IJ (1982) Occupational exposure to asbestos: Population at risk and projected mortality—1980-2030. *Am J Ind Med* 3:259-311.
- Norwegian Cancer Registry (1982) Trends in cancer incidence in Norway, 1955-1978. Oslo, The Cancer Registry of Norway.
- Owen WG (1985) Mesothelial tumors and exposure to asbestos dust. *Ann NY Acad Sci* 132:674-84.
- Peto J, Henderson BE, Pike MC (1981) Trends in mesothelioma incidence in the United States and forecast epidemic due to asbestos exposure during World War II. Banbury Report 9. In Peto R, Schneiderman M (Eds): "Quantification of Occupational Cancer." New York: Cold Spring Harbor Laboratory, pp 51-69.
- Planteydt HT (1979) Netherlands mesothelioma register. *Ann NY Acad Sci* 330:467-71.

- Selikoff JJ (1981) Disability compensation for asbestos-associated disease in the United States. Report to the U.S. Department of Labor. Contract No. J-9-M-8-0165.
- Selikoff JJ, Hammond EC, Seidman H (1979) Mortality experience of insulation workers in the United States and Canada, 1943-1976. *Ann NY Acad Sci* 330:91-116.
- Selikoff JJ, Lee DHK (1978) *Asbestos and Disease*. New York: Academic Press, pp 262-265.
- Strenio J (1984) Asbestos in Buildings: National Survey in Asbestos-containing Friable Materials. U.S. Environmental Protection Agency Report No. EPA 56015-84-006.
- Teta MJ, Lewinsohn HC, Meigs JW, Vidone RA, Howard LZ, Flannery JT (1983) Mesothelioma in Connecticut, 1955-1977: Occupational and geographic associations. *J Occup Med* 25:749-756.
- Vianna NJ, Maslowsky J, Roberts S, Spellman G, Patton RB (1981) Malignant mesothelioma: Epidemiologic patterns in New York State. *NY State J Med*, April 1981, pp 735-737.
- Wagner JC, Sleggs CA, Marchand P (1960) Diffuse pleural mesothelioma and asbestos exposures in the North-West Cape Province. *Br J Ind Med* 17:260-271.
- Walker AM, Loughlin JE, Friedlander ER, Rothman KJ, Dreyer NA (1983) Projections of asbestos-related diseases 1980-2009. *J Occup Med* 25:409-425.
- Wright WE, Sherwin RP, Dickson EA, Bernstein L, Fromm JB, Henderson BE (1984) Malignant mesothelioma: Incidence, asbestos exposures, and reclassification of histopathology. *Br J Ind Med* 41:39-45.
- Zielhuis RL, Versteeg JPI, Planteydt HT (1975) Pleural mesothelioma and exposure to asbestos. *Int Arch Occup Environ Health* 36:1-18.