File: Mesothelioma in Connecticut

Yale University
Inter-Office Correspondence

RECEIVED
Date: 5/5/83 MAY 09 1983

To: Dr. Lewinsohn
H. LEWINSOHN, M.D.

From: Jane

(no tables or appendices attached)

Attached is the final version of the meso paper with the changes we discussed and a copy of the correspondence to JOM.

I talked with Dr. Vidone. There is a possibility for some financial support for a student. Would you like to tell Dr. Cohen or shall I? Our meeting consisted of only a phone call, since my car broke down yesterday.

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May 5, 1983

Doris L. Flournoy, M.S.
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Dear Ms. Flournoy:

A revised version of the paper entitled "Mesothelioma in Connecticut 1955-1977: Occupational and Geographic Associations" was forwarded to you a few weeks ago. Unfortunately, one of the authors had not thoroughly reviewed the manuscript prior to its submission and has requested that a few minor changes be made in one section of the Discussion. These changes are unrelated to the reviewer's comments and, in effect, shorten the report. I am resubmitting the entire manuscript, although the changes involved only pages 14 and 15. I apologize for the inconvenience this may cause you and the editorial board.

Thank you for your cooperation.

Sincerely yours,

Jane Teta

Jane Teta
Associate in Research

JT/rg

Enclosure

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* ... Connecticut State Medical Society, University of Connecticut, Yale University

Title: Mesothelioma in Connecticut 1955-1977: Occupational and Geographic Associations

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Acknowledgements

The authors are grateful for the technical assistance of Lawrence Hally, Regina Robinson, and Marianne Delpo of the Connecticut Cancer Epidemiology Unit and Nora Naughton of the Connecticut Tumor Registry.

This investigation was supported by grants number N01-CP-33235 and N01-CP-61002 awarded by the National Cancer Institute, USDHHS, and by the Institute of Occupational Medicine and Hygiene, Yale University School of Medicine.

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Abstract

All cases of malignant mesothelioma (201) and other primary malignant pleural tumors (19) reported to the Connecticut Tumor Registry from 1955 through 1977 were studied to look for high risk jobs, industries and geographic locations and to try to estimate the risk attributable to asbestos exposure in the workplace. Data sources were hospital records, death certificates and city directories for cases, case spouses and a random sample (604) of Connecticut decedents (1955-1975). Three cases had worked in asbestos products manufacture, but there was no evidence of residential risk in that geographic area. "Carpenters and cabinetmakers" had a RR=2.25 ($p< 0.05$); "plumbers and pipefitters" had a RR=3.87 ($p< 0.05$); persons "ever employed" in the rubber industry had a RR=5.08 ($p< 0.01$). Occupational exposure was indicated in 85% of the cases; attributable risk (AR) was 36%. Risk increased with greater exposure and older age. AR was 81% in men aged 70-89 at diagnosis. Reduction of unnecessary occupational asbestos exposure remains the highest public health priority.

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Introduction

In 1980, Lewinsohn et al (1) provided descriptive information about mesothelioma in Connecticut from 1935-1977. Problems of diagnosis and ascertainment made results prior to 1955 of uncertain value. From 1955-1977 the age-adjusted rates in males rose from about 0.19 to 0.60/100,000 and in females from 0.13 to 0.19/100,000.

Claims have been made by Bruckman et al. in 1977 that increases in the disease are due to the increase in the "cumulative asbestos consumption" and that emissions into the environment (e.g. building construction, demolition, automobile brake-linings) are somehow involved as causative factors (2). The substantial rise, however, in the male:female ratio is more consistent with occupational exposures to men at work. Bruckman et al. were unable to provide complete occupational histories for the 133 diagnosed cases of mesothelioma (1935-1972) drawn from the Connecticut Tumor Registry (CTR) on which their report was based. Despite this limitation, the Air Compliance Unit of the Connecticut Department of Environmental Protection has proposed an ambient air standard of 30ng/m3, measured over a thirty-day interval (3). This proposal was based on estimated asbestos concentrations at several selected sites in Connecticut.

Mesothelioma is a rare disease with approximately 2.2 cases per million population expected annually (4). The proportion of cases not associated with some form of asbestos exposure has been reported to be near 15% (5,6,7). This disease may serve as a marker for unsuspected past asbestos exposure. The present study was designed primarily to examine the job categories and industry titles of identified cases of

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malignant mesothelioma recorded in the CTR to attempt 1.) to identify job categories, industries, specific employers, and Connecticut geographic locations which are associated with an excess risk for mesothelioma and which may also be associated with asbestos usage; and 2.) to determine the proportion of cases with possible exposure to asbestos in the workplace.

The health implications of the proposed ambient air standard make it desirable to estimate the kinds and numbers of cases which may be due to occupational asbestos exposure, other as yet undetermined risk factors, or possible asbestos exposure from the general environment.

There remain numerous unanswered questions concerning the existence of a threshold and the nature of the asbestos-mesothelioma dose-response relationship (8,9). The data available allowed us to approach these problems indirectly. In lieu of dust measurements, job and industry titles, ascertained for study subjects for periods up to 50 years, were used as indicators of exposure.

Methodology

Since mesothelioma has in the past often been confused with other malignant tumors, an anatomic pathology review of all cases reported to the CTR between 1955 and 1977 was undertaken. Histologic material along with gross autopsy and clinical reports were submitted to one of the authors (RAV) for review. No personal identifiers or occupational data were included. Although the final results of this review will be published separately, specific findings will be discussed in the context of the present report.

The CTR has registered 196 cases of primary malignant mesothelioma during the years 1955 to 1977 inclusive. With the exception of the Veterans' Administration (VA) Hospitals in Connecticut, it is mandatory for hospitals to report diagnosed malignant neoplasms to the central registry. A review of all autopsy records from the larger of the 2 VA hospitals in the state from 1955 through 1977 yielded 5 additional cases of mesothelioma. With the addition of these patients, the total number of mesotheliomas increased to 201. This included 137 cases with site pleura, 29 with site peritoneum, and 35 of other or unknown sites. Concerns about diagnostic sensitivity prompted the inclusion of 19 cases reported as pleural tumors other than mesothelioma during the same 23 year time period. These concerns were justified by the slide review which identified several cases of mesothelioma in this group. The total case study population size was 220 (Table 1).

Medical, demographic, and occupational data have been collected for these 220 cases. Similar information gathered by Roush (10) for a computer generated random sample of 604 decedents (1955-1975) aged 20 to 98 years provided a control group. These controls were drawn without stratification of any kind from the death certificate files of the Division of Health Statistics of the Connecticut State Department of Health Services (CSDHS). Death certificates (DC) provided demographic data and usual occupation for study subjects at time of death. City directories (CD) were searched for residential and employment histories 1, 10, 20, 25, 30, 40, and 50 years prior to date of diagnosis or death, provided that the subject was at least 20 years old at the time (11).

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The Price and Lee City Directories, which are available for about two-thirds of Connecticut towns from 1890 to 1980, have a target population of 92% of the adult males in the state. A similar occupational history and cancer search was conducted for all spouses (n=193) of the 220 cases to explore the possibilities for domestic exposure that may have originated in the workplace.

The three-digit 1970 U.S. Census industrial and occupational codes (12) were assigned to the employment information ascertained. Industrial coding was determined on the basis of product descriptions for each employer which were found in the manufacturing directories of Connecticut published by the State Department of Labor and in the Price and Lee Directories for non-manufacturing industries (13).

The study population for occupational analysis was restricted to males over 30 years of age at death or diagnosis. A large proportion of females (46% cases, 31% controls) had no known work history. Although non-occupational etiologies may be a possibility, the absence of reliable occupational data for females prevented a formal analysis of their occupational asbestos exposure. Since all cases were born after 1874, controls born prior to 1875 were excluded. There remained 611 male subjects for the occupational analysis: 136 mesothelioma cases; 11 cases of pleural tumors, other than mesothelioma; and 464 controls. The case-control ratio was approximately 1:3. There were 7 cases included in the analysis who were alive at the time of the data collection period (1978).

Study subjects were first compared on the basis of "ever worked" in selected jobs or industries with known potential for occupational asbestos exposure or for which there were sufficient numbers to be informative. Formal statistical comparisons were made for 7 job categories (engineers; brickmasons and stonemasons; cabinetmakers and carpenters;electricians; foremen; painters, construction and maintenance workers; and plumbers and pipefitters) and for 8 industry categories (construction; misc. non-metallic mineral and stone products; electrical machinery equipment and supplies; aircraft and parts; ship and boatbuilding; yarn, thread and fabric mills; rubber product; and automobile repair and related service). The Mantel-Haenszel odds ratio was the statistical method used to estimate relative risk (RR) (14).

In order to increase statistical power and provide a more direct measure of causation, efforts were made to classify study subjects in terms of the probability of occupational asbestos exposure. A subset of jobs and another subset of industries were selected for which exposure to asbestos was considered either "possible" or "likely" (Appendix A,B). These subsets were developed by one of the authors (HCL) without reference to information about disease status. Comparisons of case-control proportions with occupational asbestos exposure ("possible" and "likely") were analyzed separately for each of three sources of information - job title, industry title, job title and industry title. For each of these comparisons, adjustment was made (non-simultaneously) for age (30-49, 50-69, 70-89), year of birth (1870-1889, 1890-1909, 1910-1929, 1930-1949), and geographic location. The 1966 labor market area (LMA) divisions of Connecticut were utilized for the purpose of geographic risk analysis (15). Particular attention was given to the LMA's surrounding Connecticut's 5 largest urban areas and two rapidly expanding, previously rural regions.

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A scoring procedure was developed in an attempt to provide an indicator of the duration and severity of occupational asbestos exposure for both cases and controls. If a job title in the "likely" category could be documented from DC, CD or both for an individual, a score of "2" was assigned for each documentation. A job title from the "possible" group was given a score of "1", from the "unlikely" subset a score of "0". These values were summed across all available time periods for which employment information was available. Individuals lacking any employment history, which included those never employed and those for whom data were missing, were excluded. The remaining study subjects were each assigned a final single job index of exposure. This crude measure provided an ordered exposure variable, which was categorized into 5 levels. Level 0 included a job index of 0, level 1 included a job index of 1, level 2, a job index of 2; level 3, job indices of 3 and 4; level 4, job indices greater than 4. Each study subject with a job index of exposure was assigned to 1 of the 5 groups. (Although the medical records of some cases noted past occupational asbestos exposure, this information could not be incorporated into the analysis since such data is lacking for controls and has not been systematically collected for cases over time.)

Mantel-Haenszel standardized odds ratios were computed, comparing cases and controls across each of the 4 levels of "exposure" to "no exposure". Finally, the Cochran-Mantel-Haenszel Test of Partial Association (16) was applied to test the disease-exposure relationship for trend while controlling for the potential confounding of age, which was stratified into 20 year intervals: 30-49; 50-69; 70-89. The 90+ stratum with too few numbers to be informative (2 cases, 7 controls) was

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excluded from the "dose-response" analysis. These results are reported for an estimated exposure index based on job only. The coding of industries into the broad categories of the U.S. Census does not discriminate satisfactorily among jobs with different exposures.

Controls tended to be older at death with a mean age of 68 years as opposed to 64 for cases (Table 2). They predominated in the earlier birth cohorts with 81% born prior to 1910. Since age and year of birth are likely to be related to occupational asbestos exposure, as well as to disease status, they were considered potential confounders and controlled for in the analysis, whenever sample size permitted. The confounding effect of these variables, however, was not substantial. The standardized odds ratios differed minimally from the crude, and simultaneous adjustment was not deemed necessary.

The proportions of individuals with at least 1 job title from DC, CD or both were comparable for cases and controls and virtually complete using all sources - 98% for cases, 99% for controls (Appendix C). The percentages with 1-4 and 5-8 job titles were nearly identical. CD provided fewer job and industry titles than DC but more names of specific employers. One year prior to death or diagnosis less information was obtained for controls from CD, most likely attributable to the larger proportion of retirees in the latter group. For all other time periods the percentages of cases and controls with a job or industry title were similar. Using both CD and DC, at least 1 industry title was available for 89% of cases and 90% of controls.

Results

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Secular and time trends for mesothelioma in Connecticut, 1935 through 1977, have been described by the authors in an earlier report (1). In the present case-control occupational risk analysis for the years 1955 to 1977, based on job title alone, the more than 2-fold risk for "cabinetmakers and carpenters" and the nearly 4-fold risk for "plumbers and pipefitters" were significant ($p < 0.05$) (Table 3). Excess risk was observed for engineers, masons, electricians, foremen, and painters. None of these categories reached statistical significance at the 0.05 level. It should be noted that for the job and industry specific analyses the study provided adequate power to detect only large associations for the less common categories of employment. Fourteen of the 15 cases among the carpenters were diagnosed with pleural mesothelioma and the single case of peritoneal mesothelioma was the only one who had worked in a boat-yard. All 7 plumbers and pipefitters were registered at the CTR with pleural mesothelioma, and all were reported in this job category on their death certificate. Although CD data was available for only 4 of these cases, it was in perfect agreement with DC and revealed first employment in this category to be at least 30 years before diagnosis for each.

A parallel comparison of cases and controls using industry title alone revealed a significant association with the rubber industry (RR=5.08; $p < 0.01$) (Table 4), which was particularly striking when limited to subjects 70 to 89 years of age at death or diagnosis (RR=16.97; $p < 0.005$). Three different employers were represented among the 5 cases of pleural and 1 case of peritoneal mesothelioma who had worked at one time in the rubber industry.

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The proportion of cases with "possible" or "likely exposure" to asbestos on the basis of job title was 67% for the entire state, yielding an LMA-adjusted RR of 1.63 ($p < 0.01$). The AR in the exposed was 39%. There was little variation in risk across these geographic regions. The study provided more than 90% power to detect relative risks of 2 or more at the .05 level for this comparison.

On the basis of industry title the overall proportion considered to have been exposed was 66% with a RR of 1.36 ($p < 0.10$) and an AR of 26%. Power calculations for this portion of the analysis yielded results similar to those described above. Substantial inter-regional variation was observed in the percent "exposed" and in the risk for disease. One large industrialized region (LMA1) exhibited nearly a 4-fold risk ($p = 0.02$). One employer in LMA1 accounted for three times as many cases (6) as controls (2) with an unadjusted RR of 9.83. All the cases from LMA5 (with the exception of 1 with industry unknown) worked at one time in an industry judged to be associated with "probable" or "possible exposure". Histologic review of an male cases from LMA1 (area in which an asbestos plant is located) and LMA5 (area in which shipyards are located) resulted in 2 (8%) and 1 (17%) respectively reclassified as "not mesothelioma" or "probably not mesothelioma". There was no observable indication of diagnostic bias (false positives) in these regions where knowledge of an exposure hazard was available in the medical community.

Using "exposure" either through job or industry as a criterion, the statewide proportion of cases with an indicator of occupational exposure was 85%, yielding an age-adjusted RR of 1.57 ($p < 0.05$) and an AR of 36%.

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In an examination of a birth cohort effect, all cases, except those born between 1930 and 1949, were more likely than controls to have been exposed to asbestos on the basis of their job title. The differences were statistically significant (RR=2.16, p< 0.02) for the 1910-1929 cohort only. The overall cohort-adjusted (1870-1889; 1890-1909; 1910-1929; 1930-1949) RR was 1.69 (p< 0.01)

Utilizing the job "exposure" score as previously defined, a monotonic increase in risk associated with higher levels of estimated asbestos exposure was suggested, particularly for the oldest age group (Table 5). There was a slight increase for the 30-49 year old group, but numbers were small and the variances of the RR estimates were large. There was a sizeable number of cases (80) and controls (177) in the 50 to 69 year old group, and a fairly constant risk associated with increasing estimated exposure was indicated. Those males 70 years or older (n=272) with job exposure scores in levels 3 and 4 exhibited highly significant relative risks for this disease. The AR in the exposed for these 2 levels were 78% and 81% respectively. The test for trend which compared the relative proportions of cases and controls across increasing levels of estimated asbestos exposure, while controlling for age, was highly significant overall (p< 0.0005) and for the 70-89 year old age group (p< 0.0001).

Discussion

The major difficulties encountered in a non-interview retrospective study of an asbestos-mesothelioma association relate to the inadequacy of occupational histories, the potential for misclassification of exposure status, and errors in diagnosis. Although partial employment data were obtained for nearly all study subjects, complete work histories were available for very few and information regarding part-time work or hobbies was completely absent. The level of completeness varied geographically, with the less mobile industrialized regions having more complete CD coverage than the more rural less populated areas. Completeness by geographic region did not differ, however, between cases and controls. For the 7 living cases, occupational information could be obtained from CD only. When the analyses were repeated excluding these individuals, however, the findings were unchanged. These occupational history limitations were balanced in part by the advantage that respondent memory bias and faulty interviewing techniques, associated with widely publicized carcinogenic hazards such as asbestos, were avoided in this non-interview approach.

Although the inability to reconstruct dust measurements prevented direct examination of a dose-response relationship, the job "exposure" index, a correlate of asbestos exposure, demonstrated increasing disease risk with higher scores, particularly for the 70-89 year old age group. An attempt was made to test the possibility of a systematic inflation of case scores due to more complete occupational information for the diseased population. Job title availability for the maximum of 8 time periods searched was comparable for both groups (Appendix C) with 71% of cases and 72% of controls having 1-4 job titles and 27% of each having 5-8 job titles. In addition the age-stratified relative risk calculations made adjustment for the large proportion of retirees in the control group with fewer job titles 1 year prior to death. The elevated risks associated with the older age group and with the 1910-1929 birth

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cohort are consistent with the poor dust control measures in most workplaces prevalent in earlier years.

Peto et al (17) in their review of a number of studies showed a wide variation in the pleural:peritoneal ratio among asbestos exposed persons. We have determined this ratio in our cases and attempted to relate it to some parameters which seem to influence its distribution. An analysis of proportions of cases of mesothelioma by site within each of three age groups, 30-49, 50-69, 70-89, for each sex separately, showed that among men the proportions of pleural disease increased as age increased, while the proportions of peritoneal disease decreased. Pleural mesothelioma accounted for 79% of cases aged 50-69 and 93% of cases aged 70-89 at diagnosis. Job attributable risk in the exposed were about 80% for these older men. Results (Table 3) for "carpenters and cabinetmakers" (14 of 15 pleural) and "plumbers and pipefitters" (7 of 7 pleural) are consistent with the above proportions and with Table 5 in suggesting that pleural mesothelioma, in men over 50 in Connecticut, is highly likely to have been associated with and probably caused by exposure to asbestos at work. These data also indicate that occupational exposure to asbestos probably explains most of the disease in these older men and that it began in the 1930's.

Peto et al (17) showed that mesothelioma death rates were independent of age at first exposure, and it may therefore be assumed that age in itself has no direct influence. These authors did show a strong correlation between disease and length of time since first exposure. The fact that the incidence of mesothelioma of the pleura increases sharply in the males in the older age groups with the higher "exposure"

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scores in our cases, is consistent with the long latency known to be associated with this disease. This is also in conformity with Peto's findings.

The potential for random misclassification of exposure status, based on subjective, "blind" review of limited work histories restricts our ability to draw firm conclusions, because such errors produce attenuation toward a relative risk of one. This is particularly relevant with regard to the "true" proportion occupationally exposed and the "true" magnitude of the relative risk, which is likely to be higher than our findings indicate. "Blind" subjective review has also been used by other investigators in estimating exposure, but most often in conjunction with interview data (18,19).

It is widely held that relatively low exposure levels, 20-50 years prior to diagnosis may lead to the development of mesothelioma. The cases described with no known exposure may fall into this category, may have been exposed from the general environment, or may be related to some other unknown etiologic factor. Careful examination of the occupational data for these cases and the controls with no known exposure did not reveal any unusual differences. There were no geographical associations of peritoneal mesothelioma with asbestos cement pipe used in Connecticut in a search made by one of the authors (JWM) in a report to the Environmental Protection Agency.

The possibility of misdiagnosis is important. 964 randomly sampled autopsied cases reported to the CTR as primary lung cancer over the 45 years from 1935-79 were reviewed recently by Dr. Raymond Yesner, Chairman of the World Health Organization Committee on Nomenclature of

Lung Cancer, and one of the authors (JWM). One of these was diagnosed as a mesothelioma. The 5 cases of mesothelioma in the present study identified from VA hospital autopsies included two prior to 1963 whose initial diagnosis had been lung cancer. This suggests that in the past, as many as 1 or 2 per thousand cases diagnosed as lung cancers may have been mesotheliomas, but the proportion is probably smaller at present, because of increased awareness by clinicians and pathologists.

The association with the rubber industry requires additional exploration because of the lack of specific information regarding the many aspects of manufacturing processes lumped into this broad category and the potential for chance association due to the examination of multiple comparisons. McDonald reported (19) 3 cases and 1 control who were employed by a factory making rubber products in her North American Survey of mesothelioma. These were selected from all male cases (150) and their matched controls, who did not work in occupations associated with likely asbestos exposure. Exposure to rubber among all 344 case-control matched pairs in her survey did not reveal an elevated relative risk. The association was in fact in the opposite direction (RR=0.6).

The manufacture of asbestos-containing friction materials was associated with job histories in only 3 cases in the present study. First hire was in the 1920's and 1930's with time intervals of about 30 years before mesothelioma was diagnosed. Slide review confirmed a diagnosis of peritoneal mesothelioma in a female clerical worker (case 1) with approximately 30 years employment. In this individual asbestosis was also considered to be present. Similarly, in a male employee (case 2) with the same surname, a diagnosis of "possibly pleural mesothelioma" was made. These 2 individuals were discovered to be brother and sister-in-law. Their common relative (the husband of case 1 and brother of case 2) was employed by the same asbestos company for a period of at least 30 years and died aged 56 years of an acute coronary thrombosis. He resided consecutively with his brother for at least 17 years and with his wife for over 15 years prior to his death. The third case from the same plant, another female clerical worker who was employed there less than 5 years, was classified "probably pleural mesothelioma". In a search of city directories by single years, no other employment was found for this woman.

Two of the 3 cases employed at the asbestos plant were identified by McDonald in her recently reported cohort study, (20) which was based on death certificate information and employee records. The diagnosis of mesothelioma, however, was not ascertained since no mention of this disease was made on either death certificate. The third person, a male, employed 1921-1932, was not included in McDonald's cohort which was defined as persons employed in the period 1937 to 1959 only. These 3 cases represented only small proportions (1 of 30 males, 2 of 12 females) with mesothelioma in the LMA that included the plant making asbestos products. Most of the remaining male cases had occupational history indicators of asbestos exposure at work.

There was no support for the hypothesis of a significant residential risk to persons living in the vicinity of this plant. The original case-control proportions residing at time of death or diagnosis in LMA1 were 20% and 12% for males and 17% and 18% for females, respectively. After excluding all males with "possible" or "likely" occupational

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asbestos "exposure", based on job title or industry title or both, there remained 9.5% of all male cases and 9.2% of all male controls in that LMA. No real residential difference was now observable for either males or females. This result may be related to the asbestos fiber type used at the plant, which McDonald reported to have been the less hazardous chrysotile and would, therefore, not be extrapolated to all asbestos products manufacturers.

One of the female cases who worked at the asbestos friction materials plant may have had domestic exposure from her husband who also worked there for many years. We explored this general issue by reviewing cancer incidence among 193 spouses, the majority of whom were female. Twenty-seven case spouses have been reported to the CTR (1935-1978) with a confirmed malignancy. There are no reported tumors of the pleura, lung, peritoneum, or ovary in the spouse group. This provided no indication of domestic risk. However, since there were no control spouses, inferences involving domestic exposure were very limited.

Only 2 "probable" cases and 1 "possible" case of mesothelioma were known to have worked in shipbuilding or repair. The LMA that included these industries showed no excess proportion of cases over controls. Selikoff (personal communication) has suggested that heavy asbestos exposures occurred in the late 1940's and that cases might develop in the 1970's and later. The two "probable" cases with recorded shipbuilding employment in the present study were diagnosed in 1975 and 1976, which is consistent. The findings of Peto et al., (21) however, indicate that the consequences of wartime exposure may have been exaggerated. Future data from Connecticut should clarify this question.

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Conclusion

Difficulties in ascertaining occupational asbestos exposure histories in our study population indicate a need for better recordkeeping in industry, medical institutions, and tumor registries. Our methodology, utilizing indirect means of ascertainment, has enabled us to estimate the extent to which occupation or industry may affect the incidence of mesothelioma among males in Connecticut. Job-related or industry-related factors appear to account for a large percentage of all male mesothelioma cases diagnosed in the State between 1955 and 1977. Lack of detailed information regarding the residual cases may obscure the true number occupationally exposed. The large proportion of older male cases with some indication of occupational exposure, the increase over time in the male:female ratio, and the lack of difference between the proportion of cases and controls without evidence of occupational exposure residing in the LMA containing an asbestos plant, do not provide support that ambient air concentrations are a major factor in influencing the observed increment in mesothelioma cases over the study period. The reduction of unnecessary exposure to asbestos in the workplace remains the highest public health priority.

Future studies of the mesothelioma cases recorded in the CTR should endeavor to clarify the clusters of cases in the rubber manufacturing industry and in the plant located in LMA1 where a RR of nearly 10 was observed. Collaboration of the industry or industries concerned will be sought to explore the implications of these results. This will be attempted in conjunction with continuing surveillance of mesothelioma in

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Connecticut.

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