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Mesothelioma in Connecticut, 1955-1977

Occupational and Geographic Associations

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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 in an attempt to identify high-risk jobs, industries and geographic locations and to estimate the risk attributable to asbestos exposure in the workplace. Data were obtained from hospital records, death certificates and city directories for cases, case spouses and a random sample (604) of Connecticut decedents (1955-1975). Three cases involved histories of work in asbestos products manufacture, but there was no evidence of residential risk in that geographic area. Relative risk (RR) for carpenters and cabinetmakers was 2.25 ($p < .05$); for plumbers and pipefitters, 3.87 ($p < .05$); and for persons "ever employed" in the rubber industry, 5.08 ($p < .01$). 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 to 89 years at diagnosis. Reduction of unnecessary occupational asbestos exposure remains the highest public health priority.

In 1980, Lewinsohn et al[1] described mesothelioma in Connecticut from 1935 through 1977. Problems of diagnosis and ascertainment made results for the years prior to 1955 of uncertain value. From 1955 through 1977 the age-adjusted rates among males rose from about 0.19 to 0.60/100,000 and among females from 0.13 to 0.19/100,000.

Bruckman et al[2] claimed 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. The substantial rise, however, in the male-female ratio is more consistent with occupational exposures of 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 30 ng/m^3, measured over a 30-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%.[5-7] 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 malignant mesothelioma recorded in the CTR in an attempt to (1) identify job categories, industries, specific employers, and Connecticut geographic locations that are associated with an excess risk for mesothelioma and that may also be associated with asbestos usage; and (2) determine the proportion of cases involving 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 that 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 as-

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bestos-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 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, was submitted to one of us (R.A.V.) 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 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 two VA hospitals in the state from 1955 through 1977 yielded five additional cases of mesothelioma, bringing the total number 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 period. These concerns were justified by the slide review that 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 was gathered by Roush et al[10] for a computer-generated random sample of 604 decedents (1955-1975) aged 20 to 98

Table 1 – Sex, Age and Diagnostic Classification of 201 Cases of Malignant Mesothelioma and 19 Other Pleural Tumors Diagnosed in Connecticut, 1955-1977

Diagnosis*	Males	Females	Total	Mean Age†
Pleural mesothelioma	100	37	**137**	63
Pleural tumor (other than mesothelioma)	11	8	**19**	63
Peritoneal mesothelioma	18	11	**29**	59
Mesothelioma at other sites and at unknown sites	21	14	**35**	54
Total	**150**	**70**	**220**	**61**

* World Health Organization (1976), as originally recorded by CTR

† At diagnosis

years who 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 (DCs) provided demographic data and usual occupation for study subjects at time of death. City directories (CDs) 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] 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 nonmanufacturing 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 nonoccupational 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. Seven cases included in the analysis were those of individuals who were alive at the time of the data collection period (1978).

Study subjects were first compared on the basis of whether they had "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 seven job categories (engineers; brickmasons and stonemasons; cabinetmakers and carpenters; electricians; foremen; painters, construction and maintenance workers; and plumbers and pipefitters) and for eight industry categories (construction; miscellaneous nonmetallic mineral and stone products; electrical machinery equipment and supplies; aircraft and parts; ship and boat building; yarn, thread and fabric mills; rubber product; and automobile repair and related service). The Mantel-Haenszel odds ratio was used to estimate relative risk (RR).[14]

To increase statistical power and provide a more direct measure of causation, efforts were made to classify study stubjects 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" (Tables 2 and 3). These subsets were developed by one of us (H.C.L.) without reference to information about disease status. Comparisons of case-control proportions with occupational asbestos

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Table 2 – Estimates of the Probability of Asbestos Exposures in Two Categories by U.S. Census Code and Job Title

Category			
Likely		Possible	
U.S. Census Code	Job Title	U.S. Census Code	Job Title
*012	Electrical and electronic engineer	006	Aeronautical and astronautical engineer
013	Industrial engineer	011	Civil engineer
014	Mechanical engineer	022	Sales engineer
404	Boilermaker	023	Engineer, n.e.c.
*486	Railroad and car shop	056	Personnel and labor relations workers
*522	Plumbers and pipefitters	140	Teachers, college and university
*525	Power station operator	142	Elementary school teachers
*534	Roofers and slaters	*151	Chemical technicians
*601	Asbestos and insulation workers	152	Draftsmen
615	Dry wall installers and lathers	173	Technicians, n.e.c.
622	Furnacemen, smelter-men, and pourers	190	Painters and sculptors
*751	Construction laborers, excluding carpenters' helpers	216	Managers and superintendents, building
		221	Officers, pilots, and pursers; ship
		326	Insurance adjusters, examiners and investigators
		403	Blacksmiths
		410	Brickmasons and stonemasons
		413	Cabinetmakers
		415	Carpenters
		424	Cranemen, derrickmen, hoistmen
		*430	Electricians
		*433	Electric power linemen and cablemen
		436	Excavating, grading, and road machine operators; exc. bulldozer
		441	Foremen, n.e.c.
		442	Forgemen and hammermen
		446	Heat treaters, annealers, and temperers
		454	Job and die setters, metal
		*455	Locomotive engineer
		461	Machinists
		471	Mechanics and repairmen; aircraft
		*473	Automobile mechanics
		481	Heavy equipment mechanics; including diesel
		482	Household appliance and accessory installers and mechanics
		483	Loom fixers
		492	Miscellaneous mechanics and repairmen
		495	Not specified mechanics and repairmen
		502	Millwrights
		503	Molders, metal
		*510	Painters, construction and maintenance
		514	Pattern and model makers, excluding paper
		533	Rollers and finishers, metal
		535	Sheetmetal workers and tinsmiths
		545	Stationary engineers
		550	Structural metal craftsmen
		552	Telephone installers and repairmen
		561	Tool and die makers
		610	Checkers, examiners, and inspectors; manufacturing
		611	Clothing ironers and pressers
		621	Filers, polishers, sanders, buffers
		*623	Garage workers and gas station attendants
		641	Mixing operatives
		650	Drill press operatives
		651	Grinding machine operatives
		661	Sailors and deckhands
		662	Sawyers
		†670	Carding, lapping and combing operatives
		†672	Spinners, twisters and winders
		†673	Weavers
		†674	Textile operatives, n.e.c.
		†680	Welders and flame-cutters
		†681	Winding operatives, n.e.c.
		690	Machine operatives, miscellaneous specified
		*694	Miscellaneous operatives
		695	Not specified operatives
		710	Motormen; mine, factory, logging camp, etc.
		753	Freight and material handlers
		*760	Longshoremen and stevedores
		944	Hardressers and cosmetologists

* An occupation identified in reference sources as having potential for asbestos exposure or actually described in conjunction with a case in the literature

† Occupations in textile factories that need further investigation to determine whether asbestos textiles were involved as distinct from cotton, wool or manmade fibers

(n.e.c. = not otherwise classified)

Table 3 – Estimate of the Probability of Asbestos Exposures in Two Categories by U.S. Census Code and Industry Title

Category			
Likely		Possible	
U.S. Census Code	Industry Title	U.S. Census Code	Industry Title
057	Nonmetallic mining and quarrying except fuel	127	Cement, concrete, gypsum, and plaster products
067	General building contractors	128	Structural clay products
068	General contractors, except building	158	Fabricated structural metal products
069	Special trade contractors	289	Beverage industries
138	Miscellaneous nonmetallic mineral and stone products	318	Miscellaneous textile mill products
139	Blast furnaces, steel works, rolling and finishing mills	328	Pulp, paper, and paperboard mills
147	Other primary iron and steel industries	337	Paperboard containers and boxes
148	Primary aluminum industries	348	Plastics, synthetics and resins, excluding fibers
149	Other primary nonferrous industries	379	Rubber products
168	Miscellaneous fabricated metal products	407	Railroads and railway express service
177	Engines and turbines	417	Trucking service
199	Household appliances	419	Water transportation
207	Radio, TV, and communication equipment	427	Air transportation
208	Electrical machinery, equipment and supplies, n.e.c.	567	Alcoholic beverages – wholesale
209	Not specified electrical machinery, equipment and supplies	609	Department and mail order establishments
227	Aircraft and parts	627	Miscellaneous general merchandise stores
228	Shipbuilding and boat building and repairing	648	Gasoline service stations
229	Railroad locomotives and equipment	649	Miscellaneous vehicle dealers
239	Scientific and controlling instruments	758	Electrical repair shops
258	Ordnance	759	Miscellaneous repair services
467	Electric light and power	857	Elementary and secondary schools
477	Water supply	858	Colleges and universities
529	Electrical goods – wholesale	867	Educational services, n.e.c.
539	Machinery equipment and supplies – wholesale	888	Engineering and architectural services
558	Petroleum products – wholesale		
568	Paper and its products – wholesale		
569	Lumber and construction materials – wholesale		
607	Lumber and building material retailing		
639	Motor vehicle dealers		
647	Tire, battery, and accessory dealers		
668	Household appliances, TV and radio stores		
757	Automobile repair and related services		
779	Laundering, cleaning, and other garment services		
917	Federal public administration		
927	State public administration		
937	Local public administration		

(n.e.c. = not otherwise classified)

exposure (possible and likely) were analyzed separately for each of three sources of information – job title, industry title, and job title and industry title. For each of these comparisons, adjustment was made (nonsimultaneously) for age (30 to 49 years, 50 to 69 years, 70 to 89 years), 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 geographic risk analysis.[15] Particular attention was given to the LMAs surrounding Connecticut's five largest urban areas and two rapidly expanding, previously rural regions.

A scoring procedure was developed to provide an indicator of the duration and severity of occupational asbestos exposure for both cases and controls. For each job title in the "likely" category that could be documented from DCs, CDs or both for an individual, a score of 2 was assigned. A job title from the "possible" group was given a score of 1 and 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. Each of the remaining study subjects was assigned a final single job index of exposure. This crude measure provided an ordered exposure variable, which was categorized into five 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 indexes of 3 and 4; and level 4, job indexes greater than 4. Each study subject with a job index of exposure was assigned to one of the five 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 were 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 four 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 to 49 years; 50 to 69 years; 70 to 89 years. The 90+ stratum with too few numbers to be informative (two cases, seven controls) was 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 4). 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 one job title from DCs, CDs or both were comparable for cases and controls and virtually complete using all sources – 98% for cases, 99% for controls (Table 5). The percentages with 1-4 and 5-8 job titles were nearly identical. CDs provided fewer job and industry titles than DCs but more names of specific employers. One year prior to death or diagnosis less information was obtained for controls from CDs, 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 CDs and DCs, at least one industry title was available for 89% of cases and 90% of controls.

Table 4 – Demographic Characteristics of Cases and Controls*

	Cases	Controls
Mean year of death or diagnosis	1969	1966
Mean age at death or diagnosis	64	68
Birth Cohort Distribution, %		
1870 – 1889	8	32
1890 – 1909	56	49
1910 – 1929	33	18
1930 – 1949	3	1
	100	100

* Males older than 30 years at death or diagnosis, born after 1874

Results

We have described secular and time trends for mesothelioma in Connecticut from 1935 through 1977 in an earlier report.[1] In the present case-control occupational risk analysis for the years 1955 through 1977, based on job title alone, the more than twofold risk for cabinetmakers and carpenters and the nearly fourfold risk for plumbers and pipefitters were significant ($p < .05$) (Table 6). Excess risk was observed for engineers, masons, electricians, foremen, and painters, but in none of these categories did it reach statistical significance at the .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 as pleural mesothelioma and the single case of periotoneal mesothelioma occurred in the only individual who had worked in a boat yard. All seven plumbers and pipefitters were registered at the CTR with pleural mesothelioma, and all death certificates reported them to be in this job category. Although CD data were available for only four of these cases, it was in perfect agreement with DC data 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 (relative risk [RR] = 5.08; $p < .01$) (Table 7), which was particularly striking when limited to subjects 70 to 89 years of age at death or diagnosis (RR = 16.97; $p < .005$). Three different employers were represented among the five individuals with pleural and one with peritoneal mesothelioma who had worked at one time in the rubber industry.

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 ($p < .01$). The attributable risk (AR) in the exposed group 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 an RR of 1.36 ($p < .10$) and an AR of 26%. Power calculations for this portion of the analysis yielded results similar to those described above. Substantial interregional variation was observed in the percent "exposed" and in the risk for disease. One large industrialized region (LMA1) exhibited nearly a four-fold risk ($p = .02$). One employer in LMA1 accounted for three times as many cases (six) as controls (two) with an unadjusted RR of 9.83. All the cases from LMA5 (with the exception of one with "industry unknown") had worked at one time in an industry judged to be associated with "probable" or "possible exposure." Histologic review of all male cases from LMA1 (an area in which an asbestos plant is located) and LMA5 (an area in

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Table 5 – Completeness of Occupational Data for Cases and Controls From Death Certificates and City Directories

Source	% with Job Title*		% With Industry Title		% With Employer Name	
	Cases	Controls	Cases	Controls	Cases	Controls
DC	92†	96	73†	85	59†	41
CD	76	69	69	67	71	53
1 yr prior to Dx	46	26	45	23	47	17
10 yr prior to Dx‡	53	42	43	40	45	28
20 yr prior to Dx‡	46	45	39	45	40	29
25 yr prior to Dx‡	41	39	36	39	34	27
30 yr prior to Dx‡	30	35	30	36	31	25
40 yr prior to Dx‡	26	24	19	23	19	15
50 yr prior to Dx‡	10	18	8	14	3	8
DC and CD	98	99	89	94	NC§	NC§
1-4 job titles‖	71	72	...	...	...	...
5-8 job titles‖	27	27	...	...	...	...

* Uninformative titles such as retired, student excluded

† When seven cases in living persons excluded from the denominator, percentages become 96, 76, 62

‡ Cases less than 20 years of age at search year excluded from denominator

§ NC indicates not calculated

‖ Total number of jobs for cases = 475 (3.23/case); for controls = 1,412 (3.04/control)

which shipyards are located) resulted in reclassification of two (8%) and one (17%), respectively, 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 ($p < .05$) and an AR of 36%.

In an examination of a birth cohort effect, all individuals, 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, $p < .02$) for the 1910-1929 cohort only. The overall cohort-adjusted (1870-1889; 1890-1909; 1910-1929; 1930-1949) RR was 1.69 ($p < .01$)

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 8). There was a slight increase

Table 6 – RR of Mesothelioma Associated With Selected Job Categories

Job Title	RR	95% Confidence Interval	N*
Engineers	2.72	(.85, 8.68)	11
Brickmasons and stonemasons	2.15	(.37, 12.50)	5
Cabinetmakers and carpenters	2.25†	(1.13, 4.48)	35
Electricians	1.29	(.39, 4.24)	14
Foremen	1.57	(.84, 2.94)	50
Painters, construction, and maintenance	1.39	(.52, 3.71)	20
Plumbers and pipefitters	3.87†	(1.38, 10.82)	13

* N indicates the number of male cases and controls older than 30 years at death or diagnosis, born after 1874, who "ever worked" in the category; total N for each independently calculated RR was 611 (147 cases, 464 controls)

† $p < .05$

Table 7 – RR of Mesothelioma Associated With Selected Industry Categories

Industry Title	RR	95% Confidence Interval	N*
Construction	1.21	(.60, 2.45)	45
Miscellaneous nonmetallic mineral and stone products	1.64	(.15, 18.06)	3
Electrical machinery equipment, and supplies	2.79	(.86, 6.67)	20
Aircraft and parts	1.03	(.43, 2.49)	25
Shipbuilding and boat building	1.09	(.35, 3.42)	16
Yarn, thread and fabric mills	.57	(.17, 1.92)	20
Rubber product	5.08†	(1.60, 16.11)	10
Automobile repair and related service	.65	(.08, 5.53)	6

* N indicates number of male cases and controls older than 30 years at death or diagnosis, born after 1874, who "ever worked" in the category; total N for each independently calculated RR was 611 (147 cases, 464 controls)

† $p < .01$

Table 8 – RR of Mesothelioma Associated With Level of Occupational Asbestos Exposure by Age

	Level of Occupational Asbestos Exposure						
Age Group	0	1	2	3*	4†	N	χ^2 for Trend
30-49	1.00	.39	.47	1.17	. . .‡	66	NS
50-69	1.00	1.11	1.59	1.60	1.67	257	NS
70-89	1.00	2.19	1.78	4.59§	5.35§	272	.0001
All ages‖	1.00	1.19	1.34	2.20¶	2.73§	611	.0005

* Level 3 is exposure scores 3 or 4
† Level 4 is exposure scores 5 to 16
‡ RR could not be calculated due to 0 denominator; one case, 0 controls with "exposure"
§ $p < .001$
‖ Age-adjusted relative risks
¶ $p < .005$

for the 30 to 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 ARs for those exposed in these two levels were 78% and 81%, respectively. The test for trend that compared the relative proportions of cases and controls across increasing levels of estimated asbestos exposure, while controlling for age, was highly significant overall ($p < .0005$) and for the 70 to 89-year-old age group ($p < .0001$).

Discussion

The major difficulties encountered in a noninterview 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 seven cases in living persons, occupational information could be obtained from CDs 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 noninterview 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 to 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 eight time periods searched was comparable for both groups (Table 5) 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 one year prior to death. The elevated risks associated with the older age group and with the 1910-1929 birth 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 that seem to influence its distribution. An analysis of proportions of cases of mesothelioma by site within each of three age groups, 30 to 49 years, 50 to 69 years, and 70 to 89 years, 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 to 69 years and 93% of cases aged 70 to 89 years at diagnosis. Job AR in the exposed was about 80% for these older men. Results (Table 6) for carpenters and cabinetmakers (14 of 15 pleural) and plumbers and pipefitters (seven of seven pleural) are consistent with the above proportions and with Table 8 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 1930s.

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" scores in our cases, is consistent with the long latency known to be associated with this disease. This is also in conformity with Peto et al'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 an RR of 1. This is particularly relevant with regard to the "true" proportion occupationally exposed and the "true" magnitude of the RR, 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 to 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 us (J.W.M.) in a report to the Environmental Protection Agency.

The possibility of misdiagnosis is important. Dr. Raymond Yesner, chairman of the World Health Organization Committee on Nomenclature of Lung Cancer, and one of us (J.W.M.) recently reviewed 964 randomly sampled autopsy cases reported to the CTR as primary lung cancer during the 45 years from 1935 through 1979. One of these was diagnosed as a mesothelioma. The five cases of mesothelioma in the present study identified from VA hospital autopsies included two pre-1963 cases in which the initial diagnosis had been lung cancer. This suggests that in the past, as many as one or two 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[19] reported three cases and one 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 RR. 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 three cases in the present study. First hire was in the 1920s and 1930s 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 two 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 at age 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, that of a female clerical worker who had been employed there less than five years, was classified as "probably pleural mesothelioma." In a search of city directories by single years, no other employment was found for this woman.

Two of the three cases in employees at the asbestos plant were included by McDonald and Fry[20] in their recently reported cohort study, 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 who was employed during the period 1921 to 1932, was not included in McDonald and Fry's cohort which was defined as persons employed in the period 1937 to 1959 only. These three cases represented only small proportions (one of 30 males, two 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 among those residing in LMA1 at time of death or diagnosis were 20% and 12% for males and 17% and 18% for females, respectively. After excluding all males with "possible" or "likely" occupational 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 observed for either males or females. This result may be related to the asbestos fiber type used at the plant, which McDonald and Fry reported to have been the less hazardous chrysotile and would, therefore, not be extrapolated to all asbestos products manufacturers.

One of the female cases, an employee 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 two persons with "probable" cases and one with a "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 (oral communication, 1978) has suggested that heavy asbestos exposures occurred in the late 1940s and that cases might develop in the 1970s 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.

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 mesothelioma cases in males diagnosed in the State between 1955 and 1977. Lack of detailed informa-

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tion regarding the residual cases may obscure the true number occupationally exposed. The large proportion of cases of older men 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 for the view that ambient air concentrations were a major factor in influencing the observed increment in cases of mesothelioma during the course of 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 an 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 Connecticut.

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