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PLAINTIFF'S EXHIBIT

UC-4215

MALIGNANT MESOTHELIOMA IN CONNECTICUT 1935-1977

by

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II. Methodology

The CTR has identified 229 cases of malignant mesothelioma as well as 38 other pleural tumors, not mesothelioma, which were diagnosed in the state between 1935 and 1977 (Table 1).

Medical, demographic, and occupational data have been collected for the cases and for the respective spouses of cases diagnosed 1955-1977. Similar information has been gathered for a random sample of approximately 700 decedents (1935-75) aged 20 to 98 years from the Division of Health Statistics of the Connecticut Department of Health Services.

Descriptive epidemiology for this research pertains primarily to the forty-three year time interval. ~~Future~~ The case-control comparisions will ~~include~~ comprise cases (215) diagnosed after 1954 (Table 1), and controls (604) whose deaths occurred during this same time period. This procedure yields a case-control ratio of approximately 1:3, while reducing sources of error resulting from the limited occupational and medical data prior to 1955 and the lack of awareness of mesothelioma associated with this earlier time period (1935-1954). The Price and Lee City Directories (4) were searched for job title and name of specific employer or industry for cases, controls and spouses at 1, 10, 20,25, 30, 40 and 50 years prior to date of diagnosis, death or until the subject was less than twenty years old. An occupational history search was attempted for spouses to coincide with these intervals for their corresponding cases.

1970 U.S. Census industrial and occupational codes (U.S. Dept. of Commerce, 1971) (5) were assigned to the employment information ascertained from medical histories, death certificates, and City Directories. A computerized

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Table 1. Sex, age and diagnostic characteristics of 229 cases of malignant mesothelioma and 38 other pleural tumours diagnosed in Connecticut, 1935-1977

Diagnosis[a]	Males		Females		Total		Mean age	
Pleural mesothelioma	102	(94)[b]	45	(37)	147	(131)	61	(62)
Pleural tumour (other than mesothelioma)	24	(12)	14	(8)	38	(20)	62	(63)
Peritoneal mesothelioma	20	(18)	13	(11)	33	(29)	58	(59)
Mesothelioma at other sites & at unknown sites	29	(21)	20	(14)	49	(35)	52	(54)
Total	175	(145)	92	(70)	267	(215)	59	(60)

[a] WHO (1976) (1)

[b] Numbers in brackets refer to the period 1955-1977

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list of job and industry titles has been developed for all cases, spouses, and controls (1955-1977). This will form the basis for classification of study subjects into asbestos exposure categories for future case-control comparisons (sample from listing Fig. 1).

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III. Results

Descriptive Epidemiology

The following ~~descriptive~~ results are based upon ~~the information available from the~~ CTR and will require adjustment following ~~the~~ completion of ~~our~~ slide review. Using the 1950 US population as a standard, the age-adjusted incidence rate for mesothelioma in Connecticut is 2.1/million for the years 1935-1977. Rates per 100,000 population increased for both sexes, but there was a rapid rise from about 1960 for males (Fig. 2). The male-female ratio is approximately 2:1; the mean age at diagnosis is fifty-nine years. Average survival time from date of diagnosis to date of death is ten months.

~~Ten~~ New London Labor Market Area (LMA) ~~(New London)~~ cases were reported in ~~a~~ where shipyards are located, and ~~five~~ 5 (5%) of these were identified between 1975 and 1977 (Fig. 3). The geographical distribution of mesothelioma shows evidence of urban clusters in the 5 largest cities (Bridgeport, Hartford, Waterbury, Stamford , New Haven) where 30 % of the cases resided at time of diagnosis (Fig. 3). Since these locations have comprised 20-30% of Connecticut's population (1940-1977), the suggested urban effect may reduce to a factor of population density. These 5 large cities and New London are ~~also~~ all centers for ~~Labor Market Areas (LMA)~~ LMA's. All 6 areas exhibit a similarly increasing age-adjusted incidence rate for males. The Stamford LMA's mesothelioma rate shows an unexplained sharp increase since 1965 (Fig. 4).

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AGE-ADJUSTED INCIDENCE RATES OF MESOTHELIOMA
IN CONNECTICUT BY YEAR OF DIAGNOSIS AND SEX

RATE\100,000

10. 20. 30. 40. 50. 60.

Male
Female
Both

1935-39
40-44
45-47
48-52
53-56
57-61
62-66
67-71
72-75

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GEOGRAPHICAL MAPPING OF CASES OF MESOTHELIOMA (1955-1977)
BY TOWN OF RESIDENCE AND 1960 LABOR MARKET AREA

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Fig 7

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SLIDE REVIEW

Malignant mesothelioma is a very rare disease with only 2 cases per million population expected annually.[7] Resistance to the acceptance of mesothelioma as a disease entity persisted until the late 1960's.[8] Wagner's widely publicized association of mesothelioma with Cape Crocidolite asbestos exposure created the potential for the introduction of diagnostic bias.[9]

Positive diagnosis of mesothelioma is often complicated by its confusion with other forms of cancer..(Vidone discussion of simulators).
The controversy over criteria for positive diagnosis is well documented in the literature.[10] Most experts agree, however, that a full autopsy is required to positively distinguish diffuse mesothelioma of the pleural or peritoneum from other primary or secondary neoplasms.[11]

We examined, for all CTR reported cases of mesothelioma and for all pleural tumors other than mesothelioma (1935-77), the histological basis for diagnosis (Tables 2,3). For 12% (32) of the cases, no tissue was examined at time of diagnosis, while the origin of available material varied. Overall (1935-77) only 44% 105 (~~105~~) of the 238 deceased cases are known by the CTR to have been autopsied, but only 82 of the autopsied cases were microscopically confirmed. The percentages for all categories, except peritoneal mesothelioma, are low ranging from 33% to 40% autopsied,

These results suggested the advisability of a ~~slide~~ case review. Dr. Romeo Vidone, chief pathologist of St. Raphael's Hospital, is presently studying the medical records (except occupational data) and slides we have obtained for cases diagnosed after 1954. Cooperation was sought from 37 hospitals, of which 30 have thus far provided us with the materials requested.

(Summary of Dr. Vidone's preliminary Findings)

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Table 2: Basis for Diagnostic Evaluation
for cases of Malignant Mesothelioma
and Pleural Tumors other than
Mesothelioma Diagnosed in Connecticut, 1935-1977

Diagnosis[a]	Tissue[b] Available	%	No Tissue Available	%	Total	%
Pleural Mesothelioma	136	(93)	11	(7)	147	(100)
Pleural Tumor (other than mesothelioma)	27	(71)	11	(29)	38	(100)
Peritoneal Mesothelioma	31	(94)	2	(6)	33	(100)
Mesothelioma at other sites and unknown sites	41	(84)	8	(16)	49	(100)
Total	235	(88)	32	(12)	267	(100)

[a] WHO (1976)

[b] specimen from biopsy, frozen section, surgery, autopsy, D and C

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Table 3: Frequency of Autopsy for Cases of Malignant Mesothelioma and Pleural Tumors other than Mesothelioma Diagnosed in Connecticut, 1935-1971

Diagnosis[a]	(1) Autopsy, Evidence of Cancer	(2) Autopsy, Cause Evidence of Cancer	(3) Autopsy, Cause Undetermined Cancer	(4) Autopsy, but only Slight Evidence of Cancer	(5) Autopsy, no Report	(6) No Autopsy	Unknown	Dead Number	% Autopsy[b]
Malignant Mesothelioma of pleura, site unknown	23	8	1	1	2	12	2	38	33
Mesothelioma peritoneal	12	4				5	1	28	28
Mesothelioma (other) (unknown)									
Pleural Tumor Malignant	8	1	1		3	13	11	37	32
Pleural Mesothelioma	23	3		1	1	29	18	134	20
Total	63	16	2	1	6	59	32	242	

$$p_{\text{Total}} = \frac{(1) + (2) + (3) + (4) + (5)}{(6)} \quad \text{OR} \quad \frac{\text{Col}}{\text{Col}}$$

[a] OHM (1971)

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IV. Discussion

Although this study was initially undertaken to discover whether it would be feasible to identify the environmental factors responsible for the increase of malignant mesothelioma in the State of Connecticut, it has suffered from lack of detail in available records. Major deficiencies in the data are the low autopsy rate for the pleural mesotheliomata and the inadequacy of the pathological material available and used for diagnostic purposes.

Felton[12] has pointed out several needs for post-mortem review. A problem may arise in workers' compensation adjudication where a decision has to be made, years to decades after initial work exposure, in those instances where death has resulted from pulmonary cancer or a thoracic or peritoneal mesothelioma. It is therefore important, in such cases, to be able to confirm by the presence of asbestos related effects that there has been exposure to respirable asbestos fibers.

A further need for autopsy arises to confirm the diagnosis of malignant mesothelioma made on limited biopsy material obtained during life. This is important for workers' compensation purposes and also to improve the epidemiological data required to investigate the etiological factors involved with this disease.

Valuable information can be gained from a comparison between radiographic apperances and histological changes in the lung. Such information will help to eliminate present diagnostic uncertainties.

It has been our experience that occupational histories are not routinely obtained and included in hospital records. In our search through records stored at the CTR (i.e. hospital records), we found job titles for only 17% of the mesothelioma cases. If we exclude from this group those designated as "retired", "housewife", or "student", the figure is reduced to 12%. We were only able to ascertain type of industry in 7% of these cases. The sample size for these statistics was 220 cases, whose diagnoses were between 1955 and 1977. A recently passed Ct. statute, whose method of implementation is under study, will hopefully alleviate the paucity of employment data from medical records.

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Two other areas of epidemiological interest which are not routinely recorded for patients admitted with suspected malignant disease are smoking habits and hobbies ~~and~~ or part-time activities.

(Comment on the significance of the Slide Review)

It is evident that until the physicians investigating cases of malignancy appreciate the importance of occupational ~~factors on~~ and environmental factors ~~on the etiology of these diseases, no~~ (lifestyle, habits, hobbies, part-time activities, detailed job histories) , any attempt to apportion blame to any particular factor for disease causation or promotion will be severely hampered. It is particularly essential in the case of a rare tumor, which may present diagnostic difficulties, to obtain sufficient tissue for study before a diagnosis is made. Whenever a tumor is found and an association is suspected with a particular occupational or environmental factor, every attempt should be made to document all relevant facts and to subsequently verify the diagnosis by means of a full autopsy.

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