PLAINTIFF'S EXHIBIT

UC-2621

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from the desk of
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TITLE: The Influence of Occupational and Environmental Asbestos Exposure on the Incidence of Malignant Mesothelioma in Ct: A Retrospective Case Control Study

Investigators: J. Wister Meigs, Director, Connecticut Cancer Epidemiology Unit and Clinical Professor of Epidemiology, Yale School of Epidemiology and Public Health

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Research Plan:

1. Specific Aims of this Investigation

a. To evaluate the extent of misclassification of malignant pleural mesothelioma and other primary pleural tumors in Ct. from 1935-1977. From the entire set of primary pleural tumors a homogeneous subset will be selected on the basis of clinical, pathologic, and histologic criteria most representative of pleural mesothelioma. Comparisons will be made of these cases and those originally classified as pleural mesothelioma.

b. To bring up to date the descriptive epidemiology of all mesothelioma (pleural, peritoneal, other) and other primary pleural tumors.

c. To make case-control comparisons of occupational exposures, controlling for age, sex, and population density. Occupational histories of the population group under study will be collected in terms of job type, place of employment, and product of place of employment. Risk associated with occupational exposure of short duration will also be assessed.

d. To examine for non-occupationally exposed cases and controls the extent of risk associated with low-dose environmental exposure by utilizing information relative to occupational history of spouses and geographical distance of homes from places of asbestos manufacturing.

e. To assess the effect of occupational asbestos exposure on the disease experience of spouses.

2. Future Research Objectives

a. To examine the incidence of lung cancer, gastro-intestinal cancer, and cancer of the larynx and other cancers in Ct. in order to see whether there is any correlation between them and malignant mesothelioma in the various geographical locations which could be usefully applied to estimate the public health risk, if any.

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b. To review mesotheliomas of all sites for possible relationship to asbestos in water supplies both at home and at place of employment. Cases without evidence of exposure from ambient air, occupation, or spouses' occupation can be examined regarding the waterborne asbestos hypothesis.

c. To examine the relationship of asbestos fiber type and mesothelioma by studying the extent of geographical clustering of this disease about manufacturing firms whose products have known concentrations of crocidolite, chrysotile, and amosite.

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THE PROBLEM:

Studies of occupationally exposed populations have clearly demonstrated the health hazards associated with exposure to asbestos and asbestos products. (Doll, 1965; Mancuso and El-Atar, 1967; Wagner et al., 1960; Newhouse and Thompson, 1965; McDonald, 1973; Elmes, 1965) Three major lesions have been identified, namely, pulmonary fibrosis (asbestosis), lung cancer, and diffuse malignant mesothelioma of the pleura and peritoneum. In addition, an excess of deaths due to cancers of the gastro-intestinal tract have been reported in some studies and an association between asbestos exposure and laryngeal cancer has been demonstrated. It has been postulated that there may also be an increased risk of brain and renal cancers in asbestos workers but the epidemiological evidence for this is as yet unproven.

Thus far, the only positive evidence of non-occupational exposure is from living in close proximity to asbestos mining operations or factories with inadequate dust controls, and in a few isolated instances from domestic sources of contact with the clothing of relatives, friends or lodgers who were asbestos workers. Malignant mesothelioma has resulted from such exposures, but the number of such cases reported in the world literature remains very small.(Wagner et al., 1960; Newhouse, 1965; Champion, 1971; Selikoff and Hammond,1967, 1969)

There has been great concern in recent years about a public health risk from asbestos in the general environment, but at the present time there are no data available to substantiate or refute this fear. The presence of asbestos fibers in water, beverages, drugs, and the ambient air has not been correlated with disease in the general population. In all published series of mesothelioma. there is a small proportion of cases where exposure to asbestos is considered unlikely or impossible (McDonald et al., 1970; Webster, 1972; Greenberg and Davies, 1974; Milne, 1976), but in some cases this depends upon the care with which the evidence of exposure is sought for.Another source of confusion in the attempt to isolate causative factors in the development of mesothelioma is the different biological effects of varioustypes of asbestos fibers.(McDonald,1978) Crocidolite asbestos from certain regions appears to be the most likely to produce this disease, whereaschrysotile is least likely to do so and amosite (cummingtonite-grunerite) holdsa doubtful intermediary position. On the other hand, the possibility that mesothelioma may be incorrectly attributed to asbestos exposure, must also be taken into account.In 1978 the suspicion that other materials could be partly responsible for those cases without known exposure to asbestos, was apparently verified by the finding in Turkey that asbestos related diseases mainly calcified pleural plaques, chronic fibrosing pleuritis and malignant pleural mesothelioma are endemic is some villages without asbestos deposits. These fibers were shown to be erionite type zeolite. Thus it would seem that fiber-shape and size is important in the etiology of malignant mesothelioma and fibrous minerals from sources other than asbestos mining or processing may be implicated in the epidemiology of this disease.(Baris et al., 1978)

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The reported frequency of mesothelioma has substantially increased in Ct. in the late 1950's and has continued to increase steadily since that time. One possible explanation is increased recognition on the part of pathologists and clinicians as to the existence and etiology of this disease. It has also been suggested that this increased incidence can be attributed to the tremendous growth of the asbestos industry in the U.S. In view of the long latency period for the development of mesothelioma (Selikoff, 1977; Greenberg, 1971) a continued rise in incidence until at least the end of this century is a real fear expressed by some investigators.

When the reported measurements of ambient air are studied in the literature, we see that even the highest figure for contamination of the general atmosphere is three orders of magnitude below the current hygiene standard. In considering the public health risk we must not forget the great and continuous improvement in dust control in most workplaces where asbestos is used and, therefore, a decreasing emission of dust from these sources. The emission of fibers from brake linings has been cited as a source of asbestos in ambient air and, in Ct., such measurements as have been made, indicate that this may raise the background level where traffic is dense, where brakes are applied such as toll booths or traffic intersections. (Bruckman and Rubino, 1978)

Earlier studies suggest a significant risk associated with low-dose exposures resulting from geographical residence, occupation of spouse, or occupational exposure of short duration. (Wagner et al., 1960; Selikoff, 1965; Anderson, 1976; Newhouse, 1972; Champion, 1971) A very recent publication (Whitwell et al., 1977) reports the amount of asbestos fibers in lung tissue to be associated with occupation but not with environment. No geographical cluster about asbestos manufacturers, independent of occupation, could be demonstrated. This study provides additional evidence that the development of asbestos-induced mesothelioma is dose related, an encouraging result in the evaluation of risk in the general environment.

The question which remains unresolved is whether the minute quantities of asbestos measurable in the ambient air contribute to the incidence in the general population of those diseases which have been identified in association with asbestos exposure in occupational situations. By examining in depth the mesothelioma cases which have been reported to the Connecticut Tumor Registry between 1935 and 1977 and investigating their background, if there is indeed a public health risk it should be brought to light.

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MATERIALS AND METHODS:

Cases will be comprised of all malignant mesotheliomas, both pleural and peritoneal, with positive histology diagnosed in Ct. from 1935-77, with the possible addition of some or all other malignant primary pleural tumors with similar characteristics. The maximum number of cases for the study would be 248 - 210 cases of mesothelioma, 38 cases of pleural tumors, non-mesothelioma. Cases from 1935-77 will be analyzed descriptively only. Those from 1955 on (approximately 116 - 98 mesothelioma, 18 non-mesothelioma pleural) will receive formal statistical analyses including comparisons with a control group of about 232 randomly selected deaths from the State of Ct. Department of Vital Statistics.(Table 1)

EXPECTED FINDINGS:

An estimate of the relative importance of various sources of asbestos exposure on the rising incidence of mesothelioma in Ct. is anticipated as a result of this research. The effect of changing trends in diagnosis and classification of this disease should also be suggested. Analyses based on cases corrected for this effect will assess the level of risk associated with low-dose exposure, namely, that which might result from residential proximity to asbestos manufacturing, an occupationally exposed spouse, or an occupational exposure of short duration.

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TABLE 1

OBJECTIVE	POPULATION	DATA SOURCE	VARIABLES OF INTEREST	STATISTICAL METHODOLOGY
A	Cases(1935 to 1977)	CTR Tape & paper file	sex, age of diag.,age of death, smoking history, survival, no. of tumors, no. of primaries, grade, stage, EOD	Discriminant Analysis or Logistic Regression
B	Cases & Controls (1935-77)	CTR & State Dept. of Vital Stats.	sex; age; marital status; case survival, duration of occup. exp.,latency; incidence rates	Frequencies, Direct Age adjustment
C	Cases & Controls (1955-77)	City Dir. & U.S. Census	type job,place & duration of employment, product of place of employment, population density of residence	R.R., Chi-Square Test of equal risk,Var. & C.I. for R.R.
D	Non-Occ. Exp.Cases & Controls (1955-77)	City Dir. State Workers Comp.	occup. exp. of spouse & duration of, distance of usual resid. from asbestos manufact.	Chi-Square Test of Assoc. Mantel-Haenszel Stats(assoc. of resid. and disease, controlling for pop.) Geographical mapping of cases
E	Occ. Exp. Cases (1955-77)	CTR Tape & Death Tape	observed freq. of deaths for spouses by cause over time	R.R. comparisons of observed to expected

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