Occupational Epidemiology

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Table 9.11
OBSERVED AND EXPECTED DEATHS FROM LUNG CANCER AMONG A COHORT OF 17,800 ASBESTOS INSULATION WORKERS

Cigarette smoking habit	No. of persons	Deaths from lung cancer			
		1967—1972		1967—1975	
		Obs.	Exp.*	Obs.	Exp.*
Yes	9590	179	31.6	248	59.5
No	2066	2	7.5	6	2.3
Unknown	6144	94	16.8	—	—

* Expected numbers based on age-specific U.S. death rates for white males.

* Expected numbers based on approximate age-smoking specific U.S. death rates for white males.

5. The nature of the association between coke plant work and kidney cancer and nonoven work and digestive cancer is unclear. However, it is possible that providing respiratory protection to reduce the occurrence of lung cancer will also reduce the occurrence of other diseases.

C. Asbestos and Respiratory Cancer

There is no question that persons who work with asbestos develop excess respiratory cancer.[24] There is a question, however, as to whether asbestos exposure in the absence of cigarette smoking will lead to an excess of lung cancer. This question has recently been reviewed.[25]

In 1967, smoking habits were ascertained from 11,656 of 17,800 insulation workers who were exposed to asbestos. These workers have been followed since that time and deaths from lung cancer have been determined. In one analysis, expected numbers of deaths from lung cancer were estimated on the basis of U.S. death rates of smokers and nonsmokers combined.[26] In a second analysis, estimated rates for smokers and nonsmokers were used to compute expected numbers.[27]

The results of these two analyses are presented in Table 9.11. In the first analysis (1967 to 1971) there is no evidence that asbestos exposure in the absence of cigarette smoking leads to an excess of lung cancer. This statement, however, must be tempered by the high number of persons with an unknown smoking habit. The observed/expected ratio in these persons is essentially the same as that among the smokers. It is conceivable that a number of the persons with lung cancer among those whose smoking habits are unknown were nonsmokers. The true observed/expected ratio among nonsmokers could be above 1.0.

Another objection to these data can be raised concerning the rates upon which the expected numbers were based. Vital statistics rates are not available for smokers and nonsmokers separately. (It would be almost impossible to collect such data from the general population.) Therefore, expected numbers must be computed on the basis of the general population, which is a mixture of smokers and nonsmokers. As a result, the expected numbers of lung cancer for smokers are underestimated while the expected numbers for nonsmokers are overestimated. In the second analysis of the data,[27] an estimated smoking-specific lung cancer mortality rate was used to compute expected numbers.[24] Also, in this analysis three additional years had passed; therefore the observed number of deaths from lung cancer had increased. It can be seen in the 1967-

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Table 9.12
ASSOCIATION BETWEEN LUNG CANCER AND SHIP BUILDING ACCORDING TO SMOKING IN A CASE-CONTROL STUDY

Cigarette smoking habit	Shipbuilder	Lung cancer: Yes	Lung cancer: No	Odds ratio
No or light	Yes	11	35	1.3
	No	50	203	
Moderate	Yes	70	42	1.7
	No	217	220	
Heavy	Yes	14	3	2.4
	No	96	50	

75 data in Table 11 that there is a suggestion that nonsmoking asbestos insulation workers also had an excess of lung cancer.

The question as to the interrelationship between asbestos, cigarette smoking, and lung cancer has also been examined in a case-control study.[28] In an examination of the cancer maps by U.S. County in 1950 to 69, an excess of lung cancer was observed among white males.[29] To evaluate the reason for this excess, a case-control study of lung cancer was conducted among residents of coastal Georgia. Cases were men with lung cancer identified during several periods since 1970; controls were persons with other diseases identified either from hospital records or from death certificates. Persons with bladder cancer or chronic lung disease were not eligible to be controls, inasmuch as these diseases are known to occur to excess among cigarette smokers. Controls were matched to cases on sex, race, age, county of residence, and vital statistics.

Interviews were conducted with living cases and controls and with the next-of-kin of persons who were deceased. Information was obtained as to past smoking habits and occupational histories. At the conclusion of the interview, specific questions were asked about ship building and asbestos exposure. During World War II, ship building, which involves asbestos exposure, was common in this area.

The results are presented in Table 9.12. Among non or light smokers, the odds ratio of lung cancer in ship builders was 1.3, while among heavy smokers, the odds ratio was 2.4. While the association between lung cancer and ship building, and presumably asbestos, is much weaker than that seen among insulation workers, it is in the same direction.

The major concern to be considered in this study is in the way the data were collected. The study was done to evaluate the role of ship building in the etiology of lung cancer. Consequently, it was very important to phrase questions to the persons in the study in a neutral way, so as to avoid observation bias in the collection of occupational histories. Since the shipyards had operated for only a few years during World War II, and since the occupational histories were obtained by interview in the mid-1970s, it was possible that incomplete occupational histories might be given. If this incompleteness occurred equally among cases and controls, no bias would result. However, if cases were prompted more than controls as to past work in a shipyard, a false association between shipyard work and lung cancer could readily result. To minimize this possibility, interviewers were trained to be neutral observers, close-ended rather than open-ended questions were asked, and 10% of interviews were independently verified.

Selection bias could have occurred if knowledge of a person's occupation was used in identifying persons with lung cancer. This was avoided by selecting cases only on the basis of their diagnosis.

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Confounding by cigarette smoking was possible if shipyard workers smoked more than did nonshipyard workers. However, by stratifying on smoking as in Table 9.12, smoking was controlled in the analysis.

Based on the results of these two studies, it cannot be said with certainty that asbestos in the absence of cigarette smoke is or is not a lung carcinogen. The data upon which such a judgment would be based are simply too sparse. It would be of considerable value if asbestos by itself were not carcinogenic, for nonsmokers could be hired to work with asbestos. However, since there is no reason to believe that asbestos leads to improved health, exposure to asbestos should be minimized for all persons.

These two studies illustrate some of the practical realities of epidemiologic studies. The study of insulation workers was a prospective cohort study. This was necessary because the study was designed to determine the lung cancer experience in relation to asbestos exposure and smoking. No past information existed on smoking habits or in a cohort of insulation workers; therefore a retrospective cohort study could not be done. The study started in 1967 and, 10 years later, the data on lung cancer among nonsmokers are marginal as to size.

In contrast, the study of lung cancer in relation to prior shipyard work was completed in several years. The number of persons with lung cancer was greater than the number in the cohort study. Cigarette smoking histories were readily obtained. However, the number of persons who had worked in shipyards was only 175. Very little detail was available as to amount of exposure to asbestos. The relatively weak association between lung cancer and shipyard work may only reflect the fact that many shipyard workers were not exposed to asbestos.

D. Beryllium and Respiratory Cancer

In the 1930s and 1940s, respiratory effects of beryllium were first reported.[30] Acute beryllium disease is essentially a pneumonitis that may be severe and lead to death.[31] Chronic beryllium disease is a granulomatous disease resembling sarcoidosis. Symptoms may not develop for several years after exposure to beryllium has ceased. It has been hypothesized that chronic beryllium disease represents an autoimmune response in certain workers.[33]

In 1978 an excess of lung cancer was reported to have occurred among a group of beryllium workers.[33] Earlier versions of this report were challenged by representatives of the beryllium industry and by others.[34,35] These challenges were rebuffed.[36]

The relevant data are presented in Tables 9.13 and 9.14. As seen in Table 9.13, 47 deaths from lung cancer were observed and 34.3 were expected. The excess occurred mainly among men who worked fewer than 5 years; no excess was seen until at least 15 years after onset of exposure. A similar pattern was seen for nonneoplastic respiratory disease (Table 9.14).

Interpretation of these data must take into account not only the comments of the authors and their critics but also general problems associated with all epidemiologic studies. The decision as to whether beryllium is carcinogenic in humans should not be based solely on this one study, but also must take into account other sources of scientific data. Actions to be taken to protect persons who work with beryllium must take into account not only the results of scientific studies, but also must involve negotiation with persons whose primary concern is financial. Since none of these steps is based on an absolute process, the ultimate setting of standards of exposure must be recognized as a political rather than a scientific process.

1. Interpretation of Study Data[33]

a. Comments of Critics[34,35]

1. Cigarette smoking and geographic location of the plant were not adequately

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