Environmental Health Perspectives
Vol. 47, pp. 33-42, 1983

Assessment of the Epidemiological Data Relating Lung Cancer to Air Pollution

by Frank E. Speizer*

The epidemiological data linking air pollution and lung cancer are derived from statistical associations concerning rates of cancer among urban and rural residents, migrant studies and studies of occupational groups exposed to effluents from fossil fuel combinations. Few, if any of these studies, are adequately adjusted for both relatively simple measures of cigarette smoking or the potentially more subtle effects of the duration of smoking. Because urbanization and industrial sources of air pollution correspond chronologically with the major increases in cigarette smoking, it is not likely that the specific attributable risk to each component can be adequately assessed. Interactions between cigarette smoking and specific air pollutants, similar to those seen between cigarette smoking and asbestos and or radiation, may be occurring. Considering the various estimates made over the last 25 years, it is likely that the effect of air pollution on lung cancer is something greater than zero; however, it is unlikely that the estimate exceeds 2% of all lung cancers or 5/100,000 cases in urban males. Thus, the effect on all cancers is likely to be less than 1% of all cases.

Introduction

Epidemiologic studies to assess the association of effluents from the burning of fossil fuels with the occurrence of lung cancer, or any other cancer, generally have been hampered by the difficulty of obtaining specific information about risk factors which have far greater influence on the occurrence of lung cancer than do air pollutants. Unquestionably, cigarette smoking is the major determinant of lung cancer in humans. Secondly, for working subjects with occupational exposures to specific agents known to cause lung cancer, the risks of developing the disease are far greater than possibly could be associated with air pollutants. Thus, any efforts to assess the impact of air pollution in population studies must control in some way for the effects of cigarette smoking and occupational exposures.

Many of the epidemiologic considerations discussed over the last 25 years were presented in an excellent article, which appeared in 1955, by Stocks and Campbell (*1*). This paper summarized and evaluated the existing data which related lung cancer to smoking and air pollution as monitored by benzo(a)pyrene in several parts of England and Wales. Since that time, research has been carried out throughout the industrialized world. Although we have been able to place sharper limits on what might be the maximum attributable risk of air pollution on lung cancer, the progress in this field has been somewhat disappointing and is still in a state of great uncertainty. There are several reasons for the lack of progress. I believe the most important is that the risk related to general air pollution is so extraordinarily low relative to other risks that the time and expense involved in doing studies large enough to demonstrate the possible low relative risk have not been warranted. In addition, for other more compelling reasons over the last 15 years, the levels of pollution have generally been declining in most parts of the industrial world.

To provide a background to the discussion of the epidemiology of air pollution and cancer, I will attempt to identify some of the key studies done in the 1950s and 1960s. I will refer to several of the

*Medical School and School of Public Health, Harvard University, Boston MA. Address: Channing Laboratory, Department of Medicine, Brigham & Women's Hospital, 180 Longwood Ave., Boston, MA 02115.

reviews carried out in the 1970s and suggest that for the 1980s little further research on standard pollution sources, in terms of the relationship to cancer, needs to be conducted using epidemiologic techniques. Mainly, this conclusion results not from the likelihood of absolutely zero effects, but from the conclusion that it would be extraordinarily difficult to measure any effect from the general pollutant levels obtained over the last 25 to 30 years.

The epidemiologic data supporting the hypothesis that lung cancer is associated with air pollution result from four basic kinds of data sources. These include: (1) comparisons of lung cancer rates in immigrants and nonimmigrants, both in the country of origin and the country to which the immigrants have moved; (2) investigations of urban-rural differences in lung cancer risks in males and females; and (3) regional differences in lung cancer rates within countries related to differences in air pollution levels. The fourth category of data sources is the occupational studies of workers exposed to products of fossil fuel combustion. In these studies, levels of exposure are qualitatively similar to products in the ambient air; however, these exposures generally are quantitatively orders of magnitude larger than occur in the ambient environment. Thus, the usefulness of these studies is limited in extrapolating effects to general environmental exposures. One encouraging note is that for these occupational exposures, relatively low relative risks of lung cancer (range 2-3 times expected), particularly when compared to risks of lung cancer for cigarette smokers are found.

Assessment of the Existing Data

Much of the remaining discussion will focus on lung cancer rather than other cancers or cancer in general. The only other cancer sites affected by environmental exposures to any significant degree are the skin and upper airways. Skin cancers are poorly recorded in vital event records, and cancers of the upper airways are relatively rare; thus, they have been related to "point source" environmental exposures but generally have not been as rigorously associated with ambient pollution.

In 1977, at a conference similar to this one, Doll summarized the association between lung cancer and air pollution (*2*). He pointed out that lung cancer was consistently more common in urban areas than in rural areas and that this difference was present in both males and females. Comparing the 1966-1967 mortality rates for lung cancer in 24 countries, he noted the striking difference between males and females in all countries. He suggested that, either the disease was being overlooked in women or that men are more susceptible to the development of the disease. Neither seems to be the case. Clearly, women who do smoke develop lung cancer and, over the last several years have shown a striking increase in the disease compared to men, presumably because of the later onset of smoking than in men (*3,4*).

Doll pointed out further that there could conceivably be an interaction between smoking and known carcinogens which occur in the ambient environment. These carcinogens include, among others, polycyclic hydrocarbons, asbestos, arsenic and radon. In occupational studies, there appears to be an interaction between radon daughter exposure and cigarette smoking as well as between asbestos and cigarette smoking. The absolute risk of bronchial cancer is increased to a much greater extent in working groups exposed to these substances in association with cigarette smoking than could be expected from either the exposure or cigarette smoking alone. The differences in excess lung cancer rates among smoking urban and rural residents could reflect a similar interaction effect. Thus, the observation that there does not appear to be any significant urban-rural gradient of lung cancer in nonsmokers is not in itself conclusive evidence that there is no carcinogenic effect of ambient pollution.

In an analysis of 10% of the total lung cancer deaths in the United States in 1958-1959, Haenszel et al. (*5,6*) showed that the disease was related mainly to cigarette smoking. However, the gradient in males appeared to be steeper in heavy smoking urban residents compared to rural residents (Fig. 1). In females, there was very little gradient which suggested that something other than air pollution may have been operative at that time. Other investigators also have suggested that the differences between males and females may be due to cocarcinogens other than air pollutants.

In a prospective study of approximately one million people, Hammond and Garfinkel (*7*) compared the relative risk of lung cancers in age and smoking standardized groups of men with and without a history of occupational exposure to dust, fumes, or radiation. The analysis was limited to those men who lived in the same neighborhood for 10 or more years (Fig. 2). For men with some occupational exposure, there was an overall gradient of the ratio of observed to expected deaths of 1.23 to 0.98 between men from the metropolitan areas greater than one million and from rural areas. Within these two areas, a gradient also was observed between cities and towns. However, once occupationally exposed men were excluded, the differences in ratios between observed and expected

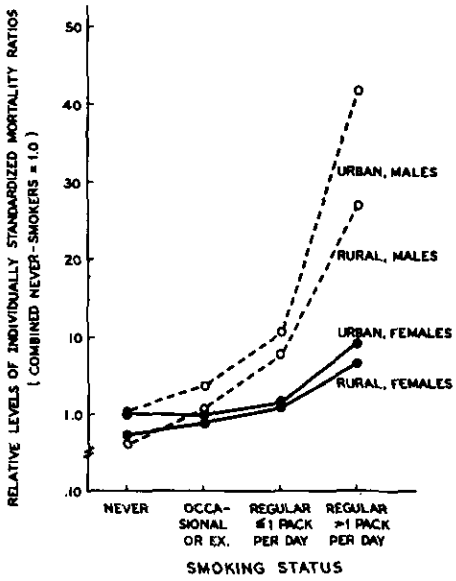

FIGURE 1. Comparison of lung cancer risk by life-long urban vs. rural residence and smoking habits; males, females. Data from Haenszel et al. (*5,6*).

between size of residence all but disappeared. There was a persistence of the city-town differences in the very large metropolitan areas and in the rural areas; however, a reversal of the effect was noted in the mid-size metropolitan areas. This leaves open the question as to the significance of these findings. In any case, the magnitude of the effect of urban-rural differences was markedly reduced by taking into account smoking, age, and occupational exposure crudely defined as exposure to dust or fumes.

Migrant studies, which suggest some factor related to country of origin influences the cancer rate in the migrant in his or her new country, have been used to postulate an air pollution effect (*8–10*). For example, migrant populations to the United States tended to have lung cancer rates which were between the rate of the country of origin and those of native-born U.S. residents, whether the rates in the country of origin were higher or lower than the rates in the United States (Fig. 3). In many of these studies cigarette smoking was not as carefully assessed as one would like. Even when assessed, no information was available on either age of starting smoking (see below) or occupation. Two hypotheses that have been proposed suggest that immigrants are exposed to more hazardous occupations in their new countries and are more likely to be cigarette smokers. This would explain why immigrants from countries with relatively low rates of lung cancer might increase their rates in their new country. However, one must conclude that immigrants who migrate from countries with higher lung cancer rates and have lower rates in their new country must be carrying some portion of their risk from their country of origin, and this risk is not likely to relate either to smoking or occupational exposures.

Other exposures to products of fossil fuel burning lend credence to the hypothesis that chronic exposure to these agents results in excess cancer rates. We are all aware of the historical reports of Sir Percivall Pott, who described scrotal cancer in

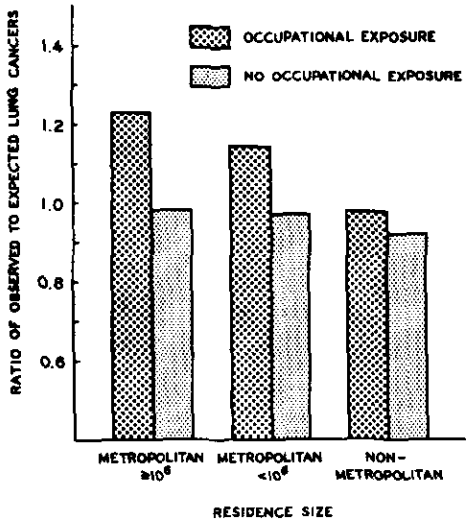

FIGURE 2. Ratio of observed to expected lung cancer rates by residence size and occupational exposure; men adjusted for age and smoking. Data from Hammond and Garfinkel (*7*).

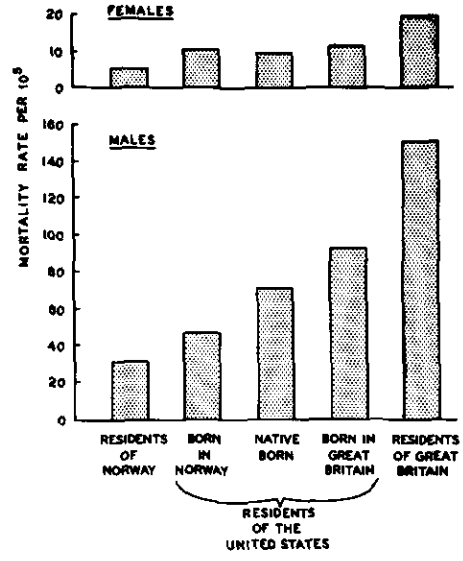

FIGURE 3. Lung cancer mortality rate per 100,000; age-adjusted by place of residence. Data of Reid et al. (*8*).

chimney sweeps more than 200 years ago. Studies in the 1920s identified coal tars to be associated with skin cancers. Subsequent studies in animals identified benzo(a)pyrene as a potent carcinogen. By the beginning of the 1950s this substance was found in ambient air and considered a surrogate for monitoring exposure to carcinogens in the environment resulting from industrial and motor vehicle fossil fuel use.

Studies in a variety of industrial settings have demonstrated excess lung cancers associated with exposures to combustion products. Of 3028 coal gas workers studied by Doll and his co-workers (*11,12*), all but one was traced up to 12 years. The men were divided into heavily exposed—i.e., retort house coal carbonization workers—and minimally exposed—i.e., to by-products only. Standardized death rates for lung cancers were found to be more than twice as high for the highly exposed workers (3.82/1000 person years at risk) compared to the minimally exposed group (1.59/1000). The differences in smoking habits in a 10% random sample of the workers suggested that the smoking habits of the retort house workers did not differ significantly from the remainder of the gas workers.

Similar studies in the United States of coke oven workers in the steel industry revealed excess lung cancer of 2.5 to 10-fold in coke oven workers compared to noncoke oven workers (*13,14*). Furthermore, the studies indicated that workers with higher exposure (topside workers) had about a fourfold excess risk compared to the lesser exposed (side oven) workers who had a better than a twofold excess risk compared to nonexposed workers. The gradient was further related to duration of exposure and was highly suggestive of an exposure-response relationship (Fig. 4).

Roofers are another group with significant occupational exposure to fumes from burning of fossil fuels. Hammond and colleagues (*15*) studied a population of union workers whose members were all involved in trades requiring the application of hot pitch or hot asphalt to repair roofs or to waterproof basements. These investigators started in 1960 with a population of 5939 men aged 39-80+ and followed the whole population to 1972. Through 1971, 1798 men had died. The only excess mortality reported for men whose cumulative time in the union was 19 or less years was in the category of respiratory diseases other than cancer and accidents. For those workers with 20 or more years of service, all cancers occurred with an excess rate of 45% with the significant excesses noted in lung cancers, upper airways and esophageal cancers, and stomach cancers. Smoking habits could be confounding the results, but unfortunately they

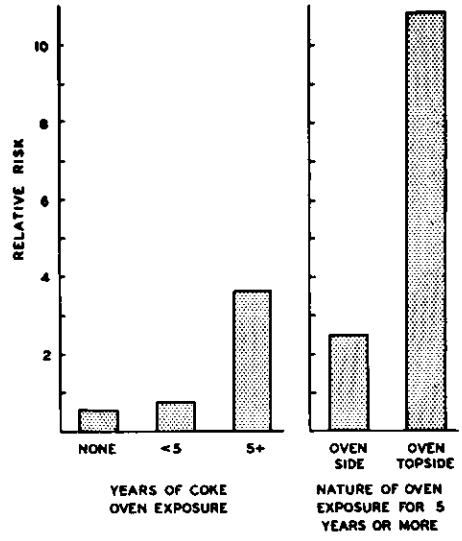

FIGURE 4. Risk of lung cancer in steel workers by exposure to coke ovens. Data of Redmond et al. (*14*).

were not measured as part of the study. If one compares the age-standardized mortality rate for lung cancer across strata of years of employment, there is a suggestion of an exposure-response relationship with a lag of 20 years and then a doubling of the risk of lung cancer over the next 20 years (Fig. 5).

An alternative potential source of polycyclic hydrocarbon exposure not considered to this point in the discussion relates to the introduction of diesel powered passenger and light duty automotive vehicles as a major mode of transportation. In the United States, estimates are that by 1985 diesel

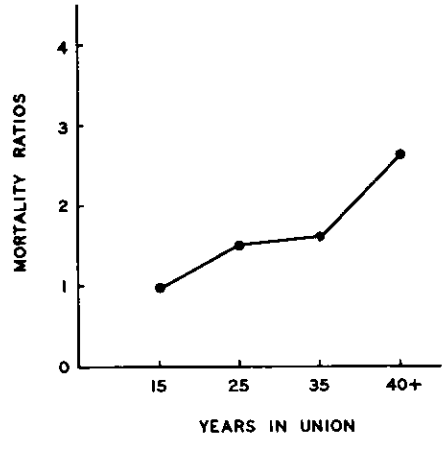

FIGURE 5. Lung cancer mortality ratios by years in roofers' union. Data of Hammond et al. (*15*).

powered vehicles will constitute 18% of sales, and that by the turn of the century 25% of all vehicles on the roads will be diesel powered.

The National Research Council of the National Academy of Sciences (NAS) recently completed an assessment of the health effects of exposure to diesel exhaust (*16*). In regard to cancer, the study represented a review of the mutagenic and carcinogenic potential of exhaust components. In terms of epidemiologic data they conclude:

> "In epidemiological studies of occupational exposure to diesel exhaust emissions, excess risk of cancer of the lung, or of any other site, has not been convincingly demonstrated. The evidence to date does not indicate that exposure to diesel exhaust is a serious cancer hazard, at least at exposure levels no greater than those that existed in London bus garages. Only two studies, one on railroad workers (Kaplan, 1959) and the other on bus garage workers (Raffle, 1957; Waller, 1979), approximate even the minimum requirements for a sound epidemiological evaluation of cancer risk. Both of these studies, however, suffer from numerous deficiencies in design. Hence, their negative conclusions must be viewed with caution." (*16*).

Review of the epidemiologic data relating to diesel exhaust is indeed disappointing. There is no question that polycyclic hydrocarbons with proven carcinogenic potential, as suggested by animal studies, are abundant in diesel exhaust. The study of Kapan mentioned above is a study of Baltimore and Ohio railroad workers (*17*). Not only were smoking habits not measured, but the potential duration of exposure to diesel exhaust was likely to have been less than 5-10 years for most of the workers studied. If diesel exhaust were to act anything like cigarette smoking, one could not expect to see many cases of lung cancer in the population with so few having long-term exposure.

The second study considered by the National Academy Task Group was the study of London Transport workers, who were characterized by job categories into relative levels of exposure to diesel exhaust (*18,19*). Mortality from lung cancer in males aged 45-64 in 1950 was followed up to 1974. Expected rates were determined by using Greater London rates. Overall, the mortality ratios for lung cancer expressed as a percent of the expected rates was 79%; however, within the various cohorts of workers there was a modest gradient of the mortality ratio which corresponded to the exposure categories. Unfortunately, smoking habits were not measured in this study, and only lung cancers that occurred while the workers were in active service were considered. This makes any conclusion about the data uncertain.*

Before proceeding further, it is worth considering in greater depth how details of smoking habits may interfere with any assessment of either an occupational exposure or a general environmental exposure effect on the rates of lung cancer determined. For this discussion I have relied on the work of Axelsson (*21*), Jarvholm and Thiringer (*22*) and the recent elegant discussion of the subject by Doll and Peto (*23*).

Two major issues need to be considered. Relatively minor differences in smoking rates for different populations may be sufficient to explain a 20% difference in lung cancer rates. For example, using the simple assumptions about relative risk of lung cancer at different levels of cigarette smoking derived from Doll and Hill (*24*), merely reducing nonsmokers from 30% to 25% and increasing heavy smokers from 5% to 10% results in a 22% increase in expected lung cancer rates (*22*). In the calculations of Harris (*20*) for an overall shift of 5% in the proportion of cigarette smoking in the London Transport garage, engineers would similarly shift relative risks of lung cancer by approximately 10–15%.

A more subtle and far more difficult effect to assess is that that lung cancer risk depends on current smoking amounts, duration of smoking and lifetime accumulated dose, the latter two of which are also dependent on age of first starting smoking (*23*). This factor may be virtually impossible to measure accurately in any cross-sectional or retrospective study. Data from Kahn (*25*) of adults aged 45-74 suggest that a 10-year difference in age of starting smoking between ages 15 and 25, for any level of smoking, may account for as great a difference in risk of lung cancer as is the difference between the rate of lung cancer at ages 55-64 and 65-74. In addition, the magnitude of the effect of duration of smoking is as great as the effect of smoking 10-20 cigarettes/day and 21-39 cigarettes/day at ages 55-64 (Fig. 6). Because most studies of lung cancer deal with people who are currently in these older age groups, the misclassification of smokers by not knowing their age of starting smoking (and thus their true duration of smoking) may easily swamp any attempt to find an association of a general environmental exposure and lung cancer.

---

*As part of the National Research Council's Diesel Impacts Study Committee, Professor Jeffrey Harris provided an assessment on the Potential Risk of Lung Cancer from Diesel Exhaust Emissions (*20*). He carefully assessed the London Transport Study, using some additional unpublished data provided by Waller and Raffle, which allowed the division of the mortality data into 2 periods, 1950-1960, and 1961-1974. The overall mortality ratios from lung cancer increased between the two periods from 71.1% to 87.0%, respectively, which is consistent with the potential for longer exposure to diesel exhaust. However, in those groups presumed to have had the highest exposures over the two periods, there was essentially no change in the mortality ratios.

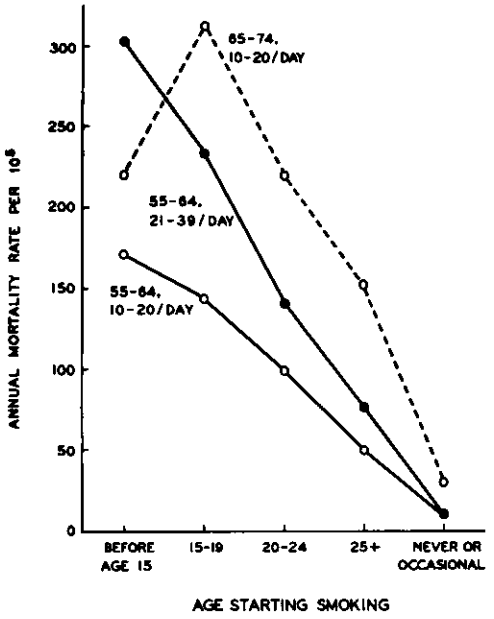

FIGURE 6. Effect of age starting smoking on annual mortality rate from lung cancer; men, 1954-1962. Data from Kahn (*25*); figure after Doll and Peto (*23*).

Most investigators have come to accept that there are significant differences of age of starting smoking between life-long urban and rural residents. For most of the studies which show urban-rural differences in lung cancer, there are few details about urban-rural smoking differences (see footnote in Doll and Peto (*23*), which quotes as one source of differences between men and women pre-World War II as coming from a magazine survey in 1935). Thus, one is left with the conclusion that a large part of the urban-rural differences and potential differences between occupational groups with different exposures might be explained by subtle difference in smoking habits (without even considering differences in the way people smoke, i.e., number of puffs, butt length, inhalation practices, and more recently, tar content of different cigarettes).

Attempts to Scale Effects of Human Exposures

All of the studies discussed thus far relate, at least superficially, to the hypothesis that the risk of lung cancer is related in some dose-response fashion to the inhalation of a product of fossil fuel combustion, whether it be from motor vehicle exhaust, effluents from coal- or oil-fired electric power plants, industrial processing or cigarette smoking. The data from these studies are consistent with the hypothesis that interactions between various environmental sources and cigarette smoking may be taking place. Common to all of these combustion products, although not necessarily directly quantitatively associated, is the exposure to polycyclic hydrocarbons. Several investigators have attempted to use some measure of polycyclic hydrocarbons, i.e., benzo(a)pyrene, as a common indicator of exposure, and to test cancer risks against this indicator (*9,26,27*). Pike et al. (*26*) discuss in detail why benzo(a)pyrene is used as an index of exposure. In spite of indicating a number of caveats for specific situations in which benzo(a)pyrene may not be correlated with other polycyclic hydrocarbon exposure, they conclude that benzo(a)pyrene is the best indicator available to assess the potential impact of general air pollution. A similar discussion is presented by the National Academy of Science (*27*), in which correlations between lung cancer rates (attempting to take cigarette smoking into account) and benzo(a)pyrene levels are actually constructed. Their review and analysis suggests that the lung cancer rate in men increases approximately 5% for each increment of air pollution, reflected by an increase of 1 μg benzo(a)pyrene/1000 m^3 air. Five years ago, the Task Group reviewing this work, for a symposium similar to one we are attending, questioned the quantitative value of the estimate and suggested that it must be considered a maximum figure (*28*). The Task Group pointed out several deficiencies (which were also considered by the NAS), which included the inadequacies of the measurements to characterize smoking histories; the sparse number of benzo(a)pyrene measurements used to characterize exposure across communities; the strikingly different estimates derived for men and women; and the remarkably high figures that were predicted for the more urban areas, particularly in face of the relatively small occupational risk observed at levels of benzo(a)pyrene several magnitudes higher than reported for urban air.

In an attempt to summarize and show relative comparisons, I have expanded on (and taken some liberties with) a figure presented in the NAS report (*27*) to indicate the relative magnitude of risk of lung cancer in several reported studies indicated above (Fig. 7).

The figure indicates the relative increase in mortality ratios found in a number of studies in relationship to estimated levels of relative benzo(a)pyrene exposure. What is clear is that the effects of cigarette smoking far exceed any other effect possibly related to polycyclic hydrocarbon exposure. In the occupationally exposed groups, even

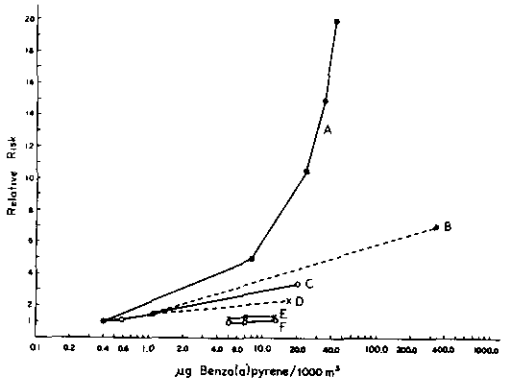

FIGURE 7. Relative risks of lung cancer in groups of men by daily benzo(a)pyrene exposure estimates: (*A*) data of Doll and Peto (*23*), British doctors by smoking habits; (*B*) data of Redmond et al. (*14*), coke oven workers; (*C*) data of Doll et al. (*12*), British gas workers; (*D*) data of Hammond et al. (*15*), U.S. roofers; (*E*) data of Hammond and Garfinkel (*7*), U.S. general population, age- and smoking-adjusted; (*F*) data of Hammond and Garfinkel (*7*), U.S. general population, adjusted for age, smoking and occupational exposures.

with assumptions about uniformity of smoking habits and extremely high levels of exposure to polycyclic hydrocarbons, the relative magnitude of mortality from lung cancer does not begin to approach those associated with cigarette smoking. Furthermore, throughout the time course of these studies, which was the 1950s and 1960s, the gradient of exposures as monitored in general environmental settings, in terms of benzo(a)pyrene, suggests that ambient levels range 100-fold (*29*). In spite of this range, in the best controlled of the general population studies, which attempted to assess gradient of exposure to benzo(a)pyrene, the gradient was only twofold (*7*). If 100-fold variations are associated with a doubling of risk, clearly, twofold variations in pollution levels cannot be expected to be associated with perceptible changes in risk.

As has been true for 25 years, specific and certain statements at this time about the magnitude of the attributable risk of lung cancer from air pollution cannot be made from the epidemiological evidence. However, over the past 25 years as more careful assessments of the available data are carried out, the attributable risk percent has declined. Table 1 summarizes a number of estimates made over the last 25 years. In each case the authors have worked with faulty data. Doll and Peto (*23*) put forward the argument that if the Pike et al. (*26*) estimate is correct and the pollution levels used by Pike have declined over the last 20 years by a factor of ten, then there should be a substantial reduction in the attributable risk of cancer. If the risk was already approaching 1–2%, then the decline should bring the attributable risk to something less than 1%. All of these estimates assume that the steady and continued decline in air pollution will persist. Unfortunately, this is not the case. For example, the introduction of diesel powered vehicles conceivably could alter the ambient hydrocarbon load significantly. In even the worst of scenarios, however, it is unlikely that the pollution loads will ever again approach those measured in the 1950s and early 1960s.

Continued study of general populations to find an effect with a maximum attributable risk percent of something less than 2% with no conceivable way of controlling for potential confounding factors and with only minimal misclassifying of subjects resulting in 20% differences in risk is a fruitless exercise. The clues for the potential magnitude of the association of air pollution and cancer have been obtained; there is no reason to repeat these kinds of studies in the future. For epidemiology studies to be useful in the future, they will have to be part of the development of multidisciplinary collaborative stud-

Table 1. Levels of "attributable risk" of lung cancer to air pollution over a 25-yr period.

Year of estimate	Comment	Author
1955	Urban air adds approximately 100 deaths/100,000	Stocks and Campbell (*1*)
1972	5% of all lung cancer	NAS (*6*)
1973	5% increase of pulmonary cancer for each increase of 1 μg/1000 m³ of benzo(a)pyrene	Carnow and Meier (*9*)
1976	Possibly a tenth of the effect of cigarette smoking	Higgins (*10*)
1976	0.4 death/100,000 per μg/1000 m³ benzo(a)pyrene in nonsmokers; 1.4 deaths/100,000 per μg/1000 m³ benzo(a)pyrene in smokers In U.S. 1 cigarette/day is equivalent to 10 μg/1000 m³ benzo(a)pyrene	Pike et al. (*26*)
1978	5-10 cases/100,000 persons acting together with cigarette smoking	Task Group (*28*)
1981	1-2% of lung cancer	
	Less than 1% of all cancers in the future	Doll and Peto (*23*)

ies. Subpopulations identified as potentially at risk will have to be studied intensively, both in terms of exposure and outcomes, using state of the art industrial hygiene and analytical chemistry techniques for defining exposures. As part of the outcome assessment, detailed smoking histories must be obtained, and even these approaches will be only partly successful in establishing an accurate lifetime history of smoking. These studies will be extraordinarily difficult and expensive to carry out and therefore, must be carefully planned and financed with long-range commitments. Because the magnitude of the air pollution effect will be small, it is not likely that one will be able to justify having studies of these kind stand alone. Therefore, they should be part of a larger effort directed toward more generalized goals. For example, in Sweden, where public commitment has been expressed to strive for the goal of a generation of nonsmokers, the evaluation of the success of such a program might very well include a component designed to assess the effects of changing levels of air pollutants on cancer outcomes.

Another alternative is to take advantage of existing data resources of relatively large population groups either known to be exposed to fossil fuel components or in which exposures can be monitored. One such group, with which I am personally familiar, I will describe in detail to illustrate the potential for use of a multidisciplinary approach to the study of carcinogens (*30*).

In the United States between 1945-1955 the entire network of railroads changed from steam to diesel powered engines. In addition, because of a rather unique pension program for railroad workers in the United States, any worker with 10 or more years of employment in the railroads and a current connection to the industry has a substantial amount of information recorded on a computer file. This file is regularly updated and contains the names of some 6 million current or former employees who are either eligible for or receiving pensions. We reasoned that with appropriate sampling techniques, documented by on-site measurements, we could identify cohorts of workers with varying levels and sufficient duration of exposure to diesel exhaust to be at risk of developing lung cancer. To the degree that we could control for potential confounding factors, and to the degree that monitored exposure to railroad engine produced diesel effluents could be compared across the cohorts, a dose–response relationship between diesel exhaust exposure and lung cancer could be detected. To make the information to be gathered relevant to ambient conditions, comparisons of the components from railroad engine diesel exhaust would have to be made with diesel powered auto exhaust.

Furthermore, the findings would be even more relevant if common specific diesel fractions from these two sources were found to be mutagenic in bacterial and animal cell preparations. Further details of study design are beyond the scope of this paper. This railroad workers study requires a high level of collaboration from biologists involved in basic mutagenic and carcinogenic testing of specific exhaust fractions, analyzed and provided by sophisticated analytic chemical techniques to fractionate specimens. Industrial hygienists are needed to obtain representative samples of the particulate in the work environments of the workers being studied. These samples not only are provided to the analytic chemist for comparison with diesel auto emissions and for carcinogenic testing but also are used to estimate exposure levels for workers in different job categories in the railroad industry. Large populations of these workers are being assessed for their risk of lung cancer and other cancers. To control for cigarette smoking effects, samples of workers who died of a variety of causes are matched to the lung cancer cases, and next-of-kin are interviewed to obtain smoking histories. In addition, relatively small samples of current workers are providing smoking histories. Even this study suffers from not being able to obtain smoking histories for prospective analyses and for this reason may not provide a definitive answer. However, the study has been designed to be large enough to measure a 20% increase in lung cancer risk at a level of exposure which is likely to be 5-10 times higher than anticipated ambient levels. If an effect at an exposure of this magnitude is not found, it is likely that no generally important environmental effect would have been missed.

The study has the distinct advantage that if an effect is found, we may be able to directly determine if a specific carcinogen is present. Unfortunately, this study is in its early stages and has not progressed far enough to report on its findings at this time.

Summary and Conclusion

The epidemiologic data relating air pollution to lung cancer have been briefly summarized and discussed. Notably, most of the studies are descriptive epidemiologic investigations carried out in the 1950s and 1960s, which have used vital event data to contrast rates of lung cancer in men and women, in urban vs. rural regions, and between migrants from different countries with different lung cancer rates. In general, random distributions of potentially confounding factors have been assumed, However, cigarette smoking and occupational exposure distributions are not equal in the groups compared,

and these factors, which have far greater impact than air pollution on lung cancer rates, make interpretation of the available data uncertain. An alternative data source has been studies of occupational groups exposed to high levels of fossil fuel combustion products. These exposures have been associated with moderate increases in lung cancer risks. However, in even these settings the risks have been substantially less than those associated with cigarette smoking.

The fact that most of these studies were carried out almost 20 years ago is not in itself unreasonable. Exposure since the early 1960s has probably declined significantly and if any effect were to be detected it would have been seen in association with pollution levels that occurred in the early part of the century.

The role of epidemiology in future studies of the carcinogenic potential of exposure to fossil fuel combustion products must be in collaborative multidisciplinary efforts directed toward identifying human populations at substantial risk of exposure. The studies will require more sophisticated approaches to understanding exposure and must be large enough to detect relatively small excesses in risk. Assessments of population groups will require measures of both environmental exposure (ambient and occupationally related) and personal exposure (cigarette smoking and other potential indoor sources). Outcomes must be determined after a sufficient period of time following onset of exposure to be sure that tumors would have developed. These kinds of studies are expensive and time consuming and must have long range financial commitment to be successfully carried out.

REFERENCES

1. Stocks, P.. and Campbell, J. M. Lung cancer death rates among non-smokers and pipe and cigarette smokers. An evaluation in relation to air pollution by benzpyrene and other substances. Brit. Med. J. 2: 923-939 (1955).
2. Doll, R. Atmospheric pollution and lung cancer. Environ. Health Perspect. 22: 23-32 (1978).
3. U.S. Dept. of Health and Human Services. The Health Consequences of Smoking for Women, A report of the Surgeon General. U.S. Government Printing Office, Washington, 1980.
4. Doll, R., Grey, R., Hafner, B., and Peto, R. Mortality in relation to smoking: 22 year's observations on female British doctors. Brit. Med. J. 2: 967-871 (1980).
5. Haenszel, W., Loveland, D. B., and Sicken, M. G. Lung cancer mortality as related to residence and smoking histories. I. White males. J. Natl. Cancer Inst. 28: 947-1001 (1962).
6. Haenszel, W., and Taeuber, K. E. Lung cancer mortality as related to residence and smoking history. II. White females. J. Natl. Cancer Inst. 32: 803-838 (1964).
7. Hammond, E. C., and Garfinkel, L. General air pollution and cancer in the United States. Prev. Med. 9: 206-211 (1980).
8. Reid, D. D., Cornfield, J., Markush, R. E., Siegel, D., Pederson, E., and Haenszel, W. Studies of disease among migrants and native populations in Great Britain, Norway, and the United States. III. Prevalence of cardiorespiratory symptoms among migrants and native born in the United States. In: Epidemiological Study of Cancer and Other Chronic Diseases, W. Haenzel (Ed.), National Cancer Inst., Bethesda, MD, 1966, pp. 221-346.
9. Carnow, B. W., and Meier, P. A. Air pollution and cancer. Arch. Environ. Health 27: 207-218 (1973).
10. Higgins, I. T. T. Epidemiological evidence on the carcinogenic risk of air pollution. INSERM 52: 41-52 (1976).
11. Doll, R., Fisher, R. E. W., Gammon, E. J., Gunn, W., Hughes, G. O., Tyrer, F. H., and Wilson, W. Mortality of gasworkers with special reference to cancers of the lung and bladder, chronic bronchitis and pneumoconiosis. Brit. J. Ind. Med. 22: 1-12 (1965).
12. Doll, R., Vessey, M. P., Beasley, R. W. R., Buckley, A. R., Fear, E. C., Fisher, R. E. W., Gammon, E. J., Gunn, W., Hughes, G. O., Lee, K., and Norman-Smith, B. Mortality of gasworkers—final report of a prospective study. Brit. J. Ind. Med. 29: 394-406 (1972).
13. Lloyd, J. W. Long-term mortality study of steelworkers. V. Respiratory cancer in coke plant workers. J. Occup. Med. 13: 53-68 (1971).
14. Redmond, C. K., Strobino, B. R. and Cypress, E. H. Cancer experience among coke byproduct workers. Ann. N.Y. Acad. Sci. 271: 102-115 (1976).
15. Hammond, E. C., Selikoff, I. J., Lawther, P. L., and Seidman, H. Inhalation of benzpyrene and cancer in man. Ann. N.Y. Acad. Sci. 271: 116-124 (1976).
16. National Research Council. Health Effects of Exposure to Diesel Exhaust. National Academy Press, Washington, 1981.
17. Kaplan, I. Relationship of noxious gases to carcinoma of the lung in railroad workers. J. Am. Med. Assoc. 171: 2039-2043 (1959).
18. Raffle, P. The health of the worker. Brit. J. Ind. Med. 14: 73-80 (1957).
19. Waller, R. Trends in lung cancer in London in relation to exposure to diesel fumes. In: Health Effects of Diesel Engine Emissions, W. E. Pepelko, N. Danner and A. N. Clarke (Eds.), EPA, Cincinnati, OH, 1980.
20. Harris, J. E. Potential Risk of Lung Cancer from Diesel Engine. National Academy Press, Washington, 1981.
21. Axelsson, O. Aspects confounding in occupational health epidemiology. Scand. J. Work Environ. Health 4: 85-89 (1978).
22. Jarvholm, B., and Thiringer, G. E. Epidemiological studies of lung cancer—influence of smoking habits. Eur. J. Respir. Dis. (Suppl. 107) 61: 125-129 (1980).
23. Doll, R., and Peto, R. The causes of cancer: quantitative estimates of avoidable risks of cancer in the United States today. J. Natl. Cancer Inst. 66: 1193-1308 (1981).
24. Doll, R. and Hill, A. B. Mortality in relation to smoking: Ten year's observations of British doctors. Brit. Med. J. 1: 1399-1410, 1460-1467 (1964).
25. Kahn, H. A. The Dorn study of smoking and mortality among U.S. veterans. Report on eight and one-half years of observation. In: Epidemiological Study of Cancer and Other Chronic Diseases, W. Haenzel (Ed.), National Cancer Inst., Bethesda, MD, 1966, pp. 1-25.
26. Pike, M. C., Gordon, R. J., Henderson, B. E., Menck, H. R., and Soo Hoo, J. Air pollution. In: Persons at High Risk of Cancer, J. F. Fraumeni (Ed.), Academic Press, New York, 1975, pp. 225-239.
27. National Research Council. Particulate Polycyclic Organic Matter. National Academy of Sciences, Washington, 1972.
28. Report of the Task Group. Air pollution and cancer: risk

assessment methodology and epidemiologic evidence. Environ. Health Perspect. 22: 1-12 (1978).

29. Sawicki, E., Elbert, W. C., Hauser, T. R., Fox, F. T., and Stanley, T. W. Benzo(a)pyrene content of the air of American communities. Am. Ind. Hyg. Assoc. J. 21: 443-451 (1960).

30. Schenker, M. B., and Speizer, F. E. A retrospective cohort study of diesel exhaust in railroad workers: study design and methodological issues. In: *Health Effects of Diesel Engine Emissions*, W. E. Pepelko, N. Danner and N. A. Clarke (Eds.), EPA, Cincinnati, OH, 1980, pp. 114-126.