

The "Urban Factor" and Lung Cancer: Cigarette Smoking or Air Pollution?

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Data are presented which suggest that cigarette smoking, and to a lesser degree, urban pollution as indexed by benzo[a]pyrene are etiologic factors in the causation of lung cancer. The dose-response relationship to benzo[a]pyrene to lung cancer death rate in the urban community was estimated by using data on lung cancer deaths among coke oven workers. It appears to be an excess of 2-5 $\mu\text{mg}/\text{m}^3$ of benzo[a]pyrene per 100,000 population, suggesting that a lifetime community exposure to benzo[a]pyrene on a continuing basis may have a greater impact on lung deaths in the community than that considered by the Royal College of Physicians.

There would appear to be no question that in industrial societies, environmental factors play an important role in disease causation, and, in regard to cancer, estimates have been made by various scientific groups that between 75 and 90 percent are environmentally related. There also would appear to be a general consensus that cancer, particularly lung cancer, has multifactorial etiology which includes cigarette smoking, urban air pollution, and occupational exposure. Separating out these factors and assessing their quantitative impact on health is critical, since a major reduction in disease will only result if all or most of the important factors are diminished or removed. The need to assess the quantitative role of air pollution relates to decision making in regard to the use of energy materials, which depends not only on their availability, but on their impact on the health of the community.

The National Academy of Sciences in its monograph, *Particulate, Polycyclic Organic Matter (1)*, suggested that polycyclic organic compounds in the form of air pollutants were a significant factor in the etiology of lung cancer. Based on a series of studies by Carnow and Meier (2), it was concluded that these epidemiological studies lead to an estimate of the effect of air pollution on pulmonary cancer death rate of a 5% increase per unit increase in

urban pollution, as indexed by benzo[a]pyrene (BaP), wherein one BaP unit equals $1\mu\text{g}$ of BaP per 1000 m^3 of air, or $1\text{ ng BaP}/\text{m}^3$.

The Royal College of Physicians of London, on the other hand, based on Doll's study of British gasworkers (3), stated that "Urban air contains carcinogenic compounds but the relatively small excess risk to men occupationally exposed to large concentrations of these compounds, raises doubt about the relevance to lung cancer of the much lower levels found in the air of even the most polluted city."

This working paper will attempt to summarize some of the results of our studies examining these relationships, particularly those data which suggest that both cigarettes and air pollution are factors in the causation of cancer.

There is agreement that cigarette smoking is by far the strongest, in fact, the overwhelming factor in the causation of lung cancer. In the face of this, it is remarkable that any other factor is able to manifest itself. If one does to any significant degree, it may even be stronger than might otherwise appear, since it must emerge from a very heavy background of cigarette use. Such factors include occupational as well as general urban pollution.

The evidence for suggesting that urban pollution is a significant etiologic factor in lung cancer can be divided into four groups of studies. For each of these groups, the best estimates of air pollution as indexed by benzo[a]pyrene were used in examining the relationship between air pollution levels and

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lung cancer mortality.

The first group of studies examined urban-rural death rates, and, while most of them did not consider cigarette smoking, a study by Prindle (4) revealed a doubling of lung cancer mortality in large cities as compared to rural areas (29.4 versus 14.6). In examining cigarette smoking in these populations on a sampling basis, he found 48.5% of adults in urban areas smoked cigarettes as compared to 42.5% in rural areas. This difference did not explain the doubling in death rates between urban and rural areas.

The other urban-rural studies give no cigarette data, but show very significant differences, again, almost a doubling. One study showed a difference in ratios between London and Wales of 1.37 to 0.79 for males and 1.32 to 0.69 for females (5). Similar data are found in two other studies of urban-rural lung cancer differences, one in Iowa (6) and one in New York (7). In this latter investigation, as a matter of fact, there appeared to be gradient between rural lung cancer death rates (15.2) to rates in metropolitan urban areas (away from central city) of 20.8, to city-urban lung cancer death rates of 29.2. Again, one sees a doubling from rural to urban with an intermediate rate in the urban, noncity area.

The second group of studies, those examining lung cancer death rates in migrants, also suggest a relationship to urban pollution. While the cigarette smoking variable is difficult to evaluate, it would appear that those leaving the United Kingdom were shown to have a 35% increase in lung cancer if they left prior to the age of 30 and a 75% increase in lung cancer if they left after the age of 30, suggesting that there may be an early influence of pollution exposure. The migrant data are not explainable on the basis of cigarette smoking, particularly since Dean (8,9) in the Australian and South African studies and Eastcott (10) in New Zealand report no decrease in the smoking of immigrants after they arrive in these countries.

A third group of studies, using regression analysis (2) were carried out by Dr. Paul Meier and myself, in an attempt to separate the effect of factors in different rural and urban environments with the aim of identifying urban factors which might be held responsible for the differences in death rates from carcinoma of the lung. The first study examined the cigarette, solid fuel and liquid fuel factors in twenty countries.

On the assumptions that the death rate is related both to cigarette consumption and to solid-fuel consumption and that the effects are at least approximately additive, the increment in the death rate per unit increase in cigarette consumption and the increment per unit increase in solid-fuel consumption

were measured.

For cigarette smoking, the coefficient is approximately 15% of the average death rate from cancer of the lung. For example, the coefficient for cigarettes in the male age-adjusted group is 110, which is 14.7% of the average rate of 749.3. Taken at face value, this suggests an increment in male deaths of 15% per 1000 cigarettes per year. For the rate of cigarettes per day, one multiplies by 365/1000, which gives a 5.4% increase in pulmonary cancer death rate per cigarette per day. This corresponds to approximately a doubling in the death rate corresponding to an increase in smoking a pack (20 cigarettes) per day. This estimate is compatible with the variation in death rates by smoking category reported by Hammond (11).

For solid fuel consumption, the regression coefficient is approximately 20% of the average death rate from cancer of the lung. This suggests an increment in male cancer deaths of 20% per metric ton of coal burned per capita. Although we have, from Pybus (12), an estimate of total benzo[a]pyrene released per ton of coal burned, we have no way to convert this to concentration of benzo[a]pyrene in air and are thus unable to express this coefficient in equivalent benzo[a]pyrene units.

The conclusion which is suggested by these results is that the products of solid fuel combustion, or of some variable highly correlated with solid fuel, may be an important etiologic factor in carcinoma of the lung.

A second study was carried out examining the relationship between cigarettes and benzo[a]pyrene concentrations and lung cancer in the forty-eight contiguous states of the United States. The variables included pulmonary cancer death rates per million persons, cigarette sales in each state per person over 15 years of age, and benzo[a]pyrene in BaP units ($1 \mu\text{g}/1000 \text{ m}^3$ equals one unit). Using data on benzo[a]pyrene measurements in 163 cities (13), each state was given an urban and rural value, based on measurements in the state, and weighted according to the percentage of the population in the urban areas in each state. The methodology is detailed elsewhere (2). While there are many weaknesses in the studies, in that the data on cigarette smoking were sales and not consumption, and there was no separation of men and women smokers, these were the best available data. Benzo[a]pyrene measurements were only made on a number of occasions for each of eight quarters for two years. The results, however, were very similar to those obtained when we examined the raw data in the urban-rural studies and in the regression studies of twenty countries; namely, there appeared to be an approximate 5% increase in lung cancer death rates

in white males for each increase in pollution as indexed by BaP. For black males the coefficient was about 15% larger. Further details and methodology can be found in Carnow and Meier (2)].

There were a number of interesting aspects to the last study. First, it did not find elevated lung cancer rates necessarily in the most urbanized areas, but rather in those areas that had the highest benzo[a]pyrene levels. Secondly, gross particulate levels were also measured in the same place at the same time by Larson and Clement (13) and these were examined in the same way as benzo[a]pyrene. They failed to show any correlation with lung cancer death rates, as was shown by benzo[a]pyrene.

Finally, a number of sampling studies were examined by us. These are of major importance, since Hammond's study (11) and the one by Buell and Dunne (14) were prospective studies and while Dean's (15), Haenzel and co-workers' (16, 17), and Hitosugi's (18) studies are retrospective, all five studies examined the cigarette smoking variable in great detail. In Buell and Dunne's study, the lung cancer death rates, adjusted for age and cigarette smoking, in Los Angeles and the San Francisco Bay area were significantly elevated above other California towns and nonindustrial areas.

In the Hammond study, a very similar gradient was shown when standardized for age and cigarette smoking from a rate of 52 in the urban areas to one of 39 per 100,000 in the rural areas.

Dean's study (15) comparing Belfast and rural areas with gradations from inner Belfast to truly rural areas, revealed a gradient, even for nonsmokers. This was from a rate of 36 to 40 lung cancer deaths per 100,000 in Belfast to a rate of 16 to 10 in the rural areas. The gradient also held true for those smoking 1 to 10 cigarettes per day and those smoking up to one package of cigarettes per day.

The very careful studies of Haenzel and co-workers (15, 17) of a 10% sample of pulmonary cancer deaths in the United States is another example. The sex, smoking habits, and location and duration of residence were considered and after standardizing for age and smoking they found a mortality ratio for white males of 113 in urban as compared to 79 in rural areas.

Hitosugi's study (18) was carried out by interviewing families of 259 individuals dying from pulmonary cancer. Age, sex, smoking habits, occupation, and residence were recorded. While the numbers were not very large, a significant relationship between lung cancer death rates and levels of air pollution was found at all levels of cigarette smoking.

A number of studies have been carried out ex-

amining the relationship between lung cancer and occupational exposure to polycyclic aromatic hydrocarbons. These include Doll's study of gas workers (19), Hammond's study of roofing workers (20), and Lloyd's large study of coke oven workers working in the United States (21). Doll and Hammond both found approximately a doubling of the lung cancer death rates among workers, the one group exposed to an estimated 2000 $\mu\text{mg}/\text{m}^3$ of benzo[a]pyrene. Lloyd, on the other hand, found that coke oven workers working top-side had ten times the lung cancer death rate found in the unexposed population. In a study by Pike and Gordon (22) the following is stated in regard to Doll's study. "The carbonization workers were exposed to an estimated 2,000 $\mu\text{mg}/\text{m}^3$ benzo[a]pyrene for about 22 percent of the year." They went on to state that, "The exposure caused an extra 160 lung cancer cases per 100,000, so that we may estimate, assuming a proportional effect, that each $\mu\text{mg}/\text{m}^3$ of benzo[a]pyrene causes 0.4 extra lung cancer cases a year per 100,000 population." They go further to state that, "A city with 15 $\mu\text{mg}/\text{m}^3$ of benzo[a]pyrene air pollution might, therefore, have an extra 18 per 100,000 lung cancer cases per year."

The implication, of course, is that a lifetime exposure to urban air pollutants, at a somewhat lower level, might still result in significant exposure and thus explain the increase in lung cancer death rates over rural death rates.

A similar calculation was carried out by our group to examine the relationship between exposure to benzo[a]pyrene and death from lung cancer among coke oven workers. Studies carried out by Jackson (23) found that workers on top of the ovens were exposed to levels of benzo[a]pyrene varying from 1.2 to 15.9 $\mu\text{g}/\text{m}^3$ of air. Assuming a 40-hr work week and a 50-week year, 2000 (hr worked/yr)/8750 (exposure/yr) = 24% of total time spent at work.

From Lloyd's study (21) of mortality among coke oven workers, there were 18 lung cancer deaths observed out of 222 workers exposed (a rate of 8108 per 100,000 with an expected rate in this group, according to Lloyd, of 2.2 deaths per 222 workers or a rate of 990 per 100,000). Thus, 7118 excess deaths per 100,000 were observed.

If one examines the minimum level of benzo[a]pyrene to which these workers might have been exposed using the results reported by Jackson (1.2 $\mu\text{g}/\text{m}^3$) or 1200 $\mu\text{mg}/\text{m}^3$ for 24% of total time, the exposure is equal to 228 $\mu\text{mg}/\text{m}^3$. The excess in cancer death rates of 7118, divided by 288 equals 24.7; that is a 24.7 per 100,000 increase in deaths per increase of 1 $\mu\text{mg}/\text{m}^3$ of benzo[a]pyrene per cubic meter of air. The increase of 24.7 divided by 990,

Table 1. Age-adjusted malignant neoplasm of trachea, and of bronchus and lung specified as primary (ICD 162); and of lung and bronchus, unspecified as to whether primary or secondary (ICD 163) for the United States; Pennsylvania and Allegheny county, Pennsylvania; and Indiana and Lake and Boone counties, Indiana, by sex and race, 1950-1969.^a

	White				Nonwhite			
	Male		Female		Male		Female	
	No.	Rate ^b	No.	Rate ^b	No.	Rate ^b	No.	Rate ^b
United States	571,226	37.98	108,326	6.29	53,910	36.67	10,222	6.27
Pennsylvania	39,924	37.73	7,521	6.20	3,532	52.96	613	8.29
Allegheny County, Pa.	6,435	43.3	1,190	7.0	699	55.7	86	6.9
Indiana	14,735	35.72	2,735	5.83	1,003	49.20	151	6.95
Lake County, Ind.	1,575	47.9	223	6.8	244	41.9	41	7.2
Boone County, Ind. (rural)	56	19.0	18	5.3	—	—	—	—

^aData of Mason and McKay (24).

^bAge-adjusted mortality rates (per 100,000).

the expected deaths in this group, represents a 2.5% increase per $\mu\text{mg}/\text{m}^3$ of benzo[a]pyrene.

Using the maximum measurements made, 1590 $\mu\text{mg}/\text{m}^3$, one finds 18.6 per 100,000 increase in lung cancer deaths per increase in nanograms per cubic meter of benzo[a]pyrene. This represents a 1.9% increase in deaths. These calculations and those of Pike and Gordon suggest that a 70-year lifetime exposure to benzo[a]pyrene on a continuous basis may have a greater impact on lung cancer deaths in the community than that considered by the Royal College of Physicians.

One further piece of data, shown in Table 1, should be noted. In examining data from Allegheny County, Pennsylvania and Lake County, Indiana, two areas in which large coke ovens are currently operating, considerably higher lung cancer death rates in white and nonwhite males as compared to lung cancer deaths in other counties in the same states and in the states as a whole, were recorded.

I noted at the onset of this discussion that any association found in the presence of such an overwhelming factor as cigarettes must be seriously considered and explained. All of the major prospective sampling studies carried out in the United States and in other countries examined by us, in addition to the regression studies we carried out, reveal a significant relationship between urbanization and lung cancer incidence, and, where benzo[a]pyrene levels were measured, an even greater relationship to levels of benzo[a]pyrene. These relationships hold, even when one standardizes for cigarette smoking, as was done in all of these studies, suggesting that air pollution is, indeed, a significant factor in the etiology of lung cancer.

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