Environmental Correlates of Intercity Variation in Age-Adjusted Cancer Mortality Rates

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Factors contributing to urban differences in cancer mortality rates are difficult to specify because of migration and the delay between exposure to carcinogens and manifestations of the disease. Proxy measures for prior migration, motor vehicle emissions, industrial pollution, factors in the water supplies, and climate, explain more than half the intercity variation in age-adjusted cancer mortality rates among 96 cities in the U.S. in 1970. The potential importance of these environmental factors as the "urban factor" in cancer is discussed.

Substantial difference in cancer mortality rates among geographic areas has implicated the urban environment as a factor in the etiology of various cancers. Chemical carcinogens and ionizing radiation in workplaces, often spilled into surrounding environments, are undoubtedly a source of some of the differences in cancer rates among certain areas (1-3). Other factors are likely to be involved but their intermix in urban environments leads to difficulties in separating them in research.

The attribution of specific deaths to specific environmental factors is also greatly complicated by population migration among environments and the long delays between exposure to harmful agents in the environment and the appearance of disease symptoms or death. In illustration, cancer mortality rates are related to prevailing wind patterns in Houston—suggesting an air pollution effect—but are not consistently related to concurrent measures of concentration in air of several pollutants (4). Unfortunately, measurement of specific pollutants in air, water, and food have not been acquired systematically until recent years. The concentrations of particular pollutants years earlier may have been substantially different from those now being measured.

Although it is not possible definitively to link specific environmental conditions in the past to later mortality rates over relatively large areas, it is possible to use proxy measures to suggest the sources of harmful environmental contamination and to estimate the relative magnitude of contribution of these sources to subsequent mortality rates. Work on source of drinking water in relation to cancer mortality rates is illustrative of this approach (5, 6).

In the research reported here, proxy measures for a wide variety of potential or known sources of harmful agents in environment were correlated to age adjusted cancer mortality rates in 98 cities in the United States in 1970. Measures of the proxy variables were obtained 8 to 16 years prior to 1970, allowing for delayed effects on mortality. Other factors such as climate and five-year residence in the cities were also included.

Data Sources

Cities were chosen for study on the basis of availability of data. Data were usable from 98 of the 100 cities for which published data existed on source of drinking water supply (surface versus wells) and concentrations of a wide variety of ele-
ments in water supplies for the year 1962 (7), and for which data on other potential correlates of mortality were available.

In addition to source of supply and pH, the water data include concentrations of silica, iron, calcium, magnesium, sodium, potassium, radium, uranium, silver, aluminum, boron, barium, beryllium, cobalt, chromium, copper, lithium, manganese, molybdenum, nickel, phosphorus, lead, rubidium, tin, titanium, vanadium, and zinc. In those cities where water was obtained from more than one source, the concentrations were weighted to reflect the contribution of each source of supply (8).

As a proxy for potential exposure of industrial workers to harmful elements as well as pollution of the environment by industrial products and wastes, the percentage of the adult population (21 years or more) employed in each city as production workers was calculated from census data (9).

As an indicator of concentration of motor vehicle emissions, the number of motor vehicles registered in each city in 1960 was divided by the total square miles of the city in 1960. Motor vehicle registrations by city are not published but were derived from published number of deaths and death rates from motor vehicle injuries per 10,000 registered vehicles (10). The number of registered vehicles is the number of deaths due to injury divided by the injury death rate per registered vehicles.

Total time of exposure of the population to a city’s environment is not known, but an indication of recent migration is included in the U.S. Census in the form of a question as to residence five years prior to the census year. As an estimate of length of exposure, the percentage of the 1970 population that was living in the same county in 1965 was used in the analysis (11). An overall indication of the degree of urbanization was included in the form of total population in the city in 1960 per square mile (12).

The climate of each city was indicated by the average annual heating degree days. A heating degree day is counted for each degree the average temperature is below 65°F on a given day (13).

Cancer mortality rates per 100,000 population were age-adjusted using the national age specific death rates applied to the number of deaths (14) and age distribution (11) in each city in 1970 by the indirect method. Deaths classified as 140-209 using the eighth revision of the International Classification of Diseases were included as cancer deaths (15).

Analysis

The data were analyzed by using linear correlation and stepwise multiple regression techniques. In stepwise regression, the potential predictor variables are examined and the variable most predictive of the outcome variable is selected into a linear regression equation. The next most predictive variable, controlling for those entered, is then selected until some preset criteria for not allowing other variables to enter is encountered. Since the number of potential predictor variables was large (41 were included), a strict level of statistical significance was used ($p < 0.01$) to consider a factor as likely to be involved in the etiology of the disease. The assumptions of linearity and additivity were checked by examining plots of bivariate distributions and residuals of the multiple regression analysis.

Results

The means and standard deviations of variables significantly related to cancer mortality rates in the regression analysis are shown in Table 1. The results of the stepwise regression analysis of the age adjusted cancer death rates are presented in Table 2. Seven of the 41 variables considered were significantly predictive of the cancer mortality rate. Cancer mortality was higher, on average, in cities which, in prior years, had more motor vehicles per square mile, a greater percentage of the population having lived there at least five years, a greater percentage of adults employed as production workers, and with higher concentrations of barium in drinking water supplies. Lower cancer mortality rates were found, on average, in cities with more bicarbonate and more sodium in water supplies, and with greater numbers of heating degree days.

| Variable                              | Mean  | SD     |
|---------------------------------------|-------|--------|
| Thousands of registered motor vehicles per square mile (1960) | 2.7   | 1.3    |
| Percent of population living in the county in 1965 | 77.5  | 6.4     |
| Percent of adults employed as production workers (1954) | 14.5  | 10.5   |
| Barium in the water supply, μg/l       | 54.0  | 46.6   |
| Bicarbonate in the water supply, mg/l  | 85.6  | 80.4   |
| Sodium in the water supply, mg/l     | 21.6  | 29.2   |
| Heating degree days                   | 4419.9 | 2012.8 |
| Age-adjusted cancer mortality per 100,000 population | 177.1 | 18.7   |

Table 1. Means and standard deviations of variables that were significantly related to cancer mortality rates in 1970.
The regression coefficients are estimates of the magnitude of the relationships. For example, the coefficient of 5.2 in relation to thousand of motor vehicles per square mile means that for every 1000 more motor vehicles per square mile in a city relative to the others in 1960 there were about five more cancer deaths per 100,000 population in 1970, controlling for the other factors considered. The coefficient of determination indicates that 51% of the variation in cancer death rates among the cities considered is explained by the seven variables in Table 2.

A number of other variables were significantly correlated with cancer mortality rates but these correlations were reduced when three of the variables that entered the regression analysis were controlled. In Table 3, the zero order correlation is shown along with the partial correlations as motor vehicles, past residence in the county, and bicarbonate in the water supply entered the equation. The correlation between population per square mile and the cancer rate was greatly reduced when motor vehicles per square mile was controlled. Similarly, correlation of the drinking water source and elements in drinking water with cancer mortality rates were reduced greatly when bicarbonate was controlled.

The changes in the partial correlations result from collinearity among the variables as shown in Table 4. Motor vehicles per square mile are highly correlated with population per square mile and a number of the elements in water are strongly correlated as are some of these elements with the source of water supply. However, the collinearity of variables that entered the stepwise regression is not large enough to distort estimates of effects.

Inspection of graphs of the bivariate relationships suggested that all of the relationships mentioned were linear except those between population per square mile and cancer mortality rates and between population per square mile and motor vehicles per square mile. Both motor vehicles per square mile and cancer mortality rates tended to increase linearly up to a point and then level off as population per square mile increased (Figs. 1 and 2). However, the relationship between motor vehicles per square mile and cancer mortality rates was linear (Fig. 3). Inspection of bivariate plots of each of the seven variables predictive of cancer mortality and residual variation from those predictions did not reveal apparent interaction effect.

Table 3. Zero-order and partial correlations of variables originally related to cancer mortality rates (p < 0.01) but not so when other variables entered the stepwise regression.

| Zero-order correlation with cancer rate | Partial correlation with cancer rate upon entry of: |
|----------------------------------------|----------------------------------------------|
|                                        | Motor vehicles | In county in 1965 | Bicarbonate in water |
| Population per square mile (1960)      | 0.44           | 0.11              | 0.05                | 0.00 |
| Drinking water source (0 = surface, 1 = wells) | -0.31          | -0.24             | -0.16              | -0.01 |
| Lithium in water                      | -0.27          | -0.20             | -0.15              | -0.10 |
| Beryllium in water                    | -0.31          | -0.23             | -0.16              | -0.08 |
| Uranium in water                      | -0.42          | -0.33             | -0.23              | -0.12 |
| Potassium in water                    | -0.34          | -0.20             | -0.10              | -0.08 |
| Magnesium in water                    | -0.34          | -0.28             | -0.25              | -0.10 |
| Silica in water                       | -0.41          | -0.33             | -0.22              | -0.11 |

Discussion

The results of this research suggest that substantial variation in cancer mortality rates among cities can be explained by relatively few variables—motor vehicle emissions, industrial production, elements in drinking water, and differential exposure of the population to city environments.
Table 4. Correlations among variables significantly related to cancer mortality rates.

| Variables                      | 2    | 3    | 4    | 5    | 6    | 7    | 8    | 9    | 10   | 11   | 12   | 13   | 14   | 15   |
|--------------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|
| 1. Motor vehicles per square mile | 0.24 | 0.33 | 0.34 | 0.84 | -0.39| -0.21| -0.35| -0.21| -0.22| -0.25| -0.20| -0.37| -0.20| -0.28|
| 2. Percent population in county in 1965 | 0.47 | 0.49 | 0.30 | -0.23| -0.17| -0.33| -0.30| -0.21| -0.27| -0.41| -0.36| -0.18| -0.41|       |
| 3. Percent adults production workers | 0.48 | 0.26 | -0.22| -0.32| -0.37| -0.19| -0.29| -0.28| -0.32| -0.16| -0.42|       |       |       |
| 4. Heating degree days | 0.34 | -0.17| -0.15| -0.39| -0.33| -0.21| -0.39| -0.19| -0.19| -0.00| -0.34|       |       |       |
| 5. Population per square mile | -0.34| -0.28| -0.33| -0.28| -0.22| -0.26| -0.27| -0.32| -0.25| -0.32|       |       |       |       |
| 6. Barium in water | 0.50 | 0.44 | 0.32 | 0.25 | 0.27 | 0.51 | 0.56 | 0.51 | 0.33 |       |       |       |       |       |
| 7. Bicarbonate in water | 0.27 | 0.60 | 0.72 | 0.36 | 0.50 | 0.20 | 0.69 | 0.51 |       |       |       |       |       |       |
| 8. Sodium in water | 0.36 | 0.60 | 0.53 | 0.49 | 0.60 | 0.26 | 0.34 |       |       |       |       |       |       |       |
| 9. Drinking water source | 0.13 | 0.21 | 0.39 | 0.22 | 0.33 | 0.63 |       |       |       |       |       |       |       |       |
| 10. Lithium in water | 0.77 | 0.61 | 0.50 | 0.34 | 0.29 |       |       |       |       |       |       |       |       |       |
| 11. Beryllium in water | 0.53 | 0.49 | 0.29 | 0.37 |       |       |       |       |       |       |       |       |       |       |
| 12. Uranium in water | 0.61 | 0.48 | 0.59 |       |       |       |       |       |       |       |       |       |       |       |
| 13. Potassium in water | 0.34 | 0.47 |       |       |       |       |       |       |       |       |       |       |       |       |
| 14. Magnesium in water | 0.34 |       |       |       |       |       |       |       |       |       |       |       |       |       |
| 15. Silica in water |       |       |       |       |       |       |       |       |       |       |       |       |       |       |

The relationships among population density, vehicle density and cancer suggest that it is the vehicle density rather than some other correlate of population density that contributes to cancer mortality. Motor vehicles per square mile do not continue to increase linearly with population density but level off in the more densely populated cities where alternative means of transportation are more often available. Cancer rates also level off in more densely populated cities but are linearly related to motor vehicle registrations per square mile. It is suggested that population density affects motor vehicle density which, in turn, affects cancer. Motor vehicles appear to be a substantial part of the "urban factor" in cancer.

At a recent symposium on cancer, claims were made that air pollution does not cause cancer based on comparison of a few cities with "clean air" compared to a few cities with "dirty air" (16), although the possibility of a synergistic effect with smoking was considered. A reviewer of this paper questioned whether the relationships observed could occur because the variables examined were surrogates for known risk factors such as smoking. Since many of the same carcinogens are present both in cigarette smoke and motor vehicle emissions, namely polycyclic aromatic hydrocarbons (17, 18), it is curious that the former would only be considered as carcinogens. More than forty years ago, experiments with mice exposed to road dust a few times per day found higher cancer rates in those exposed compared to controls. Removal of the "tars" in the dust reduced the cancer rates (19). And, it should be remembered, motor vehicle emissions are not only breathed but also settle on food (20) and are picked up by drainage into water supplies.

It is always possible that some unexamined variable is related to one or more examined variables in such a way as to mislead the researcher. The author looked for data on smoking, alcohol, and dietary intake in the cities studied but could not find satisfactory data. It is highly doubtful that smoking, drinking, and eating behavior varies enough among the cities to explain the intercity variation observed although they would undoubtedly explain some interindividual variation both between and within cities. It is even more doubtful that these factors would explain the same variation as that explained by motor vehicle emissions, migration, water supply factors and the like.

An important historical lesson is too often forgotten by scientists, who tend to be primarily interested in definitive understanding of a phenomenon. It is not necessary to have a complete understanding of every cause or of even a single cause in a disease process to prevent the disease (21). John Snow discovered that cholera was a water-borne disease, and cleanup of water supplies prevented a substantial amount of cholera before the bacillus was isolated (22). If the ten year lagged correlation of motor vehicle registration and cancer mortality, observed in the present study, accurately reflects the effect on cancer of motor vehicle emissions, and if current governmental standards for reducing emissions in new vehicles are as effective as projected, reductions in
**Figure 1.** Relation of motor vehicles and population per square mile.

**Figure 2.** Relation of population per square mile and intercity cancer mortality rates.
workers and cancer mortality rates 16 years later. If the proliferation of carcinogens into the environment by industry is not curbed, any reductions in cancers realized from other preventive measures would perhaps be more than offset by those occurring from industrial production and waste (I).

The author is aware of no straightforward explanation for the correlation of cancer mortality rates with barium, bicarbonate, and sodium concentrations in water supplies. Rats given 5 ppm soluble salts of barium in drinking water have no higher tumor incidence in their lifetimes than controls (24). This lowers the probability but does not entirely rule out the possibility that barium is a human carcinogen. The possible effects of barium, bicarbonate, and sodium in the adsorption of organic carcinogens to particulate matter in water (25) or in the metabolism of those carcinogens in the human organism deserve further investigation. The collinearity among a number of factors in water as well as the source of supply reduces confidence that the particular factors that entered the equation are of key importance in cancer causation or prevention. However, there is enough known about carcinogens in surface water supplies to justify efforts at removing them and other potential carcinogens through better treatment systems.

The higher cancer mortality rates in warmer climates, controlling for the other factors, could reflect the known effect of solar radiation on skin cancer. However, death from skin cancer is relatively rare. The relation of cancer mortality to warmer climate could indicate exposure to other environmental carcinogens as a result of the population being more frequently out of doors in warmer climates. The correlation of cancer mortality rates with percentage of the population residing in the city for at least five years is also suggestive of an effect of length of exposure to the particular urban environments involved.

The relatively large proportion of the intercity variations in cancer mortality rates explained by the relatively crude proxy measures available suggests that, as more specific and refined measures become available, the elements of the urban environment that contribute to cancer will become increasingly known, and hopefully controlled to lower the cancer burden.

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