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Lung Cancer in Relation to Environmental Pollutants Emitted from Industrial Sources

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A case–control study of residents who lived in the vicinity of a primary zinc smelter and a large steel manufacturing plant in eastern Pennsylvania was undertaken to investigate the role of environmental pollutants in the etiology of lung cancer. Lifetime residential, occupational, and smoking histories were obtained from the next of kin of 335 white male lung cancer cases and 332 white male controls. Soil samples were collected and analyzed for content in ppm of arsenic, copper, lead, manganese, zinc, and cadmium. Relative risks were determined according to distance of residence from the zinc smelter and the steel plant, and according to residence in areas with heavy and light levels of various pollutants. Twofold risks for lung cancer were associated with residence near the zinc smelter and with residence in areas with heavy levels of arsenic and cadmium, although the number of individuals living in these higher risk areas was small. These increases were not explained by the effects of cigarette smoking or by employment in the zinc or steel industry. No excess risk was associated with living near the steel plant. The limited size of the study precludes causal interpretation, but the findings suggest the need for further investigation of metallic air pollution and lung cancer.

INTRODUCTION

The finding of increased rates of lung cancer among both males and females residing in counties with copper, lead, or zinc smelting and refining operations (Blot and Fraumeni, 1975) raised the possibility that air pollution from the nonferrous smelters may present a health hazard. Each of these ores contains inorganic arsenic, a known lung carcinogen (Landrigan, 1981). A case–control study of lung cancer in a tricounty area of Pennsylvania with primary zinc smelting and refining offered the opportunity to investigate this association further. Since the study area also contained a large steel manufacturing and processing plant, we assessed the risk of lung cancer associated with living in the vicinity of either the zinc or the steel plant.

Study Area

The area studied involved three contiguous counties in eastern Pennsylvania (Fig. 1). Two industries of interest in the area were primary zinc smelting and refining and steel manufacturing and processing, each major employers (approximately 1500 and 15,000 employees, respectively) with large physical plants containing over 100 stacks. The zinc facility included two smelters, the west plant and the east plant, which began operations in 1898 and 1910, respectively. They are located approximately 4 km apart in a small town in a narrow valley bordered

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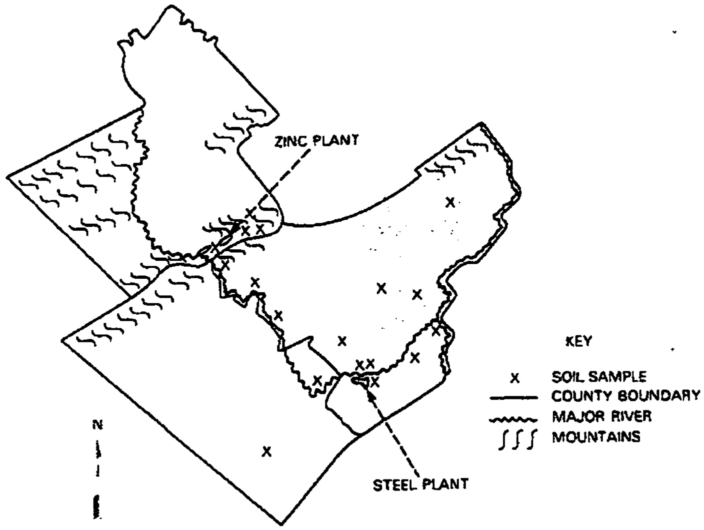

FIG. 1. Diagram of the tricounty area showing locations of the zinc plant, steel plant, soil samples, and major rivers and mountains.

by low mountains. The prevailing winds are from the northwest and southwest (Fig. 2). The integrated steel facility consisting of a coke oven, blast furnaces, steel making furnaces, finishing mill, and foundry has been in operation since 1904. Its major product line is structural steel. It extends for nearly five miles along the south bank of the Lehigh River in close proximity to an urbanized area and is bounded on the south by small mountains. The prevailing winds are from the west and northeast.

MATERIALS AND METHODS

Computerized mortality tapes from the state of Pennsylvania were used to identify all 360 deaths attributed to primary lung cancer (ICDA 162.1) among white male residents aged 30–79 of Lehigh and Northampton counties during 1976–1977 and Carbon county during 1974–1977. An equal number of controls were randomly selected from among other causes of death, excluding chronic respiratory diseases, respiratory cancer, and suicide, to be similar to the cases with respect to sex, year and age at death, and county of usual residence. Death certificates were obtained for the cases and controls and were used to locate the next of kin. Personal interviews of the next of kin were conducted during 1979–1980 by local interviewers unaware of the case–control status of decedents. A structured questionnaire was used to elicit complete residential, occupational, and smoking histories in addition to demographic and other variables of interest. All jobs held for 6 months or longer were classified into one of 15 industrial categories using a coding scheme adapted from the Standard Industrial Classification Manual (OMB, 1972). An individual's usual industry was defined as the one in which he had spent the longest number of years, provided that he had worked in this industry for at least 15 years. The usual number of cigarettes

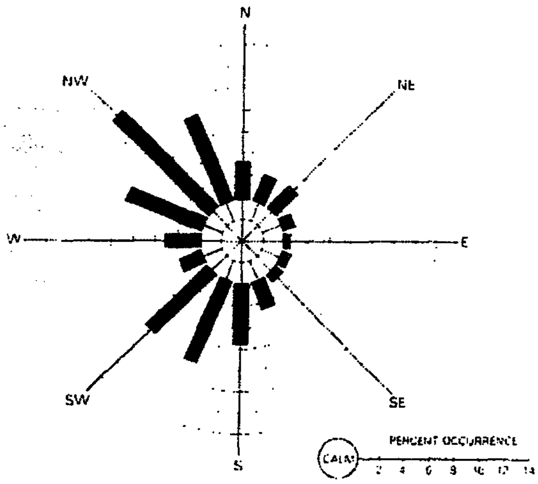

FIG. 2. Plot of percentage of occurrence for wind direction near the zinc plant (grid 5 4).

smoked per day was grouped into the following categories: nonsmoker; light or former smoker—smoked half a pack or less or quit smoking at least 1 years prior to death; moderate—smoked more than half a pack but less than two packs; and heavy—smoked two or more packs per day.

Nineteen samples of the top 5 cm of soil were collected by Lehigh University in October 1980 at locations in the three-county area where Environmental Protection Agency (EPA) air monitors had been previously located. Except for three samples collected near the zinc plant, all were in areas where the soil was "undisturbed"; that is, where trees or large shrubs were growing wild indicating no disturbance for five or more years. Heavy metal contents were determined by atomic absorption spectrophotometry using two replicate samples, background correction, and standard solutions (Grewling, 1976). Copper, lead, manganese, and zinc determinations were carried out at Lehigh University. Arsenic and cadmium determinations were performed by the Department of Agronomy, Cornell University. Limited air data for sulfur dioxide (SO_2) were obtained for stations near the zinc and steel plants from the Commonwealth of Pennsylvania's Department of Environmental Resources Bureau of Air Quality and Noise Control (personal communication, 1981).

Geologic survey maps of the three counties were used to assign each reported residence to a 1-km^2 grid. Grid coordinates were also assigned to the zinc and steel plants and to areas where soil and air sample measurements were made. Each grid from which a soil sample had been taken and the eight contiguous grids surrounding it were given a score of heavy or light based on the level of the pollutant of interest. The grid of longest residence and the grid of residence during the individual years 1920, 1930, 1940, 1950, 1960, and 1970 were determined, and case–control differences according to distance from the zinc and the steel plants and by level of heavy metals present in soil samples were analyzed.

The following model adapted from Stinnett *et al.* (1981) was also used to estimate relative exposure (X_i) according to distance (D_i) from the two zinc plants and from the steel plant. $\chi_i = \sum_{k=1}^{P} W_k\, 1/D_{ik}$ where D_{ik} is the distance from the kth grid to the ith subject. W_k is an emissions weight for the kth grid, and P is number of grids in which the zinc or steel plants were located. The measure of nearness, X_i, is based on the idea that ambient air conditions vary inversely with distance from the source of emissions and directly with emissions rate, and that concentrations from several stacks are additive. Since sufficient data were not available for the steel plant to determine the relative emissions of specific pollutants per grid, each grid was assigned an emissions weight of 1. The grids containing the east and west zinc smelters were given weights of 6 and 7 (east plant), and 4 and 3 (west plant) to represent the relative emissions of zinc and cadmium, respectively, as documented by Buchauer (1973). All zinc plant grids were given an emissions weight of 1 for the other heavy metals. Exposures from the steel and the zinc plants were not assessed simultaneously as they were over 25 km apart and the environmental pollutants emitted from each source were different. Relative exposures from each source to each grid of residence were then grouped into three proximity categories—Far, Middle, or Near—based on the combined distributions of cases and controls.

Estimates of the relative risk (RR) of lung cancer associated with residence were calculated using the odds ratio for 2 × 2 tables (Fleiss, 1981). Significance tests (one-sided because of the a priori hypotheses of increased risk with exposure) and corresponding 90% confidence intervals (CI) were calculated according to the methods described by Gart (1970). Results reported elsewhere (Blot *et al.*, 1983) revealed increased risks associated with long-term employment in both the steel and zinc smelting industries, although cigarette smoking was the predominant risk factor for lung cancer. Thus, wherever our numbers permitted, RR for residential exposures were looked at controlling for these factors. A multiple logistic model for disease incidence using stratified matching criteria [county of usual residence and five age groups (34–56, 57–62, 63–67, 68–72, and 73–79)] was applied in order to simultaneously control residential exposures for the influence of smoking and usual occupation in steel manufacturing or zinc smelting (Lubin, 1981). The four smoking categories—nonsmoker, light, moderate, and heavy—were assigned scores of 0, 0.5, 1.25, and 2.25, respectively.

RESULTS

Interviews were completed for 345 cases (96%) and 340 controls (94%). Ten cases and eight controls were deleted from the analysis because of either misdiagnosis of lung cancer determined by medical record review or incomplete questionnaires. Analyses were conducted on the remaining 335 cases and 332 controls.

The locations of the zinc and steel plants, the soil samples, and the major rivers and mountains are shown in Fig. 1. Data from the soil samples are presented in Table for each heavy metal pollutant by grid where collected. Each pollutant was assigned a value of heavy (H) or light (L) for purposes of analyses and each soil sample grid was given a value of Far (F), Middle (M), or Near (N) to indicate its relative exposure to the zinc smelter. Also presented is the range in unpolluted soil for cadmium (Rose *et al.*, 1979) and the mean in U.S. soils for the other heavy metals (Connor and Shacklette, 1975). Compared to the reported values,

TABLE 1
LEVELS OF VARIOUS POLLUTANTS MEASURED IN SOIL SAMPLES FROM 19 GRIDS

Proximity to zinc plant[a]	Grid	Arsenic ppm	Arsenic Level	Cadmium ppm	Cadmium Level	Copper ppm	Copper Level	Lead ppm	Lead Level	Manganese ppm	Manganese Level	Zinc ppm	Zinc Level
F	4569	8	L[b]	1	L	12	L	59	L	726	L	112	L
F	4841	20	L	84	H	210	H	553	H	3991	H	31,261	H
M	4939	30	L	269	H	73	H	331	H	1100	H	5,230	H
N	5036	125	H	922	H	324	H	1251	H	4689	H	27,105	H
N	5134	85	H	310	H	272	H	761	H	4602	H	35,514	H
N	5233	70	H	397	H	105	H	172	H	1049	H	4,685	H
M	5334	34	L	220	H	106	H	267	H	4697	H	4,767	H
M	5741	7	L	26	L	23	L	84	L	776	L	443	L
F	5760	5	L	1	L	19	L	66	L	800	L	148	L
F	5965	9	L	1	L	19	L	70	L	650	L	25	L
F	6343	10	L	3	L	21	L	86	L	425	L	216	L
F	6468	16	L	4	L	111	H	300	H	550	L	275	L
F	6654	2	L	2	L	13	L	91	L	343	L	108	L
F	6764	7	L	6	L	34	L	173	H	600	L	205	L
F	7156	5	L	2	L	28	L	155	H	625	L	204	L
F	7157	2	L	1	L	49	L	123	H	975	L	307	L
F	7249	15	L	4	L	39	L	175	H	1101	H	398	L
F	7357	10	L	2	L	26	L	132	H	999	L	250	L
F	8242	8	L	2	L	16	L	102	H	1573	H	216	L
Mean (range) in unpolluted soil		7.5		(0.1–0.5)		15		17		320		36	

[a] "F", "M" or "N" [illegible] proximity to the zinc plant.
[b] [illegible] each pollutant and grid indicates whether the pollutant level was considered to be heavy or light for that grid.

the levels for the pollutants tended to be substantially elevated, especially near the zinc smelter (grids 5036, 5134, 5233). Even though the soil samples taken near the smelter were from "disturbed" soil, they were similar in magnitude to values reported by Buchauer (1973). As can be seen from the table, it was impossible to separate out the effects of cadmium and zinc by an analysis of H and L grids because of the strong correlation between the two in this study. Similarly, a separate effect of arsenic could not be evaluated because grids H in cadmium and zinc, but L in arsenic contained only one person.

From the available SO_2 data, 20 measurements in 1970 downwind of the zinc smelter (grid 5334) yielded a yearly mean of 416 μg/m^3 and a 24-h maximum of 676 μg/m^3, while 35 measurements in 1974 near the steel plant (grid 7154) yielded a yearly mean of 39 μg/m^3 and a 24-hr maximum of 260 μg/m^3. The levels near the zinc smelter were higher than the National and Pennsylvania primary standards of 80 and 365 μg/m^3 for 1-year mean and 24-hr maximum values, respectively.

The RR of lung cancer associated with usual residence in areas with H and L levels of the six heavy metal pollutants are presented in Table 2. Significant increases were seen for study subjects residing in grids with high levels of arsenic (RR = 2.3, p = 0.03) and cadmium/zinc (RR = 2.0, P = 0.05) but not for copper, lead, or manganese. When these risks were adjusted for the effects of smoking and usual occupation in zinc and steel, the RR for lead and manganese were reduced to less than 1.0, while the RR for arsenic, cadmium/zinc, and copper were reduced to 1.6 (P = 0.21), 1.5 (P = 0.24), and 1.1, respectively.

Figure 3 shows the grids of usual residence for a 20-km^2 area surrounding the zinc smelter. Grids of residence at proximities far, middle, or near to the smelter are shaded. The white grids indicate areas where none of the study population usually lived. The area surrounding the smelter is sparsely populated with large unsettled areas due to mountains. The RR, however, were above 1.0 for those

TABLE 2
RR OF LUNG CANCER ACCORDING TO USUAL RESIDENCE IN GRIDS WITH LIGHT OR HEAVY LEVELS OF VARIOUS POLLUTANTS

Pollutant	Level	No. of cases	No. of controls	RR[a]	(90% CI)
Arsenic	Light	57	74	1.0	—
	Heavy	16	9	2.3	(1.0–5.4)
Cadmium (zinc)	Light	57	73	1.0	—
	Heavy	16	10	2.0	(0.9–4.6)
Copper	Light	43	56	1.0	—
	Heavy	30	27	1.4	(0.8–2.7)
Lead	Light	19	22	1.0	—
	Heavy	54	61	1.0	(0.5–2.0)
Manganese	Light	51	60	1.0	—
	Heavy	22	23	1.1	(0.6–2.1)

[a] Risk for each pollutant is relative to RR of 1.0 for light.

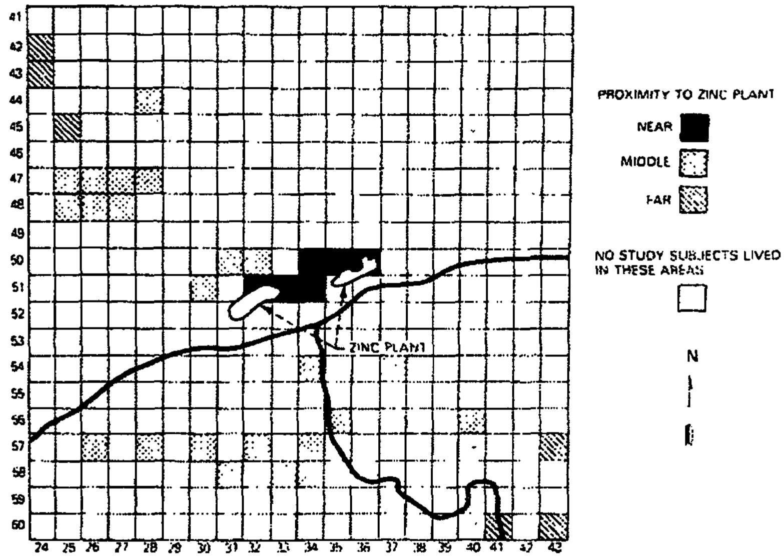

FIG. 3. Proximity to the zinc smelter for grids of usual residence in a 20-km^2 area.

study subjects who lived near the smelter (Table 3). This nonsignificant increase is apparent for both usual residence and residence in 1950. Similar patterns of risk were seen for residence in each decade year. When the RR were adjusted using a multiple logistic model which simultaneously controlled for the influence of cigarette smoking, and usual employment in steel manufacturing and zinc smelting, the RR for near proximity in 1950 was significantly elevated. For both usual and 1950 residence, there were trends of increasing risk with increasing proximity to the smelter. When the proximity patterns were redefined using the zinc and cadmium weighted exposure measurements, RR comparable to those presented for the unweighted exposures were found. When the near category was expanded to include the next three closest grids to the west of the smelter (5031, 5032, 5130) the RR were still elevated, although somewhat reduced. With the

TABLE 3

RR OF LUNG CANCER ACCORDING TO PROXIMITY TO THE ZINC SMELTER FOR USUAL RESIDENCE AND RESIDENCE IN 1950

Residence	Proximity	No. of cases	No. of controls	RR[a]	(90% CI)	RR[b]	(90% CI)
Usual	Far	292	292	1.0	—	1.0	—
	Middle	26	29	0.9	(0.5–1.5)	1.2	(0.6–2.1)
	Near	16	10	1.6	(0.8–3.4)	1.6	(0.6–4.3)
1950	Far	242	234	1.0	—	1.0	—
	Middle	27	24	1.1	(0.6–1.8)	2.3	(1.1–4.6)
	Near	14	7	1.9	(0.8–4.7)	5.0	(1.4–17.8)

[a] All risks relative to a RR of 1.0 for far proximity.
[b] RR adjusted for smoking and usual employment in steel or zinc.

prevailing winds at the smelter from the northwest and southwest, it was reasonable to assume that residents upwind of the smelter would receive less pollution than those downwind: therefore, it was felt justified to have the next three closest grids in the middle distance category.

Many of the men who lived near the zinc smelter also worked there. Table 4 shows, however, that elevated risks were seen for those with 1950 residence near the smelter regardless of their employment status. Similar results were seen for usual residence and residence in each decade year.

The shaded grids in Fig. 4 show the location of the usual residences of the study population for a 20-km^2 area surrounding the steel plant. The area surrounding the steel plant is more densely populated than that surrounding the smelter, but there are areas of sparseness due to topographical barriers. Unlike the zinc smelter, no elevated risks are seen for residence near the steel plant (Table 5). The risks for middle and near proximity become even further reduced when controlled for smoking, and usual employment in steel or zinc in the multiple logistic model.

DISCUSSION

Air pollution has long been a suspected risk factor for lung cancer, although a clear link between the two has yet to emerge. To evaluate the issue, several recent investigations have focused on the lung cancer experience of populations living around point sources of pollution. Environmental exposures near arsenic-emitting industries were examined in studies by Pershagen *et al.* (1977), Lyon *et al.* (1977), Reed *et al.* (1978), Greaves *et al.* (1981), Matanoski *et al.* (1981), Rom *et al.* (1982), and Cordier *et al.* (1983).

Cordier *et al.* (1983) found elevated rates of lung cancer in men living near a copper smelter. Matanoski *et al.* (1981) found elevated lung cancer risks in men living near a chemical plant which produced arsenicals, and Reed *et al.* (1978) found lung cancer rates to be highest in the residential areas closest to a nickel smelter. None of the other studies found significant associations, but the effects of air pollution were difficult to evaluate in these studies due to the inability to

TABLE 4

RR OF LUNG CANCER ACCORDING TO PROXIMITY OF 1950 RESIDENCE FROM THE ZINC SMELTER AND USUAL EMPLOYMENT IN ZINC SMELTING

Usual zinc employment	Proximity	No. of cases	No. of controls	RR[a]	(90% CI)	RR[b]	(90% CI)
No	Far	242	234	1.0	—	1.0	—
	Middle	22	19	1.1	(0.6–2.0)	2.4	(1.1–4.9)
	Near	5	2	2.4	(0.5–14.5)	4.2	(0.8–20.6)
Yes	Far	0	0	—	—	—	—
	Middle	5	5	1.0	(0.3–3.3)	2.0	(0.6–7.4)
	Near	9	5	1.7	(0.6–5.2)	5.6	(1.7–18.7)

[a] All risks relative to RR of 1.0 for no usual zinc employment and far proximity.
[b] RR adjusted for smoking and usual employment in steel.

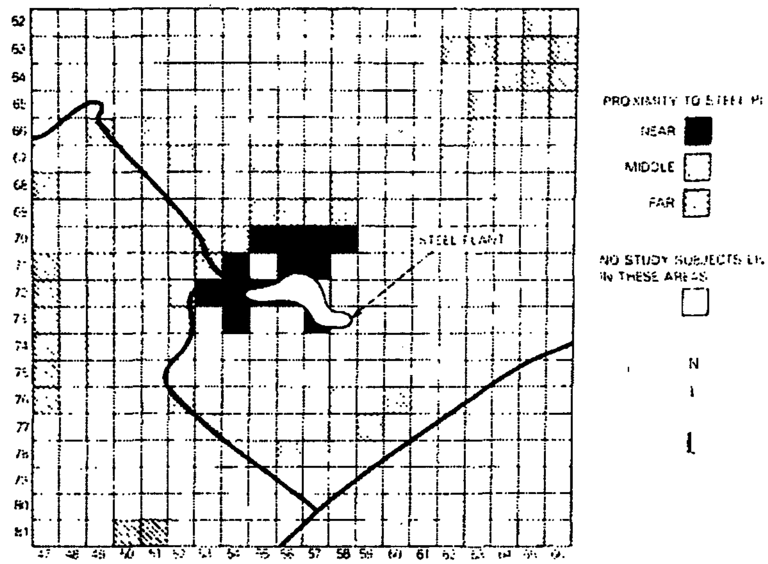

FIG. 4. Proximity to the steel plant for grids of usual residence in a 20-km² area

adjust for confounders such as cigarette smoking and occupation, and ten the absence of pollutant data.

The present study offered several advantages. Information obtained fr n complete smoking and occupational histories enabled adjustment for these i portant risk factors: and the collection of lifetime residential histories formed e basis for the estimation of pollutant exposure. Usual or longest residence, a well as residence at any point in time, was ascertained. Decade intervals were sed for convenience in the analyses and enabled examination of residential patte s prior to the development of cancer. Soil pollutant data were available, an melter stack emission levels for certain metals could be used in developing the ance-exposure index. For most of the study area historic air quality data we either unavailable or were of limited coverage. The decision to measure the c entra-

TABLE 5
RR OF LUNG CANCER ACCORDING TO PROXIMITY FROM THE STEEL PLANT FOR USUAL RE ENCE AND RESIDENCE IN 1950

Residence	Proximity	No. of cases	No. of controls	RR[a]	(90% CI)	RR[b]	(9 CI)
Usual	Far	261	252	1.0	—	1.0	
	Middle	49	53	0.9	(0.6–1.3)	0.6	(0 0.9)
	Near	24	26	0.9	(0.5–1.5)	0.7	(0. 1.3)
1950	Far	251	196	1.0	—	1.0	
	Middle	40	44	0.8	(0.5–1.3)	0.5	(0. 0.9)
	Near	28	25	1.0	(0.6–1.7)	0.8	(0. 1.6)

[a] All risks relative to a RR of 1.0 for far proximity.
[b] RR adjusted for smoking and usual employment in steel or zinc.

tion of heavy metals in soil was made with the assumption that the levels of pollutants reported in current samples of undisturbed soil may reflect an accumulation of airborne metals over several decades. The locations of our soil samples were not scientifically selected, but instead were chosen to correspond to areas where EPA had previously set up air sampling monitors. It was our intention to correlate soil and air sample data; however, due to the extremely short sampling period used by EPA their data were unrepresentative of yearly air pollution means and therefore were not useful for comparison purposes.

The case–control study revealed a higher relative risk of lung cancer in men who had lived near the zinc smelter. The soil sample analyses showed large variations in the concentration of all six metal pollutants across the study area, with the case–control comparisons showing an increased risk associated with residence in areas where arsenic and cadmium were high. The increases associated with nearness to the smelter and with the pollutant indices were not explained by the effects of cigarette smoking or by employment in the zinc or steel industry. Thus, although the study was considerably restricted by relatively small numbers of cases and controls in the high-exposure areas and by limited pollutant data, there was some indication of an increased risk associated with particulate metal pollution.

One of the major problems in a study of this nature is discriminating among the effects of so many potential exposures. In the environment near the smelter residents were exposed to heavy concentrations of complex mixtures of metals (Nordberg and Andersen, 1981) and elevated levels of SO_2. A primary suspect for an elevated lung cancer risk is inorganic arsenic, a recognized human lung carcinogen. Arsenic has been implicated in the increased risk of lung cancer among copper smelter workers in the United States, Japan, and Sweden (Lee and Fraumeni, 1969; Lubin *et al.*, 1981; Enterline and Marsh, 1980; Rencher *et al.*, 1977; Kuratsune *et al.*, 1974; Axelson *et al.*, 1978). Zinc ores typically contain smaller amounts of arsenic than copper ores, with average arsenic stack emissions from American smelters estimated at 4.9 lb per ton of copper compared to 1.3 lb per ton of zinc (Suta, 1978). Nevertheless, the soil analyses showed high levels for this substance in residential areas nearer to the smelter. One cannot, however, rule out the possibility that the other metals found in conjunction with arsenic may be involved in the development of disease. Indeed, an increased risk of lung cancer has been reported in a study of cadmium smelter workers (Lemen *et al.*, 1976). This is intriguing since the soil samples taken near the smelter had extremely high concentrations of cadmium, a finding in agreement with an earlier survey of nonferrous smelters that reported significantly elevated cadmium levels in the hair of children living near smelters (Baker *et al.*, 1977). Also, while exposure to SO_2, a lung irritant in sensitive persons at concentrations of 1–2 ppm (Welch *et al.*, 1978), has not been shown to be an independent risk factor for lung cancer, it may act synergistically with arsenic (Lubin *et al.*, 1981) or other metals.

No excess risk was found among men living near the steel facility, although long-term employment in the steel industry was associated with significantly elevated lung cancer risk in another report (Blot *et al.*, 1983). Other studies of steel workers have found substantially increased risks of lung cancer associated with coke oven operations and have implicated benzo(a)pyrene and other po: nuclear aromatic hydrocarbons (PAH) (Tanimura, 1968). Adequate environment: data on PAH concentrations in the vicinity of the steel plant were unavailable. he prevailing winds, however, were such that the majority of the emissions om the plants were probably distributed to very sparsely populated areas. The :oncentrations of the six heavy metal pollutants were generally low in areas ear the steel plant.

Of some concern in this study was the use of an exposure model whic did not include meteorological or topographical factors. However, due to the c istering of the study population we believe that the model used was adequate access whether cases resided closer to the index plants than did controls.

Also of concern was the use of deceased controls instead of a randoı sample of live controls. While it is possible that the associations may be influ ıced by the diseases among the controls that led to their death, the controls wei chosen from a variety of causes of death so that an association with any specifi disease should be minimal.

In conclusion, our results raise the possibility of an increased lung ca :er risk associated with environmental exposure to high concentrations of heav metals, including arsenic and cadmium. The small sample size and limited envir mental data preclude causal interpretation, but suggest the need for further re arch in other polluted areas of the United States.

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