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Lung Cancer among Women Residing Close to an Arsenic Emitting Copper Smelter

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ABSTRACT. Lung cancer deaths occurring between 1935 and 1969 among women residing near an arsenic emitting smelter were examined. For three geographically defined exposure groups, the observed and expected number of lung cancer deaths were compared. In none of the exposure groups did the observed number of deaths exceed the expected. However, an index of exposure based on distance of residence from the smelter and duration of residence in the area was 27% higher for cases than for age-matched controls ($p = .10$). Adjusting for a latency of 20 yr, case exposures were 23% higher than for controls ($p = .07$). Dividing individuals into quintiles of exposure yielded odds ratios ranging from 1 to 1.6 (test of trend, $p = .07$).

WORKERS exposed to high levels of ambient-air arsenic have an increased risk of lung cancer.¹ Whether lower community exposure levels also increase the risk of lung cancer is less clear. Of five community studies where exposed workers were excluded,²⁻⁶ three found significantly more lung cancer than expected among male residents. No study found excess lung cancer for female residents.

Residents of the City of Tacoma and Pierce County, Washington, have been exposed to arsenic emissions from the American Smelting and Refining Company (ASARCO) copper smelter located in the town of Ruston. The Ruston smelter has operated since 1890 and has been a copper smelter since 1905. An arsenic refinery was added in 1922-23. The copper smelter subsequently processed high arsenic copper ore and the refinery pro-

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duced a substantial fraction of the total United States arsenic supply until its closure in July 1985.

Thirty percent of Tacoma's 159,000 residents live within 3 miles of the ASARCO smelter. Significantly elevated urinary arsenic levels have been measured in children who reside near the smelter.⁷ Elevated ambient-air arsenic levels have been measured within 7 miles of the smelter.

Lung cancer in women residing close to arsenic emitting smelters is of particular interest. Until recently, women had very low rates of lung cancer, probably because older cohorts had a low prevalence of cigarette smoking. These cohorts also had few occupational exposures contributing to increased lung cancer risk.

To investigate whether ASARCO arsenic emissions increased the community lung cancer risk, a survey of lung cancer death rates among Tacoma and Pierce County women from 1935–1969 was conducted. A case-control epidemiological approach was also used to evaluate potential risk factors for lung cancer among these women.

Methods

Two separate methods were undertaken to determine whether ASARCO arsenic emissions increased lung cancer risks. The first involved comparing observed and expected lung cancer death rates for Tacoma area women in each of three geographically defined exposure groups. The second was a case-control study.

Observed and expected death rates. Population data were obtained from the 1930, 1940, 1950, 1960, and 1970 United States censuses. Census data by age and sex of resident were available for Ruston, several areas within Tacoma, and the remainder of Pierce County. For the 1930 and 1940 censuses, population counts by age and sex were given for 8 wards of Tacoma. Two of the wards (1 and 8) were in the north end of Tacoma, near the smelter. The boundaries of these wards approximate a 3-mile radius of the smelter and correspond to census tract boundaries used in the 1950, 1960, and 1970 censuses (tracts 3-9 or 603-609). Population counts for years between censuses were obtained by linear interpolation.

Three exposure groups were designated. The highest exposure group included all addresses falling within a 3-mile radial distance from the smelter (wards 1 and 8 of Tacoma and Ruston). The intermediate exposure group included addresses within Tacoma city limits but not within 3 miles of the smelter. These residences ranged from 3 to 9 miles from the smelter. The lowest exposure group—the remainder of Pierce County—included residences that were between 6 to 40 miles from the smelter.

The expected numbers of lung cancer deaths in each of the three exposure groups were derived by multiplying U.S. White female lung cancer death rates by the number of women in the exposed population. The U.S. rates each year (1935–1969) and for four age groups (35–44, 45–54, 55–64 and 65+ yr old women) were used in this calculation. United States white female rates were used since the populations of Tacoma, Ruston, and residual Pierce County were more than 95% White during this

time period. Washington State female and U.S. White female mortality rates are comparable for the periods 1939–1941, 1949–1951, 1959–1961, and 1969–1971.

Cause of death indices were used to locate death certificates for all Pierce County women who died from lung cancer between 1935 and 1969. Deaths were allocated to exposure groups using the residence address information from the death certificates. Observed death rates were calculated using these numbers and population data.

Case-control study. For the case-control study, all lung cancer deaths among female residents of Tacoma or Ruston were identified from the State death certificates for the years 1935 to 1969. A control death was matched to the case by age at death (within 5 yr), year of death, and sex. The matched control was chosen from the next eligible filed death certificate moving numerically either forward or backward from the case. Cases and controls were restricted to residents with either a Tacoma or Ruston address as determined from the death certificate.

The race, address, and the duration of residence in Tacoma for each case and control were abstracted from the death certificate. If a retirement home or a nursing home was listed as an address, a Polk City Directory for Tacoma was consulted to identify a residential address prior to entering the retirement/nursing home. If available, this address was then substituted for that of the retirement/nursing home. If length of residence was missing from the death certificate, it was estimated from the number of years during which the woman was listed in the city directory. This approach most likely underestimates length of residence for women.

The address was entered into a computerized geocoding program which assigned X and Y coordinates for the block of residence and determined if the residence was within Tacoma or Ruston city limits. The distance of residence from the smelter was calculated using the X and Y coordinates of the smelter and those of the home. Our own testing involved checking differences between manual and computer coding for geographic area (north Tacoma and Ruston, residual Tacoma and residual Pierce County). Prior to computer assignment of the geographic coordinates, each address was manually assigned to one of the three exposure groups. Differences between the manual assignment and computer assignment were examined before making a final exposure determination. In every case the computer assignment was found to be correct.

A cumulative exposure index value was then calculated for each individual using the following equation:

$$\text{cumulative exposure} = (k) \frac{(\text{years}) (\text{weighting factor})}{(\text{distance})}$$

where k is an unknown constant, years is length of residence (in years) in Tacoma/Ruston prior to death, distance is distance in feet from the smelter and the weighting factor, described below, accounts for secular variation in arsenic emissions. An illustration of a sample index calculation is given in Table 1.

The constant (k) is the same for both cases and controls. Years of exposure is approximated by length of residence

Table 1.—Index calculation for an individual with 65 yr residence in Tacoma and with a reported address at the time of death in 1963 2 miles from the smelter

Period	Residence time in years	Period weight (w)	(time) (w)	(time) (w)/distance
<1905	7	0	0	0.0
1905-1922	17	1	17	8.5
1922-1950	28	2	56	28.0
1950-1969	13	1	13	6.5
Exposure index for the individual is the sum of last column —				43.0

in Tacoma. Since data on deposition of arsenic⁹ and urinary arsenic⁷ suggest that concentration decreases in the direction of Tacoma approximately in inverse relation to the distance from the source, distance from the smelter is included in the denominator of the equation. (Fig. 1)

To account for secular variation in actual levels of arsenic emission, individual years of exposure were weighted according to emission levels for the time period of the exposure. Weighting factors for each of the time periods were determined as follows. The number of years of residence during the first period (prior to 1905) is weighted by zero since copper smelting began in 1905. Period two (1905–1920) is weighted by one since, before 1920, ASARCO sought high-grade copper ore to maximize copper production and minimize impurities such as arsenic. Period three (1920–1950) is weighted by two. During this period, the rise in the demand for arsenic pesticide formulations encouraged ASARCO to begin smelting copper ores with higher concentrations of arsenic. Arsenic became a profitable by-product of copper smelting. The weighting factor for the last period (1950–1969) is decreased to one because in 1950 ASARCO installed several engineering controls to reduce arsenic emissions. Industrial hygiene information from

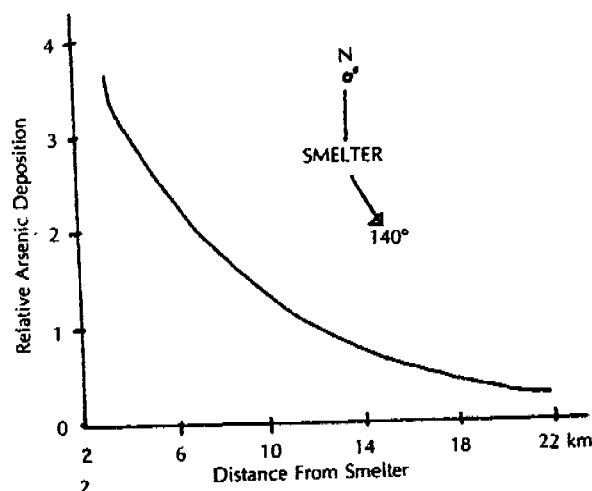


Fig. 1. Relative arsenic deposition from Tacoma smelter emissions in the direction of Tacoma (from Puget Sound Air Pollution Agency Environmental Impact Statement September 1981).

this period demonstrates a drop by half in urinary arsenic levels in the smelter workers.⁹

The weights depend on the assumption that environmental levels of exposure parallel occupational levels. This assumption is untenable if most arsenic trioxide escaped through stack emissions and remained airborne until deposited at a distance from the smelter. However, this is not the case since a large proportion of airborne arsenic trioxide is released as fugitive emissions from smelting operations such as roasting, crushing, transporting, and bagging.⁹

Two cases were excluded from the analyses because their length of residence was less than 12 mo. Four cases were excluded where length of residence could not be estimated using the methods previously described. Also excluded were two cases whose matched controls had missing information. Of 164 pairs, 156 remained for analysis.

Differences between cases and controls in their distances from the smelter and length of residence were first compared using the *t* test. The length of residence for cases and controls was compared by stratifying on residence distance from the smelter (≤ 2 miles, > 2 miles).

Within-pair differences in the cumulative exposure index value were tested with the normal approximation of Wilcoxon's sign rank test for paired data. Use of this nonparametric test denied outliers undue influence.

The influence of latency was explored in another analysis. Those pairs in which one or both members had lived in Tacoma 20 yr or more were included in the latency analysis. The Wilcoxon's sign rank test was recalculated excluding the last 19 yr residency prior to death for each member. The analysis was repeated for a residency of 40 yr or more.

Four odds ratios were calculated based on five increasing levels of the adjusted exposure index and using an analysis of trend in proportions by a grouped weighted linear regression.¹⁰ The five levels of the exposure index were formed by pooling the period-adjusted indexes of all individuals and then dividing into quintiles. The midpoint of each quintile was used for the trend analysis. The lowest quintile became the reference group.

Results

The observed and expected lung cancer deaths for the study period 1935–1969 in each of the three exposure groups are given in Table 2. In neither the Ruston area nor the remainder of Tacoma did the total number of observed deaths exceed the expected. The relative risks for lung cancer given residence in the Ruston area is 0.82 and for the remainder of Tacoma it is 0.98. For the total Tacoma-Ruston area the relative risk is 0.94 with an upper one-sided 95% confidence interval of 1.08.

In residual Pierce County, lung cancer rates were significantly below expected ($p < .01$). Since residual Pierce County was primarily rural during this time period and since lung cancer rates in rural areas tend to be lower than in urban areas,¹¹ the deficit of lung cancers in residual Pierce County is not surprising.

In the case-control study, the mean yr residence (33.2 yr for cases, 31.5 yr for controls) and mean distance from

Table 2.—Observed and expected lung cancer deaths				
Age	Ruston area	Remainder of Tacoma	Total Tacoma-Ruston	Remainder of Pierce County
0-44				
Observed	2	11	13	8
Expected	2.56	7.24	9.8	10.35
45-54				
Observed	8	30	38	23
Expected	7.50	20.44	27.94	25.47
55-64				
Observed	8	21	29	26
Expected	11.26	32.58	43.84	32.70
65+				
Observed	18	63	82	43
Expected	22.60	67.70	90.3	54.71
Total				
Observed	36	125	161	100
Expected	43.92	127.96	171.88	123.23
Relative Risk	.82	.98	.94	.81
Obs/Exp				

the smelter (4.5 miles for cases, 4.9 miles for controls) were comparable for cases and controls (Tables 3 and 4). Stratifying by distance did not alter the comparison of length of residence. No geographic clustering of the case residences was apparent when plotted on a map.

For the nonparametric analysis of the 156 pairs (Table 5), the exposure index for the cases was 26% greater than that of the matched controls (Wilcoxon rank sum test, $p = .10$). When adjusted for 20 yr latency, the index of the

case exposure was 23% greater than for the controls (Wilcoxon rank sum test, $p = .07$). Adjusting for 40 yr latency, the difference became 67% (although the p value increased to .23).

The odds ratios derived from the exposure index quintile frequencies were 1.00 (reference), 0.97, 1.07, 1.17, and 1.58 (Table 6). Using the midpoint of each quintile, the chi-squared value for the trend analysis was 2.1 (one-sided p value = 0.07). It should be noted that the midpoint of the highest quintile (211.0) was substantially higher than the midpoint of the next highest quintile (16.0).

Discussion

The findings of this study appear to be mixed. An elevated incidence of lung cancer was not detected in comparing observed with expected lung cancer rates. However, the arsenic exposure indices were higher in cases than in age-matched controls. The difference was

Table 3.—Duration of residence in Tacoma or Ruston		
Years prior to death	Cases	Controls
0-19	43	46
20-29	21	23
30-39	26	32
40-49	24	27
50-59	27	13
60+	15	15
Total	156	156
Mean duration (yr)	33.2	31.5

Table 4.—Distance of residence from the smelter at time of death		
Distance in miles	Cases	Controls
<1	8	6
1-2	6	6
2-3	17	13
3-4	38	36
4-5	24	22
5-6	21	14
6-7	25	36
7-8	9	15
>8	8	8
Total	156	156
Mean distance (miles)	4.5	4.9

Table 5.—Tests of significance for differences in exposure between cases and matched controls using the Wilcoxon rank sum test				
Number of pairs	Latency (yr)	Ratio of indices (case/control)	Wilcoxon normal approximation Z	$p(Z)$
156	0	1.26	1.3	0.097
137	>20	1.23	1.5	0.067
88	>40	1.67	0.7	0.230

Table 6.—Exposure index					
Index	0	1	2	3	4
Quintile midpoint	2.0	6.1	10.4	16.0	211.0
Case	33	34	32	31	26
Control	29	29	30	32	36
Odds ratios	1	.97	1.07	1.17	1.58
Test of trend	$p = .07$				

not significant at the .05 level. Several factors could explain these mixed results and the inability of the study to detect an effect of arsenic exposure on lung cancer incidence.

If Tacoma area physicians were more or less likely to detect lung cancer than physicians in the remainder of the U.S., then the incidence rates for Tacoma would not be comparable to national rates. During this period Tacoma had several large hospitals with advanced diagnostic and treatment facilities. Tacoma was also the site of a state tuberculosis treatment center. Because of these facilities, Tacoma area physicians were likely to be as capable of detecting lung cancer as physicians in other large metropolitan areas.

Difficulty in quantifying actual exposure levels may also contribute to the ambiguity of the results. No community arsenic exposure estimates are available prior to 1969, so it was not possible to quantify the level of exposure. However, estimated smelter emissions in 1953 were higher than those after 1960, suggesting higher ambient-air arsenic concentrations during the early years. Although some pollution control equipment (Cottrell precipitators and a baghouse) was installed in the 1920s to reduce arsenic losses during refining, emissions during 1922-1950 were undoubtedly higher than emissions after 1951. In 1951, ASARCO installed additional pollution control equipment and initiated dust control procedures.⁸ ASARCO estimated yearly arsenic emissions from the stack to be 600 tons in 1953 (six times the estimated 1983 level). Additional (fugitive) arsenic escaped during the smelting of copper and the refining and transport of arsenic. Between 1969 and 1980, the only period for which such data are available, the mean ambient-air arsenic concentration at 2100 feet of the smelter was 0.8 $\mu\text{g}/\text{m}^3$ air. At 1.5 miles it fell to 0.3 $\mu\text{g}/\text{m}^3$ air and at 3.9 miles it was 0.1 $\mu\text{g}/\text{m}^3$ air.⁹

The assumption of an inverse relationship of exposure with distance from the smelter is a simplification of the actual pattern. The prevailing wind direction changes between summer and winter with summer winds coming from the north, blowing arsenic toward Tacoma, while winter winds come from the southwest. Also, exposures to residents living close to the smelter result from ground level fugitive emissions while exposures to residents living more distant result from stack emissions. The assumed inverse relationship is an approximation to pattern of arsenic deposition and may not accurately reflect arsenic exposure for all residents.

If there is a 20-yr latency period between exposure and, in this case, death, then only slightly more than 70% of residents dying during this period had both an adequate exposure level and latency period. If the latency is 30 yr, then 56% of the deaths would have fulfilled both the exposure and latency requirements. This would reduce the ability of this study to detect an effect.

Changes in residence within Tacoma may have reduced the study's ability to detect geographic clustering. Only 15 cases and 13 controls resided within 2 miles of the smelter at the time of death.

Socioeconomic differences between north Tacoma and Ruston vs. the remainder of Tacoma are apparent. However, it is unclear how these differences would affect

the study. In the 1930 census a higher fraction of north Tacoma and Ruston residents owned a radio. In the 1950 census, 75% of north Tacoma and Ruston adult residents completed 8 or more years of school while only 53% of the remainder of Tacoma attained this level of education. However the 1940 census revealed that a higher fraction of north Tacoma and Ruston homes needed major repairs.

Finally, the smoking prevalence of women in this community during the years 1935-1969 is not known. Even if arsenic emissions increased the risk of lung cancer in the Tacoma-Ruston area, smoking would account for the majority of Tacoma area lung cancers. If the smoking prevalence for Tacoma area women is less than the national average, then the effect of arsenic exposure would be masked. Alternatively, geographic variations in smoking prevalence within Tacoma could result in cases appearing to have higher or lower arsenic exposures than controls. Such differences would not necessarily reflect risk differences from arsenic exposure. If arsenic exposure interacts synergistically with cigarette smoke exposure to increase lung cancer risk, then studies of low-risk female residents are unlikely to detect an increased risk.

Despite the limitations, the study argues against large excess lung cancer risks for communities exposed to ambient arsenic. The results may be consistent with a small elevated lung cancer risk for people who resided close to the smelter for a period of over 20 yr. Such an excess risk may be expected since even during the period 1980 to 1985, community 24-hr ambient-air arsenic exposure exceeded the 8-hr workplace standard of 10 $\mu\text{g}/\text{m}^3$ of air.

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