Lung Cancer Mortality in Workers Exposed to Sulfuric Acid Mist and Other Acid Mists [1]

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ABSTRACT—Mortality patterns were studied in 1,165 workers exposed to sulfuric acid mist and other acid mists (primarily hydrochloric acid mist) in steel-pickling operations. Standardized mortality ratio (SMR) analysis of the full "any acid exposure" cohort (n=1,165), with the use of U.S. death rates as a standard, showed that lung cancer was significantly elevated, with a mortality ratio of 1.64 [95% confidence interval (CI) = 1.14–2.28, based on 35 observed deaths]. The lung cancer mortality ratio for workers exposed only to sulfuric acid (n=722) was lower (SMR=1.39), but further restriction to the time 20 years and more from first employment in a job with probable daily sulfuric acid exposure ($\approx$0.2 mg/m^3) yielded a mortality ratio of 1.93 (95% CI = 1.10–3.13). An excess lung cancer risk was also seen in workers exposed to acids other than sulfuric acid (SMR=2.24; 95% CI = 1.02–2.46). When comparison was made to other steel workers (rather than to the U.S. general population) to control for socioeconomic and life-style factors such as smoking, the largest lung cancer excess was again seen in workers exposed to acids other than sulfuric acid (SMR = 2.00; 95% CI = 1.06–3.78). Adjustment for potential differences in smoking habits showed that increased smoking was unlikely to have entirely explained the increased risk. Mortality from causes of death other than lung cancer was unremarkable, with the exception of significantly low rates for deaths due to digestive system diseases.—JNCI 1987; 79:911–921.

Sulfuric acid is produced in greater quantities than any other chemical in the United States, with an annual production of about 80 billion pounds. Major production processes using sulfuric acid include phosphate fertilizer manufacturing, battery manufacturing, steel pickling, cellophane manufacturing, titanium dioxide manufacturing, petroleum refining, electrochemical drilling, uranium ore processing, and production of alcohol, surface-active agents, ammonium sulfate, methyl methacrylate, hydrofluoric acid, and aluminum sulfate (*1*). It has been estimated by NIOSH that over 200 different occupational categories have some potential for exposure and that these occupations include about 800,000 workers (*2*).

Until recently, little has been known about the long-term health consequences of exposure to sulfuric acid mist, except that it causes etching of tooth enamel and loss of teeth (*1*). Lung cancer rates have been examined in just two studies of acid mist-exposed workers, and these studies have been inconclusive due to small sample size. For example, Ahlborg et al. (*3*) observed 1 lung cancer (a bronchial carcinoma) versus approximately 0.6 expected in a study of Swedish pickling house workers. Another study, by Redmond et al. (*4*), reported 7 lung cancer deaths versus 8.0 expected deaths in Allegheny County, PA, steel mill pickling workers.

Atmospheric sulfur oxides and acid air pollution have been public health concerns for many years. In the Southeastern United States, where there is relatively high sulfur dioxide pollution and high humidity, it has been hypothesized that the region's high lung cancer rates may be due to an interaction between cigarette smoking and atmospheric sulfuric acid (*5*). Environmental exposure to aerosol sulfur (as sulfuric acid or sulfate particles) has been reported to be associated with lung cancer mortality in a county-based study in Florida (*6*). Atmospheric sulfuric acid results from oxidation of sulfur dioxide to sulfur trioxide, which hydrolyzes in the atmosphere to sulfuric acid (*7, 8*).

The potential for carcinogenicity or cocarcinogenicity of sulfur oxides has been discussed since 1967, when Peacock and Spence (*9*) reported that exposure to sulfur dioxide increased the incidence of lung tumors in a spontaneous tumor-susceptible strain of mice. Similarly, Laskin et al. (*10*) in 1970 reported that rats exposed simultaneously to benzo[*a*]pyrene and sulfur dioxide developed squamous cell carcinomas of the lung at a greater rate than rats exposed only to benzo[*a*]pyrene. In a study of chemical workers exposed to sulfur dioxide, Bond et al. (*11*) recently reported a significant association between lung cancer mortality and sulfur dioxide exposure, for which there was a significant dose-response relationship.

ABBREVIATIONS USED: CI = confidence interval; IRS = Internal Revenue Service; NIOSH = National Institute for Occupational Safety and Health; RR = relative risk; SMR = standardized mortality ratio; SSA = Social Security Administration.

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Interest in the relationship of respiratory cancer and acid mist exposure has been stimulated by recent reports of excessive laryngeal cancer rates in acid-exposed workers. Ahlborg et al. (*3*) in 1981 reported a significant excess of laryngeal cancer at a Swedish pickling house, Soskolne et al. (*12*) in 1984 reported a significant fourfold excess of laryngeal cancer cases in workers exposed to sulfuric acid at a Louisiana refinery and chemical manufacturing plant, Cookfair et al. (*13*) in 1985 reported a significant association between sulfuric acid exposure and laryngeal cancer among heavy smokers in a case-control study of patients at Roswell Park Memorial Institute, and Forastiere et al. (*14*) in 1986 reported a significant excess of laryngeal cancer in Italian soap-producing workers exposed to sulfuric acid.

METHODS

To investigate mortality patterns among workers exposed to sulfuric acid mist, we studied workers at three large midwestern steel-manufacturing facilities where the acid was used to remove oxides from newly manufactured steel. We chose the steel-manufacturing industry over other industries (e.g., fertilizer, battery, and sulfuric acid manufacturing), because the acid mist exposures were relatively high and the number of workers exposed at each facility was relatively large.

Pickling process and exposures.—The pickling process removes mill scale that is formed on steel during hot rolling or other hot working procedures. There are two basic pickling processes: batch and continuous. Batch pickling involves lowering steel bars or sheets into a tank of acid with a crane; continuous pickling involves running a continuous sheet of steel from a roll at one end, through the acid, to a roll at the other end. Removal of mill scale is accomplished by reaction of the acid with the metal and metal oxides, forming soluble metal salts and hydrogen gas. The hydrogen gas causes bubbling in the pickling solution and misting at the surface when the hydrogen bubbles burst as they enter the atmosphere. In so doing, the acid becomes aerosolized.

At the study plants, pickling operations began in the late 1800's and early 1900's. At facility A, pickling operations began in 1853, but most operations in existence during the study period began operations in the 1930's. At facility B, most pickling operations began in the 1920's and 1930's, and at facility C, pickling operations began in 1902, but most operations in existence during the study period began in the 1940's and 1950's.

Sulfuric acid was the predominant acid used for steel-pickling operations until the mid-1960's. Due to economic and process factors, however, sulfuric acid has largely been replaced by other acids. The other acids used at the steel plants included in our study were hydrochloric, nitric, hydrofluoric, and hydrocyanic acids, with hydrochloric acid being most commonly used. At the study plants, sulfuric acid had been replaced by other acids, or pickling operations had been shut down altogether, by the time the study began. Historical exposure data were available, however, from a NIOSH walk-through survey conducted in 1979 at facility A, from a NIOSH health hazard evaluation conducted in 1977 at facility C, and from a company survey conducted in 1975 at facility C (*15*). The data are summarized in table 1, where it can be seen that exposure levels were generally below the Occupational Safety and Health Administration standard of 1 mg/m^3 (the NIOSH recommended standard is also 1 mg/m^3) (*16, 17*). The possibility that sulfuric acid mist exposures may have been higher prior to 1975 cannot be excluded. While available evidence regarding process engineering suggests that air concentrations in past years were likely to have been similar to those reported in table 1, it is possible that exposures may have been reduced in the 1970's because of increased worker awareness about the hazards of workplace exposures.

When the sulfuric acid concentrations for the various jobs and areas were averaged, the result was 0.19 mg/m^3 for personal samples and 0.29 mg/m^3 for area samples. Since the personal samples were more directly indicative of worker exposure than the area samples, a reasonable estimate of the average exposure of workers in our exposure group 3 (sulfuric acid, probable daily exposure) is 0.2 mg/m^3. It should be noted that the figure of 0.2 mg/m^3 is based largely on samples taken at facility C. The figure is probably applicable for most of exposure group 3, however, because the pickling processes at the three facilities were similar and because most of the study population was from facility C.

The NIOSH health hazard evaluation at facility C also measured levels of iron oxide, lead, copper, manganese, nickel, chromium, zirconium, hafnium, respirable free silica, phenol, and formaldehyde (*13*). The only substances that were detectable were iron oxide and lead.

Exposure categories.—Each pickling-related job was categorized as to 1) whether the acid used was sulfuric acid or other acid and 2) the likelihood of daily exposure to acid mist. The following jobs were categorized as having probable daily exposure among steel-pickling workers employed during 1940-64:

Acid tester
Catcher (pickling), catcher scrubber
Craneman (pickling)
Feeder (pickling), feeder helper
Hooker (pickle crane), stocking hooker, pickler hooker, head hooker
Laborer (pickling), laborer pickler scrubber
Loader (pickling): feeder, feeder helper, loader-unloader, cleaner
Operator (pickling), operator helper
Pickler: feeder, helper, leader, foreman, loader, sheet pickler, piler, batch inspector, first pickler, weigher
Pickle house: craneman, hooker, laborer
Pot tender, solution tender
Scrubber operator (pickling), scrubber feeder
Stocker and pickler, stocker-feeder

TABLE 1.—*Area and personal samples of sulfuric acid air concentrations measured at two study facilities (A and C) as recorded in NIOSH and company industrial hygiene surveys in 1975, 1977, and 1979*

Facility	Batch (B) or continuous (C)[a]	Area or job sampled	No. of samples	Concentration, mg/m^3	
				Mean	Range
		Personal samples			
C	B	Pickle hooker	7	0.15	0.07–0.25
C	B	Assistant pickle hooker	4	0.20	<0.03–0.48
C	B	Craneman	4	0.22	0.15–0.29
		Average[b]		0.19	
		Area samples			
A	B	Cold finishing	2	0.09	0.04–0.14
	C	Cold strip mill	3	0.92	0.35–1.20
C	B	Pickle tanks (helper and helper's assistant)	2	0.15	0.12–0.27
C	B	Crane (operator)	10	0.25	0.01–0.50
C	B	Lunch table	2	0.21	0.18–0.24
C	B	Crane stairs	15	0.15	0.00–0.61
		Average[b]		0.29	

[a] Batch or continuous pickling process (*see* text for description).
[b] Average of the mean concentrations for each job and area.

The job categorizations were based on company industrial hygiene and engineering records, NIOSH industrial hygiene surveys, and expert opinion of company safety and health personnel.

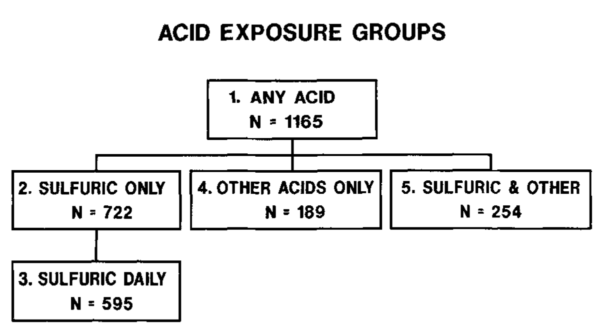
After the jobs were categorized for acid used and exposure potential, exposure groups were defined as follows: group 1—any acid exposure, group 2—sulfuric acid exposure only, group 3—sulfuric acid only with probable daily exposure, group 4—other (nonsulfuric) acid exposure only, and group 5—exposure to both sulfuric acid and other acids. The relationship between the exposure groups is graphically illustrated in text-figure 1. A worker had to have been employed in appropriate jobs for at least 6 months to be included in an exposure group. The workers were further categorized by the steel-manufacturing facility at which they worked. The facilities were referred to as facility A, facility B, and facility C.

Mortality analysis.—Persons employed in pickling operations at the three steel-manufacturing facilities were entered into the study if they were employed for at least 6 months in a pickling-related job, of which at least 1 day was prior to 1965. At two facilities (B and C), incomplete records prevented inclusion of workers who terminated employment prior to January 1, 1950 (facility B), and November 12, 1950 (facility C). Person-years at risk were not, therefore, accumulated prior to those dates for workers at facilities B and C. At facility A, records were complete for all years, but person-years at risk were not calculated prior to 1940 because comparison death rates were not readily available and because nosology of death certificates is difficult for early revisions of the International Classification of Diseases.

Excluded from the study were 11 pickling workers who had additionally been employed in coke oven operations. These workers were excluded because coke oven emissions have previously been associated with excess risk of lung and genitourinary cancers (*3*).

Vital status follow-up of each employee was performed by examining current company records, by linking to records of the SSA and the IRS, and by sending U.S. Postal Service address correction postcards. The follow-up end date was October 27, 1981, which was the most recent date for which SSA and IRS death notifications were complete at the time follow-up was conducted. Results of the follow-up process for the total cohort and for each facility are shown in table 2. Vital status could not be ascertained for 1.3% of the total cohort. The loss to follow-up ranged from 0.0 to 1.6% for the three study facilities and (not shown in table 2) from 0.5 to 1.7% for the exposure subgroups. Subjects who were lost to follow-up were assumed to have survived to the end of the study.

Of the 326 total deaths, 189 were first identified from company records, 135 were identified from SSA records, 1 was identified from IRS records, and 1 was identified



TEXT-FIGURE 1.—Relationship of the acid exposure groups defined by acid used and likelihood of daily exposure for steel-pickling workers employed 1940–64.

TABLE 2.—*Vital status of the total cohort and of the subcohorts from each steel-manufacturing facility as of the end of vital status follow-up, October 27, 1981 (steel-pickling workers employed 1940-64)*

Vital status	Study facility			
	Total (%)	Facility A (%)	Facility B (%)	Facility C (%)
Alive	824 (71)	87 (55)	224 (68)	513 (76)
Deceased	326 (28)	70 (45)	103 (31)	153 (23)
Certificate received	304	67	102	135
Certificate not received[a]	22	3	1	18
Unknown[b]	15 (1)	0 (0)	4 (1)	11 (2)
Total	1,165 (100)	157 (100)	331 (100)	677 (100)

[a] Two deaths for which no death certificate was received also did not have a date of death. These deaths were considered to have occurred on the last day of the study.
[b] Subjects of unknown vital status were assumed to have survived to the end of the study.

from U.S. Postal Service address correction postcards. Certificates of death were obtained from the States where death occurred. Certificates could not be obtained for 22 of the deaths; these deaths were included in overall death counts only. Two of the 22 deaths for which there was no certificate additionally did not have a valid death date and were assumed to have occurred on the last day of the study. Underlying causes of death were coded according to the rules and codes of the revision of the International Classification of Diseases in effect at the time of death.

Person-years at risk and expected numbers of deaths were calculated with the NIOSH life table analysis system (*18*), which adjusts for the effects of age, calendar time, sex, and race via stratification of the data. The data were further stratified into length of employment and time since first employment categories to examine the importance of those variables. The measure of effect used for the mortality analyses was the SMR, which uses indirect standardization to adjust for age and calendar time.

For calculation of the expected numbers of deaths, two comparison populations were used. The first was the U.S. general population, for which death rates were based on deaths from 1940 through 1978 and population data from 1940 through 1980. For the U.S. comparison, statistical tests (including tests of trend and heterogeneity) and confidence limits were calculated, assuming the Poisson statistical distribution (*19*).

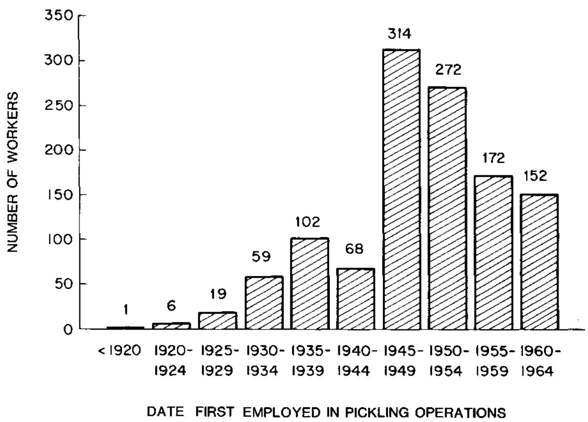
The second comparison population was 51,472 white male steel workers at 7 Allegheny County, PA, steel plants studied by the University of Pittsburgh. The Allegheny County steel workers cohort consisted of all hourly workers employed in 1953. Their vital status had previously been followed through 1975, and their death rates had been calculated in 5-year age-time intervals (*4*). The rates (and numerators and denominators) for lung cancer were supplied for the present study by the University of Pittsburgh. Rates for 1975 were extrapolated through the 1975-79 and 1980-81 periods. Statistical testing and confidence limit calculations for the SMRs were based on Mantel-Haenszel chi-square and test-based confidence limits for incidence density ratios, where variance is contributed by both the study population and the comparison population (*20*).

For comparability to the Allegheny County steelworkers cohort, which was comprised only of those steel workers employed in 1953, a subcohort of workers from our study was selected that was employed in the period 1950-54. The 1950-54 selection was performed to create a subcohort that would be similar to the Allegheny County steel workers in terms of calendar time and age. The 1950-54 subcohort was restricted to white males, because this was the only race-sex group in the Allegheny County cohort that was large enough to be used as a comparison.

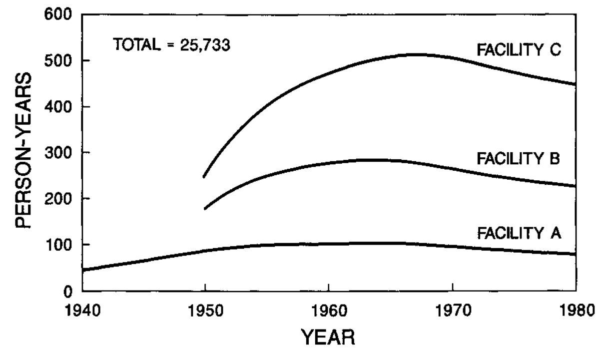
While we had no direct data on the individual smoking habits of the workers, we were able to address the potential influence of smoking habits on our lung cancer results in three ways: 1) by comparison to other steel workers who were likely to have had similar smoking habits, 2) by examination of the results for other diseases that are caused by smoking, and 3) by estimation of the potential effects of smoking differences on our risk estimates (*21*). For the third method (estimation of potential effects of smoking differences), we used methodology described by Axelson (*22*) for evaluation of confounding and National Center for Health Statistics smoking survey data for the United States for 1965 (*23*), the approximate midpoint of our observation period. The smoking categories and their assumed RRs were as follows: ex-smoker, RR = 5.00; light smoker (<15 cigarettes/day), RR = 7.00; moderate smoker (15-24 cigarettes/day), RR = 10.00; and heavy smoker (≥25 cigarettes/day), RR = 20.00.

RESULTS

A total of 1,165 workers met the study entry criteria of 6 months' employment in pickling-related jobs where at least 1 day was prior to 1965 and 1 day was in 1940 or later. It was found that the dates of first employment in pickling operations ranged from 1920 to 1964 and that about half of the cohort first began employment in pickling operations in the late 1940's and early 1950's (text-fig. 2). The distribution of person-years at risk by age and year was examined for the three study facilities. The age distributions were similar (text-fig. 3), with facility C having a slightly younger age distribution. The distributions of person-years by year for the three



TEXT-FIGURE 2.—Distribution of the steel-pickling workers employed 1940-64 by date of first employment in pickling operations.



TEXT-FIGURE 4.—Distribution by year of person-years at risk for workers at each study facility (steel-pickling workers employed 1940-64).

facilities (text-fig. 4) were dissimilar, due to person-years accumulation beginning at different dates (records were not complete at two of the facilities until 1950) and due to different employment patterns during the study period.

Of the 326 workers who were deceased as of the study end date (table 2), cause of death could not be determined for 22 (7%), and date of death could not be determined for 2 (the date of death for the 2 unknown date of death workers was assumed to be the study end date). One facility (facility C) contributed over half of the workers in the total cohort, and the percentage from each plant who were deceased varied from 23 to 45%. The cohort was predominantly (87%) white male; there were 1,017 white males, 139 nonwhite males, 9 white females, and no nonwhite females.

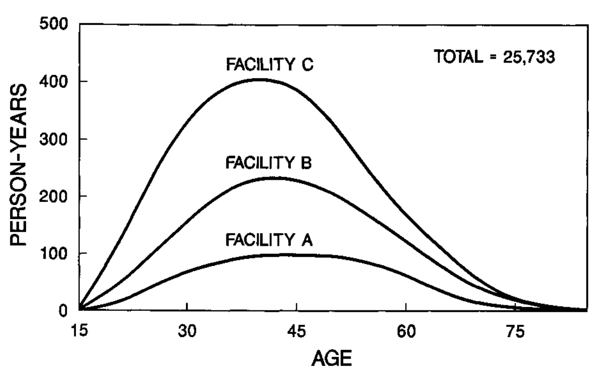
Work History

When the work histories for the individual workers were examined to determine the acids to which the workers were exposed for at least 6 months (table 3), it was found that 722 were exposed to sulfuric acid only (exposure group 2); of those, 595 held jobs with probable daily exposure to sulfuric acid (exposure group 3); 189 were exposed only to other acids (exposure group 4); and 254 were exposed to both sulfuric acid and other acids (exposure group 5). The percent that were deceased in the exposure groups ranged from 15 to 36%.

Mortality

Among those who were in any pickling-related job for at least 6 months (exposure group 1), there were 326 deaths observed when 334.4 were expected on the basis of U.S. mortality rates (SMR = 0.97) (table 4). Seventy-three of the deaths were due to cancer, when 66.1 were expected (SMR = 1.10). There was a significantly decreased risk of digestive system diseases (SMR = 0.31), which was primarily due to a deficit of cirrhosis of the liver (4 observed deaths vs. 9.2 expected deaths). Nonmalignant diseases of the respiratory system occurred at a lower rate than expected (SMR = 0.75), primarily due to a deficit of pneumonia deaths (2 observed deaths vs. 7.6 expected deaths).

When malignant neoplasms were examined in detail (table 5), a significantly increased lung cancer risk was found, based on 35 observed and 21.3 expected deaths (SMR = 1.64; $P < .01$; 95% CI = 1.14-2.28). There were 2 deaths from laryngeal cancer when 1.0 was expected. The results for cancers of other organs were unremark-



TEXT-FIGURE 3.—Distribution by age of person-years at risk for workers at each study facility (steel-pickling workers employed 1940-64).

TABLE 3.—*Description of exposure groups by acid used, number in group, number deceased, and percent deceased (steel-pickling workers employed 1940-64)*

Group No.	Exposure[a]	No. in group	No. deceased	Percent deceased
1	Any acid	1,165	326	28
2	Sulfuric acid only	722	221	31
3	Sulfuric acid only, probable daily exposure	595	178	30
4	Other acid only	189	68	36
5	Sulfuric acid and other acid	254	37	15

[a] Six months of appropriate exposure was required for inclusion in an exposure group.

TABLE 4.—*SMRs in exposure group 1 (any acid), with the use of U.S. death rates for comparison (steel-pickling workers employed 1940–64)*

Cause	Deaths		Ratio	95% confidence limits
	Observed	Expected		
All causes	326	334.3	0.97	0.87–1.09
All malignant neoplasms	73	66.1	1.10	0.87–1.39
Diabetes mellitus	8	4.8	1.65	0.71–3.26
Diseases of blood and blood-forming organs	0	0.9	0.00	0.00–4.26
Mental, psychoneurotic, and personality disorders	0	2.1	0.00	0.00–1.86
Diseases of the nervous system	20	23.3	0.85	0.52–1.33
Diseases of the circulatory system	142	144.7	0.98	0.83–1.16
Diseases of the respiratory system	14	18.5	0.75	0.41–2.27
Diseases of the digestive system	4	12.9	0.31	0.08–0.80
Diseases of the genitourinary system	2	4.0	0.50	0.06–1.81
Diseases of the skin, bone, and organs of movement	0	0.6	0.00	0.00–6.39
Accidents and violence	24	35.6	0.67	0.45–1.05
Other and unknown causes	17	21.9	0.78	0.49–1.34
Certificate not received	22			

able, including the results for sites that would have had direct exposure to acid mist. For example, in the category "malignant neoplasms of the buccal cavity and pharynx," which includes lips and tongue, there were just 2 deaths observed and 2.2 deaths expected.

When the findings for lung cancer were examined by exposure group and facility, several patterns emerged (table 6). First, the SMR of 1.39 for workers exposed only to sulfuric acid (exposure group 2) was lower than the SMR of 1.64 for workers exposed to any acid (exposure group 1). Restriction to those who had daily sulfuric acid exposure (exposure group 3), however, yielded an SMR of 1.58. Second, there was no excess risk at facility A, which was the smallest contributor to the study population and which was the only facility where sulfuric acid was the only acid used. Third, it was found that the workers who were exposed only to other acids (exposure group 4) were all from facility B, where the SMR for exposure group 4 was 2.24 (based on 9 observed and 4.0 expected deaths, $P<.05$).

SMRs by race were calculated for lung cancer for the group of workers exposed only to sulfuric acid with probable daily exposure (exposure group 3), the exposure group of most a priori interest (table 7). It was found that nonwhite men had a higher mortality ratio (SMR = 2.16) than white men (SMR = 1.43); however, the difference was not statistically significant.

To determine whether a dose-response relationship with lung cancer might exist for those holding jobs with probable daily sulfuric acid exposure (exposure group 3), we used length of employment as a measure of exposure (table 8). For this analysis, only employment in jobs with probable daily sulfuric acid exposure was counted; gaps in employment and employment in other jobs were excluded. No dose-response relationship was evident in this analysis, however. The excess risks were approximately the same in the lowest (0.5–<5 yr) and highest (≥15 yr) exposure categories, and there were no observed deaths in the 10–<15 years category.

To determine whether there was a latent period for

TABLE 5.—*SMRs for malignant neoplasms in exposure group 1 (any acid), with the use of U.S. death rates for comparison (steel-pickling workers employed 1940–64)*

Cause[a]	Deaths		Ratio	95% confidence limits
	Observed	Expected		
All MN	73	66.1	1.10	0.87–1.39
MN of buccal cavity and pharynx	2	2.2	0.90	0.11–3.28
MN of digestive organs and peritoneum	12	18.9	0.63	0.33–1.11
MN of stomach	2	3.7	0.53	0.07–1.95
MN of intestine except rectum	3	5.8	0.52	0.11–1.52
MN of pancreas	3	3.6	0.82	0.17–2.41
MN of other digestive organs	4	5.8	0.69	0.19–1.89
MN of the respiratory system	37	22.6	1.63	1.15–2.26
MN of larynx	2	1.0	1.93	0.23–6.99
MN of trachea, bronchus, and lung	35	21.3	1.64	1.14–2.28
MN of other parts of the respiratory system	0	0.3	0.00	0.00–15.84
MN of male genital organs	4	4.7	0.86	0.23–2.20
MN of urinary organs	3	3.4	0.88	0.18–2.57
Neoplasms of lymphatic and hematopoietic tissues	7	6.2	1.13	0.46–2.35
MN of other and unspecified sites	8	8.1	0.99	0.50–2.30

[a] MN = malignant neoplasms.

TABLE 6.—*Lung cancer mortality ratios and observed deaths by exposure group and facility, with the use of U.S. death rates for comparison (steel-pickling workers employed 1940-64)*

Facility	Lung cancer mortality ratios (observed deaths) by exposure group				
	1, any acid	2, sulfuric acid only	3, sulfuric acid only, daily	4, other acid only	5, sulfuric acid and other acid
A	0.86 (3)	0.86 (3)	0.62 (2)	—	—
B	1.86 (12)	1.37 (2)	2.17 (2)	2.24 (9)[a]	1.03 (1)
C	1.75 (20)[a]	1.60 (14)	1.92 (14)[a]	—	2.24 (6)
Total	1.64 (35)[a]	1.39 (19)	1.58 (18)	2.24 (9)[a]	1.92 (7)

[a] The 95% CI for the mortality ratio excluded 1.00.

the lung cancer risk, we examined the SMRs for each exposure group by time since first employment (table 9). For this analysis, "first employment" was defined as first employment in a job included in the definition of the particular exposure group. The SMRs were substantially higher 20 years after first employment for all exposure groups except exposure group 4 (the "never sulfuric" group), where the mortality ratio under 20 years (based on just 2 observed deaths) was higher than that over 20 years. The risks after 20 years were statistically significant for exposure group 1 (any acid) (SMR=1.85; 95% CI=1.25-2.64) and exposure group 3 (sulfuric acid only, probable daily exposure) (SMR=1.93; 95% CI=1.10-3.13).

Comparison was also made to Allegheny County steel workers, in addition to the U.S. general population, to control for the possibility that steel workers differ from the U.S. general population with regard to smoking habits, socioeconomic status, and other variables. For this comparison, the study population was restricted to white males employed in 1950-54 to ensure similarity to Allegheny County steel workers (white males employed in 1953) used for comparison. This reduced the overall number of subjects from 1,165 to 813. The distribution of person-years by age and year for the subcohort is shown in table 10, where it can be seen that most of the person-years were on a diagonal; i.e., there were more person-years at younger ages in the 1950's and more person-years at older ages in the later time periods. When lung cancer mortality ratios were calculated for this subcohort with the use of Allegheny County steel workers for comparison (table 11), it was found that the mortality ratios were about 15-30% lower than those obtained by use of U.S. comparison rates. The ratio for exposure group 4 (other acid only) was the only significantly elevated ratio (SMR=2.00; 95% CI=1.06-3.78) in the comparison to Allegheny County steel workers.

Finally, estimates were made of the potential impact on our lung cancer findings of possible differences in smoking habits between the study population and the U.S. general population. As shown in table 12, where increases in ever smoking of 5, 10, 15, and 20% were hypothesized, the lung cancer mortality ratios that could be expected on the basis of smoking alone ranged from 1.06 to 1.24. These estimates were well below the overall lung cancer mortality ratio of 1.64 that was found for the study population.

DISCUSSION

The biological plausibility of acid mist-associated respiratory cancer is related to several possible mechanisms, including low-pH-induced changes in mitotic activity and cell differentiation (*24*), direct damage to genetic material (*25-27*), impairment of pH-sensitive enzyme activity (*28*), pH modulation of chemical toxicity (*29-31*), and chronic irritation of respiratory tissue (*32, 33*).

Several investigators have shown that sulfuric acid aerosol can induce changes in respiratory tract clearance rates. The slowing or speeding of clearance depends on the region in the bronchial tree where the clearance is being measured (alveolar clearance is accelerated and mucociliary clearance is retarded) and on the concentration and particle size of the aerosol (*34*). As noted by Schlesinger (*34*), the long-term significance of impaired respiratory tract defenses is not clear, but it is reasonable to conclude that impairment may lead to increased systemic absorption of inhaled materials and render the host more susceptible to chronic respiratory disease.

TABLE 7.—*Lung cancer mortality by race in men*[a] *in exposure group 3 (sulfuric acid only, probable daily exposure), with the use of U.S. death rates for comparison (steel-pickling workers employed 1940-64)*

Race	Deaths		Ratio
	Observed	Expected	
White	13	9.1	1.43
Nonwhite	5	2.3	2.16
Total	18	11.4	1.58

[a] There were no women in exposure group 3.

TABLE 8.—*Lung cancer mortality by length of employment in workers in exposure group 3 (sulfuric acid only, probable daily exposure), with the use of U.S. death rates for comparison (steel-pickling workers employed 1940-64)*

Length of employment, yr	Deaths		Ratio
	Observed	Expected	
0.5-<5	10	6.2	1.61
5-<10	5	2.0	2.49
10-<15	0	1.0	0.00
≥15	3	2.1	1.40
Total	18	11.4	1.58

TABLE 9.—*Mortality ratios and observed deaths for lung cancer by time since first employment, with the use of U.S. death rates for comparison (steel-pickling workers employed 1940-64)*

Group No.	Exposure	Mortality ratios (observed deaths) by time since first employment, yr[a]	
		0.5-<20	≥20
1	Any acid	0.98 (5)	1.85 (30)[b]
2	Sulfuric acid only	0.55 (2)	1.70 (17)
3	Sulfuric acid only, probable daily exposure	0.65 (2)	1.93 (16)[b]
4	Other acid only	3.26 (2)	2.06 (7)
5	Sulfuric acid and other acid	1.64 (1)	2.13 (6)

[a] Calculated from the date first employed in a job defined as exposed for the exposure group.
[b] The 95% CI for the mortality ratio excluded 1.00.

TABLE 10.—*Distribution of person-years by age and year for the subcohort of white male steel-pickling workers employed in any steel facility job in the period 1950-54 (the subcohort used for the comparison to Allegheny County steel worker rates)*

Age, yr	Years				Total
	1950-59	1960-69	1970-79	1980-81	
<30	1,340	256	0	0	1,596
30-39	2,253	1,987	283	0	4,523
40-49	1,627	2,530	1,965	153	6,275
50-59	767	1,642	2,321	442	5,172
60-69	295	685	1,367	325	2,672
≥70	24	183	469	141	817
Total	6,306	7,283	6,405	1,061	21,055

The site of deposition of the acid mist in the respiratory tract was difficult to predict due to the hygroscopic nature of acid mist and neutralization that occurs from naturally occurring ammonia gas in the respiratory system (*35-37*). Martonen et al. (*38*) showed that the amount of sulfuric acid mist that deposits in the pulmonary region is very dependent on the particle size upon entry to the trachea, with maximal deposition (50% of particles) occurring at about 1.5 μm. Larger particles are deposited largely in the tracheobronchial region, and smaller particles are largely exhaled. The particle size of the sulfuric acid mist in our study facilities could not be measured due to cessation of sulfuric acid use, but a recent study by Jones and Gamble (*39*) of sulfuric acid mist in plate formation in battery-manufacturing plants (where exposure levels are very similar to those in steel pickling) showed an average particle size (mass median aerodynamic diameter based on Anderson impactor sampling) of 5 μm. The geometric standard deviation of the particle size was 4 μm. Thus, if the sulfuric acid mist particle size distribution in our steel-pickling facilities was similar to that in battery manufacturing, it would be reasonable to conclude that a portion of the mist particles was respirable to the pulmonary region.

The only respiratory disease category that showed increased mortality in our study was cancer of the trachea, bronchus, and lung. Deaths from other malignancies of the respiratory system (buccal cavity, pharynx, and larynx) occurred at normal rates. Deaths from nonmalignant respiratory diseases occurred at lower than normal rates, indicating that acid mist exposure does not cause fibrogenic or other nonmalignant response sufficiently to affect mortality rates.

The lung cancer excess occurred both in workers exposed only to sulfuric acid (exposure group 2) (SMR = 1.39) and in workers exposed only to other acids (exposure group 4) (SMR = 2.24). The increased risk appeared to be higher in those exposed to other acids, but the difference was not statistically significant. The increased risk in sulfuric acid-exposed workers also appeared to be higher in nonwhites than whites, but again the difference was not statistically significant.

Length of employment and time since first employment in jobs with probable daily exposure were examined to address the possibility that dose-response and latency trends might exist. No dose-response relationship was found, but there was a strong latent effect in that all of the excess risk occurred 20 years or more after first exposure (SMR=1.93; 95% CI = 1.10-3.13). The lack of a dose-response relationship may have been due to use of an incorrect dose model; i.e., all exposures were given equal weight when it may be true that recent exposures have little bearing on cancer risk, or the lack of dose response may have been due to use of dose cate-

TABLE 11.—*Mortality ratios for lung cancer for white male pickling workers employed 1950-54, with the use of Allegheny County steel worker and U.S. death rates for comparison*

Group No.	Exposure group	Observed deaths	Allegheny County			United States		
			Expected deaths	Ratio	95% confidence limits[a]	Expected deaths	Ratio	95% confidence limits
1	Any acid	28	20.8	1.35	0.92-1.97	17.3	1.62	1.08-2.34
2	Sulfuric acid only	13	12.3	1.06	0.59-1.90	10.2	1.26	0.67-2.17
3	Sulfuric acid only, probable daily exposure	12	9.8	1.23	0.68-2.20	8.2	1.47	0.76-2.57
4	Other acid only	9	4.5	2.00	1.06-3.78	3.7	2.42	1.11-4.61
5	Sulfuric acid and other acid	6	4.0	1.49	0.54-3.86	3.3	1.81	0.66-3.93

[a] The confidence limits calculations for the comparison to Allegheny County steel workers took into account statistical variance contributed by the comparison population (*see* "Methods").

TABLE 12.—*Hypothesized increases in smoking and lung cancer mortality rate ratios attributable to increased smoking in steel-pickling workers employed 1940–64*

Percent increased smoking[a]	Population percentages by smoking category					Rate ratio[c]
	Never smoker	Ever smokers[b]				
		Ex-smoker	Light smoker	Moderate smoker	Heavy smoker	
0[d]	27	21	13	24	14	1.00
5	22	23	14	26	15	1.06
10	17	24	15	27	16	1.12
15	12	26	16	29	17	1.18
20	7	27	17	31	18	1.24

[a] Hypothesized increase in the number of "ever" smokers relative to the number in the U.S. white male population in 1965. The increase was distributed among the smoking categories proportionally, with the use of the proportions of ever smokers in the 1965 U.S. white male population.
[b] The hypothesized RRs for "ever" smokers were ex-smoker = 5, light smoker = 7, moderate smoker = 10, and heavy smoker = 20.
[c] Rate ratios that would be expected in the study population due to increased smoking.
[d] The population percentages in this row are the actual percentages that existed in U.S. white males in 1965.

gories that were too large. For example, the lowest exposure category included exposures up to 5 years in length.

Influence of Cigarette Smoking

We were able to address the potential influence of smoking habits on our lung cancer results in three ways: by comparison to other steel workers (who were likely to have had similar smoking habits), by examination of the results for other diseases caused by smoking, and by estimation of the potential effects of smoking differences on our risk estimates. When other steel workers were used as a comparison group, the mortality ratios for lung cancer were generally smaller, with workers exposed to other acids (exposure group 4) showing the only statistically significant excess (SMR = 2.00; 95% CI = 1.06–3.78). Because the ratios were generally smaller, it appears that increased smoking may explain some of the excess lung cancer risk that was found in the U.S. comparison. However, the smaller rate ratios may have been partly due to industrial exposures in the steel workers used for comparison and partly due to restriction of the analysis to white males, which excluded the higher excess lung cancer risk in nonwhite males.

Results for other smoking-related diseases (other than lung cancer) were examined under the assumption that their rates should also be elevated if the lung cancer excess was due to smoking. There were fewer nonmalignant respiratory disease deaths than expected (14 observed deaths vs. 18.5 expected deaths), however, and there were 142 cardiovascular disease deaths observed when 144.6 were expected.

A third method of addressing the smoking question was estimation of the potential effect of differences in smoking habits. In the most extreme situation estimated, where 93% of the study population ever smoked (as opposed to 73% of the general population), the increase in the lung cancer SMR that would have been expected was 24%. This was well below the overall increase of 64% that was found in our study population.

Other Findings

The absence of excess laryngeal cancer was interesting, given previous studies showing substantially increased risk in sulfuric acid-exposed populations. The previous studies of laryngeal cancer were incidence studies, however, where cases were enumerated rather than deaths. Since laryngeal cancer is a survivable cancer, incidence is a better measure of disease occurrence. For this reason, a study of laryngeal cancer incidence in our population is currently being conducted. Another reason why our study did not find a statistically significant laryngeal cancer mortality excess may be that it had too small a sample size. Only 1.03 such deaths were expected in our study.

There were notable deficits of deaths from digestive system diseases (SMR = 0.31; $P<.05$) and from malignant neoplasms of the digestive system (SMR = 0.63). Whether these were chance findings or whether acid mist exposure may have favorably influenced the occurrence of digestive diseases can only be speculated. That they were chance findings is very possible, given the many comparisons made in the study. Part of the deficit of digestive system diseases was due to a low rate of death from cirrhosis of the liver, however, so lower alcohol consumption may explain some of the decreased risk.

A noteworthy finding was that one of the study facilities, facility A, had no increased risk of lung cancer associated with it. Facility A was not different from the other plants in any important way that is known to us. Its racial makeup was similar to that of the other plants (17% vs. 12% nonwhite), and its pickling processes were similar to those at the other facilities.

Study Limitations

There were several limitations to the study that should be noted. First, chance findings may have occurred due to the many diseases examined and comparisons made.

The lung cancer risk was probably real, however, given that it had a latency trend typically associated with environmental cancer and that it was consistent at two of the three study facilities (the third facility had a small sample size). A second limitation is that comparison of SMRs can be misleading if the age distributions of the populations upon which the SMRs are based are different and age is an "effect modifier" for the exposure. None of our SMR comparisons (e.g., the sulfuric acid-other acid comparison) were statistically significant, however. Third, there may have been a slight inflationary bias for the respiratory cancer mortality ratios due to use of U.S. rates based on deaths through 1978 and the study period extending to 1981. (Respiratory cancer rates have been going up over calendar time.) Fourth, information on level of exposure was limited, and it was not possible to associate specific milligrams per cubic meter exposure with specific jobs. For those with daily exposure to sulfuric acid mist (exposure group 3), however, industrial hygiene surveys conducted in the 1970's showed that the average exposure level was about 0.2 mg/m^3. Fifth, there may have been mobility of employees to or from other jobs with potential exposure to lung carcinogens. This was partially addressed by excluding subjects who had additionally worked in coke oven operations (which have previously been associated with lung cancer risk) and by comparing study cohort death rates to rates of steelworkers in general. Finally, many of the jobs and exposures that existed historically at the three steel-making facilities no longer exist. The study findings may not all be directly relevant, therefore, to the current work forces at the study facilities.

CONCLUSION

In conclusion, there was an increased risk of lung cancer in workers exposed to acid mists in steel-pickling operations. The excess risk was seen in workers exposed to sulfuric acid mist and in workers exposed to other acids. Continued monitoring of lung cancer rates in pickling operations is recommended. Since acid mist exposure occurs in many industries (NIOSH estimates that 800,000 workers in the United States have some potential for exposure), it may be prudent to monitor lung cancer rates in these other industries as well. The generalizability of the present findings extends fully to industries where acid mist concentrations and particle sizes are similar (e.g., battery manufacturing) and to a lesser extent to other industries and the general population exposed to atmospheric acid pollution. Additional studies are needed to confirm these findings, to examine the histopathology of acid-associated tumors, and to delineate possible interactions between acid mist exposure and other exposures in the workplace. Since the average exposure levels in the present study were well below the current exposure standard, accurate exposure characterization for possible use in standard setting is needed.

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