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Original Contribution

Chronic and Acute Effects of Coal Tar Pitch Exposure and Cardiopulmonary Mortality Among Aluminum Smelter Workers

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Air pollution causes several adverse cardiovascular and respiratory effects. In occupational studies, where levels of particulate matter and polycyclic aromatic hydrocarbons (PAHs) are higher, the evidence is inconsistent. The effects of acute and chronic PAH exposure on cardiopulmonary mortality were examined within a Kitimat, Canada, aluminum smelter cohort ($n = 7{,}026$) linked to a national mortality database (1957–1999). No standardized mortality ratio was significantly elevated compared with the province's population. Smoking-adjusted internal comparisons were conducted using Cox regression for male subjects ($n = 6{,}423$). Ischemic heart disease (IHD) mortality ($n = 281$) was associated with cumulative benzo[*a*]pyrene (B(*a*)P) exposure (hazard ratio = 1.62, 95% confidence interval: 1.06, 2.46) in the highest category. A monotonic but nonsignificant trend was observed with chronic B(*a*)P exposure and acute myocardial infarction ($n = 184$). When follow-up was restricted to active employment, the hazard ratio for IHD was 2.39 (95% confidence interval: 0.95, 6.05) in the highest cumulative B(*a*)P category. The stronger associations observed during employment suggest that risk may not persist after exposure cessation. No associations with recent or current exposure were observed. IHD was associated with chronic (but not current) PAH exposure in a high-exposure occupational setting. Given the widespread workplace exposure to PAHs and heart disease's high prevalence, even modest associations produce a high burden.

air pollutants; cohort studies; heart diseases; occupational diseases; polycyclic hydrocarbons, aromatic

Abbreviations: AMI, acute myocardial infarction; B(*a*)P, benzo[*a*]pyrene; CI, confidence interval; COPD, chronic obstructive pulmonary disease; IHD, ischemic heart disease; PAH(s), polycyclic aromatic hydrocarbon(s); SMR, standardized mortality ratio.

Air pollution causes a wide range of adverse cardiovascular effects, from inflammation identified in biomarkers to increased mortality (1, 2). Its adverse effects have been associated with both short- and long-term exposure to particulate matter (1, 3), more specifically particulate matter from combustion rather than crustal sources (4, 5). Combustion-based particulate matter carries metals and reactive organic compounds, including polycyclic aromatic hydrocarbons (PAHs), on its surface (1).

Particulate matter and PAH exposures are prevalent in occupational settings at levels 1–3 orders of magnitude higher than those in environmental settings, yet occupational studies have been less conclusive. Some studies have demonstrated elevated heart disease mortality with PAH-exposed jobs in industries with exposure to combustion productions, including aluminum smelting (6, 7), chimney sweeping (8), and gas work (9). However, heart disease mortality rates in occupational cohorts are typically lower than those in the general population (6, 10, 11). The strongest evidence thus far is from a cohort of European asphalt pavers: Burstyn et al. (12) reported monotonic exposure-response relations between quantitative PAH exposure and fatal heart disease in internal comparisons. Recent morbidity studies add to the growing occupational evidence, with adverse cardiovascular effects with particulate matter and PAH exposure being identified using biomarkers of cardiovascular disease, such as markers of inflammation, blood pressure, and heart rate variability (1, 13–15).

In this paper, we examine heart disease mortality in a cohort of aluminum smelter workers in British Columbia, Canada. We expand on the previously reported study of acute myocardial infarction (AMI) mortality in this cohort (16) to include all causes of ischemic heart disease (IHD); and for the first time in an occupational setting, we examine heart disease exposure-response relations with both acute and chronic exposure to benzo[*a*]pyrene (B(*a*)P). We also report on the relative mortality risk for heart disease and other chronic diseases as compared with the British Columbia general population, and we examine exposure-response relations with chronic respiratory diseases and cerebrovascular disease.

MATERIALS AND METHODS

Cohort enumeration and follow-up

This study was a 14-year update of data on a vertical-stud Söderberg aluminum smelter cohort in British Columbia, Canada (11). The updated cohort consisted of 6,423 males and 603 females who worked for 3 or more years at the aluminum smelter or its power-generating station between 1954, when the smelter opened, and 1997. Work histories through December 31, 1999, were abstracted from company records. Using probabilistic linkage, we linked the cohort to the Canadian national mortality database (1957–1999). We updated vital status through linkage with the British Columbia Client Registry to determine the workers' last known dates of residence in the province. The British Columbia Client Registry, administered by the British Columbia Ministry of Health, has kept all records of health-care recipients in the provincial medical system since 1984 and includes over 95% of the province's population. Vital status ascertainment was supplemented by data from the original study, including company pension lists and active follow-up conducted using union lists and advertisements in the company's newsletter and by contacting people who had additional relevant data, such as last employers. If a worker did not link to the client registry, he or she was censored at the last contact date if the last contact was the company or was not in Canada or if he/she had been censored in the original study prior to 1985. In this paper, we examine mortality due to nonmalignant chronic diseases; cancer outcomes were examined separately (11). An institutional review board approved this study's protocols.

Smoking status

Smoking status for the study update was ascertained using self-administered questionnaires sent to current workers and pensioners and was supplemented with smoking information obtained for 88% of the original cohort from a similar mailed questionnaire sent to workers or their survivors. Categorical smoking information (75% ever smokers, 25% never smokers) was obtained for 77% of this updated cohort.

Exposure assessment

Approximately half of the cohort had ever been exposed to coal tar pitch volatiles. Exposure to coal tar pitch volatiles occurs within the potrooms, potlining, potshell repair, and the anode plant. Workers in casting, wharf, power operations, and administration departments have minimal exposure. Quantitative levels of coal tar pitch volatiles were estimated using B(*a*)P, a specific PAH in the mixture. A cumulative exposure metric using the benzene-soluble fraction, an alternative marker of the mixture, was highly correlated with B(*a*)P in this cohort (Pearson correlation >0.94, $P < 0.001$) (17, 18).

The development of the quantitative B(*a*)P job exposure matrix is described elsewhere (18). Briefly, a B(*a*)P job exposure matrix was developed using approaches to maximize the personal exposure measurements ($n = 1{,}275$) that had been collected by the company and WorkSafe British Columbia from the mid-1970s onwards. Statistical models were developed to derive annual arithmetic mean values for each operations and maintenance job in the potrooms for the period 1977–2000. A key aspect of the models was the use of a linear spline time trend that accounted for different rates of exposure decline by time period and potline. For nonpotroom locations, mean exposures were directly calculated if measurements were available. Exposure estimates for jobs without measurements were extrapolated from exposure estimates from the statistical models by adjusting for the amount of time worked in exposed areas. Pre-1977 exposure levels were backwards-extrapolated from 1977 exposure levels and incorporated major technological changes. The job- and time-period-specific B(*a*)P exposure levels were linked to each worker's work history for calculation of cumulative and current B(*a*)P exposure levels, which were time-varying variables across the study follow-up period.

Statistical analyses

The mortality experience of the cohort for select causes of death was compared with that of the British Columbia population using standardized mortality ratios (SMRs) adjusted for age, sex, and time period. All causes of death were recoded to the *International Classification of Diseases*, Ninth Revision. Follow-up began from the point at which the worker attained 3 years of employment and extended to the earliest of the following dates: the date of death, the date last known to be alive, or December 31, 1999. Ninety-five percent confidence intervals for the SMRs were calculated assuming a Poisson distribution.

For IHD mortality, we conducted internal comparisons for 3 outcomes: 1) all IHD occurring from 1957 onwards; 2) AMI occurring from 1969 onwards; and 3) non-AMI IHD occurring from 1969 onwards. The 1969 restriction was necessary, because AMI could not be separated from other IHD codes on death certificates for prior years. We also conducted internal comparisons for cerebrovascular disease and chronic obstructive pulmonary disease (COPD), for which we had sufficient numbers of cases. All internal comparisons were restricted to males, because there were too few female cases. All tests of statistical significance were 2-sided.

For internal comparisons, we obtained adjusted hazard ratios using Cox regression models (Stata/SE, version 9.2; Stata Corporation, College Station, Texas). Because age is a strong risk factor for chronic disease outcomes and is

Table 1. Standardized Mortality Ratios for Nonmalignant Chronic Diseases in an Aluminum Smelter Cohort, by Sex, Kitimat, British Columbia, Canada, 1954–1999

Cause of Death	Males				Females				*International Classification of Diseases*, Ninth Revision, Code(s)
	Obs[a]	Exp[b]	SMR	95% CI	Obs	Exp	SMR	95% CI	
Diabetes mellitus	16	19.4	0.82	0.47, 1.34	0	1.2			250
Mental disorder	19	17.7	1.08	0.65, 1.68	1	1.0	0.98	0.02, 5.47	290–319
Disease of the nervous system	11	20.8	0.53	0.26, 0.95	2	1.5	1.35	0.16, 4.88	320–389
IHD (1969 onward)[c]	281	311.8	0.90	0.80, 1.01	8	9.53	0.84	0.39, 1.59	410–414, 429.2
IHD excluding AMI	78	103.9	0.75	0.62, 0.91	1	3.70	0.27	0.01, 1.28	411–414, 429.2
AMI	184	183.9	1.00	0.88, 1.13	7	5.50	1.27	0.60, 2.40	410
Cerebrovascular disease	58	65.2	0.89	0.68, 1.15	8	4.9	1.64	0.71, 3.23	430–438
Other circulatory disease	63	71.0	0.89	0.68, 1.14	4	3.7	1.08	0.30, 2.82	399–400, 406–409, 415–423.9, 424.4–429.1, 429.3–429.9, 439–459, 480–486
Pneumonia	26	28.6	0.91	0.59, 1.33	0	1.7			480–486
Chronic obstructive pulmonary disease	27	41.9	0.64	0.42, 0.94	1	1.7	0.59	0.01, 3.26	490–496
Other respiratory disease	12	9.6	1.24	0.64, 2.17	0	0.5			470–478, 494–519
Cirrhosis of the liver	20	33.8	0.59	0.36, 0.91	0	1.3			571
Other digestive disease	28	19.8	1.41	0.94, 2.04	0	1.4			520–530, 540–543, 555–558, 562–570, 572–579
All deaths	1,079	1,242	0.87	0.82, 0.92	51	60.4	0.85	0.63, 1.11	

Abbreviations: AMI, acute myocardial infarction; CI, confidence interval; Exp, expected; IHD, ischemic heart disease; Obs, observed; SMR, standardized mortality ratio.

[a] Observed number of deaths.

[b] Expected number of deaths.

[c] These analyses were restricted to 1969 onward because AMI could not be separated from other IHD causes of death prior to 1969.

associated with cumulative exposure, we used age as the metameter of time. The models included smoking status (ever, never, or unknown) and time-dependent covariates for year (5-year categories), time since first employed (years; continuous), and work status (employed at smelter: yes/no). All exposure metrics were time-dependent variables. For cerebrovascular disease and COPD, exposure effects were examined using cumulative B(*a*)P metrics (0-, 2-, 5-, and 10-year lags).

In the full cohort analyses of heart disease outcomes, we examined 2 time windows of B(*a*)P exposure in the same model: 1) past exposure based on cumulative B(*a*)P exposure (lagged 0, 2, 5, and 10 years); and 2) recent exposure based on cumulative B(*a*)P exposure in the recent time periods (<2 and <5 years). The past- and recent-exposure time windows were categorized with the cutpoints defined by the exposure distribution of the cases. Exposure-disease relations were also examined with a continuous, linear variable for cumulative B(*a*)P exposure. The trend across categories was tested using the person-year-weighted mean of each category in the model as a continuous variable.

We also examined exposure-response associations for IHD fatalities that occurred during active employment to examine the acute effects of B(*a*)P exposure. Active person-years of follow-up were truncated at either the date of death or 30 days past the last date worked, whichever was earlier. Current B(*a*)P exposure was defined as average B(*a*)P exposure in the past year and was categorized as none, <5 $\mu g/m^3$, or ≥ 5 $\mu g/m^3$. Both cumulative past B(*a*)P exposure and current B(*a*)P exposure were examined in the same model. Results derived from the active employment models were adjusted for smoking status and calendar year.

RESULTS

Standardized mortality ratios

The SMRs for nonmalignant chronic diseases are listed in Table 1. The all-cause mortality SMR was lower than that in the British Columbia general population for both males (SMR = 0.87, 95% confidence interval (CI): 0.82, 0.92) and females (SMR = 0.85, 95% CI: 0.63, 1.11). Elevated mortality rates were observed in males for other respiratory disease mortality (SMR = 1.24, 95% CI: 0.64, 2.17) and other digestive diseases (SMR = 1.41, 95% CI: 0.94, 2.04) and in

Table 2. Demographic Characteristics of Male Aluminum Smelter Workers and Numbers of Deaths From All Ischemic Heart Disease and Acute Myocardial Infarction, Kitimat, British Columbia, Canada, 1954–1999

	Male Sex	IHD Mortality		AMI Mortality	
		All IHD Deaths	Deaths During Employment	All AMI Deaths	Deaths During Employment
No.	6,423	281	52	184	34
Smoking status, %					
Ever smoker	57	70	65	75	64
Never smoker	19	16	17	15	25
Unknown	24	14	17	10	11
Mean year of hire (range)	1967 (1947–1996)	1957 (1951–1989)	1958 (1954–1977)	1957 (1951–1989)	1958 (1954–1977)
Mean duration of employment, years (SD)	14.5 (10.0)	14.6 (8.5)	18.6 (8.1)	15.0 (8.2)	20.3 (5.6)
Mean year of birth (range)	1937 (1893–1976)	1919 (1897–1946)	1923 (1901–1944)	1920 (1898–1946)	1924 (1906–1944)
Mean age at death, years (SD)		65.7 (11.0)	54.1 (6.8)	65.3 (10.9)	55.0 (7.5)

Abbreviations: AMI, acute myocardial infarction; IHD, ischemic heart disease; SD, standard deviation.

females for AMI (SMR = 1.27, 95% CI: 0.60, 2.40) and cerebrovascular disease (SMR = 1.64, 95% CI: 0.71, 3.23).

Study population for internal comparisons

The demographic characteristics of the entire male cohort and the heart disease cases are shown in Table 2. The workers entered the study at a mean age of 32.4 years (range, 18–65), were employed an average of 14.5 years (range, 3–45), and contributed an average of 23.5 years (maximum, 47) to study follow-up. Workers who died of IHD were more likely to have ever smoked than the average worker in the cohort (65%–70% vs. 57%). Those who died of IHD while employed had a similar mean employment start year as all workers who died of IHD; their deaths occurred, on average, 10 years earlier (age 54.1 years vs. age 65.7 years).

Exposure metrics

Exposure estimates were extrapolated backwards from pre-1977 levels in the IHD analyses for 44% of the exposed person-years: 27.6% of exposed person-years were pre-1970 and 16.3% were between 1970 and 1976. For the AMI analyses, backwards extrapolation was required for 25% of the exposed person-years: 3.4% of exposed person-years were pre-1970 and 21.7% were between 1970 and 1976.

The cumulative exposure metrics were highly skewed. For cumulative exposure with a 5-year lag, the mean, 95th percentile, and maximum exposure for exposed workers (77%) were 29.8 $\mu g/m^3$-year, 112 $\mu g/m^3$-year, and 300 $\mu g/m^3$-year, respectively. For cumulative B(*a*)P exposure within the most recent 5 years, the mean, 95th percentile, and maximum exposure for exposed workers (34%) were 7.1 $\mu g/m^3$-year, 28.0 $\mu g/m^3$-year, and 74.6 $\mu g/m^3$-year, respectively. For current B(*a*)P exposure, the mean, 95th percentile, and maximum exposure for exposed workers (24% of person-years) were 2.3 $\mu g/m^3$-year, 7 $\mu g/m^3$-year, and 18 $\mu g/m^3$-year, respectively.

Past B(*a*)P exposure (cumulative B(*a*)P with a 5-year lag) and recent B(*a*)P exposure (cumulative B(*a*)P in the most recent 5 years) were only slightly positively correlated (Spearman's $r = 0.10$, $P < 0.001$). Current B(*a*)P exposure was highly correlated with cumulative exposure in the most recent 5 years of exposure ($r = 0.86$, $P < 0.001$) but not with cumulative exposure with a 5-year lag ($r = 0.03$, $P < 0.001$). The lagged cumulative exposure metrics (0-, 2-, 5-, and 10-year) were all highly correlated with each other (all r's ≥ 0.96, all P's < 0.001). Using the lagged metrics for cumulative exposure allowed us to distinguish effects of current exposure from those of long-term exposure.

Internal comparisons for heart disease mortality

The internal comparisons for male heart disease mortality with past and recent exposure are shown in Table 3. Elevated risk of IHD mortality was observed for past cumulative B(*a*)P exposure (5-year lag) but not more recent B(*a*)P exposure. Monotonic but weaker patterns were observed when the outcome was restricted to AMI deaths. No exposure-response trends were observed with non-AMI IHD. The association with the 5-year-lagged cumulative B(*a*)P metric was marginally stronger (based on the log-likelihood model fit statistics and trend P values) than the unlagged and 2-year-lagged metrics; a 10-year lag resulted in weaker associations (not shown). Restricting the analyses to persons with known smoking status resulted in similar risk estimates and trends but wider confidence intervals due to the reduced power (not shown). The risk estimates were stronger when time since being hired and work status were included to account for the healthy worker effect. For instance, for IHD, the hazard ratio was strengthened from 1.51 (95% CI: 1.03, 2.22) to 1.61 (95% CI: 1.08, 2.39) in the highest category for past B(*a*)P exposure when time since being hired and work status were included. Adjusting for time

Table 3. Smoking-Adjusted Hazard Ratios for Heart Disease Mortality According to Past Cumulative (5-Year Lag) and Recent Cumulative (Most Recent 5 Years) Benzo[*a*]Pyrene Exposure in Male Aluminum Smelter Workers, Kitimat, British Columbia, Canada, 1954–1999

Cumulative B(*a*)P Exposure With 5-Year Lag[a]					B(*a*)P Exposure in Most Recent 5 Years[a]				
Exposure Category, μg/m^3-year	No. of Deaths	P-Y of Follow-up	HR	95% CI	Exposure Category, μg/m^3-year	No. of Deaths	P-Y of Follow-up	HR	95% CI
All IHD (1957 onward)									
Categorical									
0	56	33,111	1	Referent	0	221	82,796	1	Referent
>0–<7.79[b]	56	37,581	1.11	0.76, 1.62	>0–<0.15[b]	15	7,075	1.03	0.61, 1.75
7.79–<24.3	57	34,838	1.48	1.01, 2.17	0.15–<2.86	15	18,979	0.77	0.44, 1.36
24.3–<66.7	56	31,533	1.28	0.86, 1.91	2.86–<10.5	15	20,073	1.02	0.56, 1.87
≥66.7	56	13,688	1.62	1.06, 2.46	≥10.5	15	21,827	1.09	0.57, 20.9
Trend *P*[c]				0.053					0.61
Continuous[d]	281	150,751	1.002	1.000, 1.005					
IHD excluding AMI (1969 onward)									
Categorical									
0	15	25,071	1	Referent	0	68	75,600	1	Referent
>0–<14.6[e]	21	44,861	1.24	0.63, 2.43	<2.38[f]	5	20,966	0.63	0.25, 1.62
14.6–<39.1	21	30,395	1.88	0.94, 3.74	≥2.38	5	30,923	1.29	0.40, 4.16
≥39.1	21	27,161	1.25	0.61, 2.57					
Trend *P*				0.88					0.55
Continuous[d]	78	127,488	1.003	0.997, 1.008					
AMI (1969 onward)									
Categorical									
0	35	25,071	1	Referent	0	144	75,600	1	Referent
>0–<7.51[b]	37	30,454	1.14	0.71, 1.82	>0–<0.04[b]	10	5,596	1.19	0.62, 2.28
7.51–<27.7	37	34,621	1.21	0.75, 1.96	0.04–<2.15	10	14,664	0.77	0.39, 1.55
27.7–<67.4	38	24,081	1.36	0.84, 2.22	2.15–<9.19	10	17,611	0.96	0.46, 2.00
≥67.4	37	13,261	1.46	0.87, 2.45	≥9.19	10	14,017	0.98	0.44, 2.19
Trend *P*				0.19					0.92
Continuous[d]	184	127,488	1.001	0.997, 1.005					

Abbreviations: AMI, acute myocardial infarction; B(*a*)P, benzo[*a*]pyrene; CI, confidence interval; HR, hazard ratio; IHD, ischemic heart disease; P-Y, person-years.

[a] For each outcome, both the past and recent B(*a*)P time windows were included in the same model. Results were adjusted for smoking status (ever smoker, never smoker, or unknown) and time-dependent covariates for calendar year (5-year categories), employment status (working/not working), and time since first employed (10-year categories).

[b] Quartiles of the exposure distribution among cases.

[c] Two-sided test for trend using the person-year-weighted mean value for each category as a linear, continuous variable.

[d] Exposure variable was entered as a continuous, linear variable in the model.

[e] Tertiles of the exposure distribution among cases.

[f] Dichotomized at the median exposure among cases.

since last employment had no impact on the associations (not shown).

Using a continuous variable, the risk per μg/m^3-year was 1.002 (95% CI: 1.000, 1.005) for IHD and cumulative B(*a*)P exposure. Visual inspection of the categorical relations, however, indicated that the association was nonlinear and that the hazard ratio per unit of exposure may have been an underestimate.

To examine the acute effects of B(*a*)P exposure, we restricted the models to active employment (Table 4). The lowest exposure category and the unexposed cumulative B(*a*)P categories were combined with the unexposed because of small numbers of cases. In these restricted analyses, current B(*a*)P exposure was not associated with IHD or AMI. The hazard ratios for cumulative B(*a*)P exposure (5-year lag) were higher in the restricted analyses than in the full analyses, with hazard ratios reaching 2.39 in the highest cumulative B(*a*)P category for IHD; however, the confidence intervals were wider. Similar but weaker patterns were observed with AMI. There were too few deaths among the actively employed to examine associations with non-AMI IHD separately.

Table 4. Smoking-Adjusted Hazard Ratios for Heart Disease Mortality According to Past Cumulative (5-Year Lag) and Current Benzo[*a*]Pyrene Exposure, With Person-Years Restricted to Active Employment (End Date + 30 Days), in Male Aluminum Smelter Workers, Kitimat, British Columbia, Canada, 1954–1999

Cumulative B(*a*)P Exposure With 5-Year Lag[a]					Current B(*a*)P Exposure[a]				
Exposure Category, μg/m^3-year	No. of Deaths	P-Y of Follow-up	HR	95% CI	Exposure Category, μg/m^3-year	No. of Deaths	P-Y of Follow-up	HR	95% CI
All ischemic heart disease (1957 onward)									
Categorical									
<8.75[b]	16	39,736	1	Referent	0	22	28,614	1	Referent
8.75–<35.7	12	19,829	1.88	0.84, 4.19	>0–<5[c]	19	31,519	0.84	0.43, 1.64
35.7–<77.0	12	9,411	1.99	0.85, 4.65	≥5	11	13,899	1.25	0.51, 3.04
≥77.0	12	5,057	2.39	0.95, 6.05					
Trend *P*[d]				0.10					
Continuous[e]	56	74,033	1.002	0.995, 1.009					
Acute myocardial infarction (1969 onward)									
Categorical									
<9.18[b]	10	28,079	1	Referent	0	16	21,475	1	Referent
9.18–<41.4	8	16,145	1.59	0.60, 4.22	>0–<5	11	28,188	0.63	0.27, 1.44
41.4–<76.0	8	6,223	1.95	0.71, 5.40	≥5	7	5,847	1.39	0.44, 4.33
≥76.0	8	5,064	1.87	0.62, 5.60					
Trend *P*[d]				0.29					
Continuous[e]	34	55,511	1.001	0.993, 1.010					

Abbreviations: B(*a*)P, benzo[*a*]pyrene; CI, confidence interval; HR, hazard ratio; P-Y, person-years.

[a] For each outcome, both the past cumulative and current B(*a*)P time windows were included in the same model. Results were adjusted for smoking status (ever smoker, never smoker, or unknown), and calendar year (5-year categories).

[b] Quartiles of the exposure distribution among cases. The unexposed category and the lowest quartile were combined.

[c] Current B(*a*)P exposure ranged from 0 μg/m^3 to 18 μg/m^3; 5 μg/m^3 corresponds to the 70th percentile of current B(*a*)P exposure in exposed workers.

[d] Two-sided test for trend using the person-year-weighted mean value for each category as a linear, continuous variable.

[e] Exposure variable was entered as a continuous, linear variable in the model.

Other mortality outcomes

We examined exposure-response relations for COPD and cerebrovascular disease for male smelter workers. Neither disease had elevated mortality ratios in external comparisons with the province's population, and neither disease was associated with cumulative B(*a*)P exposure in internal comparisons (Table 5).

DISCUSSION

In this paper, we report an increased risk of IHD with chronic B(*a*)P exposure, but not acute B(*a*)P exposure, in an occupational cohort of aluminum smelter workers. Two previous smelter studies have shown an increased risk of heart disease with potroom work (7) and cumulative coal tar exposure (6). Environmental studies of air pollution, with much lower particulate matter and PAH exposure levels (19), have found consistent associations between particulate matter and IHD mortality with both short- and long-term exposure (3). Our strongest associations were with chronic B(*a*)P exposure and all IHD combined. Our separate analyses of AMI and non-AMI causes suggested that the association may be limited to AMI, although nonsignificant risks were observed in all exposure categories for both outcomes. PAHs have been found to enhance the progression of atherosclerosis in toxicologic studies (20–24), which is relevant to both AMI and non-AMI causes of IHD. We could not determine whether there was a latency period for the effects of chronic exposure, since cumulative metrics with lags ranging from 0 years through 5 years provided nearly identical results.

B(*a*)P, a specific PAH, was used as a surrogate for the complex mixture of PAHs and other compounds emitted from the coal tar pitch used in the anode in the electrolytic process of aluminum smelting. The emissions in aluminum smelters include coal tar pitch volatiles such as PAHs, fluorides, sulfur dioxide, and carbon monoxide, among other substances (25); however, in Söderberg smelters, these exposures are highly related. Previous analyses in this and other smelters have found B(*a*)P to be a good surrogate measure of coal tar pitch volatile emissions for evaluation of cancer outcomes (16, 17, 26, 27). The causal components for heart disease are unknown; however, PAHs have been implicated in toxicologic studies (20, 21).

Table 5. Smoking-Adjusted Hazard Ratios for Chronic Obstructive Lung Disease and Cerebrovascular Disease Mortality According to Cumulative Benzo[*a*]pyrene Exposure (5-Year Lag) in Male Aluminum Smelter Workers, Kitimat, British Columbia, Canada, 1954–1999

Exposure Category, μg/m^3-year	No. of Deaths	Person-Years of Follow-up	Hazard Ratio[a]	95% Confidence Interval
Chronic obstructive pulmonary disease				
<9.78[b]	12	75,755	1	Referent
9.78–<36.8	8	44,108	1.58	0.63, 3.93
≥36.8	8	30,887	1.21	0.47, 3.13
Trend *P*[c]				0.76
Cerebrovascular disease				
0	15	33,111	1	Referent
>0–<11.4[b]	14	46,347	0.88	0.42, 1.83
11.4–<76.8	15	60,656	0.65	0.31, 1.34
≥76.8	14	10,636	1.42	0.67, 2.99
Trend *P*[c]				0.20

[a] Hazard ratios were obtained from Cox regression models. Results were adjusted for smoking status (ever smoker, never smoker, or unknown) and calendar year.

[b] Tertiles of the exposure distribution among cases. For chronic obstructive pulmonary disease, the unexposed category and the lowest tertile were combined.

[c] Two-sided test for trend using the person-year-weighted mean value for each category as a linear, continuous variable.

The development of quantitative exposure estimates is a major strength of this cohort study and a substantial improvement over the semiquantitative estimates used in the original study of this cohort (11, 18). Although we used sophisticated statistical models to maximize the use of exposure measurements, the nonlinear relations observed between cumulative B(*a*)P and disease suggest that some exposure misclassification remained. Backwards extrapolation of pre-1977 levels was necessary for 44% of the person-years in the IHD analyses and may have resulted in underestimated exposure levels for this earlier period. However, the exposure measurements covered the time periods in which the majority of the technological improvements occurred (18). Although measurements anchored the exposure estimates wherever possible, interpolation based on proportion of time spent in exposed work areas was required for jobs without measurements. These jobs generally fell within the low exposure category and were primarily jobs held by maintenance workers who worked in multiple plant and workshop areas.

For the hypothesized inflammation pathways for particulate matter and cardiovascular disease, the most relevant size fractions have been the fine (<2.5 μm) and ultrafine (<0.1 μm) particles (1). The B(*a*)P metric, however, was based on PAHs bound on particles collected using 37-mm cassettes (18), which has a >50% sampling efficiency for particles with mean aerodynamic diameter less than 30 μm (28). A study characterizing the particulates from smelter emissions have found several different types of particles that are less than 3 μm in diameter, including soot, but the predominant ultrafine particulates were fluoride-containing agglomerates in the 0.1- to 1-μm range (29). We were unable to develop exposure metrics specific to these small particle sizes and thus assumed that the respirable fraction was a constant proportion of the measured particulate. If the proportion varied by job or time, exposure misclassification would have been introduced.

Other exposures relevant to an aluminum smelter environment, such as noise, heat, and high energy expenditures (30–35), have also been associated with heart disease but were not evaluated in this study. Confounding by these exposures is unlikely, since our nonexposed reference group (50% of the cohort) included persons who worked in other noisy and high-physical-activity areas such as electrical operations, nonpotroom maintenance areas, the wharves, and the casting department, which also had high heat exposures.

We previously reported differences in exposure levels between smokers and nonsmokers (mean cumulative B(*a*)P exposure of 30.9 μg/m^3-year and 20.9 μg/m^3-year, respectively) (36). To account for the potential confounding from smoking, we adjusted for smoking status (ever smoker, never smoker, or unknown) in all analyses. Our internal comparisons for COPD, another disease with smoking as a risk factor, did not show an association with B(*a*)P exposure, further supporting our findings of only modest confounding by smoking. Although residual confounding may remain, since we could not adjust for the workers' pack-years of smoking, it is unlikely to account for the entirety of the elevated risk of heart disease mortality seen here, as previous studies have shown only modest confounding by smoking in occupational cohorts (37, 38).

A strength of our study was the use of internal comparisons to reduce bias due to the healthy worker effect. External comparisons of occupational cohorts with the general population have rarely shown an elevated SMR with cardiovascular disease, because of the healthy hire effect (39).

That was indeed the case with heart disease in our external comparisons. There is no simple way to address residual bias in the other component of the healthy worker effect, the healthy worker survivor effect. When people leave work or change to less-exposed jobs as their health declines, the healthier workers accrue the largest exposures while symptomatic persons truncate their exposures, resulting in attenuated exposure-response associations (40, 41). In light of the healthy worker survivor effect, we generally see weaker associations among active workers, since less healthy workers typically leave behind a survivor population of healthier employed subjects. We found the opposite, with higher hazard ratios for chronic B(*a*)P exposure in our analyses restricted to active employment than in our full analyses; albeit the restricted analyses had much wider confidence intervals from the reduced power. The lower hazard ratios in the full cohort compared with the actively employed suggest that cardiovascular effects may be reversible with time away from exposure.

Although our a priori interest was heart disease outcomes, we also examined external comparisons for other nonmalignant chronic diseases and internal comparisons for cerebrovascular disease and COPD. The decreased all-cause mortality rate in this cohort is typical in an occupational cohort (39). Cerebrovascular disease was elevated in the cohort's women (SMR = 1.64, 95% CI: 0.71, 3.23) but was not elevated in the men; no association with PAH exposure was observed in our internal comparisons. COPD mortality was lower than that of the province's population for both men and women, and we found no indication of a trend with PAH exposure in the internal comparisons. Other studies of aluminum smelter workers and of asphalt pavers have shown some weak evidence for an increased risk of respiratory symptoms and COPD mortality with PAH exposure (42–45). In a Norwegian aluminum smelter study, Romundstad et al. (46, 47) found elevated COPD mortality with fluoride exposure, a coexposure in Söderberg smelters that was not examined in this study.

A limitation of our study was the use of mortality rather than morbidity for cardiopulmonary outcomes. We expected nearly complete ascertainment of mortality causes with the linkage of this cohort to the national mortality database, to the national cancer incidence database, and to tax data for confirmation of vital status. However, the good survival rates for cardiopulmonary outcomes indicated that we captured only a portion of the cardiopulmonary outcomes that might have arisen from occupational exposures. Further studies of cardiopulmonary morbidity and PAH exposure are warranted.

In summary, our results support those of previous environmental studies by finding exposure-response relations between chronic PAH exposure and heart disease in a highly exposed occupational cohort. Given the widespread prevalence of workplace exposure to PAHs and particulate matter and the high prevalence of heart disease worldwide, even modest associations can result in a high burden of heart disease. Our results provide additional evidence that the downward bias due to the healthy worker survivor effect in occupational studies requires the development and incorporation of more sophisticated analytical approaches, such as causal models that can account for variables (e.g., leaving work) that are both confounders and intermediates on the causal pathway (40, 41, 48, 49).

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