AMERICAN JOURNAL OF INDUSTRIAL MEDICINE 37:175–183 (2000)

Cancer Incidence and Cause Specific Mortality Among Workers in Two Norwegian Aluminum Reduction Plants

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Background Concern about the health hazards in the aluminum industry has initiated this study where we have investigated associations between exposure to polycyclic aromatic hydrocarbons (PAH) and fluorides, and cancer incidence and cause specific mortality among workers in two Norwegian aluminum plants in operation since 1954 and 1957, respectively.

Methods The study was designed as a historical cohort study and comprised 5627 identified men employed for more than six months. Cancer incidence was investigated from start of employment to 1995, and cause specific mortality was investigated from 1962 to 1995. The observed cases of cancers and observed deaths were compared with expected numbers calculated from national rates. Internal comparisons were made using Poisson regression with age and smoking included in the models. Historical exposure to PAH and fluoride had been estimated previously by use of statistical modeling on industrial hygiene measurements and process parameters. A job exposure matrix was used to investigate possible associations between cumulative exposures, and cancer incidence and cause specific mortality. Smoking habits were identified for 92% of the cohort members.

Results The study showed a significant excess risk for urinary bladder cancer among workers exposed to PAH, but no clear dose–response relationship. When using a 30-year lag period, a significant excess of bladder cancer in the highest exposure category ($> 2000\ \mu g/m^3$ .year PAH) was shown (SIR 4.08). The data also suggested an association between exposure to PAH and pancreatic cancer, but no association with lung cancer was seen. The mortality analysis indicated an association between exposure to potroom emissions (fluorides) and mortality from chronic bronchitis, emphysema and asthma, but no associations with cardiovascular diseases.

Conclusions The study findings are compatible with an excess risk for bladder cancer for aluminum plant workers exposed to PAH. The increased risk for cancer of the pancreas indicated, should be further evaluated in larger exposed populations. Am. J. Ind. Med. 37:175–183, 2000. © 2000 Wiley-Liss, Inc.

KEY WORDS: aluminum reduction plants; cancer incidence; mortality; søderberg; PAH; fluorides; bladder cancer; pancreatic cancer; COLD

INTRODUCTION

Several epidemiological studies of aluminum plant workers have shown excess risk of urinary bladder cancer [Tremblay et al., 1995; Spinelli et al., 1991: Ranneberg and Andersen. 1995], and some studies have also reported a moderately increased risk of lung cancer [Armstrong et al..

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Contract grant sponsor: The Nordic aluminium Industry's Secretanat for Health Environment and Safety Contract grant sponsor Confederation of Norwegian Business and Industry
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Accepted 27 September 1999

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1994; Spinelli et al., 1991; Andersen et al., 1982]. The excess risk has mainly been related to exposure to carcinogenic substances in coal tar pitch volatiles (CTPV) in Søderberg potrooms. Other types of cancers found in excess among workers in aluminum reduction plants in epidemiological studies are cancer of the pancreas [Rockette and Arena, 1983; Milham. 1979; Carta et al., 1992; Mur et al., 1987], kidney cancer [Gibbs, 1985; Spinelli et al.. 1991; Rockette and Arena, 19831, lymphatic cancer [Gibbs, 1985; Spinelli et al., 1991; Rockette and Arena. 19831, and leukemia [Andersen et al., 1982; Rockette and Arena, 1983; Mur et al., 19871. In an overall summary report, the International Agency for Research on Cancer (IARC) concluded that there was sufficient evidence implying that certain exposures occurring during aluminum production cause cancer and sufficient evidence from animal carcinogeneity studies implicating several of the individual components of the CTPV [IARC, 1987].

Epidemiological studies have shown associations between work in potrooms and mortality from cardiovascular diseases [Thériault et al., 1988; Rønneberg and Andersen, 1995], and both mortality studies and morbidity studies have shown relationships between work in potrooms and chronic obstructive lung diseases (COLD) [Milham, 1979; Rønneberg, 1995; Kongerud et al.. 1994].

Aluminum is produced by electrolysis of alumina (Al_2O_3) dissolved in molten cryolite (Na_3AlF_6). The electrolysis takes place in several carbon-lined steel shells (potlines). Alumina dust. solid fluoride salts. and hydrogen fluoride gas are emitted from the pots. The anode, which is situated at the top of the pot, is produced from coke with coal tar pitch as a binder. The anode is consumed during the process liberating carbon dioxide (CO_2), carbon monoxide (CO), and sulfur dioxide (SO_2). Two main types of anodes are used for electrolysis: continuous Søderberg anodes and prebaked carbon blocks. The Ssderberg anode is regularly supplied with unbaked anode paste at the top. The heating of the uncarbonized paste in the Søderberg anode leads to emissions of coal tar pitch volatiles. The prebaked anodes are baked in furnaces at a separate facility before being fitted into the pots, and they emit only small amounts of CTPV during electrolysis.

The present study concerned two Norwegian aluminum reduction plants: Hydro Aluminium Sunndal and Elkem Aluminium Mosjøen, which have been in operation since 1954 and 1957, respectively. The plants have mainly been operated by the Ssderberg process. The study focused on quantitative exposure to PAH and fluorides, and cancer incidence and cause specific mortality.

A description of the plants has been given elsewhere, where the historical exposure to polycyclic aromatic hydrocarbons (PAH) and fluoride was estimated objectively by using statistical modeling and industrial hygiene data describing the relationship between industrial hygiene measurements and process parameters [Romundstad et al., 19991.

MATERIAL AND METHODS

Before identification. the study group included 5663 men who had worked for six months or more at one of the two plants studied (Table I). Information on each employee was obtained from company records giving name, date of birth, departments,jobs, and dates for job changes. After the linkage of names. birth dates and available personal identification numbers to data from Statistics Norway, we were able to identify 5627 men by a personal identification number and the date of deaths and emigrations.

The cohort was divided into two subcohorts based on length of employment. Short-term employment was defined as less than three years of total employment and long-term employment as three or more years of total employment. All workers available for follow-up contributed with person-years in the short-term subcohort based on the first three years of employment. the remaining person-years were allocated to the long-term employment subcohort. The splitting of the cohort was performed due to a lack of accurate job descriptions and to a substantial lack of smoking data for those employed for less than three years.

TABLE I. The Study Cohort, Workers in Aluminum Reduction Plants, Norway

	Male employees with at least six months employment	Male employees with at least three years employment
The Sunndal plant	2938	2194
not identified (excluded)	14	3
The Mosjøen plant	2725	1867
not identified (excluded)	22	2
Included in the cancer incidence study	5627	4056
excluded in the mortality study due to death before 01.01.1962	16	8
Included in the mortality study	5611	4048

Dose–response analyses were only performed for those employed for more than three years.

Cancer Incidence

Each individual was observed for the event of cancer from the time of hire. Observation continued until 31 December 1995 or the time of death or emigration. For this period, the Cancer Registry of Norway gives a complete coverage of the population for all cancer sites except basal cell carcinoma of the skin, which was excluded in the present analysis. The analysis of cancer incidence was based on the ICD-7 code (3-digit code. International Classification of Diseases, ICD-7) as registered by the Cancer Registry of Norway. In the analyses of cancer incidence we used the standardized incidence ratio (SIR) and Poisson regression. SIRs were calculated as ratios between observed and expected numbers of all cancers as well as site-specific cancers. The expected numbers were calculated from five-year national cancer incidence rates among men by five-years age groups. The 95% confidence intervals (95% CI) were calculated assuming a Poisson distribution of the observed numbers.

Cause Specific Mortality

Each individual was observed from 1 January 1952 or time of hire if later. Observation continued until 31 December 1995 or the time of death or emigration. In the mortality analysis, observations during the first six months of employment were excluded due to the inclusion criteria of minimum six months employment. Sixteen persons who died before the follow-up started in 1962 were excluded from the mortality analysis. The mortality analysis was based on the classification code of death (3-digit code. International Classification of Diseases, ICD-9) as registered by Statistics Norway. The observation period spanned the 7th. 8th, and 9th revision of the ICD and the codes in the 7th and 8th revision were, therefore, transformed to the 9th revision [Rønneberg, 1995]. Cause specific mortality was analyzed by calculation of the standardized mortality ratio (SMR) and by use of Poisson regression for internal analysis.

The standardized mortality ratio (SMR) was calculated as the ratio between the observed and the expected numbers of deaths. The expected numbers were calculated from the biannual national mortality among men by five-years age groups. The 95% confidence intervals (95% CI) were calculated assuming a Poisson distribution for the observed numbers.

Exposure Data

The following agents were considered in this study: total paniculate PAH. total fluorides (gaseous and particulate), asbestos, and electromagnetic fields. The estimation of exposure to PAH and fluorides in the Søderberg potrooms is described in another paper [Romundstad et al., 1999]. The estimation was based on statistical modeling of personal measurements, stationary measurements and process data in order to obtain valid and objective estimates of job specific exposures from the start of operation to 1995. The estimation was performed in several steps. The relationship between measured area concentrations and process parameters were investigated by statistical modeling. Process parameters and the models were then used to estimate area concentrations in periods lacking area measurement data. Next, the relationships between the area measurements and job specific exposure (personal measurements) were investigated by use of a measurement model. In the last step, the obtained relationships were used to estimate job specific exposure. The job specific exposure estimates for PAH at the plants ranged from 2 to $> 3000\ \mu g/m^3$ and the fluoride estimates ranged from 0.1 to $1.7\ mg/m^3$. The exposure estimates of PAH and fluorides for jobs in departments other than the potrooms were mainly based on personal measurements.

Personal sampling did not include the maintenance personnel (mainly mechanics and electricians). Maintenance personnel working in the potrooms were assigned half the average exposure estimated for potmen in the respective potrooms. Maintenance personnel working in the carbon plant were assigned half the average exposure estimated for the carbon plant workers. The assignment of exposure was based on annual reports from the maintenance department, where maintenance work in these process departments was estimated at about 50% of the total work time.

Exposure to asbestos (mainly chrysotile) was assessed qualitatively based on the frequency and duration of dusty work involving asbestos handling. Workers in the cast house, pothers. and metal tappers were assigned as exposed to asbestos.

Exposures to static and time varying magnetic fields were estimated quantitatively based on the cell current and the cell design. A previous survey of Norwegian aluminum smelters showed a constant relation of about 0.06 mT//kA cell current for static fields. The time varying fields were between 0.01% and 0.1% of the static fields. and the time varying fields were therefore calculated as 0.05% of the static fields [Thommesen and Bjølseth, 19921. In the rectifiers the measurements indicated a level around $10\ \mu T$ for time varying fields [Thommesen and Bjdseth, 19921. As our estimates of static fields and time varying fields were strongly correlated. we only used the latter in the analysis.

Smoking Habits

Individual smoking habits abstracted from medical files at the health departments of the smelters included smoking

data for about 80% of the workers employed for more than three years. Additional information was gathered for about 12% of the workers through interviews with long time employees at each plant. The data were categorized into never smokers, current smokers, former smokers, and persons with unknown smoking status. In all, we had complete information on smoking habits for 92% of the workers employed for more than three years. Of these 27% were never smokers, 53% were current smokers, and 20% were ex-smokers. The general distribution of smoking habits was similar at the two plants.

Analysis of Dose–Response Relations

Cumulative exposure was used as an indicator of individual dose. This was calculated for each person-year under observation as the product of the estimated exposure intensity and duration summed for all jobs held. Thus, each person could contribute person-time to more than one exposure category in each analysis. 'Unexposed' person-time constituted one exposure category and the exposed person-years were divided into *two* or three cumulative exposure categories. We used two exposure categories if the number of expected cases was less than *25.*

In all the dose–response analyses involving cancer, we used a minimum lag of three years to exclude exposure in time periods when exposure was not likely to be related to cancer development. We also performed analyses applying lags of 10.20, and 30 years. In this study, lag was defined as the time period from causal action until the date of diagnosis [Rothman. 1981: Checkoway et ai., 1990].

Poisson Regression Analysis

Poisson regression analysis was used for internal dose–response analysis and for investigation of potential confounding effects from smoking. The calculation of SMR and the SIR and the Poisson regression analyses were performed using the program package 'EPICURE' [Preston et al.. 1993].

RESULTS

The study cohort comprised 5627 men who contributed 139,554 person-years to the investigation of cancer incidence and 5611 men who contributed 128,020 person-years to the investigation of cause specific mortality. The 4056 men who satisfied the long-term employment criteria Contributed 88.468 person-years in the cancer incidence analysis. In the mortality analysis. 4048 men contributed 85,089 person-years to the long-term employment subcohort.

Cancer Incidence

As shown in Table II, the cohort's incidence of cancer did not differ significantly from the expected values. except for a low incidence of malignant melanomas. The SIR of 1.97 for multiple myeloma is mainly due to an excess at one of the plants, where we observed 9 cases among the long-term employees vs. 3.6 expected (SIR = 2.5). A further evaluation of this unexpected finding showed that the increase was restricted to workers in the unexposed departments.

We found an excess risk of bladder cancer among the PAH-exposed subjects, but no dose–response relation (Table III). The SIR's for bladder cancer showed no increase with increasing lag time. An exception is the highest exposure category ($> 2000\ \mu g/m^3$ .year), where 30-years lag period showed a significant excess SIR of 4.08. This site was further evaluated by Poisson regression with a 30-year lag period in a model where age and smoking were included (Table IV). A non-significant increasing trend was shown ($P = 0.06$). no confounding from smoking was seen. There appeared to be a relationship between cumulative PAH exposure and cancer of the pancreas (Table V), but when cumulative exposure to PAH was lagged by 20 and 30 years, the association gradually diminished (not in Table). The result of the Poisson regression analysis of cumulative PAH exposure (lagged by 10 year). age and smoking, and the risk of pancreatic cancer is presented in Table VI. We found no indications of an association between cumulative exposure to PAH and the incidence of lung cancer (Tables VII, VIII).

We also investigated the potential associations between cumulative exposure to asbestos and the incidence of lung cancer, as well as between cumulative exposure *to* magnetic fields and lymphatic and hematopoietic cancers and between cumulative PAH exposure and kidney cancer. but found no associations (results not shown).

Cause Specific Mortality

Table IX shows mortality from selected causes of death by short time employment and long time employment. Neither total mortality nor cause specific mortality differed significantly from the expected value. The all cause mortality (SMR = 0.93) for those with more than three years of employment is at the same level as in other Norwegian industrial cohorts {Rønneberg, 1995; Hobbesland et al.. 1996]. The mortality in the long time employment group was somewhat lower than in the short time employment group.

There was no indication of an association between cumulative exposure *to* fluoride and mortality from cerebrovascular disease or between cumulative exposure to PAH and mortality from ischemic heart disease (results not shown). However, we found a dose–response relation-

TABLE II. Observed (Obs) and Expected (Exp) Number of Different Types of Cancer and Standardized Incidence Ratio (SIR) by Length of Employment Among 5627 Male Aluminum Smelter Workers in the follow-up Period from 1954 to 1995

		Less than 3 years of employment (51,076 person-years)				More than 3 years of employment (88,468 person-years)			
Cancer site	ICD-7 codes	Obs	Exp	SIR	95% CI	Obs	Exp	SIR	95% CI
All sites	140–204	83	98.5	0.84	0.67–1.04	342	358.4	0.95	0.86–1.06
Lip	140	0	1.2	0.00	0.00–3.07	2	4.2	0.48	0.06–1.72
Stomach	151	7	6.3	1.11	0.45–2.29	25	23.1	1.08	0.70–1.60
Colon	153	10	7.5	1.33	0.64–2.45	20	29.7	0.67	0.41–1.04
Rectum	154	4	4.8	0.83	0.23–2.13	20	19.4	1.03	0.63–1.60
Pancreas	157	2	2.9	0.70	0.08–2.49	13	11.5	1.13	0.60–1.94
Larynx	161	0	1.3	0.00	0.00–2.82	7	5.1	1.37	0.55–2.38
Lung	162	15	12.1	1.24	0.69–2.04	46	49.3	0.93	0.68–1.24
Pleura	163	0	0.4	0.00	0.00–10.3	0	1.5	0.00	0.00–2.46
Prostate	177	6	12.6	0.48	0.17–1.04	61	57.7	1.06	0.81–1.36
Testes	178	6	4.8	1.26	0.46–2.72	7	7.8	0.90	0.36–1.85
Kidney	180	3	3.7	0.82	0.17–2.37	12	14.0	0.86	0.44–1.50
Bladder	181	5	6.4	0.78	0.25–1.82	36	26.2	1.37	0.96–1.90
Malignant melanoma	190	3	6.0	0.50	0.10–1.46	6	16.8	0.36	0.13–0.78
other skin	191	3	2.9	1.05	0.21–3.02	10	11.6	0.86	0.41–1.58
Brain, nervous system	193	3	4.6	0.66	0.13–1.91	11	11.9	0.92	0.46–1.65
Unspecified	199	1	3.4	0.30	0.01–1.64	18	12.8	1.41	0.84–2.23
	201	3	1.5	2.00	0.41–5.84	4	2.8	1.43	0.39–3.67
Non-Hodgkins	200.202	1	2.8	0.36	0.01–1.99	5	8.9	0.56	0.18–1.31
Leukemia	204	2	2.4	0.84	0.10–3.05	9	7.3	1.23	0.56–2.34
Multiple myeloma	203	2	1.4	1.43	0.17–5.16	11	5.6	1.97	0.98–3.52
Another sites	–	7	9.5	0.73	0.30–1.51	19	30.8	0.62	0.37–0.96

ship between cumulative exposure to fluoride and mortality from COLD (Tables X. XI). As we had no cases in the lowest exposure group in the SMR analysis (X), we had to change the exposure cutpoints for the exposure groups in the Poisson regression analysis (Table XI).

DISCUSSION

Our study showed an increased risk of bladder cancer among aluminurn production workers exposed to PAH, indications of an increased risk of cancer of the pancreas and a relationship between mortality from chronic bronchitis, asthma, and emphysema. and exposure to potroom emissions (fluorides). We found no association between exposure to PAH and lung cancer. no association between magnetic field exposure and lymphatic and hematopoietic cancers. and no association between exposure to fluoride or PAH and mortality from cardiovascular diseases.

Our finding of an excess risk of bladder cancer among the PAH-exposed workers was in accordance with several other studies, though in the present study the finding is weaker than in the other studies [Tremblay et al., 1995; Spinelli et al., 1991]. A case–control study nested in a large Canadian cohort of aluminum plant workers showed a strong dose–response relationship between exposure to coal tar pitch volatiles and the risk of bladder cancer. and only small changes were seen with increasing lag time [Tremblay et al., 1995]. A possible explanation for these differences might be differences in the length and the magnitude of exposure [Tremblay et al., 1995].

In contrast to other studies of aluminum production workers and cancer [Armstrong et al., 1994; Spinelli et al., 1991; Andersen et al., 1982], we were not able to find an increased risk of lung cancer. The risk of lung cancer among aluminum plant workers has, however. not been consistent among epidemiological studies. Length and magnitude of exposure as well as variations in exposure to other lung carcinogens (asbestos. smoking) might explain some of the discrepancies. But it is interesting that the high exposure to PAH. experienced by the workers in the Ssderberg departments. did not seem to result in an increased risk of

TABLE III. Observed (Obs) and Expected (Exp) Number of Bladder Cancer and Standardized Incidence Ratio (SIR) by Cumulative Exposure to PAH ($\mu g/m^3 \cdot$ year)

Cumulative PAH exposure ($\mu g/m^3 \cdot$ year)	Obs	Exp	SIR	95% CI
Lag = 3 year				
<50	8	9.45	0.85	0.37–1.67
50–500	9	3.90	2.31	1.05–4.38
500–2000	8	6.55	1.22	0.53–2.41
>2000	11	6.30	1.75	0.87–3.12
Lag = 20 year				
<50	14	12.59	1.11	0.61–1.87
50–500	9	4.04	2.23	1.02–4.23
500–2000	5	5.56	0.90	0.29–2.10
>2000	8	4.01	1.99	0.86–3.93
Lag = 30 year				
<50	24	19.03	1.29	0.83–1.92
50–500	3	2.41	1.04	0.21–3.03
500–2000	4	3.99	1.16	0.32–2.97
>2000	5	1.25	4.08	1.32–9.51

TABLE IV. Poisson Regression Analysis of Bladder Cancer Risk by Cumulative Exposure to PAH ($\mu g/m^3 \cdot$ year), Age, and Smoking

Variable	Rate ratio	95% CI	P-value trend test
Age			
<55	1.0	–	
55–65	6.18	2.34–16.3	
65–70	10.69	3.46–33.0	
70–80	22.04	7.95–61.1	
80+	17.30	2.02–147	
Smoking			
Never smokers	1.0	–	
Former smokers	4.56	0.99–20.9	
Smokers	4.69	1.10–20.0	
unknown	1.23	0.11–13.6	
Cumulative PAH exposure ($\mu g/m^3 \cdot$ year), lag = 30 year			
<50	1.0	–	
50–500	1.07	0.31–3.40	
500–2000	1.13	0.38–3.40	0.06
<2000	3.71	1.33–10.3	

TABLE V. Observed (Obs) and Expected (Exp) Number of Pancreatic Cancer and Standardized Incidence Ratio (SIR) by Cumulative Exposure to PAH ($\mu g/m^3 \cdot$ year)

Cumulative PAH exposure $\mu g/m^3 \cdot$ year	Obs	Exp	SIR	95% CI
Lag = 3 year				
<50	2	4.21	0.47	0.06–1.72
50–500	2	1.71	1.17	0.14–4.22
>500	9	5.53	1.63	0.74–3.09
Lag = 10 year				
<50	2	4.61	0.43	0.05–1.57
50–500	2	1.76	1.14	0.14–4.11
>500	9	5.09	1.77	0.81–3.36

TABLE VI. Poisson Regression Analysis of Pancreatic Cancer Risk by Cumulative Exposure to PAH ($\mu g/m^3 \cdot$ year), Age, and Smoking

Variable	Rate ratio	95% CI	P-value trend test
Age			
<60	1.0	–	
60–70	3.68	0.64–3.56	
70–80	8.17	1.89–35.2	
80+	23.9	2.74–208	
Smoking			
Never smokers	1.0	–	
Smokers/former smokers	2.20	0.58–8.30	
Unknown	3.77	0.61–23.2	
Cumulative PAH exposure ($\mu g/m^3 \cdot$ year, lag = 10 year)			
<50	1.0	–	
50–500	2.55	0.36–18.2	0.016
>500	6.38	1.33–30.6	

lung cancer in this study. Our use of national rates in the calculation of SIR instead of regional rates has probably lowered the overall SIR of lung cancer in the present study somewhat due to a low background rate in one of the plants region. This has not affected our conclusions of no association, as no increasing trend in risk with exposure was found in the internal comparisons.

The indication of an increased risk of pancreatic cancers in this study, has also earlier been noted in epidemiological studies of aluminum workers [Rockette et al..

TABLE VII. Observed (Obs) and Expected (Exp) Number of Lung Cancer and Standardized Incidence Ratio (SIR) by Cumulative Exposure to PAH ($\mu g/m^3 \cdot$ year)

Cumulative PAH exposure ($\mu g/m^3 \cdot$ year)	Obs	Exp	SIR	95% CI
Lag = 3 year				
<50	17	17.51	0.97	0.57–1.55
50–500	8	7.45	1.07	0.46–1.98
500–2000	15	12.51	1.20	0.67–1.90
>2000	6	11.84	0.51	0.19–1.10
Lag = 20 year				
<50	23	24.46	0.94	0.60–1.41
50–500	13	7.54	1.72	0.92–2.95
500–2000	8	10.25	0.78	0.34–1.54
>2000	2	7.06	0.28	0.03–1.02

TABLE VIII. Poisson Regression Analysis of Lung Cancer R i by Cumulative Exposure to PAH ($\mu g/m^3 \cdot$ year), Age, and Smoking

Variable	Rate ratio	95% CI	P-value trend test
Age			
<55	1.0	–	
55–65	6.70	3.01–15.0	
65–70	14.91	6.09–36.5	
70–80	22.21	9.47–52.1	
80+	16.93	2.17–132.2	
Smoking			
Never smokers	1.0	–	
Former smokers/smokers	12.15	1.70–88.5	
Unknown	8.37	0.93–75.2	
Cumulative PAH exposure ($\mu g/m^3$. year), lag = 3 year			
<50	1.0	–	
50–500	0.91	0.37–2.25	
500–2000	1.39	0.70–2.75	>0.5
>2000	0.61	0.24–1.58	

1983; Milham, 1979; Carta et al., 1992; Mur et al., 19871. However, the low incidence of this type of cancer demands a larger study population at risk to be more conclusive.

The mortality analysis indicated an association between exposure to pot emissions measured by cumulative fluoride exposure and death from chronic bronchitis, emphysema, and asthma. This association was also to be expected since both morbidity and mortality studies have shown relationships between pot emissions and obstructive lung diseases [Milham, 1979: Rønneberg, 1995; Kongerud et al., 1994].

Recently, a paper has been published showing an increased mortality due to arrythmia related conditions and due to acute myocardial infarction among electric utility workers exposed to alternating magnetic fields [Savitz et al., 1999]. We, therefore, performed an additional analysis to investigate potential relations between magnetic field exposure and acute myocardial infarction, but we found no indication of an association.

TABLE IX. Observed (Obs) and Expected (Exp) Number of Deaths and Standardized Mortality Ratio (SMA) by Length of Employment and Causes of Death Among 5611 Male Aluminum Smelter Workers *in the* Follow-up Period from 1962 to 1995

		Less than 3 years of employment (42,931 person-years)				More than 3 years of employment (85,089 person-years)			
Cause of death	ICD-9 codes	Obs	Exp	SMR	95% CI	Obs	Exp	SMR	95% CI
All causes	1–999	207	208.35	0.99	0.9–12	712	766.27	0.93	am–1.00
cancer	140–209	46	47.93	0.96	0.7–1.3	180	189.73	0.95	0.82–1.10
Ischemic heart disease	410–414	62	57.77	1.07	0.8–1.4	240	240.52	1.00	0.88–1.13
Sudden death	798	6	6.69	0.90	0.3–2.1	21	25.21	0.83	0.52–1.27
Peripheral arteriosclerosis	440, 444, 785	2	1.21	1.65	0.2–6.0	5	5.36	0.93	0.30–2.18
Cerebrovascular disease	431–438	18	12.54	1.44	0.9–2.3	48	53.51	0.90	0.66–1.19
Hypertensive disease	401–405	2	1.99	1.00	0.1–3.8	5	8.31	0.60	0.20–1.40
Kidney disease	580–587,791	1	1.15	0.87	0.03–5.5	6	4.04	1.49	0.55–3.23
Chronic obstructive lung disease	490–493, 496	2	4.66	0.43	0.05–1.6	18	20.49	0.88	0.52–1.39
Pneumoconiosis	501–503.505	0	0.14	0.00	0.00–27.4	0	0.60	0.00	0.00–6.18
External causes	E800–999	33	32.93	1.00	0.7–1.4	60	69.83	0.86	0.66–1.11

TABLE X. Observed (Obs) and Expected (Exp) Number of Deaths from Chronic Obstructive Lung Disease (Bronchitis, Emphysem and Asthma) and Standardbed Mortality Ratio (SMR) by Cumulative Exposure to Fluoride (mg/m^3 fluoride . year)

Cumulative exposure Fluoride-mg/m^3 . year	Obs	Exp	SMR	95% CI
No lag				
<0.5	0	5.46	0.00	0.00–0.68
0.5–4.9	6	5.89	102	0.37–222
>5	12	9.14	1.31	0.68–2.29

TABLE XI. Poisson Regression Analysis of Mortality from Chronic Obstructive Lung Diseases (Bronchitis, Emphysem and Asthma) by Cumulative Exposure to fluoride (mg/m^3 Fluoride · year), Age, and Smoking

Variable	Rate ratio	95% CI	P-value trend test
Age			
<60	1.0	–	
60–70	6.29	1.66–23.8	
70–80	27.49	7.94–95.2	
80+	80.55	14.7–442	
Smoking			
Never smokers/ former smokers/ unknown smoking habits	1.0	–	
Smokers	17.3	2.8–130	
Cumulative fluoride exposure (mg/m^3 year, no lag)			
<2.5[a]	1.0	–	
2.5–7.5	3.26	0.66–16.2	0.004
>7.5	5.78	1.25–26.7	

[a]As we had no cases in the lowest exposure group (below 0.5 mg/m^3 · year), we had to change the cutoff point for this analysis in order to achieve cases in all groups.

The results from this study are not likely to have been seriously confounded by smoking as the internal analyses were only slightly affected after the inclusion and adjustment for smoking habits. Although the smoking variable was crude, well known associations between smoking and bladder cancer, lung cancer. pancreatic cancer, and COLD were obtained.

We had difficulties in specifically disentangling a risk posed by an individual agent as several of the exposure variables were correlated or appeared in mixtures (CTPV). Industrial hygiene measurements that had been performed indicated a strong correlation between exposure to SO_2, total particulates and the fluoride measurements. The fluoride exposure estimates might, therefore, be viewed as a surrogate measure also for these agents.

The use of respiratory protection became substantial during the early eighties when about 70% of the workers reported to have used such devices. Our exposure estimates have not been adjusted for the use of respiratory protection. as we had no data on individual use. This has probably not affected the results since the exposure was dramatically reduced during the same period of time [Romundstad et al., 1999].

We are reasonably sure that the exposure estimates used in this study described the actual exposure experienced by most of the workers [Romundstad et al., 19991. A potential limitation of the exposure evaluation of PAH is the possible qualitative differences in exposure to various PAHs or various components of the CTPV in different departments and jobs.

There is probably an important difference in the bioavailability of PAH in various industries and settings due to differences in the bonding properties of PAH to various particles. Dissolution or desorption of crystalline PAHs from a particle is normally a rapid reaction [Gerde et al., 1991]. However, when the binding energies for adsorbed PAHs are sufficiently high. the hydrocarbon will be tied almost irreversibly to the surface [Rivin and Atkins, 1987]. High binding energies has been found for carbonaceous particles in particular [Rivin and Atkins, 1987]. Recently, it has been shown that particulate PAH at aluminum smelters are more strongly adsorbed in soot carbon matrix in both effluent and recipient waters of aluminum reduction plants than was earlier believed [Næs et al., 1998]. Compared to petroleum derived PAHs, they are less available to desorption processes and presumably less bioavailable [Næs and Oug, 19971. The low solubility of the carcinogenic PAH relative to the greater solubility of less carcinogenic PAHs, and a strong adsorbance of carcinogenic PAH to carbon soot and alumina, might only give a negligible mass flux of carcinogenic PAHs to the lung tissue. If this is correct, most of the potentially harmful PAHs might pass through the body, or at least the target tissue in the lung, without being metabolized. This might explain why an apparently massive exposure to PAH have not resulted in an increased risk of lung cancer in this study.

The strength of this study lies in the exposure assessment, the available smoking data, and the possibility of a reliable computation of cancer morbidity. The Cancer Registry of Norway gives a near 100% complete coverage of all cancers in Norway based on information from pathological laboratories. compulsory reporting from physicians and clinical departments. and death certificates from Statistics Norway. Since 1953. about 85% of the cancers have been histologically verified and <2% are based on the death certificate alone.

A complete cohort with few unidentified persons should also give confidence to the results of this study. Furthermore, the findings in this study are strengthened by the use of both internal and external groups for comparisons and by the fact that the findings were similar at the two plants investigated.

ACKNOWLEDGMENTS

We acknowledge the support from the project committee members Eirik Nordheim, Erle Grieg Astrup, Arvid Bastiansen, Bjørn Bergan Skar, Per Iver Øksne, Sverre Langård and Bjørn Hilt. We thank Jahn Ivar Martinsen for valuable help in programming and data analysis, and Håkon Lasse Leira for constructive comments.

REFERENCES

Andersen A. Dahlberg BE, Magnus K, Wannag A. 1982. Risk of cancer in the Norwegian aluminum industry. Int J Cancer 29:295–298.

Andersen KE, Potter JD, Mack TM. 1996. Pancreatic cancer. In. Schottenfield D. Fraumeni JF Jr. editors. Cancer epidemiology and prevention. New York: Oxford University Press, p 725-771.

Armstrong B. Tremblay C. Baris D. Thériault G. 1994. Lung cancer mortality and polynuclear aromatic hydrocarbons: a case-cohort study of aluminum production workers in Arvida, Quebec, Canada. *Am* J Epidemiol 139:250–262.

Breslow NE, Day NE. 1987. Statistical methods in cancer research; vol II (The design and analysis of cohort studies). Lyoo: International Agency for Research on Cancer (IARC).

Carta P, Cocco PL. Flore C, Pau M, Grussu M, Cherchi P. 1992 Mortality in workers of a primary aluminum foundry in Portovesme in Sardinia. Med Lav 83(5):530–535.

Checkoway H. Pearce N. Hickey JLS, Dement JM. 1990. Latency analysis in occupational epidemiology. Arch Environ Health 45:95–100.

Gerde P, Medinsky MA. Bond JA. 1991. Particle associated polycyclic aromatic hydrocarbons—a reappraisal of their possible role in pulmonary carcinogenesis. Toxicol Appl Pharmacol 15:108 (1):1–13.

Gibbs GW. 1985. Mortality of aluminum reduction plant workers. 1950 through 1977. J Occup Med 27:761–770.

Grandjean P. Olsen JH. Juel K. 1983. Excess cancer incidence among workers exposed to fluoride. Scand J Work Environ Health (19 Suppl.) 1:108–109.

Hobbesland A, Kjuus H. Thelle DS. 1996. A study of mortality among 14,730 male workers in 12 Norwegian Ferroalloy plants: Cohort characteristics and the main cause of death. Occup Environ Med 53(8):540–546.

IARC. 1987. IARC Monographs on the evaluation of the carcinogenic risk of chemicals to humans. Supplement 7: Overall evaluations of carcinogenicity: an updating of IARC. Monographs volumes 1 to 42. Lyon, France: International Agency for Research on Cancer, 1987;89-91 IARC scientific publications no. 82:96–7.

Kongerud J, Bøe J. Søyseth V. 1994. Aluminum potroom asthma: the Norwegian experience. Eur Respir J 7(1):165–172.

Milham S. Mortality in aluminum reduction plant workers. 1979. J Occup Med 21:475–480.

Mur JM. Moulin JJ, Meyer-Bisch C, Massin N, Coulon JP, Loulergue J. 1987. Mortality of aluminum reduction plant workers in France. Int J Epiderniol 16257-264.

Næs K, Axelman J, Naf C, Broman D. 1998. Role of soot carbon and other carbon matrices in the distribution of PAHs among particles, DOC. and the dissolved phase in the effluents and recipient waters of an aluminum reduction plant. Environ Sci Technol 32(12):1786-1792.

Næs K, Oug E. 1997. Multivariate approach to distribution patterns and fate of polycyclic aromatic hydrocarbons in sediments from smelter-affected Norwegian fjords and coastal waters. Environ Sci Technol 31(5):1253–1258.

Preston DL, Lubin JH, Pierce DA, McConney ME. 1993. Epicure. Seattle, Washington: Hirosoft International Corporation. 1993.

Rivin D, Atkins DH. 1987. Sorption of bioactive material on carbon. Carbon 25:135-145.

Rockette HE, Arena VC. 1983. Mortality studies of aluminum reduction plant workers: potroom and carbon department. J Occup Med 25:549–557.

Romundstad PR Haldorsen T. Rønneberg A. 1999. Exposure to PAH and fluoride in aluminum reduction plants in Norway: historical estimation of exposure using process parameters and industrial hygiene measurements. *Am* J Ind Med 35:164-174.

Rothman KJ. Induction and latent periods. 1981. *Am* J Epidemiol 114253-259.

Rønneberg A, Andersen A. 1995. Mortality and cancer morbidity in workers from an aluminum smelter with prebaked carbon anodes—part II: cancer morbidity. Occup Environ Med 52:250–254.

Rønneberg A. 1995. Mortality and cancer morbidity in workers from an aluminum smelter with prebaked carbon modes—part III: mortality from circulatory and respiratory diseases. Occup Environ Med 52255 –261.

Savitz DA. Liao D, Sastre A. Kleckner RC. Kavet R. 1999. Magnetic field exposure and cardiovascular disease mortality among electric utility workers. *Am* J Epidemiol 149135-142.

Spinelli JJ, Band PR, Svirchev L. Gallagher RP. 1991. Mortality and cancer incidence in aluminum reduction plant workers. J Occup Med 33:1150-1155.

Thériault GP, Tremblay CG. Armstrong BG. 1988. Risk of ischemic heart disease among *primary* aluminum production workers. Am J Ind Med 13:659–666.

Thommesen G. Bjølseth P. 1992. Static and low frequency magnetic fields in Norwegian alloy and electrolysis plants. Report 1992.1. Oslo: National Institute of Radiation Hygiene, 1992 (in Norwegian).

Tremblay C. Armstrong B, Thériault G, Brodeur J. 1995. Estimation of risk of developing bladder cancer among workers exposed to coal tar pitch volatiles in the primary aluminum industry. Am J Ind Med 27:335–348.