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A mortality study among workers in a French aluminium reduction plant

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Abstract ***Objective:*** A mortality study on the association between lung cancer and occupational exposure to polycyclic aromatic hydrocarbons (PAHs) was carried out in a French aluminium reduction plant. This study updated a previous mortality study. ***Method:*** The historical cohort included every male worker who had been employed in the plant for at least 1 year between 1950 and 1994. Workers were followed-up for mortality from 1968 to 1994. Causes of death were obtained from death certificates. Standardised mortality ratios (SMRs) and 95% confidence intervals (CI) were computed using regional mortality rates as external reference to compare observed and expected numbers of deaths, adjusted for gender, age and calendar time. ***Results:*** The cohort comprised 2,133 men, of whom 335 died during the follow-up period. The observed mortality was lower than expected for all causes of death (SMR = 0.81, CI 0.72–0.90) and for lung cancer (observed = 19, SMR = 0.63, CI 0.38–0.98). No lung cancer excess was observed in workshops where PAH exposure was likely to have occurred, and no trend was observed according to duration of exposure and time since first exposure. This low lung cancer mortality could be partly explained by a marked healthy worker effect and a possible negative confounding by smoking. An excess was observed for bladder cancer (observed = 7, SMR = 1.77, CI 0.71–3.64) in the whole cohort, that was higher among workers employed in workshops where PAH exposure was likely to have occurred (observed = 6, SMR = 2.15, CI 0.79–4.68). In addition, an SMR higher than unity was observed for ''psychoses and neuro-degenerative diseases'' (observed = 6, SMR = 2.39, CI 0.88–5.21), that could not be related to occupational aluminium exposure. ***Conclusion:*** No lung cancer risk was detected. Non-significant excesses were observed for bladder cancer and for psychoses and neuro-degenerative diseases.

Key words Lung cancer · Bladder cancer · Alzheimer's disease · Aluminium · Polycyclic aromatic hydrocarbons

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Introduction

A mortality study was carried out by the French National Institute for Research and Safety (INRS), among workers in one aluminium reduction plant. The study was conducted by request of the Aluminium Pechiney company. The aim was to assess the possible relationship between lung cancer mortality and employment in workshops where exposure to polycyclic aromatic hydrocarbons (PAHs) was likely to have occurred [17]. Such a relationship has been assessed by the International Agency for Research on Cancer (IARC) [17, 19], and recently reviewed by Boffetta et al. [4] from the international literature [1, 2, 7, 12, 13, 23, 26, 27, 31, 32, 36, 39].

A previous mortality study, that had been conducted by the INRS in workers of the 11 French plants of the Aluminium Pechiney company, covered the follow-up period 1950–1976 [26]. The present study was an update of the mortality study of workers in one of these plants.

Material and methods

Industrial process and occupational exposure to PAHs

Aluminium is produced by reducing alumina in large electrolytic cells called ''pots''. The anodes are made of a baked mixture of coke and petroleum pitch, and lie in an electrolytic bath containing

alumina and a fluxing agent (cryolite). Two types of anodes are used: continuous Söderberg, and prebaked. In the Söderberg process, anode paste is supplied to permanent anodes and baked continuously in the potroom. Exposure to PAHs may occur due to the evaporation of volatile coal-tar pitch from the anode [17]. Prebaked electrodes are manufactured in a carbon-workshop which is separated from the potrooms, so that PAH exposure is much lower than that in the Söderberg process [17]. The two types of anode co-existed in the plant under study: prebaked anodes have been used since 1902, whereas Söderberg cells had been used between 1952 and 1982, so only prebaked anodes have been used since 1982.

Aluminium from the pots is carried to the casthouse to be moulded into wires, plaques, ingots, and so on. Delining consists of removing the old cathodes and crusts of solidified baths out of the pots, using pneumatic hammers.

Cohort definition and data collection

The cohort included every male worker who had been employed in the plant for at least 1 year between 1 January 1950 and 31 December 1994. The required individual information was name, date and place of birth, and job history, i.e. successive periods of employment in the different workshops with dates of starting and leaving. In order to obtain a complete cohort, we collected these data from several sources:

- Data already recorded in the previous study for the period 1950–1976 [26]
- Computerised data in an available file from the Personnel department for the period 1980–1994
- Administrative registers for the hiring and the leaving of workers for the period 1977–1979
- Individual administrative records of the Personnel department, to obtain complete job histories.

The information available on smoking was that previously collected by the occupational physician of the plant, during the yearly clinical examination of workers. This information was classified as "never", "former", and "current" smoker. Current smokers were further divided into "slight", "medium" and "heavy" smokers (1–10, 11–20 and >20 cigarettes/day respectively). Only the latest available information, i.e. more often the smoking status of each worker at the date of leaving the plant, was abstracted from medical records. No information was available on whether a subject might have changed smoking habits after having left the plant.

Vital status was assessed using registers of birthplaces for people born in France, and the national file of deaths from the Institut National de la Statistique et des Etudes Economiques (INSEE). Causes of death were abstracted from the death certificate national file of the Institut National de la Santé et de la Recherche Médicale (INSERM). As this file was set up in 1968, the follow-up period of the study covered the period 1 January 1968 to 31 December 1994. The file of the INSERM, which contains all causes of death given on French death certificates, is the only available source of information. The eighth and ninth revisions of the International Classification of Diseases (ICD8 and ICD9) (three-digit codes) [40, 41] were used for the periods 1968–1978 and 1979–1994 respectively. The source of information on causes of death, i.e. death certificates registered by the INSERM, was the same for the study cohort and the general population used as a reference.

Statistical analysis

Standard methods as described by Breslow and Day [6] were used to compute person-years at risk, expected numbers of causes of death, and standardised mortality ratios (SMRs) adjusted for gender, age and calendar time, using the program written by Coleman et al. [10]. Regional death rates were used for the calculation of expected numbers of causes of death. Ninety five percent confidence intervals (95% CI) of the SMRs were computed under the standard Poisson assumption [6, 10].

Due to the lack of reliable information on their vital status, workers lost to follow-up, i.e. workers born abroad and those with no known birth place in France, were censored from the calculation of person-years on the date of leaving the plant. Moreover, the calculation of person-years was limited to age groups of under 85 years since (1) the information on the number of individuals provided by census of the general population is not sufficiently detailed or precise for individuals above the age of 85, and (2) the lack of precise information on causes of death is important among the elderly [16]. We tested the trends with quantitative parameters using the exposure ranks as dose levels in the method described by Breslow and Day [6].

Description of the study population

The initial database was comprised of 2,465 male workers. As the follow-up period started on 1 January 1968, some individuals were excluded from the study: those who had died or who had reached the age of 85 before 1 January 1968, and those who were lost to follow-up before this date. As a result, 2,133 workers were included in the study, leading to 35,145 person-years. The mean follow-up period was 16.5 years, and the number of workers considered as lost to follow-up was 235. The causes of death were ascertained for 94% (316 deaths) of the 335 recorded deaths. Table 1 gives the distribution of workers according to date of first employment, and the numbers of workers employed at different cross-sectional times over the decades.

Exposure assessment

An attempt was made to assess occupational exposure to PAHs. This required the identification of periods of employment in workshops where such exposure was likely to have occurred, i.e. Söderberg and prebake potrooms, electrode manufacture department, exhaust ventilation operations, pot-lining, and maintenance [2, 17, 39]. Unfortunately, the data available on individual job histories did not provide any relevant information, since the only category available was "potroom", and no data with further details on whether they referred to Söderberg or prebake, were available. Furthermore, considering periods of time when only the prebake process was used, in particular the earliest period between 1910 and 1952, no assessment of exposure levels was possible due to the lack of exposure measurements. This made it impossible to consider the groups definitely exposed to PAHs. Consequently, only a broad definition of PAH exposure was employed, based on "having ever been employed in the potroom, electrode manufacture department, exhaust ventilation operations, pot-lining, and maintenance".

Asbestos exposure should be considered, as it may be a confounding factor in the investigation of lung cancer risk due to PAHs. Unfortunately, no relevant information was available, either on periods of employment in specific jobs giving rise to

Table 1 Description of the study population

Years of first employment	Numbers	%	Active workers over time	
1910–1919	7	0.33	1950	423
1920–1929	36	1.69	1955	538
1930–1939	134	6.28	1960	688
1940–1949	246	11.53	1965	768
1950–1959	402	18.85	1970	800
1960–1969	332	15.56	1975	746
1970–1979	407	19.08	1980	844
1980–1989	444	20.82	1985	716
≥1990	125	5.86	1990	728
			1994	645

asbestos exposure, or on exposure levels in workshops. The only surrogate that could be used was periods of employment in workshops where asbestos exposure might have occurred, that is, potroom, casting, electrode manufacture department, exhaust ventilation operations, pot-lining, and maintenance.

Results

Selected causes of death

The observed overall mortality (observed = 335, SMR = 0.81, CI 0.72–0.90) (Table 2) and the mortality from all cardiovascular diseases (SMR = 0.81, CI 0.65–0.99), cerebro-vascular diseases (SMR = 0.47, CI 0.26–0.79), travel accidents (SMR = 0.37, CI 0.12–0.87), and all cancer sites (SMR = 0.78, CI 0.63–0.94) were lower than expected. A significant low mortality was also observed for lung cancer (SMR = 0.63, CI 0.38–0.98). Conversely, some of the excesses that we observed for mortality due to bronchitis and emphysema (SMR = 1.40, CI 0.51–3.05), bladder cancer (SMR = 1.77, CI 0.71–3.64), and cancer of the pleura (SMR = 1.42 based on one observed case) were non-significant.

Table 2 Mortality from selected causes of deaths. Standardised mortality ratio (SMR): observed (obs) / expected numbers of death. Reference: French regional population. Follow-up period: 01.01.1968 to 31.12.1994 (*CI* confidence intervals)

	Obs	SMR	95% CI
All causes	335	0.81	0.72–0.90
Circulatory system	93	0.81	0.65–0.99
Hypertensive diseases	3	1.05	0.22–3.08
Ischaemic heart diseases	39	0.97	0.69–1.33
Cardiac arrhythmias	3	0.43	0.09–1.25
Cerebrovascular diseases	14	0.47	0.26–0.79
Heart failure	12	0.88	0.46–1.54
Respiratory system	17	0.74	0.43–1.18
Pneumoconiosis	0	0.00	0.00–2.91
Chronic bronchitis. Emphysema	6	1.40	0.51–3.05
Fibrosis	0	0.00	0.00–9.30
Digestive system	28	0.83	0.55–1.21
Cirrhosis of the liver	19	0.88	0.53–1.38
Endocrinous diseases	3	0.50	0.10–1.46
Mental diseases	4	0.38	0.10–0.98
Nervous system and sense organs	8	1.05	0.46–2.08
Psychoses and neuro-degenerative diseases	6	2.39	0.88–5.21
Accidents and violence	43	0.79	0.57–1.07
Suicides	11	0.81	0.41–1.45
Travel accidents	5	0.37	0.12–0.87
All malignant neoplasms	101	0.78	0.63–0.94
Buccal cavity. Pharynx	8	0.70	0.30–1.38
Larynx	7	1.11	0.45–2.29
Oesophagus	5	0.55	0.18–1.28
Stomach	6	0.84	0.31–1.83
Colon-intestine	6	0.76	0.28–1.65
Rectum	1	0.27	0.01–1.53
Liver	4	0.71	0.19–1.81
Pancreas	5	1.10	0.36–2.57
Lung, bronchus	19	0.63	0.38–0.98
Pleura	1	1.42	0.04–7.90
Bone and sarcoma	0	0.00	0.00–2.35
Prostate	6	0.63	0.23–1.36
Bladder	7	1.77	0.71–3.64
Brain	1	0.54	0.01–2.99
Hodgkin and lymphoma	1	0.24	0.01–1.33
Leukaemia	2	0.57	0.07–2.07

With respect to central nervous system diseases, the SMR was close to unity for "diseases of the nervous system and sense organs" (SMR = 1.05, CI 0.46–2.08), whereas a significantly low mortality appeared for "all mental disorders" (SMR = 0.38, CI 0.10–0.98). However, the grouping together of the codes which included Alzheimer's disease, i.e. codes 290 of ICD8 and ICD9 and 331 of ICD9 [40, 41], hereafter named "psychoses and neuro-degenerative diseases", led to a high but non statistically significant SMR (SMR = 2.39, CI 0.88–5.21). Three of these six observed cases were Alzheimer's disease (ICD9 four-digit code 331.0), the other three being coded "unspecified neuro-degenerative diseases" (ICD9 four-digit code 331.9) [40, 41]. As these diseases generally occur in the elderly, person-years and expected numbers were further estimated, including age groups of over 85: the rough estimate of the SMR thus obtained was 1.89 (observed = 6, estimated expected = 3.18, estimated CI 0.69–4.11).

Qualitative and quantitative parameters

Using time since first exposure, we observed a significant, increasing trend for the overall mortality (Table 3). No trend appeared for lung and bladder cancer. Regarding "psychoses and neuro-degenerative diseases", we obtained a significant excess for workers with more than 30 years since first employment (SMR = 2.88, CI 1.06–6.27).

The overall mortality increased significantly with duration of employment, whereas no clear pattern was observed for the other selected causes of death (Table 3).

Tables 4 and 5 give SMRs by workshop and SMR according to duration of employment in workshops where PAH exposure was likely to have occurred, i.e. electrolysis, electrode manufacture department, exhaust ventilation operations, pot-lining, and maintenance workshops. The SMR for all causes of death was significantly lower than unity among maintenance workers (SMR = 0.74, CI 0.59–0.92). No trend was observed for lung cancer mortality according to duration of PAH exposure.

Regarding bladder cancer, we observed no clear pattern with regard to workshops (Table 4). Although non-significant, the SMR of workers considered as exposed to PAHs (SMR = 2.15) contrasted with that of non-exposed (SMR = 0.85) (Table 5), and a non-significant trend was observed according to duration of exposure, with an SMR of 2.54 (observed = 5, CI 0.82–5.92) for workers exposed for more than 10 years (Table 5).

As the Söderberg process started in 1952, workers who left the plant before this date would have been employed in the prebake potroom only. The SMRs of these workers were 0/0.52 for lung cancer and 0/0.10 for cancer of the bladder. These results could not be interpreted due to the low numbers involved.

Table 3 Mortality from selected causes of death according to time since first employment and duration of employment (*Obs* observed, *SMR* standardised mortality ratio, *CI* confidence intervals)

Time since first employment	All causes			Lung cancer			Cancer of the bladder			Psychoses and neuro–degenerative diseases[a]		
	Obs	SMR	95% CI	Obs	SMR	95% CI	Obs	SMR	95% CI	Obs	SMR	95% CI
0–9 years	17	0.59	0.34–0.94	0	0.00	0.00–2.52	0	0.00	0.00–36.19	0	0.00	0.00–80.18
10–19 years	33	0.67	0.46–0.94	3	0.91	0.19–2.66	1	3.96	0.10–22.07	0	0.00	0.00–39.54
20–29 years	69	0.74	0.57–0.93	4	0.53	0.14–1.36	0	0.00	0.00–4.74	0	0.00	0.00–13.09
≥30 years	216	0.89	0.77–1.01	12	0.67	0.35–1.18	6	2.12	0.78–4.62	6	2.88	1.06–6.27
Test for trend (*P*)	0.023			0.65			0.68			0.33		
Duration of employment												
0–9 years	68	0.63	0.49–0.79	3	0.37	0.08–1.08	1	1.12	0.03–6.25	1	1.96	0.05–10.92
10–19 years	59	0.70	0.53–0.90	6	1.07	0.39–2.34	2	2.76	0.33–9.99	1	2.20	0.06–12.28
20–29 years	108	1.00	0.82–1.20	4	0.49	0.13–1.24	2	1.84	0.22–6.65	1	1.53	0.04–8.54
≥30 years	100	0.88	0.72–1.08	6	0.73	0.27–1.60	2	1.59	0.19–5.74	3	3.37	0.70–9.85
Test for trend (*P*)	0.006			0.60			0.95			0.62		

[a] ICD8 and ICD9: 290; ICD9: 331

Table 4 Mortality from selected causes of death according to workshop (*Obs* observed, *SMR* standardised mortality ratio, *CI* confidence intervals)

	All causes			Lung cancer			Bladder Cancer			Psychoses and neuro-degenerative diseases[a]		
	Obs	SMR	95% CI	Obs	SMR	95% CI	Obs	SMR	95% CI	Obs	SMR	95% CI
Potroom	148	0.88	0.74–1.03	11	0.88	0.44–1.57	3	1.88	0.39–5.50	0	0.00	0.00–3.79
Casthouse	58	0.81	0.61–1.04	2	0.40	0.05–1.43	2	2.96	0.36–10.68	0	0.00	0.00–8.45
Exhaust ventilation operations	2	0.93	0.11–3.37	1	6.13	0.16–34.14	0	0.00	0.00	0	0.00	0.00
Pot-lining	5	0.51	0.17–1.19	0	0.00	0.00–3.97	0	0.00	0.00–35.44	0	0.00	0.00–68.82
Electrode manufacture department	67	1.07	0.83–1.36	3	0.72	0.15–2.09	2	3.35	0.41–12.09	0	0.00	0.00–9.03
Maintenance	81	0.74	0.59–0.92	5	0.60	0.19–1.40	3	2.83	0.58–8.28	3	4.66	0.96–13.62
Manutention	51	1.17	0.87–1.54	2	0.66	0.08–2.37	2	4.49	0.54–16.24	1	3.41	0.09–18.98
Control laboratory	7	0.99	0.40–2.05	1	1.57	0.04–8.73	0	0.00	0.00–54.89	0	0.00	0.00
Research laboratory	45	0.88	0.64–1.17	5	1.26	0.41–2.93	0	0.00	0.00–7.57	2	7.34	0.89–26.52
General services	43	0.86	0.63–1.16	2	0.51	0.06–1.85	0	0.00	0.00–6.92	1	2.84	0.07–15.82

[a] ICD8 and ICD9: 290; ICD9: 331

Table 5 Mortality from selected causes of death according to duration of employment in workshops where PAH exposure was likely to have occurred (*Obs* observed, *SMR* Standardised Mortality Ratio, *CI* confidence intervals)

	All causes			Lung cancer			Cancer of the bladder		
	Obs	SMR	95% CI	Obs	SMR	95% CI	Obs	SMR	95% CI
Non-exposed	87	0.72	0.58–0.89	4	0.47	0.13–1.20	1	0.85	0.02–4.76
Exposed									
< 10 years	68	0.71	0.55–0.90	5	0.69	0.22–1.61	1	1.22	0.03–6.79
10–19 years	58	0.80	0.60–1.03	4	0.84	0.23–2.15	2	3.13	0.38–11.32
20–29 years	59	0.87	0.66–1.12	3	0.56	0.11–1.65	1	1.46	0.04–8.11
≥30 years	63	1.09	0.84–1.39	3	0.70	0.14–2.05	2	3.11	0.38–11.24
P for trend	0.01			0.68			0.29		
Total exposed	248	0.84	0.74–0.95	15	0.69	0.39–1.15	6	2.15	0.79–4.68

Although three subjects who died from "psychoses and neuro-degenerative diseases" had been employed in maintenance activities, no death was observed among workers employed in workshops where aluminium was produced (Table 4).

Regarding asbestos exposure, the grouping of workers who had ever been employed in workshops where such exposure might have occurred did not show any specific pattern, since the lung cancer SMR was 0.62 (observed = 15, CI 0.35–1.02).

Smoking

Information on tobacco consumption was available for 1,560 employees, i.e. 73% of the study population. The

percentages of never, former and current smokers were 35.4%, 22.9%, and 41.7%, respectively. The distribution of current smokers was light (11.4%), medium (24.7%), and heavy (5.6%) smokers. Although the numbers involved were low, slight dose-response relationships were observed when we considered never, light, medium and heavy smokers, the SMRs being (1) 0.68 (observed = 65), 0.67 (observed = 29), 1.05 (observed = 113), and 1.20 (observed = 17), respectively, for mortality due to all causes of death, (2) 0.29 (observed = 2), 0.00, 0.99 (observed = 7), and 1.72 (observed = 2), respectively, for mortality due to lung cancer, and (3) 2.23 (observed = 2), 2.29 (observed = 1), 1.88 (observed = 2), and 7.32 (observed = 1), respectively, for mortality due to bladder cancer.

Discussion

Follow-up update

An industry-wide study had been carried out in the 11 plants of the French aluminium smelting industry [26]. This study included 6,455 workers followed-up for mortality between 1950 and 1976. It showed a slight but non-significant lung cancer excess of 1.14 based on 37 observed deaths in the full cohort, that could not be related to occupational exposure to PAHs [26]. However, the interpretation of this study was hampered by the fact that (1) the information on periods of employment in Söderberg vs prebake potrooms was available for only 31% of the population under study, (2) causes of death had been collected from general and hospital practitioners which led to only 71.3% of known causes of death (access to death certificates was not possible at this time in France), and (3) the source of information on causes of death was not the same in the cohort (general practitioners) and in the reference group (death certificates) [26]. Due to the high proportion of unknown causes of death, we had to transform the actual observed numbers of causes of death into estimated observed numbers, using a correcting factor [26].

The present paper is an update of the mortality investigation in the largest plant in the previous study. An improvement was made by the collecting of causes of death from death certificates over the period 1968-1994: this led not only to an increased number of known causes of death (94%) but also to the use of the same source of information as in the reference population.

Cohort definition

Some mechanisms of selection might have resulted from the criteria adopted for the inclusion of subjects in the cohort [8, 20]:

- The study population was made up of two sub-cohorts: the cross-sectional sub-cohort of 423 workers active at 1 January 1950 (Table 1) and the dynamic sub-cohort of 1,710 workers first employed between 1 January 1950 and 31 December 1994 [26]. The possible healthiness selection among workers of the cross-sectional sub-cohort is likely to be balanced by the dynamic sub-cohort for which there is no selection resulting from survival [20].
- The follow up period 1950–1967 was not included in the present study as causes of death prior to 1968 had been provided by general practitioners (about 30% of unknown causes). However, this could be another healthiness selection because only workers still alive in 1968 were included in the present study cohort. This survival selection is likely to result in a loss of statistical power to investigate risks due to the earliest periods of employment.
- Workers born abroad contributed to person-years for as long as they were employed in the plant, and were censored from the calculation of person-years at the date of leaving. This was due to the lack of reliable information on their vital status since they were not born in France and the file of the INSEE is not exhaustive for foreign subjects. Although this results in a loss of statistical power, it is unlikely to be a bias as we had no information indicating that foreign workers have had jobs with heavier exposure than other workers.

These mechanisms of selection may account for a part of the overall low mortality observed in the study.

External reference

In order to control for possible geographic factors [30], we used the death rates of the regional general population to calculate expected numbers of deaths. Since a large proportion of the workforce might have left this district, one may consider that regional death rates are inappropriate. The SMRs were slightly modified when we used national death rates: SMR = 0.80 (CI 0.72–0.89) for all causes of death, SMR = 0.77 (CI 0.62–0.95) for cardiovascular diseases, SMR = 0.74 (CI 0.61–0.90) for all malignant neoplasms, and SMR = 0.61 (CI 0.37–0.95) for lung cancer. This indicates that regional death rates were likely to be relevant.

Exposure assessment

When writing the study protocol, the investigators considered that, in addition to the cohort study, further investigations could be performed: a nested case-control study for the collection of relevant information on job histories and smoking, and a job-exposure matrix to assess PAH and asbestos exposure levels. The feasibility of the nested case-control study was assessed through (1) a complete review of available information on job histories from administrative records of the plant, and (2)

the possibility of interviewing former workers, providing data on past working conditions. The investigators concluded that the relevant information for such a study was not available, so that no further nested case-control study could be conducted.

Söderberg cells had been used between 1952 and 1982 only, whereas prebaked anodes started to be utilised in 1902. Table 1 indicates that the relevant periods of employment in this study date from the 1910s to the 1920s for the earliest ones. This made it difficult to assess occupational exposure due to the lack of information on exposure levels in workshops, in particular in prebake workshops in the 1910s and 1920s. As a consequence, the investigators of the study decided not to attempt any further exposure assessment, in particular not to develop a job-exposure matrix.

This lack of accurate assessment of PAH exposure is a weakness of this study, meaning that periods of employment in the Söderberg potroom could not be distinguished from periods in the prebake potroom. As a consequence, only broad exposure definitions were used, which decreased the statistical power to detect a lung cancer excess due to exposure to PAHs.

Smoking

Occupational cohort mortality studies are often carried out using company records for the data collection. These studies use historical cohorts, so that a large proportion of the study workers is no longer currently employed when information is collected. As a consequence, no smoking data are available in most historical cohort studies [3, 37]. However, due to the fact that French workers have to undergo a yearly clinical examination, an attempt was made to take smoking into account.

This information on smoking must be interpreted with caution, firstly because a smoking-habit was known for only 73% of the study population, and secondly, because misclassifications are likely to have been introduced. In the first case, the smoking information was known more often about living subjects, since the lung cancer SMR was 0.57 for workers with known smoking-habits, as compared with 0.81 for unknown smoking information. Other misclassifications may be due to the fact that (1) information on smoking had been asked for by different occupational physicians, and at different times over the period 1950-1994, (2) only the latest available information, more often at the date of leaving the plant, for non active workers, was collected for the study, and (3) some individuals may have changed their tobacco consumption after leaving. As an example, the less relevant information is ''former smoker'' since the time elapsed between the date of giving up smoking was unknown. Despite these limitations, the observed dose-response relationship provides some credibility to the quality of smoking data.

The percentage of smokers was found to be 41.7%. According to several surveys of the French male population, performed over the past few decades, the proportion of smokers decreased from approximately 70% in the 1960s to approximately 40% in the 1990s [25]. In so far as the smoking data collected for this study are considered as partly relevant, this may suggest that the workers of the study cohort smoked less than did the general population. This may be due to advice against smoking provided by the occupational physicians of the plant during yearly clinical examinations.

Such a tobacco under-consumption may decrease SMRs for smoking-related diseases. The method proposed by Axelson enables this lung cancer deficit to be assessed [3]. Assuming a lung cancer relative risk of 12.0 for smokers vs. non-smokers [18], and a proportion of 55% of smokers in the general population (an average value from Moulin et al. [25]), the lung cancer relative risk would be 0.80, when the cohort is compared with the general population. This value is higher than the observed SMR (0.63), suggesting that, if a negative confounding due to smoking exists, it is unlikely to account for the totality of the lung cancer deficit. Another outcome of this assessment is that the excess observed for cancer of the bladder (SMR = 1.77) cannot be attributed to smoking.

All causes of death

A marked healthy worker effect [9, 22, 24, 38] appeared in the present study, as the SMR for all causes of death was significantly below unity. As described in the literature [24], we observe that the healthy worker effect tends to disappear as time since first employment increases (see Table 3).

A similar result had been observed in the previous nation-wide study carried out in the French aluminium industry (observed = 996, SMR = 0.85, CI 0.80–0.91) [26]. However, in the sub-cohort concerning only the present study, such a healthy worker effect did not appear, the SMR being 1.04 (observed = 285, CI 0.92–1.17) for all causes of death (40% of these 285 deaths that occurred between 1950 and 1976 were included in the present follow-up between 1968 and 1994) (unpublished results). The SMRs were close to unity for the main causes of death: 0.99 (actual observed number = 58, CI 0.78–1.23) for cardiovascular diseases, 0.92 (actual observed number = 42, CI 0.68–1.22) for accidents and violence, 0.96 (actual observed number = 54, CI 0.75–1.21) for all malignant neoplasms, and 1.12 (actual observed number = 13, CI 0.64–1.83) for lung cancer (unpublished results).

Lung cancer

The observed mortality from lung cancer (19 deaths) was significantly lower than expected. No trend was obtained, when duration of employment and time since first exposure were taken as quantitative parameters.

The SMR was not increased for workers who had ever been employed in workshops where exposure to PAHs was likely to have occurred. The SMR observed for workers employed in prebake potrooms, i.e. those who left the plant before 1952, cannot be interpreted due to the small numbers involved.

Misclassifications between PAH exposed vs non-exposed workers, which have been introduced because the actual PAH exposed group could not be defined, are likely to have biased the SMR towards unity [5]. Also, selection mechanisms due to cohort definition, and possible negative confounding due to smoking, may have contributed to decrease lung cancer SMRs. Nevertheless, the low level of the observed SMRs seems to preclude any lung cancer risk in this plant.

According to Boffetta et al., the results of the literature regarding the risk of lung cancer in the aluminium production industry, were not consistent between studies [4]. Our results seem to be in agreement with previous studies which did not detect a risk of lung cancer [7, 13, 26, 31, 34, 36].

Bladder cancer

The statistical analysis showed a non-significant excess of mortality from bladder cancer, based on seven deaths. Although no clear pattern appeared when the duration of employment and time since first exposure were considered as parameters, it is noteworthy that the relative risk was higher, SMR = 2.15 (Table 5), among individuals ever employed in workshops where PAH exposure was likely to have occurred. In addition, the SMR was 2.54 for workers employed for more than 10 years in these workshops.

This excess is unlikely to be attributable to smoking, since we found some evidence to suggest that the study subjects had smoked less than had members of the general population. It is worth noting that selection mechanisms, and possible negative confounding due to smoking, did not prevent the risk of cancer of the bladder from being observed.

The epidemiological evidence seems more consistent in indicating an occupational risk of bladder cancer than of lung cancer due to the Söderberg process [4, 34], particularly when considering the dose-response relationship observed by Tremblay et al. [39]. The excess observed in the present study agrees with those previous results in the literature.

Central nervous system diseases

The literature provides some evidence suggesting possible neuro-toxic effects of aluminium, i.e. renal dialysis and drinking aluminium-containing water [11, 21]. However, the literature provides no evidence of a risk of diseases of the central nervous system and of Alzheimer's disease within the aluminium production industry. In the study by Gibbs in Canada [12], where 1,539 deaths in two cohorts of 5,406 and 485 men were analysed, the observed number for Alzheimer's disease was zero (expected number not given). The study by Ronneberg [32], in a cohort of 1,137 Norwegian men, of whom 501 had died, showed a somewhat increased SMR for "senile psychoses" (ICD 290) based on three cases (SMR = 2.40), however two of the three cases had had less than 3 years of employment (expected = 0.33). Furthermore, considering all occupational exposure to aluminium, three recent case-control studies provided negative results [14, 15, 35].

The results of the present study do not provide any clear evidence, as (1) the excess we observed for "psychoses and neuro-degenerative diseases" is balanced by a low mortality for "all mental disorders", and (2) a misclassification in the assessment of the causes of death cannot be excluded.

However, the larger and significant excess among subjects 30 years and more after first employment may suggest a risk of Alzheimer's disease. That this risk is related to aluminium exposure appears unlikely as no excess was found in workshops where exposure to aluminium was likely to have occurred, in particular the potroom and casthouse [28, 29]. A more precise assessment of aluminium exposure could unfortunately not be performed.

Conclusion

This study showed a marked healthy worker effect, and a statistically significant low lung cancer mortality, which could be partly explained by some healthiness selection mechanisms and a possible negative confounding due to smoking. The non-significant excess that appeared for cancer of the bladder is consistent with previous results in the literature. The non-significant excess observed for "psychoses and neuro-degenerative diseases", based on six cases, could not be clearly interpreted.

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