Mortality study of employees in a factory of recovery and refining of catalytic converters in Rome, Italy

Roberto Pasetto[(a)], M. Giuseppina Bosco[(b)], Stefania Palange[(c)], Pietro Comba[(a)], Marco De Santis[(a)], Maria Di Fabio[(b)], Francesco Forastiere[(c)], Fabrizio Magrelli[(b)], Giulia Castellani[(e)], Carlo Alberto Perucci[(c)], Sergio Rovetta[(b)] and Roberta Pirastu[(d)]

[(a)]Dipartimento di Ambiente e Connessa Prevenzione Primaria, Istituto Superiore di Sanità, Rome, Italy
[(b)]Servizio Prevenzione, Igiene e Sicurezza nei Luoghi di Lavoro. Dipartimento di Prevenzione, ASL Roma B, Rome, Italy
[(c)]Dipartimento di Epidemiologia, ASL Roma E, Rome, Italy
[(d)]Dipartimento di Biologia Animale e dell'Uomo, Università degli Studi "La Sapienza", Rome, Italy
[(e)]Consulting Occupational Physician

Summary. The study objective is to describe cause specific mortality of employees in a plant engaged in production, recovery and refining of catalytic converters located in Rome. Previous epidemiological studies conducted in similar plants are not available. A total of 828 workers (642 males and 186 females) were followed up between 1956 and 31-12-2003. Cause specific standardized mortality ratio (SMR) and 90% confidence intervals (CI) were computed using regional rates for comparison. Among males hired between 1956 and 1993, followed up until 31/12/2003, mortality for all causes (SMR 0,8; 90% CI 0,7-1,0; 85 observed) and all neoplasms (SMR 0,6; 90% CI 0,42-0,87; 20 observed) is below expected; an increase is present for liver cirrhosis (SMR 2,74; 90% CI 1,47-5,1; 7 observed) and brain cancer (SMR 5,24; 90% CI 2,3-11,90; 4 observed). The present investigation complies with the proposed scientific standards for occupational cohort studies. The study was not prompted by well defined a priori hypotheses but it is included in a process intended to typify a potentially polluted site; the absence of a priori hypotheses and of previous epidemiological evidence, prevent from a causal interpretation of the increased mortality from liver cirrhosis and brain cancer. The implementation of cohort studies in industrial sites where industrial activities similar to the one here examined are present, are highly recommended.

Key words: mortality, cohort study, chemical industry, Italy.

Riassunto *(Studio di mortalità in un'azienda di produzione e recupero di catalizzatori esausti)*. Lo scopo dell'indagine è la descrizione della mortalità dei dipendenti di un'industria di produzione, recupero e raffinazione di catalizzatori esausti localizzata nel comune di Roma. Non sono disponibili studi epidemiologici condotti in impianti produttivi sovrapponibili a quello in esame. La coorte è costituita dai dipendenti dell'impianto industriale a partire dal 1956 e successivamente assunti fino al 31/12/2003 (828 soggetti, 642 uomini e 186 donne). La mortalità della coorte è stata confrontata con quella della popolazione dei residenti nella regione Lazio utilizzando i tassi di mortalità specifici per causa, sesso, età e periodo di calendario e calcolando il rapporto standardizzato di mortalità (standardized mortality ratio, SMR) al quale è stato associato l'intervallo di confidenza al 90% (IC 90%). Tra gli uomini, assunti nel periodo 1956-1993 e con follow-up fino al 2003, la mortalità osservata per tutte le cause (SMR 0,8; IC 90% 0,7-1,0; 85 osservati) e per tutti i tumori (SMR 0,6; IC 90% 0,42-0,87; 20 osservati) è inferiore all'attesa; si osserva un incremento per cirrosi epatica (SMR 2,74; IC 90% 1,47-5,1; 7 osservati) e tumore dell'encefalo (SMR 5,24; IC 90% 2,3-11,90; 4 osservati). Dall'esame degli aspetti di validità dell'indagine è possibile concludere che essa rientra negli standard scientifici proposti per gli studi di coorte in ambito professionale. L'indagine non è stata condotta sulla base di definite ipotesi eziologiche a priori ma nell'ambito di un processo di caratterizzazione di un sito potenzialmente inquinato. Questo elemento, insieme alla mancanza, nella letteratura scientifica, di studi di coorte relativi a insediamenti produttivi analoghi, preclude un'interpretazione in termini causali degli incrementi di mortalità per cirrosi epatica e tumori encefalici. È invece da raccomandare la replicazione dello studio in siti industriali caratterizzati da siti produttivi simili.

Parole chiave: mortalità, studio di coorte, industria chimica, Italia.

Indirizzo per la corrispondenza (Address for correspondence): Roberto Pasetto, Dipartimento di Ambiente e Connessa Prevenzione Primaria, Istituto Superiore di Sanità, Viale Regina Elena 299, 00161 Roma. E-mail: roberto.pasetto@iss.it.

INTRODUCTION

The study objective is to describe cause specific mortality of employees in a plant engaged in production, recovery and refining of catalytic converters located in Rome, Italy. Occupational cohort mortality study is a cornerstone in the investigation of health risks in a geographic area where industrial risk is hypothesized [1].

PRODUCTION PROCESSES AND POSSIBLE EXPOSURES: A BRIEF DESCRIPTION

Production of chemical catalysts and recycling of precious metals through pyrolysis and thermodistruction of exhausted catalysts are the main processes taking place in the plant. Production started in 1957 and remained essentially the same over time, the main change being an expansion of activities related to recovery of precious metals originating from exhausted catalysts and other industrial processes. Residues from chemical industries located in Italy and abroad for ashing and recovery of precious metals are currently conveyed to the plant which is authorized by Latium Region for treating 1600 Tons/year of such residues.

The plant is organized in departments where different phases of production and recycling take place:

1. in the department salts and solution, solutions of complex salts of precious metals are produced. Metals are dissoluted in acids or chlorine, hydrolysed in bases and precipitated with organic acids, subsequently filtrated and dispersed in organic acids/organic products to be finally dried and crystallized;
2. in the department chemical catalysts, precious metal based catalysts are produced. Metals are absorbed/impregnated on the support (coal or alumina), washed, mixed and dried;
3. in the department coating, precious metals are dispersed in solutions of acetic acid or other organic products, ceramic/metallic supports are soaked with alumina, zirconium, cerium and subsequently dried and calcined;
4. in the department Sampling-oven, precious metals are recovered from exhausted catalysts which are burned in oven, the ashes are sampled to measure the content of precious metals and subsequently sent to refining;
5. in the Refining Department ashes are treated with acids and then purified;
6. in the laboratories starting chemicals and products are analysed;
7. in another department waters and scrubbers are treated for fumes elimination.

Some activities of the production process (receipts, storing, oven loading with exhausts materials, ashing and ashes and treatment) possibly entail exposure to metals (mercury, cadmium, chromium, nickel and various precious metals) and different carcinogens as labelled by producers. In all departments emissions' fall out from ashing is possible; in such emissions, given the current presence of post combustion systems, the levels of polycyclic aromatic hydrocarbons and metals (cadmium, mercury, vanadium, nickel, chromium, arsenic) are below exposure limits, the presence of dioxin in traces cannot be excluded.

EPIDEMIOLOGICAL EVIDENCE

Studies in plants where production processes are similar to the one under investigation were not retrieved from the epidemiological literature. A recent study carried out in the plant showed that in two areas where the metallic elements are treated with acids, precipitated, and dissolved in inorganic and organic additives, exposure to platinum (Pt) in air particulates, blood, urine and hair was higher in blue collar workers than in white collars and an external comparison group [2].

The epidemiological studies on health risks of workers in the chemical industry and a recent meta-analysis of 181 cohort studies of chemical workers in Europe and the United States [3] provide results on job titles and/or exposures which are different from the ones present in the plant under investigation.

MATERIALS AND METHODS

The cohort includes all workers who began employment in 1956 (year of plant starting operation) and those subjects subsequently hired until 31/12/2003. Cohort enumeration started from a company file subsequently completed from company payrolls and data from periodical medical examinations; a further check to ensure cohort completeness was carried out in 2005 from data of Italian national social security (Istituto Nazionale Previdenza Sociale, INPS). The cohort includes 828 individuals, 642 men and 186 women.

Ascertainment of vital status and causes of deaths for the follow-up period 01/01/1956- 31/12/2003, was carried out through the Register Office of the place of residence of cohort members, this procedure allowed to distinguish the subjects into four groups: a) alive, b) emigrated to a different village/city where a request for vital status ascertainment was sent, c) not found at the place of residence/birth and therefore classified as lost to follow-up, d) deceased. For those individuals deceased out of Latium region cause of death was requested from the local health unit (Unità Sanitaria Locale, USL) of the place of residence, for those deceased in Latium region a linkage with regional death index (Registro nominativo delle cause di morte, Re.N.Ca.M) was carried out. Causes of death were classified following the rules of the IX ICD Revision. Individuals lost to follow-up contributed to person-years until the date at which presence in the plant was known from company records.

Standardized mortality ratios (SMR) were computed and mortality rates for the population resident in Latium region were applied for comparison; for each SMR value a 90% confidence interval (CI) was calculated with the maximum likelihood method on the assumption of a Poisson distribution; mortality rates for the years 1995-1998 (the most recent made available from the National Institute of Statistics at the National Health Institute at

Table 1 | *Cohort of employees in a catalysts production and recycling plant: vital status, distribution of person years by age. Follow-up 1956-2003. Men*

	Period of hire 1956-1993 no. (%)	Period of hire 1956-1993 Blue collars (ever blue collar) no. (%)	Period of hire 1956-2003 no. (%)
Alive	377	253	531
Deceased	85	74	85
with cause of death	80 (94.1)	70 (94.6)	80 (94.1)
Lost to follow-up	20 (4.2)	15 (4.4)	26 (4.05)
Total	482	342	642
Total person years	12635	9296	
age (person years)			
< 40 years	5021 (39.7)	3497 (37.2)	7874 (46.1)
40-65 years	6450 (51.0)	4898 (51.3)	7898 (46.2)

the time of study was analyses) were applied to the periods 1995-1999 and 2000-2003; mortality rates for the years 1970-1975 were applied to person-years accrued before 1970.

Mortality analysis was carried out only for men who worked in the plant starting in 1956 and subsequently hired until 31/12/1993, *a priori* adopting a restriction criterion which ensured a minimum 10 years follow-up period to all cohort members; in addition a separate analysis was completed for those who ever worked as blue collar. Mortality of women was not investigated given the small number of observed deaths (5 deaths).

RESULTS

Table 1 describes vital status ascertainment and person-years distribution of men hired in the years 1956-1993 and for those who ever worked as blue collar. In the overall cohort and among ever blue collars the percentage of lost to follow-up is about 4% and causes of death is known for 94% of deceased individuals, about 40% of person-years is below age 40; *Table 1* also shows vital status ascertainment and person-years distribution for men hired in the years 1956-2003.

For both latency *(Table 2)* and duration *(Table 3)* about 35% of person-years is allocated to the category "0-10 years".

Workers hired in the years 1956-1993 *(Table 4)* and those who ever worked as blue collar in the same period *(Table 5)* show a decreased mortality for all causes (SMR respectively equal to 0,80; 90% CI; 90% CI 90% 0,7-1,0; observed (obs.) 85 and SMR 0,83; 90% CI 0,69-1,00; obs. 74) and all neoplasms (total cohort SMR 0,60; 90% CI 0,42-0,87; obs. 20; ever blue collars SMR 0,59 90% CI 0,40-0,89; obs. 17). Mortality for circulatory system diseases is similar to expectation, observed is above expected for hypertension (total cohort SMR 2,20; 90% CI 1,06-4,6; obs. 5; ever blue collars SMR 1,91 90% CI 0,84-4,35 obs. 4).

Among men hired in the period 1956-1993 an increased mortality is observed for brain cancer (SMR 5,24; 90% CI 2,3-11,90; obs. 4) and liver cirrhosis (SMR 2,74; 90% CI 1,47-5,1; 7 obs.); similar results are observed among ever blue collars, brain cancer SMR equals to 4,88 (90% CI 1,89-12,63; obs. 3) and liver cirrhosis SMR equals to 2,7 (90% CI 1,45-5,55, obs. 6).

In the total cohort (hired 1956-1993) observed mortality for brain cancer is above expected in the categories of duration of employment 0-9 and 10-19 years,

Table 2 | *Cohort of employees in a catalysts production and recycling plant. Men hired 1956-1993. Distribution of person years by latency (years from hire). Follow-up 1956-2003*

	Person years no. (%)	Blue collars (ever blue collar) no. (%)
Latency (years)		
< 1	479 (3.8)	338 (3.6)
1- 9	4206 (33.3)	2953 (31.4)
10-29	6621 (52.4)	5038 (53.6)
30+	1329 (10.5)	1067 (11.4)
Total	12635	9396

Table 3 | *Cohort of employees in a catalysts production and recycling plant. Men hired 1956-1993. Distribution of person years by duration of employment (years). Follow-up 1956-2003*

	Person years no. (%)	Blue collars (ever blue collar) no. (%)
Duration (years)		
0-9	4503 (35.6)	3448 (36.7)
10- 19	3026 (23.9)	2306 (24.6)
20-29	2828 (22.4)	1785 (19.0)
30+	2278 (18.1)	1857 (19.8)
Total	12635	9396

Table 4 | *Cohort of employees in a catalysts production and recycling plant. SMR by causes of death, men hired 1956-1993. Reference population Latium Region*

Cause of death (IX ICD)	Observed	Expected	SMR	90% CI
All causes (001-999)	85	101.4	0.8	0.7-1
Malignant neoplasms (140-208)	20	33	0.6	0.42-0.87
Oral cavity and pharynx (149.8)	1	0.9	1.22	0.24-6.28
Digestive organs (150-9)	5	10.7	0.46	0.23-0.97
Oesophagus (150)	-	0.4		
Stomach (151)	-	2.9		
Intestine and rectum (152-154)	2	3.1	0.65	0.2-2.06
Colon and sigma (153)	-	2		
Rectum (154)	2	1	1.97	0.61-6.32
Liver and intrahepatic ducts (155.0-155.2)	1	1.9	0.51	0.09-2.67
Liver primary (155.0)	-	1.05		
Liver (not spec.) (155.2)	1	0.8	1.17	0.23-6.08
Gallbladder (156)	-	0.4		
Pancreas (157)	2	1.2	1.56	0.49-5
Peritoneum and retroperitoneum (158)	-	0.1		
Respiratory organs (160-5)	6	11.8	0.51	0.26-0.99
Larynx (161)	-	0.9		
Lung (162)	6	10.7	0.55	0.28-1.09
Pleura (163)	-	0.1		
Mediastinum (164)	-	0.1		
Melanoma (172)	1	0.3	3.15	0.6-16.31
Skin (173)	-	0.1		
Genitourinary organs (179-189)	2	4.2	0.48	0.15-1.53
Prostate (185)	-	1.9		
Bladder (188)	1	1.5	0.6	0.14-3.6
Kidney and other not spec. (189)	1	0.7	1.33	0.26-6.89
Nervous system (190-2)	4	0.8	4.81	2.11-10.97
Brain (191)	4	0.8	5.24	2.3-11.91
Site unspecified (195)	-	0.3		
Malignant neoplasms, not spec. (199)	-	0.9		
Lympho-hematopoietic (200-8)	1	2.6	0.39	0.07-2.03
Hodgkin's lymphoma (201)	-	0.2		
Non-Hodgkin's lymphoma (200, 202)	-	0.7		
Mieloma (203)	-	0.3		
Leukaemia (204-8)	1	1.1	0.84	0.16-4.33
Lymphoid leukaemia (204)	1	0.3	2.95	0.57-15.33
Myeloid leukaemia (205)	-	0.5		
Neoplasms unspecified (239)	-	0.7		
Diseases of blood (280-89)	1	0.4	3.09	0.59-16.05
Diabetes mellitus (250)	1	2.9	0.34	0.06-1.77
Nervous system (320-359)	1	1.6	0.6	0.11-3.08
Anterior horn cell disease (335)	-	0.2		
Circulatory system (390-459)	36	37.3	1.02	0.78-1.32
Hypertension (400-404)	5	2.3	2.2	1.06-4.6
Ischaemic heart disease (410-414)	13	16.7	0.78	0.5-1.22
Cerebrovascular disease (430-438)	6	8.3	0.72	0.37-1.42
Respiratory system (460-519)	4	5.64	0.7	0.31-1.62
Bronchitis, Emphysema and Asthma (490-493)	3	3.2	0.93	0.36-2.41
Digestive system (520-579)	10	6.9	1.45	0.86-2.43
Cirrhosis (571)	7	2.5	2.74	1.47-5.1
Genitourinary system (580-629)	-	1.4		
Ill-defined conditions (780.0-799.8)	-	0.7		
Unknown causes (799.9)	5	0.1		
Injury and poisoning (800-999)	4	7.1	0.57	0.25-1.29

SMR: standardized mortality ratio; 90% CI: 90% confidence intervals.

Table 5 | *Cohort of employees in a catalysts production and recycling plant. SMR by causes of death, men hired 1956-1993, blue collars (ever blue collar). Reference population Latium Region*

Cause of death (IX ICD)	Observed	Expected	SMR	90% CI
All causes (001-999)	74	88.8	0.83	0.69-1
Malignant neoplasms (140-208)	17	28.6	0.59	0.4-0.89
Oral cavity and pharynx (149.8)	1	0.7	1.47	0.28-7.62
Digestive organs (150-9)	5	9.4	0.53	0.26-1.11
Oesophagus (150)	-	0.42		
Stomach (151)	-	2.59		
Intestine and rectum (152-154)	2	2.7	0.74	0.23-2.37
Colon and sigma (153)	-	1.78		
Rectum (154)	2	0.88	2.26	0.7-7.25
Liver and intrahepatic ducts. (155.0-155.2)	1	1.69	0.59	0.11-3.07
Liver primary (155.0)	-	0.9		
Liver (not sec.) (155.2)	1	0.75	1.33	0.26-6.92
Gallbladder (156)	-	0.36		
Pancreas (157)	2	1.08	1.85	0.58-5.91
Peritoneum e retroperitoneum (158)	-	0.15		
Respiratory organs (160-5)	5	10.23	0.49	0.23-1.02
Larynx (161)	-	0.74		
Lung (162)	5	9.26	0.54	0.26-1.13
Pleura (163)	-	0.09		
Mediastinum (164)	-	0.08		
Melanoma (172)	1	0.25	4.01	0.77-20.79
Skin (173)	-	0.09		
Genitourinary organs (179-189)	1	3.76	0.27	0.05-1.38
Prostate (185)	-	1.72		
Bladder (188)	1	1.3	0.77	0.15-3.97
Kidney and other not spec. (189)	-	0.64		
Nervous system (190-2)	3	0.67	4.47	1.73-11.56
Brain (191)	3	0.61	4.88	1.89-12.63
Site unspecified (195)	-	0.2		
Malignant neoplasm not spec. (199)	-	0.77		
Lympho-hematopoietic (200-8)	1	2.16	0.46	0.09-2.4
Hodgkin's lymphoma (201)	-	0.18		
Non-Hodgkin lymphoma (200, 202)	-	0.63		
Mieloma (203)	-	0.33		
Leukaemia (204-8)	1	1.02	0.98	0.19-5.1
Lymphoid leukaemia (204)	1	0.29	3.42	0.66-17.69
Myeloid leukaemia (205)	-	0.43		
Neoplasms unspecified (239)	-	0.69		
Diseases of blood (280-89)				
Diabetes mellitus (250)	1	2.65	0.38	0.07-1.95
Nervous system (320-359)	1	1.47	0.68	0.13-3.53
Anterior horn cell disease (335)	-	0.13		
Circulatory system (390-459)	36	33.65	1.07	0.81-1.41
Hypertension (400-404)	4	2.09	1.91	0.84-4.35
Ischaemic heart disease (410-414)	13	14.84	0.88	0.55-1.38
Cerebrovascular disease (430-438)	6	7.6	0.79	0.4-1.55
Respiratory system (460-519)	3	5.22	0.57	0.22-1.48
Bronchitis, Emphysema and Asthma (490-493)	2	3.01	0.66	0.2-2.12
Digestive system (520-579)	9	6	1.5	0.87-2.6
Cirrhosis (571.5)	6	2.12	2.83	1.45-5.55
Genitourinary system (580-629)	-	1.26		
Ill-defined causes (780.0-799.8)	-	0.56		
Unknown causes (799.9)	4	0.15	27.06	11.89-61.60
Injury and poisoning (800-999)	3	5.62	0.53	0.2-1.38

SMR: standardized mortality ratio; 90% CI 90% confidence intervals.

the respective values of SMR is 6,81 (90% CI 2,13-21,79; 2 obs.) and 9,18 (90% CI 2,87-29,38; 2 obs.).

The results of the analyses carried out using national rates for comparison are similar to the ones obtained with regional rates, a trivial change in the SMR values is the only difference.

No deaths were observed among those hired in the years 1994-2003.

For the causes of death showing an increase versus expectation, i.e. brain cancer, liver cirrhosis and hypertension the values of 95% Confidence Intervals are as follows: 1.97-13.95 (SMR 5.24), 1.31-5.74 (SMR 2.74) and 0.92-5.29 (SMR 2,20).

DISCUSSION

The main findings of the present study are an increased mortality for liver cirrhosis and brain cancer among men hired from 1956 through 1993 and followed-up till 2003.

Before commenting these findings, it is appropriate to briefly review the main validity aspects of the adopted study design.

The cohort was enumerated from payrolls, which are regarded as the best source in retrospective occupational cohort studies [4]. The data collected were then integrated with information derived from other sources in order to improve the initial completeness and accuracy.

Ascertainment of vital status was completed for about 96% of study subjects (overall cohort and ever blue collar subcohort), thus the proportion of lost to follow-up was lower than 5%, the percentage commonly regarded as acceptable for the calculation of a valid SMR [4].

The underlying cause of death was retrieved for about 94% of deceased subjects. The cause of death was not identified for five subjects.

Completeness and accuracy of data concerning enrollment and follow-up of the cohort ensure validity of SMR.

Estimates of SMR computed among male subjects using as reference Latium Region mortality rates, were contrasted with those obtained using national rates as reference: SMR do not substantially vary as a consequence of use of one or the other reference population.

The finding of a decreased overall mortality, partly explained by the decreased occurrence of respiratory and digestive tract diseases, is consistent with the so-called "Healthy Worker Effect", that may be explained with selection and self-selection to work, and with a longer duration of work for subjects with better health conditions [4]. The present study also indicates a reduced mortality for all neoplastic causes, in this respect the evaluation of the healthy worker effect is more complex [5].

Hepatic cirrhosis is clearly in excess in the cohort, with 7 observed cases and 2,5 expected. The most frequent causes of this disease are chronic hepatitis virus infection and alcohol abuse; with respect to occupational exposures, an increased incidence has been observed among workers exposed to a variety of organic solvents, vinyl chloride, arsenical pesticides and polichlorobiphenyls in capacitor manufacture [6]. No figures are available on the frequency of hepatitis virus infection in the study population, but the geographic distribution of birthplaces does not suggest a high occurrence of subjects from parts of Italy with a high viral circulation. No figures are available on alcohol consumption in the cohort, as well, but no excess in death rates from alcohol-related causes has been obseved.

As far as brain cancer is concerned (4 observed versus 0,8 expected), the only ascertained risk factor is exposure to ionizing radiation; heredity, smoking, alcohol consumption and exposure to N-nitroso compounds are suspected to play an etiologic role [7]. With regards to job titles increased risks have been reported for fire fighters [8], petrochemical workers, rubber workers, electric utility workers, farmers and health professionals. Exposure to polyciclic aromatic hydrocarbons, benzene and pesticides are common in some of those occupations, but no specific associations have been described [9]. A meta-analysis of 181 cohort studies of chemical workers from industries in Europe and USA, published from 1966 through 1997, reported and increased mortality from neoplasms of brain and central nervous system, especially for subjects with 10 or more years of duration of employment and of latency; this increased risk was not attributed to defined exposures or job-titles [10].

The case-control study on glioma diagnosed in San Francisco Bay Area [11], whose findings are adjusted for gender, education and ethnicity, confirmed an increased risk for fire fighters, oil and gas production workers and health professionals; the study also reports an increased risk for painters, who are traditionally exposed to solvents. A subsequent investigation in the same area, based on the same crude categorization of exposures but including also cases diagnosed in 1997-99, confirmed the previous findings for fire fighters and health professionals, and observed increased risks workers in the rubber and plastic, electric and metal industry as well as for truck and car drivers and garage workers [12].

An investigation on 17 cases of intracranial neoplasms among employees of the Amoco Chemical Research Centre in Illinois was published in 1999; the cases had worked in three buildings characterizated by the presence of several organic solvents, plastics, monomers and polymers, catalites, organometallic catalyzers and their complexes and, to a lower extent, aminoacids [13]. The subsequent case-control study included histologically confirmed cases and was based on information on work history derived from a questionnaire and from Company records with respect to the occurrence of 15 chemicals. An increased risk for glioma associated with self-reported n-hexane exposure and with possible use of n-hexane for at least 4 years was detected; an increased risk was also associated with self-reported exposure to organometallic compounds, and amines other than nitrosoamines [14].

In Sweden, a record linkage of subjects active in 1970 with the National Cancer Registry for the years 1971-1989 showed an increased risk of glioma in men associated with possible exposure to arsenic (RR 1.61, 95% CI 1.12-2.32; 34 observed cases) and probable exposure to mercury (RR 1.76, 95% CI 0.99-3.14;

12 observed cases), estimated through a job-exposure matrix [15].

The findings of a case-control study on brain cancer in Canada, 1994-97, show an increased risk in men associated with benzene exposure (OR 1.56, 95% CI 1.05-2.31; 38 cases) and with work as a welder; the latter increases with increasing duration of work with a significant trend [16].

A case-control study on glioma diagnosed in the years 1980-1991, performed in six European and US centers, detected an increased risk of low-grade glioma among metal workers (OR 1.59, 95% CI 1.00-2.52; 45 exposed cases) and among subjects exposed to solvents and detergents (OR 1.15, 95% CI 0.73-1.82; 42 observed cases) [17].

The present study also showed a weak association with hypertensive disease (5 observed and 2.3 expected). Individual life-style factors and diet are the main determinants of hypertension. As far as occupational exposures are concerned, an increased prevalence of hypertension has been observed among subjects exposed to carbon disulphide, CS2, a solvent largely used in the manufacture of viscose and rayon, in a carbon production and as a fumigant in wheat disinfestations [18].

CONCLUDING REMARKS

The review of the validity aspects of the present investigation has documented that it complies with currently adopted scientific standards for occupational cohort studies [4].

The study was not conducted in order to test *a priori* defined etiologic hypotheses, but it was planned and completed in the frame of a complex process of characterization of a polluted site. The lack of background information due to the absence of epidemiologic studies conducted in similar industrial settings, does not allow a causal interpretation of the observed excesses of brain cancer and hepatic cirrhosis.

The replication of the study in industrial sites characterized by the presence of comparable production facilities and work processes should be encouraged.

Submitted on invitation.
Accepted on 10 April 2006.

References

1. Pasetto R, Pirastu R. Lo studio di coorte nel contesto dei siti inquinati. In: Bianchi F, Comba P (Ed.). *Indagini epidemiologiche nei siti inquinati: basi scientifiche, procedure metodologiche e gestionali, prospettive di equità*. Roma: Istituto Superiore di Sanità; 2006. (Rapporti ISTISAN, 06/19).
2. Petrucci F, Violante N, Senofonte O, Cristaudo A, Di Gregorio M, Forte G, Alimonti A. Biomonitoring of a worker population exposed to platinum dust in a catalyst production plant. *Occup Environ Med* 2005;62:27-33.
3. Greenberg RS, Mandel JS, Pastides H, Britton NL, Rudenko L, Starr TB. A meta-analysis of cohort studies describing mortality and cancer incidence among chemical workers in the United States and Western Europe. *Epidemiology* 2001;12:727-40.
4. Checkoway H, Pearce N, Kriebel D. *Research methods in occupational epidemiology.* Oxford: University Press; 2004.
5. Higginson J, Muir CS, Muñoz N. *Human cancer. Epidemiology and environmental causes*. Cambridge: University Press; 2004.
6. Wang JS, Groopman JD. Toxic liver disorders. In: Rom WM (Ed.). *Occupational and environmental medicine.* Philadelphia-New York: Lippincott-Raven; 1998. p. 831-41.
7. Preston-Martin S, Mack WJ. Neoplasms of the nervous system. In: Schottenfeld D, Fraumeni JF (Ed.). *Cancer epidemiology and prevention.* New York-Oxford: Oxford University Press, 1996. p. 1230-81.
8. Barnhart S, Pappas GP. Firefighters' health and safety. In: Rom WM (Ed.). *Occupational and environmental medicine.* Philadelphia-New York: Lippincott-Raven; 1998. p. 1455-64.
9. Preston-Martin S, Mack WJ. Neoplasms of the nervous system In: Schottenfeld D, Fraumeni JF (Ed.). *Cancer epidemiology and prevention.* New York-Oxford: Oxford University Press; 1996. p. 1230-81.
10. Greenberg RS, Mandel JS, Pastides H, Britton NL, Rudenko L, Starr TB. A meta-analysis of cohort studies describing mortality and cancer incidence among chemical workers in the United States and Western Europe. *Epidemiology* 2001;12:727-40.
11. Carozza S, Wrensch M, Miike R, Newman B, Savitz D, Olshan A, Savitz DA, Yost M, Lee M. Occupation and adult glioma. *Am J Epidemiol* 2000;152(9):838-46.
12. Krishnan G, Felini M, Carozza SE, Miike R, Chew T, Wrensch M. Occupation and adult gliomas in the San Francisco Bay Area. *J Occup Environ Med* 2003;45(6):639-47.
13. Delzell E, Beall C, Rodu B, Lees PS, Breysse PN, Cole P. Case-series investigation of intracranial neoplasms at a petrochemical research facility. *Am J Ind Med* 1999;36(4):450-8.
14. Beall C, Delzell E, Rodu B, Sathiakumar N, Lees PS, Breysse PN, Meyers M. Case-control study of intracranial tumors among employees at a petrochemical research facility. *J Occup Environ Med* 2001;43(12):1103-13.
15. Navas-Acién A, Pollan A, Gustavsson P, Plato N. Occupation, exposure to chemicals and risk of glioma and meningioma in Sweden. *Am J Ind Med* 2002;42:214-27.
16. Pan SY, Ugnat AM, Mao Y, Canadian Cancer Registries Epidemiology Research Group. Occupational risk factors for brain cancer in Canada. *J Occup Environ Med* 2005;47:704-17.
17. Schlehofer B, Hettinger I, Ryan P, Blettner M, Preston-Martin S, Little J, Arslan A, Ahlbom A, Giles GG, Howe GR, Menegoz F, Rodvall Y, Choi WN, Wahrendorf J. Occupational risk factors for low grade and high grade glioma: results from an International case control study of adult brain tumours. *Int J Cancer* 2005;113:116-25.
18. Levin SM, Lilis R. Carbon disulfide. In: Rom WM (Ed.). *Occupational and environmental medicine.* Philadelphia-New York: Lippincott-Raven; 1998. p. 1221-6.