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ORIGINAL ARTICLE

Welding, a risk factor of lung cancer: the ICARE study

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ABSTRACT

Objectives We investigated the relationship between lung cancer and occupational exposure to welding activity in ICARE, a population-based case–control study.

Methods Analyses were restricted to men (2276 cases, 2780 controls). Welding exposure was assessed through detailed questionnaires, including lifelong occupational history. ORs were computed using unconditional logistic regression, adjusted for lifelong cigarette smoking and occupational exposure to asbestos.

Results Among the regular welders, welding was associated with a risk of lung cancer (OR=1.7, 95% CI 1.1 to 2.5), which increased with the duration (OR=2.0, 95% CI 1.0 to 3.9 when duration >10 years), and was maximum 10–20 years since last welding. The risk was more pronounced in case of gas welding (OR=2.0, 95% CI 1.2 to 3.3), when the workpiece was covered by paint, grease, or other substances (OR=2.0, 95% CI 1.2 to 3.4) and when it was cleaned with chemical substances before welding. No statistically significant increase in lung cancer risk was observed among occasional welders.

Conclusions Although these results should be confirmed, we showed that type of welding and mode of workpiece preparation are important determinants of the lung cancer risk in regular welders.

What this paper adds

- In 1990, the International Agency for Research on Cancer (IARC) reviewed the scientific literature addressing the risk of cancer in relation to welding, a technique extensively used all over the world: the reported findings pointed to an excess risk of lung cancer, which was finally considered as limited evidence of carcinogenicity in humans.
- The present analysis, conducted on the data set of a large population-based case–control study, highlighted a clear dose–response relationship between regular welding and lung cancer.
- Gas welding resulted to be more harmful than arc welding.
- The risk was increased when the workpiece was covered by paint, grease or other substances.
- Surface cleaning with chemicals before welding may increase the risk of lung cancer, compared with mechanical cleaning.

In 1990, the International Agency for Research on Cancer (IARC) reviewed the scientific literature addressing the risk of cancer in relation to welding, a technique extensively used all over the world. The reported findings pointed to an excess risk of lung cancer, which was finally considered as limited evidence of carcinogenicity in humans.[1] Since then, numerous cohort and case–control studies have been carried out. These studies were synthesised in several meta-analyses, including the most recent one, a pooled analysis of case–control studies that demonstrated a 50% increase in the risk of lung cancer associated with exposure to welding fumes.[2–4]

Welding fumes are complex mixtures formed by the filler material, gas flows, the metal surface to be welded and its coverings.[5 6] Different carcinogens are found in welding fumes, but many studies focused on hexavalent chromium (Cr VI) and nickel oxides. Cohort studies have tried to disentangle these complex exposures investigating some specific sectors, for example, shipyards and stainless steel or mild steel welders. On the other hand, case–control studies were based on job titles as a proxy of welding fume exposure. Very few studies have focused on the type of welding, mostly arc welding. The paper by t'Mannetje *et al*[7] pooled data from several case–control studies and identified gas welding as potentially more harmful than arc welding, leading to an increased (but not statistically significant) risk of lung cancer. We could not retrieve any study investigating the risk of lung cancer associated either with metal surface coatings, such as paints and greases, or with the type of treatment applied before welding. Furthermore, most of these studies had methodological weaknesses, such as residual confounding by smoking (particularly true in historical cohort studies) or lack of adjustment for asbestos exposure. Thus, although welding was consistently identified as a risk factor for lung cancer, the variety of welding processes made it difficult to identify one or several determinants of the risk.

We investigated the relationship between lung cancer and occupational exposure to welding in detail, using a large population-based case–control

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study conducted in France in the 2000s, the ICARE study.[8] We were particularly interested in the type of welding (torch or arc welding, etc) as well as the preparation of workpieces (ie, removing the paint or grease prior to welding). Smoking and asbestos exposure were carefully taken into account.

METHODS

Study design

ICARE is a large multicentre population-based case–control study on cancers of the respiratory tract conducted in France from 2001 to 2007. The study was set-up in 10 out of the 11 French administrative *départements* with a general cancer registry (see ref 8 for details). As regards the lung cancer part, all patients between 18 and 75 years of age identified during the study period were eligible for the study. The cases were all histologically confirmed primary lung cancer (C33-C34 ICD-O), which included all histological types. Participation in the study was proposed to 3360 participants, but 434 refused (13%).

Throughout the recruitment period, population controls from the same *départements* as the cases were selected every 2 months by a polling institute using a random digit dialling procedure. Each number was called 10 times before being abandoned as not answered. Calls were made in the evening on weekdays and during the day on Saturday, so that each home had the same probability of being contacted. Controls were frequency matched with cases for gender and age (in 4 categories: less than 40, 40–54, 55–64, ≥65 years of age). An additional stratification was performed to achieve a distribution of controls by socioeconomic status[i] comparable to that of the general population in each *départment*, as obtained by census data and the surveys on employment by the French National Institute of Statistics. After a brief presentation of the general objectives of the study, the names and addresses of eligible persons who agreed to participate were transmitted to the ICARE interviewers, who arranged interview appointments. Among the 4673 eligible controls, 4411 were contacted and 3555 agreed to participate in the study (refusal rate: 19%).

Each participant gave written and informed consent. The study was approved by the Institutional Review Board of the French National Institute of Health and Medical Research (IRB-INSERM, n° 01-036) and by the French Data Protection Authority (CNIL n° 90120).

Data collection and occupational data coding

Face-to-face interviews were conducted by trained interviewers using standardised questionnaires. The general questionnaire collected the lifelong occupational history, including the beginning and ending dates of each job, the type of industry and a description of the tasks carried out in the job. Each occupation lasting 1 month or more, including unpaid work, unofficial jobs and occupational activity during national service or apprenticeship, was defined as a 'job period'.

In addition, 20 job-specific questionnaires were available for certain tasks or job titles, including one on welding, brazing or metal cutting. Occupations and branches of industry were coded by trained coders, according to the *International Standard Classification of Occupations* (ISCO) and the French Nomenclature of Activities (*Nomenclature d'Activités Françaises*: NAF) and blindly with respect to case or control status of the participants.[9,10]

Definition of welding activity

Welding was first caught for each job period with a single question in the general questionnaire: 'During this job period, were you exposed to welding/brazing/gas cutting?' For those who declared that more than 5% of worktime was devoted to this task (n=612), the participant was asked to answer the four-page job-specific questionnaire, investigating the process of welding, the type of metals welded, the type of coating covering the metal, the treatments applied before welding and the use of protective clothing. We defined 'regular welders' as those participants with at least one job period as welder in the strict sense of the word (ie, coded 8-72 in ISCO code), and 'occasional welders' as those participants who simply responded positively at least once to the above reported specific question.

Assessment of asbestos exposure

ICARE's questionnaires were designed with multiple closed questions, allowing the identification of exposure tasks or circumstances and the construction of a task-exposure matrix (TEM) specific for asbestos exposure (see details in ref [11]) based on the participant's replies. The TEM assigned a probability of exposure (possible, probable or definite) and an intensity of exposure (0.001 to 0.1; 0.1 to 1; 1 to 10; ≥10 fibres/cm^3) to each task of interest. The probability of exposure of a job was defined by the maximum amount of probability among all tasks described in that job, while the intensity of exposure corresponded to the maximum amount of intensity among all tasks with maximum probability. For adjustment, we calculated an asbestos cumulative exposure index (CEI) as $CEI_{TEM}=\Sigma(D_i \times P_i \times I_i)$, with D_i, the duration of task job, i; P_i, the probability of exposure; and I_i, the intensity of exposure. The CEI_{TEM} was categorised into four classes, according to the distribution among controls (0; 0 to 0.15; 0.15 to 3.35; >3.35).

However, to improve the definition of the not exposed group and because it was not possible to be sure that participants had answered all requested specific questionnaires, we additionally applied an asbestos-specific job-exposure matrix (JEM) developed according to the combination of ISCO and NAF codes (available on demand from dst-matgene@invs.sante.fr).[12,13] Briefly, for each job i, the asbestos-JEM assigned a probability (percentage of workers exposed in the considered combination: none or less than 1% of workers; <5%; 5% to 30%; 30% to 70% and >70%), a frequency (percentage of working time during which a participant would be exposed (<5%, 5% to 30%; 30% to 70% ≥70%) and an intensity (in fibres/mL: <0.01; 0.01 to 0.1; 0.1 to 1;1 to 10; >10) of exposure related to specific tasks. In addition, the JEM attributed a frequency and an intensity of exposure related to work environment contamination. Based on this JEM, we calculated an asbestos CEI (CEI_{JEM}).

Participants with $CEI_{JEM}=0$ and $CEI_{TEM}=0$ were defined as not exposed to asbestos, while asbestos exposure was considered as missing when $CEI_{TEM}=0$ and $CEI_{JEM}>0$ (n=519).

Statistical analyses

Overall, 6481 participants were included in the study: 2926 cases and 3555 controls. We restricted the analysis to men, who represented 78% of our population: 2276 cases and 2780 controls.

We estimated the effect of welding separately for the regular or occasional welders. The reference group included

[i]Farmers, self-employed workers, managers/professionals, intermediate occupations, clerical workers, sales and services workers, blue-collar workers, inactive individuals.

participants who had not welded throughout their entire occupational history if not specified otherwise.

Multivariable unconditional logistic regression was used to estimate ORs and 95% CIs for association between lung cancer and welding exposure. No OR was estimated when less than 10 participants were included in a category. Association of histological types of lung cancer with welding was tested by multinomial regression to evaluate their heterogeneity.

Lifelong cigarette smoking was captured by the cumulative smoking index (CSI),[ii] which takes into account total duration of smoking, time since cessation and intensity, measured as the average number of cigarettes smoked per day.[14 15] A non-smoker was defined as a participant having smoked less than 100 cigarettes in his lifetime (CSI=0).

Models were adjusted for age at interview, *département*, CSI, CEI_{TEM} and the total number of working periods (<3; 3 to 4; 4 to 6; and >6 jobs, according to the quartiles in controls).

Dose–response relationships were investigated for frequency of welding during working time, total duration of exposure to welding activity, delay between first exposure to welding fumes and interview (≤35 or >35 years, which is the median of the delay among controls (38 years) rounded off to 35) and time since last welding. Sensitivity analysis was performed restricting the study population to blue-collar workers, as defined by the last job period held.

Statistical analyses were performed using SAS software V.9.3 (SAS Institute Inc, Cary, North Carolina, USA).

RESULTS

A total of 5056 men were included in this analysis (table 1). Cases had a mean age at diagnosis of 60 years, while controls were slightly younger (58 years old). Cases had a statistically significant lower educational level than the controls. We observed a clear increase in the risk of lung cancer with CSI (p trend $<10^{-4}$).

A similar proportion of cases and controls (23%) reported welding at least once during their occupational history; 5% and 3% of the cases and controls, respectively, were regular welders (table 2). Compared with participants who were never exposed to welding (reference group), regular welders had a significantly higher risk of lung cancer (OR=1.7, 95% CI 1.1 to 2.5). We explored dose–response relationships and did not find any substantial increase in the risk of lung cancer among occasional welders. On the other hand, among regular welders, we found that a frequency of welding over 5% of working time was associated with a 70% increase in the risk of lung cancer, statistically significant and the risk increased with duration of welding activity (p for trend 0.02).

These findings were strengthened when considering time since first exposure, up to a double risk (statistically significant) for regular welders who started welding more than 35 years before the interview and had an exposure duration longer than 10 years, with respect to reference participants. Interestingly, we found that the association with lung cancer was maximal 10–20 years since last welding, then decreasing slightly when delay was between 20 and 30 years or more. Sensitivity analysis restricted to blue-collar workers (1102 cases and 972 controls) did not modify the results (data not shown). No heterogeneity was observed in the association among regular welders between welding and lung cancer according to histological types, with ORs estimated to OR=1.8, 95% CI 1.1 to 3.0; OR=1.6, 95% CI 0.8 to 3.1; OR=1.6, 95% CI 1.0 to 2.8, respectively, for squamous cell carcinoma, small cell carcinoma and adenocarcinoma, p=0.4.

We estimated the risk of lung cancer according to the metal welded. As each worker had welded all types of metals, it was unfortunately not possible to isolate groups of workers that had welded a unique type of metal. Associations between each metal and the risk of lung cancer were therefore rather homogeneous, in the range of 1.05–1.75, and not significant (data not shown).

Estimations of the risk of lung cancer according to the welding process are presented in table 3.

Gas welding (76%) and arc welding (65%) were the two main welding processes reported by regular and occasional welders together. Among the occasional welders, each specific process was not associated with lung cancer, compared with non-exposed participants. However, among those who reported welding exclusively with one specific process, the OR corresponding to gas welding was 1.6, 95% CI 0.7 to 3.9, while the arc welding process did not produce any substantial increase (OR=0.9, 95% CI 0.4 to 2.0). It was not possible to perform this separate analysis among regular welders, given the small number of participants who reported welding only with one specific process. However, after pooling occasional and regular welders together, we observed that participants who reported gas welding exclusively had an OR of lung cancer of 2.3, 95% CI 1.0 to 5.0, while for those who reported arc welding activity, no association was observed (OR=1.1, 95% CI 0.6 to 2.3; data not shown).

We explored the role of substances covering the metal surface to be welded and of the cleaning procedure (table 4).

We found that, among regular welders, the risk of lung cancer increased to 2.0, 95% CI 1.1 to 3.4 when the work piece was covered with a substance, primarily paint or grease (33 controls and 53 cases). Cleaning the surface before welding is mainly done with mechanical treatment or, rarely, with a chemical treatment. We did not observe any increase in the risk of lung cancer for occasional welders who mechanically cleaned the metal before welding. In contrast, the small number of participants using only chemical substances had a higher risk of lung cancer, compared with non-exposed participants (not statistically significant). The same analysis performed among regular welders gave similar results, although the very low number of participants using chemicals only, allowed us to reliably estimate the association solely for those who used both kinds of cleaning (mechanical and chemical): in this case, the OR was 2.79, 95% CI 1.35 to 5.77.

In table 5, we show the risk of lung cancer according to the chemicals used to clean the metal before welding after pooling occasional and regular welders together, in view of the small number of participants in each subgroup.

For this analysis, the reference group was composed of participants who welded but did not use any chemical treatment before starting, either because they did not need to clean the metal or because it was mechanically cleaned. The highest risk of lung cancer was observed for participants cleaning the surface with acid (OR=2.5, 95% CI 1.0 to 6.1), which was the least used substance, followed by gasoline (OR=1.9, 95% CI 1.0 to 3.6).

DISCUSSION

This study shows that welding was associated with an increased risk of lung cancer among regular welders.

[ii]$CSI=(1-0.5^{dur^*/t})\times(0.5^{tsc^*/t})\times\ln(int+1)$, with t a half-life parameter, int the average daily cigarettes consumption, tsc*=max (tsc−d, 0), tsc, the time after smoking cessation, dur*=max (dur+tsc−d, 0)−tsc*, dur, the total duration of cigarette smoking and d a lag time parameter.

Table 1 Characteristics of the study population

	Controls (2780)		Cases (2276)			
	n	Per cent	n	Per cent	OR	95% CI
'Département'						
Bas-Rhin	360	12.9	302	13.3		
Calvados	358	12.9	272	12.0		
Doubs+Territoire de Belfort	112	4.0	106	4.7		
Haut-Rhin	89	3.2	56	2.5		
Hérault	360	12.9	252	11.1		
Isère	407	14.6	371	16.3		
Loire Atlantique	311	11.2	273	12.0		
Manche	247	8.9	262	11.5		
Somme	387	13.9	269	11.8		
Vendée	149	5.3	113	5.0		
Age at recruitment, years						
Mean (SD)	58 (9.9)		60 (9.0) $p<10^{-4}$			
<50	664	23.9	312	13.7	1.00	(ref)
50–60	858	30.9	774	34.0	1.25	1.02 to 1.52
60–70	927	33.4	826	36.3	1.46	1.19 to 1.77
≥70	331	11.9	364	16.0	2.32	1.82 to 2.97
Highest educational level						
Elementary school or less	521	19.4	675	33.3	1.00	(ref)
Middle school	1081	40.3	869	42.9	0.69	0.57 to 0.83
High school	310	11.6	185	9.1	0.53	0.40 to 0.69
University	752	28.0	273	13.5	0.39	0.31 to 0.49
Unknown	19	0.7	25	1.2	1.51	0.71 to 3.23
Number of jobs held						
Mean (SD)	4.6 (2.6)		4.4 (2.7) $p\leq 10^{-3}$			
Smoking history						
CSI=0	813	29.3	59	2.6	1.00	(ref)
0< CSI ≤0.5	611	22.1	105	4.7	2.32	1.67 to 3.25
0.5< CSI ≤1	513	18.5	234	10.4	6.22	4.57 to 8.46
1< CSI ≤1.5	393	14.2	391	17.4	14.51	10.7 to 19.6
1.5< CSI ≤2	355	12.1	779	34.6	34.55	25.6 to 46.5
CSI >2	106	3.8	683	30.3	89.17	63.5 to 125.1
Mean (SD)	0.65 (0.7)		1.62 (0.6) $p<10^{-4}$			
Histological type*						
Squamous cell carcinoma			808	35.3		
Adenocarcinoma			800	34.9		
Small cell carcinoma			335	14.6		
Large cell carcinoma			200	8.8		
Other			130	5.7		
Sarcoma			6	0.3		
Non-specified			13	0.6		

All participants were men. All estimated ORs have been adjusted for age, *département*, CSI.
*Sixteen patients had multiple tumours.
CSI, cumulative smoking index.

Our study has several strengths: the inclusion of incident cases, population controls randomly selected in the same *départements* as cases through incidence density sampling, participation rates over 80% in cases and controls, and face-to-face interviews by trained interviewers using structured questionnaires. Case–control study is often considered to have a weaker design compared with cohort (mostly historical in the context of occupational settings); in particular, this is usually due to recall bias. This real limitation is balanced by the knowledge of the entire occupational history, which allows the addressing of other carcinogenic exposures more accurately. Asbestos exposure is certainly the main occupational confounder in this debate and must be considered in all analyses. Assessment of exposure was performed through precise questionnaires allowing us to set up a TEM, which determines the exposure of the participant himself and not the exposure of a job, as is carried out with a JEM. Adjustments for asbestos can be therefore considered as accurately as possible, as previously shown.[11] Moreover, the case–control design allowed us to consider the entire smoking history of each participant.

Table 2 Risk of lung cancer associated with welding among occasional and regular welders*

	Controls		Cases			
	n	Per cent	N	Per cent	OR	95% CI
No welding	2037	77.4	1629	76.6	1.00	(ref)
Occasional welders	525	20.0	397	18.7	0.88	0.71 to 1.10
Regular welders	69	2.6	100	4.7	1.66	1.11 to 2.49
Occasional welders						
Frequency of welding						
≤5%	286	54.5	180	45.3	0.70	0.53 to 0.92
>5%	239	45.5	217	54.7	1.11	0.85 to 1.46
Test for trend, p					*0.93*	
Duration (years)†						
≤10	111	46.4	95	43.8	1.00	0.69 to 1.45
>10	128	53.6	122	56.2	1.20	0.85 to 1.70
Test for trend, p					*0.30*	
Time since first exposure†‡						
Duration (years)						
≤35						
≤10	48	20.1	34	15.7	1.16	0.67 to 2.03
>10	48	20.1	30	13.8	0.81	0.45 to 1.46
>35						
≤10	63	26.4	61	28.1	0.89	0.55 to 1.44
>10	80	33.5	92	42.4	1.44	0.95 to 2.16
Time since last welding†‡						
Years						
0	44	18.4	24	11.1	0.82	0.44 to 1.53
]0,10[	39	16.3	44	20.3	1.76	0.99 to 3.14
[10,20[	44	18.4	41	18.9	1.03	0.60 to 1.77
[20,30[	32	13.4	37	17.0	1.10	0.61 to 1.98
[30,40[	48	20.1	37	17.0	0.94	0.53 to 1.67
>40	32	13.4	34	15.7	1.17	0.62 to 2.19
Regular welders						
Frequency of welding						
≤5%	5	0.7	8	0.4	1.17	0.31 to 4.51
>5%	64	2.4	92	4.3	1.67	1.10 to 2.54
Test for trend, p					*0.19*	
Duration (years)†						
≤10	29	1.8	34	2.3	1.53	0.91 to 2.55
>10	35	0.6	58	2.0	1.96	0.98 to 3.92
Test for trend, p					*0.02*	
Time since first exposure†‡						
Duration (years)						
≤35						
≤10	11	17.2	10	10.9	1.08	0.38 to 3.01
>10	12	18.8	19	20.6	1.54	0.62 to 3.79
>35						
≤10	18	28.1	24	26.1	1.64	0.75 to 3.62
>10	23	35.9	39	42.4	2.05	1.08 to 3.91
Time since last welding†‡						
Years						
0	10	15.6	12	13.0	1.22	0.43 to 3.47
]0,10[	10	15.6	21	22.8	2.53	1.01 to 6.37
[10,20[	8	12.5	15	16.3	2.84	0.95 to 8.53
[20,30[	10	15.6	16	17.4	1.92	0.71 to 5.22
[30,40[	17	26.6	17	18.5	1.11	0.48 to 2.57
>40	9	14.1	11	12.0	1.24	0.42 to 3.67

All estimated ORs have been adjusted for age, *département*, number of jobs, cumulative smoking index (CSI) and asbestos exposure.
*'Regular welders' were those participants with at least one job period as welder in the strict sense of the word (ie, coded with International Standard Classification of Occupations (ISCO) code 8-72), and 'occasional welders' were those participants who declared to have at least once been exposed to welding/brazing/gas cutting.
†Participants with a frequency of welding <5% of the working time were not included.
‡p trend was not tested, as the curve departed from linearity.

Table 3 Risk of lung cancer according to the type of welding activity

	Controls		Cases			
	N	Per cent	n	Per cent	OR	95% CI
No welding activity	2037	87.1	1629	84.1	1.00	(ref)
*Occasional welders**	239	10.2	217	11.2	1.11	0.85 to 1.47
Soldering						
Ever†	107	44.8	89	41.0	0.98	0.67 to 1.42
Exclusively†	9	3.8	6	2.8	1.97	0.55 to 7.08
Brazing						
Ever	77	32.2	75	34.6	1.21	0.79 to 3.87
Exclusively	0	0	0	0	–	–
Gas welding‡						
Ever	188	78.7	172	79.3	1.10	0.81 to 1.50
Exclusively	13	5.4	24	11.1	1.64	0.69 to 3.90
Arc welding						
Ever	159	66.5	126	58.1	0.97	0.70 to 1.35
Exclusively	20	8.4	15	6.9	0.89	0.39 to 2.04
Spot welding						
Ever	72	30.1	67	30.9	1.22	0.78 to 1.90
Exclusively	3	1.3	4	1.8	–	–
Other welding						
Ever	32	13.4	23	10.6	0.79	0.39 to 1.57
Exclusively	5	2.1	6	2.8	1.02	0.23 to 4.44
*Regular welders**	64	2.7	92	4.7	1.69	1.12 to 2.57
Soldering						
Ever	14	21.9	29	31.5	2.62	1.20 to 5.72
Brazing						
Ever	18	28.1	26	28.3	1.20	0.58 to 2.49
Gas welding‡						
Ever	39	74.9	64	76.4	1.98	1.20 to 3.29
Arc welding						
Ever	47	68.0	65	62.8	1.99	1.21 to 3.26
Spot welding						
Ever	25	39.1	38	41.3	1.35	0.72 to 2.53
Other welding						
Ever	13	20.3	17	18.5	1.80	0.72 to 4.51

All estimated ORs have been adjusted for age, *département*, number of jobs, cumulative smoking index (CSI) and asbestos exposure.
*Participants with a frequency of welding <5% of the working time were not included in the analysis. 'Regular welders' were those participants with at least one job period as welder in the strict sense of the word (ie, coded with International Standard Classification of Occupations (ISCO) code 8-72), and 'occasional welders' were those participants who declared to have at least once been exposed to welding/brazing/gas cutting.
†Exclusively defines participants who used only one type of welding as opposed to ever.
‡Including blowtorch welding.

Recall bias should be formally addressed: welding activity was similarly self-reported by cases and controls (23%); this was expected, as welding is very common. In contrast, regular welders were significantly more represented among cases than among controls, and it is very unlikely that cases were overestimated as regular welders. The large number of very detailed questions may have generated false answers; however, many precautions were taken in order to minimise differential recall bias, including the fact that the ICARE study was presented as a study focusing on 'health and environment' instead of lung cancer risk factors.

In 1990, IARC classified welding fumes as possibly carcinogenic (2B): there was no significant increase of lung cancer in the cohort studies and a significant increase in some case–control studies, when adjusting for smoking.[1] Since then, other studies that were able to adjust for both smoking and occupational exposure to asbestos have found significant excess risk of lung cancer, when compared with participants who were not exposed to welding, with ORs between 1.4 and 1.9.[4 7 16–18] It should be noted once again that most epidemiological studies used welding activity as a proxy of welding fumes. In accordance with these studies, we also observed a significantly increased risk of lung cancer among regular welders (OR 1.7, 95% CI 1.1 to 2.5). A dose–response relationship is a key issue in the discussion of causality, which was often lacking or not very sharply observed in previous epidemiological studies.[1 17 19–23] Our results showed that the association with lung cancer increased with frequency of welding during the working time, and with total duration of exposure. The time elapsed from the first exposure is also important when considering the carcinogenic effect of exposure to a mixture. In our population, first exposure to welding dated extremely far back in time, with a median that was about 35 years in the controls. We found a higher risk of lung cancer among those who started welding more than 35 years ago, especially when the duration of welding was longer than 10 years. This observation reinforces the hypothesis of a carcinogenic effect of welding fumes. The shape of the curve describing the relationship with time since last welding was consistent with what we expected, considering the natural history of the disease. On the other hand, no association was found for occasional welders, suggesting that the increase in risk also depended on the level of exposure. Similar findings have been observed by Sörensen *et al*[16] and Kendzia *et al*.[4]

Despite the large number of epidemiological studies investigating the association between welding and lung cancer, knowledge of the carcinogenic mechanism remains poor. Different carcinogens are found in welding fumes, depending on the welding process and the type of metal, for example, Cr VI, nickel oxides and cadmium.[24] Cr VI in particular is considered as one of the possible causative agents of the association. It is found particularly in stainless steel welding and it has been shown that, among the types of arc welding, the manual metal arc (MMA) process entails higher exposure to Cr VI than tungsten inert gas (TIG), metal inert gas (MIG) or metal active gas (MAG) processes.[3 25] Gray and Gérin[25] estimated that the average Cr VI concentrations are substantially high and similar for MMA (arc welding) and oxy-gas welding (gas welding) with stainless steel (120 and 100 $\mu g/m^3$, respectively). Nickel oxides are found with the arc process (MIG, MAG, TIG), brazing or gas welding, according to the type of metal used.[25] In order to disentangle the effect of such complex exposures, epidemiological studies either investigated a specific industry (eg, shipyards),[20 23 26–28] or focused on the welded material (stainless steel, mild steel),[16 17 20 26 27 29–35] or on the specific chemicals released by the welding (Cr VI, nickel compounds).[1 26 28 31 36 37] Our questionnaire included detailed questions on the type of metal and the welding process; however, most participants reported welding several metals with different processes, since the study was set up in the general population. As a consequence, we could investigate only the major processes used (arc, gas, spot, etc), without going into further detail (ie, TIG, MIG, MAG, plasma). Our results showed that welding exclusively with gas was associated with a higher risk of lung cancer, with respect to arc welding, in agreement with t'Mannetje *et al*.[7] One hypothesis to support this result would be an exposure to higher Cr VI levels with gas welding as compared with arc

Table 4 Risk of lung cancer according to the covering and preparation of surfaces to be welded

	Controls		Cases			
	n	Per cent	N	Per cent	OR	95% CI
No welding	2037	89.5	1629	88.2	1.00	(ref)
Occasional welders	239	10.5	217	11.8		
Presence of grease or paint on the pieces	107	4.7	115	6.2	1.36	0.94 to 1.97
Cleaning with mechanical preparation only	84	3.7	69	3.7	0.94	0.61 to 1.42
Cleaning with chemical preparation only	18	0.8	18	1.0	1.44	0.60 to 3.42
Cleaning with chemical or mechanical preparation	89	3.9	78	4.2	1.03	0.69 to 1.56
Regular welders	64	3.1	92	3.4		
Presence of grease or paint on the pieces	33	1.6	53	3.1	1.98	1.15 to 3.43
Cleaning with mechanical preparation only	26	1.2	25	1.2	0.97	0.48 to 1.97
Cleaning with chemical preparation only	2	0.1	6	0.3	–	–
Cleaning with chemical or mechanical preparation	17	0.8	26	1.2	2.79	1.35 to 5.77

Participants with a frequency of welding <5% of the working time were not included in the analysis. All estimated ORs have been adjusted for age, *département*, number of jobs, cumulative smoking index (CSI) and asbestos exposure.

welding, when separating the subcategories MIG, MAG, TIG or MMA is unreachable. However, it is also possible that this increase in risk was related to blow torch cut, an activity that does not require any cleaning before cutting and that therefore generates many pollutants. Unfortunately, our questionnaire did not include any specific questions regarding blowtorch use, it was simply included in gas welding.

Our welding-specific questionnaire explored whether the surfaces to be welded were covered by paint or grease and identified the treatment applied to clean the surface before welding. Indeed, in case of the presence of paint, oil or grease on the surfaces to be welded, substances considered carcinogenic to the lung by the IARC may be found in the welding fumes (eg, metals such as chromium, or compounds issued from the decomposition of solvents leading to acidic substances). The presence of these substances generated during welding may contribute to the excess of lung cancer in welders, as observed in our study. Often, the cleaning is carried out in a mechanical way (ie, sanding or grinding) but some workers reported using chemical agents. For these workers, we observed a higher risk of lung cancer compared with those who had never welded, although this difference was not significant. To further investigate this association, we estimated the risk of lung cancer according to the chemical agent used, taking as the reference group those who worked without any chemical cleaning before welding. Because workers generally used several products, we were unable to isolate one agent as being more harmful; however, the strongest association was observed with acid (OR 2.6, 95% CI 1.1 to 6.4). These results constitute one of the original aspects of this analysis.

In conclusion, although further studies are needed to confirm our results, we show that the type of welding (gas welding) and the process used to clean the metal piece before welding, contribute as causes of occupational lung cancer.

Table 5 Risk of lung cancer according to the chemicals used to clean the surface to be welded

	Controls		Cases			
	n	Per cent	n	Per cent	OR	95% CI
Occasional and regular welders	303		309			
Never used any chemical	174	57.4	180	58.2	1.00	(ref)
Ever used chemicals						
Paint stripper	32	10.6	33	10.7	1.46	0.76 to 2.83
Trichloroethylene	58	19.1	59	19.1	1.30	0.77 to 2.20
Gasoline	29	9.6	41	13.3	1.92	1.01 to 3.65
White spirit	28	9.2	34	11.0	1.69	0.86 to 3.31
Acid	16	5.3	26	8.4	2.54	1.05 to 6.13

Participants with a frequency of welding <5% of the working time were not included in the analysis. All estimated ORs have been adjusted for age, *département*, number of jobs, cumulative smoking index (CSI) and asbestos exposure.

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Welding, a risk factor of lung cancer: the ICARE study

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