Case–Control Study on Renal Cell Cancer and Occupational Exposure to Trichloroethylene. Part I: Exposure Assessment

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A method for a semi-quantitative retrospective assessment of exposure to trichloroethylene (TCE) was implemented for a case–control study conducted in the Arve valley (France), an area with a widely developed screw-cutting industry, where teams of occupational physicians have collected a large quantity of well-documented measurements. A task-exposure matrix was developed to link the main working circumstances in a screw-cutting workshop to corresponding TCE-exposure levels: a ‘basic level’ was assigned to each task, standing for usual working procedures; exposure circumstances, such as duration or distance from the TCE source, were introduced as corrective factors. In parallel, a detailed occupational questionnaire was designed, setting subjects’ descriptions of their successive jobs and working circumstances against levels assessed in the matrix. Possible exposure to TCE, plus some other occupational compounds (other solvents, oils, some metals, asbestos, welding fumes and ionizing radiations), were assessed for any job in all job histories. An average level of exposure to TCE, related to an 8 h usual working day, was attributed to each job period in turn, which was then categorized into six classes: 0; 1–35; 35–50; 50–75; 75–100; and >100 p.p.m. A total of 402 study subjects described their occupational life (average 3.7 jobs/subject, from 1924 to 2003). About 19% of the 1486 job periods described were assessed as being exposed to TCE; of these, 72.2% involved levels <35 p.p.m., 13.2% involved levels >50 p.p.m. and 5.4% above the French occupational exposure limit of 75 p.p.m. (TWA 8 h). A total of 41 job periods included exposure with peaks. Compared with levels encountered in other studies, the more severely exposed part of our study population seemed more exposed than most other populations previously studied, owing to vapor degreasing practices.

Keywords: cancer epidemiology; cutting fluid; exposure assessment; solvents; trichloroethylene

A hospital based case–control study on renal cell cancer was conducted in the Arve Valley (France). This valley is traditionally devoted to screw cutting, a kind of lathe work on metal parts that makes considerable use of cutting fluids and, hence, of degreasing agents. In 1965, 450 workshops were devoted to that activity, 330 having <10 workers. During the 1970s there were 650 workshops, with a total of about 7000 workers, but 500 of them employed <5 workers. In 1982, 750 companies employed about 12 000 workers, 600 involving <10 workers. This paper describes the methodology developed for the semi-quantitative assessment of exposure to trichloroethylene (TCE), the main culprit agent hypothesized in the study. Exposure assessment is a key part of occupational epidemiological studies, and exposures need to be characterized as accurately as possible in terms of intensity, route, duration and frequency (Semple, 2005). Various

*Author to whom correspondence should be addressed. Tel: +33 4 78772827; fax: +33 4 78742582; e-mail: barbara.charbotel@rockefeller.univ-lyon1.fr
rtoscopic methods may be used for occupational-exposure assessment in case-control studies such as use of job–exposure matrices (Bouyer and Hénon 1993; Golberg and Hénon, 1993; Tielemans et al., 1999) or task–exposure matrix (Van der Gulden et al., 1993) and expert assessment from self reporting of task by study subjects (Siemiatycki et al., 1981; Gerin and Siemiatycki, 1991; Siemiatycki, 1996). Hybrid approaches that use expert assessments based on detailed job information in combination with a substance-specific exposure matrix have been suggested recently (Fritschi et al., 2001). In this approach the quality of the retrospective assessment by experts is thought to be enhanced by a more accurate knowledge of a specific exposure and of the specific tasks and occupational environment of each subject (Benke et al., 2001).

Few epidemiological studies have assessed TCE-exposure levels quantitatively by means of actual measurements (Wartenberg et al., 2000). In an incidence study by Antilla et al. (1995), exposure was assessed by biological monitoring: Urine concentrations of trichloroacetic acid (U-TCA) were recorded from 1965 to 1982. The overall median U-TCA was 63 μmol l⁻¹ for women and 48 μmol l⁻¹ for men (respectively 80–90 μmol l⁻¹ before 1970). No data on air contaminants were available, but in measurements performed by the Finnish Institute of Occupational Health between 1982 and 1985 the concentration of TCE in degreasing was usually <50 p.p.m. In a Swedish cohort (Axelson et al., 1994), 81% of male subjects showed a mean U-TCA level <50 mg l⁻¹, corresponding to 20 p.p.m. in the air (TWA 8 h) according to the authors. In a cohort of workers at a US aircraft maintenance facility (Stewart et al., 1991), available industrial health data were collected but could not be straightforwardly linked to chemicals in use in work areas, and exposure to TCE was estimated in terms of tasks; an equation was developed to take account of conditions of use. In a German cardboard factory, Henschler et al. (1995) did not have measurement data but interviewed long-term employees to assess exposure levels. Vamvakas et al. (2001) quantified TCE levels from the description of exposure conditions (duration, frequency, intensity) and of acute symptoms following exposure (frequency and type), graded from none to severe.

In the Arve Valley many measurements have been carried out over a long period (1960s until now) focusing especially on atmospheric TCE levels near degreasing machines or on biological monitoring of screw-cutting workers [urinary levels of trichloroacetic acid (U-TCA), or trichloroethanol (U-TCE)]. Some of the studies have been published and are presented in Table 1.

In addition to these studies, occupational physicians in the Valley have a policy of routine monitoring: workers in the screw-cutting industry regularly undergo U-TCA assessment and workshop measurements are undertaken when excessive levels are detected.

Because of this knowledge on occupational exposure to TCE, the Arve valley in France was of special interest for a case–control study based on a specific semi-quantitative exposure assessment.

**MATERIALS AND METHODS**

A Task/TCE-Exposure Matrix was designed using all these well-documented levels of exposure, set against answers to a detailed occupational questionnaire where all study subjects were asked to describe accurately their successive jobs, with the help of a trained interviewer.

**The task-exposure matrix**

The main tasks or working circumstances in a screw-cutting workshop were linked to corresponding TCE-exposure levels: a ‘basic level’ (atmospheric level of TCE) was assigned to each task/machine, representing the average level for usual working procedures. These levels have been assessed from observed atmospheric levels and from biological measurements on workers. The resulting estimates represent the global uptake from both the respiratory pathway and some cutaneous penetration due to deposition of solvent vapors on the bare skin of hands, forearm or face. Task duration and various exposure circumstances, such as distance from the TCE source or use of personal or collective protective equipment, were introduced as corrective factors (additive or subtractive) for these basic levels.

- For degreasing machines, the ‘basic level’ represents its potential emission of TCE vapor, to which corrective factors should be applied depending on whether workers were actively using the machine, or were simply located in the same workshop, and their distance from it.

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early 1980s, and 10 p.p.m. for closed machines in use after 1990.

- Corrective factors for distance from the degreasing machine.

It is quite impossible to come up with a general rule, as specific workshop geometry, ventilation and activity are critical (Cherrie, 1999); nevertheless, generally speaking, levels decrease only slightly in the immediate vicinity of the machine (the near-field) then drop off, proportionally to distance between 10 and 30 m and according to the number and kinds of activities going on there. It was impossible in such a retrospective study to be aware of all parameters required to reconstruct exposure levels in various locations of each workshop, but at least the size of the shop, and distance to the source of TCE, as given by subjects in their job descriptions could be used to appreciate a potential decrease of the exposure.

The corrective factors arbitrarily chosen for this study were reductions of 10% at 5 m, 25% at 10 m, 40% at 15 m, 55% at 20 m and 75% at 30 m.

- Emptying, cleaning and refilling the degreaser.

Old degreasing machines are cleaned manually or semi-manually. Although these tasks were performed after one night of cooling the degreaser (generally done by the employer or the foreman on Saturday morning), they involved high levels of exposure either from respiratory intake because of the large quantities of solvent and some confined tasks inside the tank, or from dermal intake. All workers used gloves during such tasks, but their faces were exposed, and their overcoats were likely to have been at least partially impregnated with TCE.

Many atmospheric and biological measurements have been carried out by Occupational Physicians of the Valley. Although less frequent, it is the longest and most exposing task for their workers, and average equivalent atmospheric levels assessed have taken into account these two ways of exposure. The most exposing parts of the tasks (emptying the tank; removing the sludge of oily solvent—physically entering the tank; cleaning it with jets of TCE) led to an average level of 300 p.p.m., with presence of peaks up to 600 p.p.m. and an average duration of 2 h.

- Peaks of exposure.

Exposure peaks obviously contribute to higher average levels and, thus, have already partially been taken account of by the assessment. Nevertheless, they could not be totally integrated in the average TCE concentration as they represent additional short but

<table>
<thead>
<tr>
<th>Job description</th>
<th>Atmospheric TCE levels</th>
<th>Biological data</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tolot et al. (1964)</td>
<td>Attributed survey in a very large degreasing workshop using three half-open machines</td>
<td>Between 180 and 600 p.p.m.</td>
</tr>
<tr>
<td>Bonnavion et al. (1980)</td>
<td>Exposure during washing and drying activities in six workshops (886 workers)</td>
<td>From 70 to 800 p.p.m. in the washing areas</td>
</tr>
<tr>
<td>Routhier et al. (1982)</td>
<td>Description of the usual working day (9 h) of 188 workers from 89 workshops of various sizes</td>
<td>93 (49%) of the workers were never/only seldom using TCE, 54 (58%) worked in the same area as the degreasing machines. The remaining workers were located in separated shops</td>
</tr>
<tr>
<td>Coudert (1984)</td>
<td>Survey of 18 non-washing workers from one workshop, after introduction of a new half-open degreasing machine</td>
<td>From 15 to 20 p.p.m. in the general surroundings (TWA 8 h), to 200 p.p.m. at 6 m from the machine when it was opened</td>
</tr>
<tr>
<td>Venjean et al. (1989)</td>
<td>General survey run on 31 washing machines currently in use and representing the 5 main specifications of interest (open, half-open or closed, and manual or with a conveyer)</td>
<td>Levels near open manual machines were all above the threshold limit value (TLV), with some up to 300 p.p.m., while only one of the four closed washing machines with a conveyor presented excessive values</td>
</tr>
<tr>
<td>Barnavol et al. (2003)</td>
<td>Biological survey of 104 workers from 78 different workshops</td>
<td>Seven workers (screw cutters and storekeepers) were not exposed, 13 presented results above the French Biological Limits (U-TCA + TCE &gt;300, or U-TCA &gt;100 mg g⁻¹ creatinine)</td>
</tr>
</tbody>
</table>
extreme exposures (such as moving the boiling TCE when removing the baskets, Challen et al., 1958; Lefèvre et al., 1965; Kay 1973).

As a result, the occurrence of exposure peaks was also assessed, as an additive factor, according to the following rules:

—Peak = any exposure reaching 200 p.p.m.
   (the French Ceiling Value for 15 min), for at least 15 min a day, either by repeated very short-term tasks (1 min), such as those done by a degreaser dipping and removing baskets at each stage of the degreasing process, or during a less frequent but longer task involving higher quantities of solvent, such as cleaning floors or degreasing tanks each week or month. This level means that only people exposed to hot TCE (either in a direct task or by close contact with the hot degreaser) or cold TCE in large quantity and/or evaporation surface were involved in this assessment.
—Peak Level 1 = workers seldom exposed to peaks, a few times a year.
—Peak Level 2 = workers exposed to peaks, a few times a month.
—Peak Level 3 = workers frequently exposed to peaks, a few times a week.

• Hand-dipping in cold TCE.

Until the 1990s, many workers had at their disposal little tins of cold TCE, to dip and check their production samples with bare hands. Although the area of skin in contact was quite small, mainly the tips of three fingers, the question arises of the actual dermal uptake, as the activity was repeated a number of times a day. Although, out of eight countries, the UK was the only one who assigned a skin notation to TCE (Johanson, 2001), various studies from a long time (Sato and Nakajima, 1978; Kezic et al., 2000), and biological measurements taken on Arve Valley workers, have clearly shown that some uptake occurred from such dermal TCE penetration. A basic level (expressed as an ‘equivalent airborne concentration, TWA 8 h’) of 30 p.p.m. has been attributed to a worker dipping metal parts in an individual open tin every 10 min throughout the working day. This equivalent level was assessed from local data: a biological survey conducted on workers in screw-cutting shops, who were exposed only cutaneously (no large degreaser in the assembly or control room) (Venjean et al., 1999), and annual reports (1998–2001) by some occupational physicians of the valley. Among all monitored workers, 26 were only exposed to TCE from a dermal penetration of cold solvent (no degreasing machine in the room, no receipt of baskets full of wet pieces, etc.) and showed U-TCA + TCE from 0 to 176.6 mg g⁻¹ (mean 38.4 mg g⁻¹). Obviously this dermal penetration is linked to some inhalation from the evaporation of the open tin of cold solvent, but the biological levels obtained take into account these two totally correlated intakes. According to the physicians in charge of this survey, this biological level can be linked to an atmospheric level of 30 p.p.m. (TWA 8 h).

ASSESSMENT BASED ON THIS MATRIX

This Task-Exposure Matrix enabled average TCE doses to be calculated for each job, insofar as the job’s tasks, duration and relevant working circumstances were described in the occupational questionnaire (see below). These doses were then used to categorize job periods into five classes, with the French and international legal values as cut-off levels:

- Very low exposure = 1–35 p.p.m. (35 p.p.m. = 1/2 French occupational exposure limit. INRS, 1999a).
- Low exposure = 35–50 p.p.m. (50 p.p.m. = ACGIH limit. INRS, 1999b).
- Medium exposure = 50–75 p.p.m.
- High exposure = 75–100 p.p.m.
- Very high exposure >100 p.p.m.

As these categories are the result of exposure levels averaged over a working day and over the year, they may represent any pattern of exposure, ranging from a single constant source of exposure throughout the working day to a variety of unstable exposures resulting in discontinuous levels; they also include seasonal variations, as only jobs held for 1 year or more were taken into account.

THE OCCUPATIONAL QUESTIONNAIRE
(AVAILABLE ON http://www.inrets.fr/ur/umrestte/index.e.html)

The first part of the occupational questionnaire was devoted to the respondent’s job history, listing any job she/he had held. Subjects were then asked to describe each job in turn, either with the support of a Screw-Cutting Questionnaire (SCQ), if the job was related to that business, or of a General Occupational Questionnaire (GOQ), if not.

The GOQ and SCQ followed the same structure:

- some questions devoted to the company (production, size, ...), the workshop (production, size, equipment, ...) and other workers (number, tasks, ...);
- list of main tasks and working conditions (duration, etc.);
- as many activities or jobs might involve exposure to TCE (textile cleaning, or metal cleaning in workshops other than screw-cutting), the GOQ, like the SCQ, asked about possible exposure to solvents in general and to TCE in particular;
- some questions devoted to possible exposures to other occupational risk factors for Renal Cell

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Cancer (asbestos, petroleum oils, other solvents, cadmium, lead and welding fumes). (Partanen et al., 1991; Edelman et al., 1992; Fowler, 1992; Steenland et al., 1992; McCredie and Stewart, 1993; Poole et al., 1993; Schnatter et al., 1993; Mellemgaard et al., 1994; Fu and Boffetta, 1995; Mandel et al., 1995; Sali and Boffetta 2000).

After blinding (identity and diagnosis), the occupational questionnaires filled in by subjects were analyzed as follows:

In the first step of the occupational assessment, the career of each subject was first examined job by job, so as to get a detailed overview of the whole job history. If necessary a job in turn was split into two or more homogeneous job periods in case of evolution of tasks or process. Then for each job period, the employer’s activity and the job title were encoded (ISCO, 1968; NACE Rev 1, 1999; respectively) and a qualitative assessment of low/medium/high level was made of all exposures except to TCE.

In addition, job periods were grouped into three categories: (i) screw-cutting jobs: all job periods in screw-cutting workshops; (ii) non-screw-cutting but possibly TCE-exposed jobs; and (iii) job periods definitely not exposed even to a minimal level of TCE.

In the second step, all the screw-cutting jobs were reviewed. A range of exposure was attributed to each screw-cutting job period, using both the matrix and the SCQ description, taking into account tasks with their duration, use of hot or cold TCE, description of the workshop, and presence and distance of a hot or cold degreasing machine. Based on TCE levels during tasks and reported duration of tasks a 8 h time weighted average (TWA) exposure was calculated:

\[ 8\text{h} - \text{TWA TCE} = \frac{\sum_i (\text{TCE}_i \times D_i)}{8}; \]

where TCE\(_i\) is the estimated TCE level for task-\(i\) and D\(_i\) is the reported duration of task-\(i\) (in hours).

The final 8 h TWA TCE estimate was assigned a confidence score: certain/probable/possible exposure to TCE based on subjective assessment by the exposure rater and quality of the job descriptions. In addition to this average level of exposure, peak exposure was also assessed, in terms of three levels as described above.

In the third step, all non-screw cutting jobs attributed at least possible TCE exposure in the first step were reviewed to estimate TCE exposure, using the qualitative description of the tasks together with detailed information from the GOQ.

**RESULTS**

**Occupations and other exposures**

A total of 86 cases and 316 controls were included. The mean age of the cases was 61.8 (±10.7), 59 were men (68.6%). The mean age of the controls was 61.1 (10.4), 221 were men (69.9%).

For the 402 subjects, 1341 jobs were initially described leading to 1486 job periods after splitting some of these into two or more homogeneous jobs, in case of evolution in the career of the worker or in the technology of the workshop (average: 3.7 job periods per subject). The distribution of activity codes showed, as expected, a high proportion of metalwork (20%), with construction (8%), farming (4%), workshop jobs (3%), chemical production (3%) and garages (2.5%) being the other main ‘blue collar’ activities in the study population. For metal workers, 138 jobs were initially described in a SCQ, leading to 175 job periods (12% of the final number of job periods, but 20% of subjects). About 120 job periods in various other activities were assessed as possibly/probably/certainly exposed to some TCE. As expected for this area with a high metal-working population, relatively high prevalences of petroleum oils (cutting and lubricating), metals (especially cadmium), petroleum solvents (including gasoline and white-spirit), welding (but not brazing) and asbestos were observed (see Table 2).

**EXPOSURE TO TCE**

**Information about TCE exposure as given by subjects**

As seen in Table 3, subjects were able to answer questions concerning possible exposure to TCE, in both the general and in the SCQ. Based on information from the 1203 GOQs filled in, ~14% of the jobs described the use of TCE, 86% of them (woodworkers, machine fitters, etc.) in a cold way and in small quantities. In contrast, in the 138 initial SCQs, within 34 jobs describing the use of TCE, 18 (53% of these jobs) used it hot.

**Trichloroethylene exposure assessment**

In total, 295 out of 1486 job periods (19%) involved TCE exposure; 120 were not in the screw-cutting industry, though mainly in other metal workshops. Table 4 shows that the prevalence of TCE exposure has increased between the 1950s and 1970s in this population. The number of job periods involving TCE exposure reached a maximum (146) during the 1970s, as did the percentage of periods with an exposure (19.8%) and the percentage of highly exposed subjects (8.2% exposed above 75 p.p.m.). Then, during the 1980s, a decline in TCE use is observed: the percentage of job periods involving TCE exposure was lower (14.8% during 1980s and 7.1% during 1990s), although exposure levels were still high (9.1% above 75 p.p.m. during 1980s).
Table 2. Frequency and levels of other exposures for job periods

<table>
<thead>
<tr>
<th>Level exposure</th>
<th>Low (1) Number (% of 1486 job periods)</th>
<th>Medium (2) Number (% of 1486 job periods)</th>
<th>High (3) Number (% of 1486 job periods)</th>
<th>Total Number (% of 1486 job periods)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Solvents</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chlorinated (Other than TCE)</td>
<td>36 (2.4)</td>
<td>10 (0.7)</td>
<td>4 (0.3)</td>
<td>50 (3.4)</td>
</tr>
<tr>
<td>Petroleum derivates</td>
<td>220 (14.8)</td>
<td>63 (4.2)</td>
<td>7 (0.5)</td>
<td>290 (19.5)</td>
</tr>
<tr>
<td>Oxygenated</td>
<td>56 (3.8)</td>
<td>16 (1.1)</td>
<td>2 (0.1)</td>
<td>74 (5.0)</td>
</tr>
<tr>
<td>Other</td>
<td>8 (0.5)</td>
<td>3 (0.2)</td>
<td>0 (0.0)</td>
<td>11 (0.7)</td>
</tr>
<tr>
<td>Oils</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cutting fluids</td>
<td>99 (6.7)</td>
<td>44 (3.0)</td>
<td>80 (5.3)</td>
<td>223 (15.0)</td>
</tr>
<tr>
<td>Other petroleum oils</td>
<td>82 (5.5)</td>
<td>17 (1.1)</td>
<td>4 (0.3)</td>
<td>103 (6.9)</td>
</tr>
<tr>
<td>Welding</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Brazing</td>
<td>24 (1.6)</td>
<td>12 (0.8)</td>
<td>3 (0.2)</td>
<td>39 (2.6)</td>
</tr>
<tr>
<td>Other</td>
<td>82 (5.5)</td>
<td>33 (2.2)</td>
<td>17 (1.1)</td>
<td>132 (8.9)</td>
</tr>
<tr>
<td>Lead</td>
<td>62 (4.2)</td>
<td>8 (0.5)</td>
<td>2 (0.1)</td>
<td>72 (4.8)</td>
</tr>
<tr>
<td>Cadmium</td>
<td>29 (2.0)</td>
<td>7 (0.5)</td>
<td>2 (0.1)</td>
<td>38 (2.6)</td>
</tr>
<tr>
<td>Asbestos</td>
<td>143 (9.6)</td>
<td>20 (1.3)</td>
<td>1 (0.1)</td>
<td>164 (11.0)</td>
</tr>
<tr>
<td>Ionizing radiation (source)</td>
<td></td>
<td></td>
<td></td>
<td>17 (1.1)</td>
</tr>
</tbody>
</table>

Table 3. Quality of Information about TCE exposure given by subjects in occupational questionnaires

<table>
<thead>
<tr>
<th></th>
<th>Number and percentage of answers (%)</th>
<th>Number and percentage of 'YES' responses in answers (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>In the 138 initial Screw cutting questionnaires: ‘Which machines and materials were in the main workshop or room you were working in, (and in the other ones if applicable)?’</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Screw-cutting machines</td>
<td>133 (96.7)</td>
<td>92 (69.2)</td>
</tr>
<tr>
<td>Digitally driven machines</td>
<td>130 (94.2)</td>
<td>78 (60.0)</td>
</tr>
<tr>
<td>Washing machines in cold phase</td>
<td>126 (91.3)</td>
<td>26 (20.6)</td>
</tr>
<tr>
<td>Washing machines in hot phase (or vapor)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Open washing machine</td>
<td>121 (87.7)</td>
<td>18 (14.9)</td>
</tr>
<tr>
<td>Half open washing machine</td>
<td>121 (87.7)</td>
<td>16 (13.2)</td>
</tr>
<tr>
<td>Closed</td>
<td>121 (87.7)</td>
<td>18 (14.9)</td>
</tr>
<tr>
<td>With a drying channel</td>
<td>119 (86.2)</td>
<td>10 (8.4)</td>
</tr>
<tr>
<td>Did you do one or more of the following jobs?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Screw-cutter, or screw-cutting assistant</td>
<td>136 (98.6)</td>
<td>63 (46.3)</td>
</tr>
<tr>
<td>Digitally driven machine operator</td>
<td>135 (97.8)</td>
<td>38 (28.1)</td>
</tr>
<tr>
<td>If yes, were metal parts still wet with TCE when you received them?</td>
<td>37 (94.4)</td>
<td>7 (18.9)</td>
</tr>
<tr>
<td>Metal parts checking</td>
<td>135 (97.8)</td>
<td>12 (8.9)</td>
</tr>
<tr>
<td>If yes, were metal parts still wet with TCE when you received them?</td>
<td>10 (83.3)</td>
<td>4 (40.0)</td>
</tr>
<tr>
<td>Washing with cold trichloroethylene</td>
<td>130 (94.2)</td>
<td>22 (16.9)</td>
</tr>
<tr>
<td>Washing with hot trichloroethylene</td>
<td>130 (94.2)</td>
<td>18 (13.8)</td>
</tr>
<tr>
<td>Cleaning the washing machine, scraping sludge, etc.</td>
<td>131 (94.9)</td>
<td>10 (8.3)</td>
</tr>
<tr>
<td>In the 1203 GOQs: ‘Were you exposed, in your own jobs or via those of a neighboring worker, to any chemical used as solvent, thinner, degreasing agent or cleaning agent (except detergents or soaps)? How did you use it, or how was it used by your neighbor?’</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Trichloroethylene</td>
<td>1,149 (95.5)</td>
<td>162 (14.1)</td>
</tr>
<tr>
<td>Cold use</td>
<td>150 (92.6)</td>
<td>140 (93.3)</td>
</tr>
<tr>
<td>Hot use, or as vapor</td>
<td>151 (93.2)</td>
<td>19 (12.6)</td>
</tr>
<tr>
<td>In a large open batch</td>
<td>150 (92.6)</td>
<td>141 (94.0)</td>
</tr>
<tr>
<td>In a large closed batch</td>
<td>150 (92.6)</td>
<td>8 (5.3)</td>
</tr>
</tbody>
</table>
Of the 295 job periods, 72.2% involved levels <35 p.p.m., 13.2% involved levels 50 p.p.m. and 5.4% above the French occupational exposure limit of 75 p.p.m. (TWA 8 h). For 88.8% of these job periods, the TCE exposure assessment confidence score was 2 or more. A total of 41 job periods included exposure with peaks; all but one of the highest exposure levels and peaks occurred before 1980 (Table 5), which is consistent with technological evolution.

Validation of the assessment of TCE in screw-cutting shops

A validation was attempted with information gathered from occupational physicians in the valley during systematic biological survey of degreasers, resulting in a biological classification that might be compared with our classes of exposure. While not exactly identical in terms of level, mainly because of the shift from biological to atmospheric values (Lowry et al., 1974; Vincent et al., 1980; Magadur and Morel, 1981; Ulander et al., 1992; Axelson et al., 1994), the two types of classification may be related as follows:

Table 4. Levels of TCE exposure by decade and job period

<table>
<thead>
<tr>
<th></th>
<th></th>
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<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;35</td>
<td>3</td>
<td>17</td>
<td>54</td>
<td>103</td>
<td>99</td>
<td>72</td>
<td>33</td>
<td>6</td>
</tr>
<tr>
<td>[35–50]</td>
<td>0</td>
<td>3</td>
<td>13</td>
<td>22</td>
<td>22</td>
<td>12</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>[50–75]</td>
<td>0</td>
<td>2</td>
<td>6</td>
<td>10</td>
<td>13</td>
<td>6</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>≥75</td>
<td>0</td>
<td>1</td>
<td>3</td>
<td>4</td>
<td>12</td>
<td>9</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Total periods with an exposure</td>
<td>3</td>
<td>23</td>
<td>76</td>
<td>139</td>
<td>146</td>
<td>99</td>
<td>41</td>
<td>8</td>
</tr>
<tr>
<td>Rate of exposure over 75 ppm among periods with an exposure</td>
<td>0</td>
<td>4.3%</td>
<td>3.9%</td>
<td>2.9%</td>
<td>8.2%</td>
<td>9.1%</td>
<td>4.9%</td>
<td>0</td>
</tr>
<tr>
<td>Total number of periods</td>
<td>77</td>
<td>334</td>
<td>573</td>
<td>736</td>
<td>736</td>
<td>671</td>
<td>575</td>
<td>128</td>
</tr>
<tr>
<td>Rate of periods with an exposure</td>
<td>3.9%</td>
<td>6.9%</td>
<td>13.3%</td>
<td>18.9%</td>
<td>19.8%</td>
<td>14.8%</td>
<td>7.1%</td>
<td>6.3%</td>
</tr>
</tbody>
</table>

Level 1 = some times a year; level 2 = some times a month; level 3 = some times a week.

Table 5. Exposure to peaks according to level of TCE exposure (job periods)

<table>
<thead>
<tr>
<th>Class of exposure (p.p.m.)</th>
<th>Peaks</th>
<th>Total N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>0.1–35</td>
<td>201 (79.1)</td>
<td>11 (31.6)</td>
</tr>
<tr>
<td>[35–50]</td>
<td>36 (14.2)</td>
<td>4 (47.4)</td>
</tr>
<tr>
<td>[50–75]</td>
<td>14 (5.5)</td>
<td>2 (10.5)</td>
</tr>
<tr>
<td>[75–100]</td>
<td>1 (0.4)</td>
<td>2 (10.5)</td>
</tr>
<tr>
<td>100 and more</td>
<td>2 (0.8)</td>
<td>—</td>
</tr>
<tr>
<td>Total</td>
<td>254 (100.0)</td>
<td>19 (100.0)</td>
</tr>
</tbody>
</table>

Level 1 = some times a year; level 2 = some times a month; level 3 = some times a week.

Of the 295 job periods, 72.2% involved levels <35 p.p.m., 13.2% involved levels >50 p.p.m. and 5.4% above the French occupational exposure limit of 75 p.p.m. (TWA 8 h). For 88.8% of these job periods, the TCE exposure assessment confidence score was 2 or more. A total of 41 job periods included exposure with peaks; all but one of the highest exposure levels and peaks occurred before 1980 (Table 5), which is consistent with technological evolution.

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A validation was attempted with information gathered from occupational physicians in the valley during systematic biological survey of degreasers, resulting in a biological classification that might be compared with our classes of exposure. While not exactly identical in terms of level, mainly because of the shift from biological to atmospheric values (Lowry et al., 1974; Vincent et al., 1980; Magadur and Morel, 1981; Ulander et al., 1992; Axelson et al., 1994), the two types of classification may be related as follows:

—Low exposure: U-TCA + TCE < 40 mg per g creatinine (50 mg l⁻¹); corresponding to atmospheric levels <30 p.p.m. over an 8 h working day.

—Medium exposure: U-TCA + TCE = 40–100 mg g⁻¹ (50–130 mg l⁻¹), corresponding to atmospheric levels from 30 to 60 p.p.m. (TWA 8 h).

—High exposure: U-TCA + TCE = 100–170 mg g⁻¹ (130–220 mg l⁻¹) and/or U-TCA > 70 mg g⁻¹, corresponding to atmospheric levels from 60 to 80 p.p.m. (TWA 8 h).

—Toxic level: U-TCA + TCE = 170–300 mg g⁻¹ (>220 mg l⁻¹), corresponding to atmospheric levels above 80 ppm (TWA 8 h), and/or peaks.

The eight occupational physicians from the valley who participated in the validation received a file including: subject ID number, period of job, job title and tasks, name and location of factory and technical description as given in the questionnaire; thus, validation was not carried out by subject but by job in a given workshop at a given time.

Out of these job periods, the physicians identified 32 in workshops, which were in their catchment area at one time or another since they had joined the group (mainly in the 1980s), and made their own assessment.
for these, based on their knowledge, and on atmospheric and biological data in their possession. This was done blind to any other assessment.

For 23 (72%) of these periods, there was a good agreement between occupational physicians and our assessment. Three periods initially assessed as being not exposed were attributed low exposure levels by the physicians (general workshop conditions). The low level of exposure initially assessed for one job period proved inappropriate, as TCE was not yet in use at that date according to the physicians. One job period initially assessed in the low category (35–50 p.p.m.) was to split into two different jobs, the first with medium exposure (probably <60 p.p.m.) as assessed by the physicians and the second with low exposure. One subject was assessed as low-exposed in the second part of his job, according to the change in tasks he described, whereas the physicians had attributed high exposure for the whole period. Finally, three job periods were considered as involving medium exposure by the physicians in contrast to the very low exposure assessed.

**DISCUSSION**

Few epidemiological studies of TCE exposure have been based on a detailed exposure assessment. Indeed, assessing historical exposure levels is always difficult and rather imprecise, especially in the general population where working conditions are diverse and industrial hygiene measurements often not available. In the present study area, however, all the different screw-cutting plants could almost be considered to be part of one single large factory, as all occupational physicians in this area work together and are dedicated to the same industrial network almost totally specialized in that activity. Moreover, they have collaborated in many health and safety surveys over a range of workshops, so that the local hygiene data are more plentiful and coherent than one could expect in a general population.

The aim of the exposure-assessment approach used in the present study was to make ‘semi-quantitative’ estimates, combining existing data with detailed and accurate job descriptions. A specific occupational questionnaire was developed for this study, information from which was used alongside a task-exposure matrix (based on both biological and air-monitoring data from local workshops) to provide exposure estimates for the main routine tasks in screw-cutting shops.

This kind of process combining an expert assessment from Job Specific Questionnaires with the use of substance-specific exposure matrix has been demonstrated to enhance the quality of the retrospective assessment by experts (Benke et al., 2001).

As far as possible, comparisons were made between the levels obtained from the present task-estimates and those in the industrial hygiene literature that testify to the same range of levels. All exposures have been assessed as a TWA on an 8 h shift, but as intense solvent exposures of short to very short duration are frequent in hot degreasing, the possibility to be over exposed in that way was of special concern in that study. Various parameters have been used to define peaks of exposure (Kumagai and Matsunaga, 1999; Preller et al., 2004), yet no real consensus exists on what constitutes toxicologically relevant parameters. Nevertheless, magnitude, duration and frequency of these peaks are of main interest to define them. In this study peaks were defined as a partially additional exposure with a magnitude of 200 p.p.m. (French Ceiling Value) or more, a minimum duration of 15 min, but possibly shared into serial exposures of 1 min or more, and on a daily, weekly or monthly frequency. It means that we have considered very short exposures even those averaging 1 min, if they were repeated during the shift. These very high atmospheric levels could also lead to an additional dermal intake that we were not able to quantify. That is the reason why our peaks are not quantified but only defined as an additional exposure to the average level during a shift.

TCE estimates for cold washing were of 18 p.p.m. as the basic emission level around the tank, and 50 p.p.m. directly above the tank, compared with a TCE level of 15 p.p.m. from an open-top cold tank, with 30–100 p.p.m. directly above it as reported in the literature (Lefevre et al., 1965; Dahlberg and Myrin, 1971). We estimated peaks of 120 p.p.m. as basic level, and 300 p.p.m. + peaks above 400 p.p.m. directly above the tank, compared with peaks reported in the literature that ranged from 400 to 600 p.p.m. for work above an open-top vapor degreaser, with an average emission level from 100 to 150 p.p.m. (Bedford et al., 1956; Wadden et al., 1989; Stewart et al., 1991). We estimated peak exposure of 35 p.p.m. as basic level, and 75 p.p.m. + peaks above 200 p.p.m. directly above the tank, compared with peaks reported in the literature that ranged from 200 to 400 p.p.m. for work above a half-open vapor degreaser, with an average level from 20 to 70 p.p.m. (Bresson, 1985; Landrigan et al., 1987).

Corrective factors for distance have been applied, using the subject’s description of the shops and of their location in it. These factors are very crude estimates as a lot of parameters, such as number of air-changes per hour, were not available. Simulated exposure levels and the concentration at a fixed location of different workshops have shown a ratio of far to near field concentration close to 0.9 in small poorly ventilated workrooms, and ~0.35 in small well-ventilated, or larger but medium-ventilated rooms (Cherrie, 1999). Knowing that most of the
subjects in that study were located in small to medium-sized workshops with poor to medium ventilation (open or closed doors and windows, according to summer or winter) these results compare well with our reduction of 10% for people working 5 m from the source of exposure and of 25–55% for people working 10–20 m from the source.

Experiences on volunteers dermally exposed to TCE on a defined area (arms, hands) and for a measured duration have shown comparable airborne exposure equivalent to those applied in this study. TCE applied on 360 cm² of skin (palm + fingers) for 3 min, each hour of a working day was assessed to be equivalent to 60 p.p.m. (8 h TWA) (Kezic et al., 2001). We assumed the equivalent airborne TCE exposure to be 30 p.p.m. for the tip of three fingers (90 cm²) dipped 50 times for 1 min each day. Assessment of the dermal penetration is not totally comparable, from different parts of the body. The estimates provided by Kezic et al. were based on the absorption through the skin of the forearm, which is considered to be higher than through the skin of the fingers (Ectec, 1993). Nevertheless, equivalent dose as assessed in the present study is either quite similar or a bit lower than that in the experiment on volunteers.

Regarding job descriptions, it appeared that most subjects were able to answer technical questions about TCE, giving a detailed description of their jobs/tasks/activities. Not surprisingly, in the part of the study population not involved in screw-cutting, use of TCE was limited to cold degreasing tasks while 60% of workers involved in screw-cutting shops described hot TCE use—which was one of the features that led us to undertake a study in that particular area.

Whenever it was possible, assessments obtained from our estimates were compared with levels of TCE observed in workshops by occupational physicians. On a total of 175 job periods described in a screw-cutting shop, 32 (18.2%) were compared, leading to an equivalent assessment for 72% of them. This high rate of agreement between atmospheric levels obtained from the matrix and biomonitoring data collected by occupational physicians suggests that, although not specifically assessed, dermal exposures have been taken account of rather adequately in our assessment.

Temporal changes in exposure, as noted in our assessment, seem coherent with economical evolution of screw-cutting in the Arve Valley, with a growing use of TCE until the 1970s, and a decline during the 1980s, corresponding to a period of economic crisis when some workshops were closed (coherent with the lower number of job periods observed in the study) and others made no long-term investments such as expensive closed washing machines (coherent with high levels still observed at this time in our assessment).

The level of information about TCE asked for in screw-cutting shops was quite different from that asked for in other occupations. While the usual way of using TCE, as a cold degreaser on a rag, was easy to describe and, therefore, to assess from the general questionnaire, unusual tasks (chemical industry, etc) were less easy for subjects to describe, with resultant imprecision and possible underestimation or over-estimation.

Though comparison between our matrix and exposure levels reported in the scientific literature showed more-or-less equivalent assessments for equivalent tasks, it is also important to compare the final levels assessed in our study population with those in other epidemiological populations exposed to TCE.

In the Swedish cohort (Axelson et al., 1978), almost all workers exposed to TCE were biomonitored; exposure was assumed to be ~20 p.p.m. for >80% of subjects. In almost the same way, the cohort of all Finnish workers ‘regularly exposed’ to TCE was biomonitored between 1963 and 1992 (Tola et al., 1980; Anttila et al., 1995), with very low U-TCA levels: median exposure <15 p.p.m. before 1970 and <10 p.p.m. later. The populations in these two studies came from the general working population of their countries, as did those of our subjects who answered the general questionnaire and were assessed in the 1–35 p.p.m. exposure bracket.

In their study of aircraft workers, Stewart et al. (1991) provided a semi-quantitative exposure assessment related to descriptions of the main exposing tasks in the facility. These descriptions were close to what was observed in the Arve Valley workshops (degreasers located in the general hangars, poor maintenance and ventilation at the beginning of the study period, etc.) leading to peak levels consistent with those observed in our study. While not explicitly stated, average exposure may be estimated from information given (frequency, duration and level of tasks). Depending on how they are calculated, these averages may reach 50 p.p.m. for vapor degreasers (Cherrie et al., 2001b); or, applying our own matrix estimates to Stewart’s task descriptions: [(300 p.p.m. x 15 min x 5 times a day) + a background exposure of ~20 p.p.m. in the shops housing the degreasers] = 65 p.p.m. + peaks, as a maximum average exposure to TCE for our study. As far as it is possible to make comparisons, levels of ‘high’ exposure, even in the worst period were lower than ours, probably due to the lower frequency of degreasing tasks for the ‘washers’ described by Stewart and to slower technological progress in degreasing machines in the small French workshops.

A small cohort study in a cardboard factory (Henschler et al., 1995) included some exposure descriptions to correlate with levels of TCE exposure there. As in Stewart’s study, an assessment of TCE levels may be attempted. Cherrie proposed a
CONCLUSION

This method of retrospective assessment of exposure to TCE among patients included in a case–control study on renal cell cancer in a French area has combined individual information with a task–exposure matrix constructed from a large set of local monitoring data. Assessments obtained have been validated by local occupational physicians’ direct observations and seem coherent with levels described in other occupational studies. Nevertheless with 13.2% of the exposed jobs with level of exposure >50 p.p.m., the safety limits in use in many countries, and 7.5% of exposed jobs having peaks >200 p.p.m., our study population cannot be regarded as a typical general population.

Legal agreements

Approvals by the French Ministry of Research (Comité consultatif pour le traitement de l’information en matière de recherche dans le domaine de la santé) and the French data protection authority (Commission Nationale de l’Informatique et des Libertés) were obtained before starting the study.

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