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Dear Dr. Jameson,

Dr. Daniel T. Teitelbaum asked that I send you the enclosed recent article ["Urinary concentrations of trichloroacetic acid in Danish workers exposed to trichloroethylene, 1947-1985", Am J Ind Med 2001; 39:320-327] by Raaschou-Nielsen and colleagues for NTP's review regarding trichloroethylene's listing in the 10th RoC.

Dr. Teitelbaum hopes that you will find this document enlightening.

Sincerely,

[redacted]

Ms. BJ Croall, MA
Technical Librarian

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Urinary Concentrations of Trichloroacetic Acid in Danish Workers Exposed to Trichloroethylene, 1947–1985

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Background *Since 1947, the National Labour Inspection Service in Denmark has relied upon urinary measurements of trichloroacetic acid (TCA) in surveys of the occupational exposure to trichloroethylene (TCE).*
Methods *We examined the paper files relating to 2397 TCA measurements to extract information about the year, the company, the work process and the worker. We used multiple regression models to analyze the effects of various factors on the urinary concentration of TCA.*
Results *The regression analyses showed that (1) a four-fold decrease in TCA concentrations occurred from 1947 to 1985; (2) the highest concentrations were observed in the iron and metal, chemical, and dry cleaning industries; (3) TCA levels were two times higher among men compared with women in the iron and metal and dry cleaning industries; (4) TCA concentrations were higher among younger compared with older workers; and (5) persons working in an area in which TCE was used, but not working with TCE themselves, also showed urinary TCA levels indicative of exposure.*
Conclusion *Calendar year, type of industry, degree of contact with TCE, sex and age were predictors of TCA concentration in the urine of Danish workers.* Am. J. Ind. Med. 39:320–327, 2001. *© 2001 Wiley-Liss, Inc.*

KEY WORDS: ***trichloroethylene; trichloroacetic acid; urine; metabolite; occupational exposure; industry; age; sex***

INTRODUCTION

Trichloroethylene (TCE) has been widely used in many industries since the Second World War, mainly because of its degreasing properties and non-flammable character. In 1980, an estimated 377,000 tons were used in the United States, western Europe and Japan [International Agency for Research on Cancer, 1995] and 2,433 tons were used in Denmark [Danish Bureau of Statistics, 1981]. About 5,000 Danish workers were regularly exposed to TCE in the late 1980, [Christensen and Rasmussen, 1990].

The toxic effects of TCE on the human nervous system have been known for some time [Grandjean et al., 1955], and

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exposure to TCE has induced cancer in the liver, kidney and other organs in experimental animals [International Agency for Research on Cancer, 1995]. On the basis of experimental data and limited evidence from epidemiological studies, the International Agency for Research on Cancer classified TCE as a probable human carcinogen (2A) [International Agency for Research on Cancer, 1995]. However, the question of a carcinogenic effect in humans remains a matter of controversy [Weiss, 1996; McLaughlin and Blot, 1997; Boice et al., 1999].

Between 35 and 45% of inhaled TCE is retained in the human body. Of the retained TCE, about 15% is expired while the remaining 85% is metabolized and excreted in the urine, with 45–50% as trichloroethanol, 20–40% as trichloroacetic acid (TCA) and about 4% as monochloroacetic acid [Soucek and Blachová, 1960; Bartonícek and Teisinger, 1962; Nomiyama and Nomiyama, 1971]. The biological half-life of TCA is about 100 h [Müller et al., 1974]. TCA accumulates in the body [Vesterberg et al., 1976] and the urinary concentration can be used as an indicator of TCE exposure during the preceding week [Ulander et al., 1992]. Ikeda et al. [1972] found that the urinary concentration of TCA was linearly related to the average concentration of TCE in the work environment for concentrations below approximately 70 ppm ($TCA_{mg/L\ urine} = 2.74\ TCE_{ppm} + 0.7$); a similar relationship was reported in other studies [Grandjean et al., 1955; Inoue et al., 1989].

In Denmark, the occupational health authorities have regulated the TCE exposure of workers according to the following occupational exposure limit: 1947–1957: 37 ppm; 1957–1975: 47 ppm; 1975–1994: 30 ppm and since 1994: 10 ppm (1 ppm = 5.37 mg/m^3). Moreover, the National Labour Inspection Service has conducted information campaigns to improve hygienic standards and measurements of TCA in the urine of workers have been used as an instrument to survey occupational exposure to TCE between 1947 and 1985.

The aim of this study was to investigate the occupational exposure of Danish workers to TCE by evaluating urinary concentrations of TCA measured during the period 1947–1985, and the factors which affected those concentrations.

METHODS

Data Source

Between 1947 and 1985, the National Labour Inspection Service monitored TCA in the urine of workers exposed to TCE. The urine samples were usually taken following a request from the local labour inspection agency or medical officer. The original paper files of each of the 2,397 TCA samples were examined to extract information about the urinary concentration of TCA, the calendar year, the company, the work process and the worker.

Measurement Method

During the entire study period, the Fujiwara method was used to measure TCA in urine [Fujiwara, 1914; Tanaka and Ikeda, 1968]. The method is based on a reaction between TCA and pyridine in an alkaline medium, followed by spectrophotometric detection at 530 nm. All analyses were made at the Danish National Institute for Occupational Health following a standard protocol and the spectrophotometric method has been compared with a head space gas-chromatograhpic method; good agreement was found between the two methods [Christensen et al., 1988].

Explanatory Variables

Calendar period was divided into seven categories defined by year of measurement: 1947–1953, 1954–1959, 1960–1964, 1965–1969, 1970–1974, 1975–1979 and 1980–1985. *Industry* was defined as the activity in the working area and included 10 categories. The first three categories were divisions of the iron and metal industry, which included galvanizing/electroplating, production of fittings, razor blades, ammunition, kitchen hardware, engines, lamps, silverware, etc., according to the work tasks: (1) 'painting department' which included work in a large company or in a small company specializing in painting/lacquering metal products; (2) 'skilled work' which included all skilled or highly specialized work (except painting), e.g., smiths, tinsmiths, welders, shipwrights, engine fitters, turners and repairmen; and (3) *not otherwise specified* (NOS) which included all others. The remaining seven categories represented: (4) the electronic industry which included production of telephones, radios, televisions, hearing aids, capacitors, and precision mechanics; (5) the chemical industry which included production of cosmetics, medicine, shoe polish, rubber, polymer, paint, lacquer, and work with polyester; (6) the printing industry which included production of printed matter, production of printing plates and cleaning of the machines; (7) the dry cleaning industry which included mainly small dry cleaning shops; (8) laboratories of large companies, irrespective of the main product; (9) 'others', which included cleaning or gluing of non-metallic products and production of furniture (not specified as metal furniture), mattresses, double glazed windows, bricks and motion pictures; and finally (10) the category 'unknown' was used if the paper files did not indicate the industry. Workers were classified according to degree of *contact with TCE* as determined from information on the work process of the person monitored. Workers were said to have 'direct contact with TCE if they used TCE themselves, e.g., immersed metal products in TCE, wiped the products afterwards or cleaned machines with TCE. 'Indirect contact with TCE' was defined as very limited direct contact with TCE, such as among those who hung up parts on a conveyer before automatic degreasing or processed the product after degreasing. A worker was said to have 'no contact with TCE' if it was stated in the paper files that he/she did not use TCE. Such a statement was often followed by a remark like 'a degreaser was present in the department' or 'TCE was used in the same room'. *Previous work with TCE* referred to the duration of work with TCE in the present and previous jobs. We used the 33th and the 67th percentile to define three duration levels: 0–8, 9–34 and 35 months or more. 'Age' referred to the age of the worker at the time of the measurement. We used the 33th and the 67th percentile to define three levels: 12–33 years, 34–47 years and 48 years or more. *Sex* of the worker was the final variable considered.

Statistical Analyses

We used multiple regression analyses (the 'GLM' procedure of SAS [SAS Institute, Inc., 1988]) to measure effects of the explanatory variables on the outcome variable, urinary TCA concentration. The distribution of the outcome variable was highly right-skewed, and therefore the variable was transformed by the natural logarithm. Three hundred and fifty-eight measurements had the value '0 mg/L'; before the log-transformation those observations were assigned a concentration that corresponded to half of the lowest concentration during the relevant calendar period (the assumed detection limit).

The basic model included 'calendar period' and 'industry'. To minimize the loss of power due to missing values for the four other variables, these variables were entered in the basic model one at a time. The effect of adjustment for the other three variables was investigated on the limited data set with no missing value in any variable. If this adjustment changed the estimate for the actual variable less than one standard error, the adjustment was disregarded.

When the effect of 'industry' was analyzed, 183 measurements from the heterogeneous categories 'unknown' and 'others' were disregarded. When the effect of 'contact with TCE' was analyzed, observations from the categories 'chemical', 'laboratories', 'others' and 'unknown' were disregarded because of too many observations with a missing value. Moreover, measurements from the dry cleaning industry were disregarded because the distinction between 'direct', 'indirect' and 'no' contact with TCE was not possible for the small dry cleaning shops; all employees seemed to be in direct as well as indirect contact with TCE.

We used the *F*-statistic to test if a variable or interaction term contributed significantly to a model and the *T*-statistic to determine if a given variable was associated with TCA concentration. Statistical significance was set at $P < 0.05$.

RESULTS

Summary Statistics

The data included 2397 TCA measurements at 275 different companies during the period 1947–1985; the number of measurements per year ranged from 5 to 150. Seven hundred and fourteen different workers gave urine for 1519 of the measurements; it was not possible to unambiguously identify the workers who corresponded to the remainder 878 measurements. Table I shows the number of measurements, the median and the mean concentrations of TCA in urine for each combination of calendar period and industry. Sixty-two percent of the measurements were from workers in one of the three categories of the iron and metal industry, 15% were from workers in the electronic industry, 9% from dry cleaning shops, and the remainder were from different industries, each representing 3% of the measurements or less; the industry was unknown for 3% of the measurements. In general, mean concentrations were substantially higher than median concentrations because of a right-skewed distribution of the concentrations. The table indicates decreasing concentrations over time for most industries. Figure 1 shows that median concentrations for all industries combined decreased from about 30 mg/L before 1960 to about 5 mg/L in the 1980s and that concentrations above 500 mg/L were measured during all periods except 1980–1985. The decrease in concentrations temporarily weakened in the 1960s following the implementation of higher exposure limits in 1957. Figure 2 shows decreasing concentrations for all industries from 1947 to 1985, but the reductions occurred at different times for the different industries. Using the formula given by Ikeda et al. [1972] to transform the occupational exposure limits from ppm TCE to mg TCA per liter urine, 20, 11 and 6% of the measurements indicated exposure above the occupational exposure limits for the periods 1947–1957, 1958–1975 and 1976–1985, respectively. Forty percent of all measurements indicated levels of exposure above the occupational limit of today.

Multiple Regression Analyses

Calendar period and industry. Table II shows that mean TCA concentrations decreased four-fold between 1947 and 1985, and that the highest mean concentrations were seen in the dry cleaning shops, in the iron and metal (NOS) and chemical industries. Figure 2 indicates that the relationship between TCA concentration and industry varied by calendar period. This was confirmed in the regression analyses: the interaction term 'industry* calendar period' was statistically significant ($P < 0.0001$) when added to the basic model. In particular, TCA concentrations in the dry cleaning shops were higher than in the iron and metal industry (NOS) in the first period (1947–1953) ($P < 0.0001$), but the reverse was

TABLE I. Median and Mean Concentrations of Trichloroacetic Acid in Urine (mg/L) among Danish Workers Exposed to Trichloroethylene, by Calendar Period and Industry (N = 2397)

		Median/mean (N)													
Industry	**N**	**1947–1953**		**1954–1959**		**1960–1964**		**1965–1969**		**1970–1974**		**1975–1979**		**1980–1985**	
Iron and metal, not otherwise specified	1302	25/62	(223)	30/59	(156)	25/62	(189)	30/57	(236)	5/39	(223)	15/36	(225)	5/22	(50)
Iron and metal, skilled work	35	—	(0)	—	(0)	—	(0)	3/3	(1)	4/4	(18)	5/6	(16)	—	(0)
Iron and metal, painting dept.	145	0.5/7	(3)	25/47	(3)	—	(0)	5/6	(10)	28/58	(50)	15/34	(72)	5/4	(7)
Electronic	354	20/19	(8)	45/97	(22)	13/38	(16)	5/15	(92)	10/17	(131)	10/21	(71)	5/24	(14)
Dry cleaning shops	204	60/119	(97)	15/19	(8)	20/109	(31)	5/66	(37)	25/60	(16)	3/7	(5)	1/2	(10)
Printing	81	38/44	(4)	—	(0)	8/14	(30)	—	(0)	2/3	(5)	3/3	(37)	1/3	(5)
Chemical	76	70/70	(17)	28/46	(6)	15/15	(12)	20/32	(18)	—	(0)	23/22	(4)	7/8	(19)
Laboratories	17	—	(0)	8/8	(2)	10/8	(3)	—	(0)	30/30	(1)	3/3	(6)	1/2	(5)
Others (known)	111	20/66	(6)	8/8	(12)	78/79	(6)	73/101	(16)	150/184	(52)	5/9	(13)	1/2	(6)
Unknown	72	55/92	(38)	30/34	(5)	15/32	(3)	55/270	(3)	10/26	(3)	5/33	(10)	1/3	(10)
All industries	2397	35/78	(396)	28/57	(214)	20/58	(290)	20/49	(413)	15/49	(499)	10/28	(459)	5/14	(126)

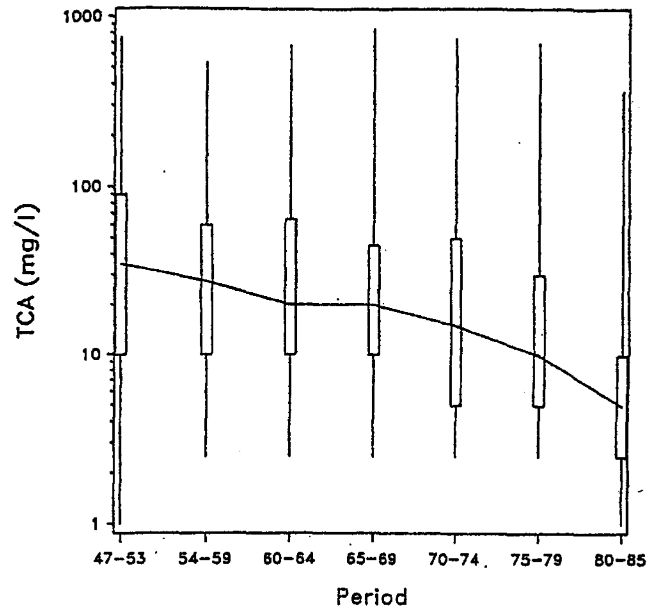

FIGURE 1. Box-and-whisker plots of 2,397 measurements of trichloroacetic acid (TCA) in the urine from Danish workers, 1947–1985. The box encloses the middle half of the data and the line joins the median values for each period. The upper whisker represents the concentrations above the 75th percentile and the lower whisker those below the 25th percentile.

true during the two last periods (1975–1979 and 1980–1985) ($P = 0.02$ and $P < 0.0001$, respectively).

Previous work with TCE, sex, age and contact with TCE. The duration of the worker's 'previous work with TCE' was known for 684 of the 2,397 measurements. The variable was

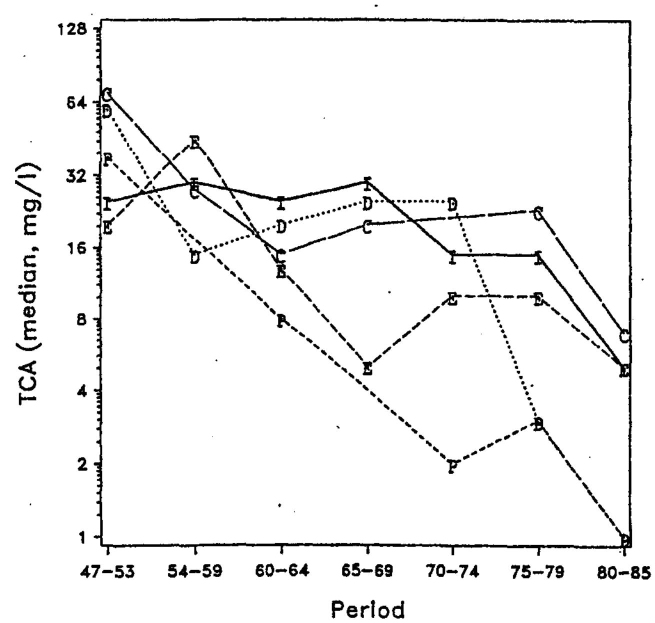

FIGURE 2. Median concentrations of trichloroacetic acid (TCA) in the urine from Danish workers in the iron and metal industry ('I'), the electronic industry ('E'), in dry cleaning shops ('D'), in the printing industry ('P') and in the chemical industry ('C'), by period.

TABLE II. Relative Concentrations of Trichloroacetic Acid According to Calendar Period and Industry, Adjusted for the Other Variable* (N = 2214)

Variable	Relative concentration	95% CI	P
Period			
1980–1985	1.0	—	—
1975–1979	2.2	1.7–2.9	<0.0001
1970–1974	2.6	2.0–3.4	<0.0001
1965–1969	3.0	2.3–4.0	<0.0001
1960–1964	3.7	2.8–5.0	<0.0001
1954–1959	3.8	2.8–5.1	<0.0001
1947–1953	4.0	3.0–5.3	<0.0001
Industry			
Iron and metal, not otherwise specified	1.0	—	—
Iron and metal, skilled work	0.2	0.2–0.4	<0.0001
Iron and metal, painting dept.	0.9	0.8–1.2	0.65
Electronic	0.5	0.4–0.6	<0.0001
Dry cleaning shops	1.3	1.1–1.6	0.003
Printing	0.3	0.2–0.3	<0.0001
Chemical	0.9	0.6–1.2	0.34
Laboratories	0.3	0.2–0.6	0.0002

*The model included the variables 'calendar periods' and 'industry'.

not statistically significant ($P = 0.16$) when added to either the basic model including 'calendar period' and 'industry' or to a model also including 'sex', 'age' and 'contact with TCE' ($P = 0.56$, N = 401, data not shown). Thus, 'previous work with TCE' was dropped from further analyses.

The sex of the worker was known for 2,094 measurements (1,785 men and 309 women). The proportion of females ranged from 2% in the iron and metal industry (printing department) to 50% in the dry cleaning shops. In a model including 'calendar period', 'industry' and 'sex', the mean concentration for men was 1.8 times that for women ($P < 0.0001$). Further adjustment for 'age' and 'contact with TCE' changed the estimate for 'sex' only marginally. The interaction term 'industry*sex' was statistically significant ($P = 0.001$), indicating varying effects of sex on TCA concentrations in the different industries. Table III shows that

TABLE III. Concentrations of Urinary Trichloroacetic Acid in Men Relative to Women Workers, by Industry, Adjusted for Calendar Period (N = 2094)

Industry	Relative concentration[a] (male/female)	95% CI	P[b]	N_{men}	N_{women}
Iron and metal, not otherwise specified	2.1	1.6–2.7	<0.0001	997	118
Iron and metal, skilled work	0.5	0.1–2.3	0.76	32	3
Iron and metal, painting dept.	0.5	0.1–2.2	0.37	139	3
Electronic	1.2	0.8–1.7	0.51	300	42
Dry cleaning shops	2.3	1.5–3.3	<0.0001	84	85
Printing	1.2	0.2–6.7	0.88	67	2
Chemical	1.0	0.5–1.9	0.95	29	28
Laboratories	0.9	0.1–5.6	0.89	14	2
Others (known)	5.1	2.3–11.2	<0.0001	99	11
Unknown	0.8	0.4–1.9	0.63	24	15

[a] The relative concentrations were estimated from a model including the variables 'calendar period', 'industry', and an industry-specific effect of sex.
[b] P for no difference between males and females

TABLE IV. Concentrations of Urinary Trichloroacetic Acid in Younger Workers Relative to Workers Aged 48 Years or More, by Industry; Adjusted for Calendar Period (N = 1511)

Industry	12–33 years				37–47 years				≥ 48 years	
	Relative concentration[a]	95% CI	P	N	Relative concentration	95% CI	P	N	Relative concentration	N
Iron and metal, not otherwise specified	1.0	0.8–1.2	0.64	269	1.1	0.9–1.4	0.36	290	1.0	243
Iron and metal, skilled work	1.4	0.6–3.7	0.44	19	1.2	0.4–3.9	0.75	7	1.0	9
Iron and metal, painting dept.	2.0	1.3–3.1	0.002	63	1.0	0.5–1.8	0.91	21	1.0	49
Electronic	1.8	1.3–2.5	0.0005	79	1.3	0.9–1.8	0.12	98	1.0	122
Dry cleaning shops	7.5	4.9–11.7	<0.0001	13	3.4	1.5–7.6	0.003	25	1.0	13
Printing	2.0	0.8–4.5	0.12	12	0.9	0.5–1.8	0.85	27	1.0	27
Chemical	1.3	0.3–5.8	0.71	7	1.5	0.4–5.7	0.54	15	1.0	4
Laboratories	1.4	0.3–6.3	0.65	6	1.1	0.2–5.7	0.93	4	1.0	4
Others (known)	0.4	0.2–0.9	0.03	26	0.4	0.2–1.0	0.04	18	1.0	17
Unknown	0.9	0.3–3.2	0.92	5	1.3	0.4–4.5	0.66	5	1.0	14

[a]The relative concentrations were estimated from a model including the variables 'calendar period,' 'industry,' and an industry-specific effect of age.

males had about two times higher concentrations than females in the iron and metal (NOS) industry and in the dry cleaning shops (both $P < 0.0001$) and that in the category 'other industries' the difference between the sexes was even greater (based on only 11 measurements from females). There was no statistically significant difference between the sexes in any other industry.

The age of the worker was known for 1,511 measurements and the variable was statistically significant in a model including 'calendar period' and 'industry' ($P = 0.01$). The concentrations among workers aged 12–33 and 34–47 years were, respectively, 1.3 ($P = 0.004$) and 1.2 ($P = 0.05$) times higher than that among workers aged 48 years or more. Adjustment for 'sex' and 'contact with TCE' changed the estimates for 'age' less than one standard error and was disregarded. The interaction term 'industry∗age' was statistically significant ($P = 0.0004$), and Table IV shows that in the iron and metal industry (NOS), with the majority of the measurements, no effect of age could be detected. In all other specified industries, the highest concentrations were found for the youngest workers. The most notable effect was in the dry cleaning shops, where a 7.5 times higher concentration was seen for the youngest age group ($P < 0.0001$).

For 655 measurements in the iron and metal, electronic and printing industries, the work process could be characterized as involving 'direct contact with TCE' (N = 545), 'indirect contact with TCE' (N = 61) or 'no contact with TCE' (N = 49). Significant differences in concentrations of TCA were found across these categories in a model with 'calendar period' and 'industry' ($P < 0.0001$). Concentrations associated with 'indirect contact' and 'no contact' were 0.3 ($P < 0.0001$) and 0.5 ($P = 0.002$) times, respectively, the concentration for 'direct contact'. The estimates for 'contact with TCE' were affected only marginally by adjustment for 'sex' and 'age'. The interaction term 'industry∗workprocess' was not statistically significant ($P = 0.21$); in all included industries, 'no contact' and 'indirect contact' were associated with lower concentrations than 'direct contact'. Eighty percent of the measurements from workers with 'no contact' showed concentrations of TCA above the detection limit.

DISCUSSION

In our study, we observed the following: (1) decreasing concentrations over the study period of TCA in the urine of Danish workers exposed to TCE; (2) highest concentrations in the iron and metal (except for skilled workers), chemical, and dry cleaning industries; (3) higher concentrations among men than among women workers in the iron and metal and dry cleaning industries; (4) higher concentrations among younger compared with older workers; and (5) work not involving direct contact with TCE was still associated with exposure, as assessed by urinary TCA concentration.

It should be noted that the measurements in this study were not obtained from random samples of workers. Instead, over the years, measurements were used for general surveillance, as an instrument to identify 'hot spots' or 'worst cases', as evaluation following improved hygienic standards or as a response to acute poisoning symptoms of workers. Thus, the TCA measurements might be unevenly distributed across industries and, more importantly, concentrations might not be representative of those of a random sample. However, a study of air measurements for organic solvents in the work environment (1985–1986) showed that, in general, the measurements that are part of the usual practice of the Danish Labour Inspection Service were fairly consistent with those from a random sampling of companies [National Institute for Occupational Health, 1988]. The degree to which this finding can be generalized to measurements of TCA in the urine (which reflects long-term exposure) or to measurements performed in other calendar periods is not known, but the correlation for air measurements suggests that the urinary measurements in this study may be indicative of typical exposure patterns.

The concentrations of TCA found in this study correspond well with those found in three other studies. In Finland, median concentrations (all industries) decreased from about 18 mg/L in 1965 to about 6 mg/L in the beginning of the 1980s [Antilla et al., 1993]. Grandjean et al. [1955] found mean concentrations of 87 mg/L TCA in the urine from 73 Swiss workers degreasing ion and metal parts in the beginning of the 1950s. In Sweden, median concentrations (all industries) were about 20 mg/L until 1955, 20–35 mg/L between 1955 and 1970, and decreasing to about 14 mg/L in 1976 [Ulfvarson, 1983].

We considered the urinary concentration of TCA as a marker of TCE exposure. However, TCA in urine is not specific to TCE exposure. Perchloroethylene (PCE) and 1.1.1 trichloroethane also metabolize to TCA, although much lower urinary concentrations of TCA follow exposure to PCE [Ikeda et al., 1972] and 1.1.1 trichloroethane [Kaneko et al., 1994]. The Local Labour Inspection Services intended to measure TCA in the urine of workers exposed to TCE, but if PCE or 1.1.1 trichloroethane was the primary exposure, the TCA concentration would be much lower compared with a situation in which TCE was the only solvent. Due to the much higher levels of TCA as a result of TCE exposure and due to the strategy of the Labour Inspection Service to assess only exposure to TCE–not PCE or 1.1.1 trichloroethane–by urinary TCA measurements, we would expect that the measured TCA concentrations reflect almost entirely exposure to TCE. Although TCA is a byproduct of chlorinating drinking water, this is not an important source of the TCA measured in this study because (1) in Denmark, drinking water in households is typically not chlorinated and 2) the amount of TCA due to chlorinated drinking water is negligible compared to the amount of TCA measured in this study [Weisel et al., 1999]. The finding of decreasing concentrations over time was expected and a similar trend was found by Anttila et al. [1993]. The low concentrations from the dry cleaning shops measured in the period 1975–1985 are consistent with the substitution in most dry cleaning shops of TCE with PCE in the 1970s [Danish Technological Institute, 1978]. Furthermore, in the 1980's, some dry cleaning shops switched to Freon 113 as the main solvent [Brandt et al., 1987], although TCE was used as a spot remover. Thus, the low concentrations of TCA may reflect the introduction of new solvents, rather than a decrease in exposure to halogenated solvents in general.

Different levels of exposure and/or different metabolizing capacities may play a role in the differences in urinary TCA concentrations among men and women workers. Nomiyama and Nomiyama [1971] found higher urinary concentrations of TCA among women than among men exposed to the same concentrations of TCE. Thus, the inverse results in this study are likely to be explained by higher exposures among men than among women workers. In the dry cleaning shops, for example, men usually took care of the functions in the machine room where high concentrations occurred. Few other studies have addressed the difference between men and women workers as regards urinary concentrations of TCA. In a metal plating industry in China, Inoue et al. [1989] found no differences in TCA concentrations in the urine from 52 men and 10 women. TCA measurements from different industries in Finland between 1965 and 1982 showed 24% lower concentrations among men than among women [Anttila et al., 1995]. Differences in exposure between sexes probably depend on traditions related to enrollment of workers, which again depend on industry and country.

We found higher concentrations among younger than older workers in most industries. This result might be caused by higher exposures in the kind of jobs available for young, relatively inexperienced workers although age-dependent biological differences may have contributed to the different concentrations across ages. It seems likely that this result can be generalized to other countries and other chemicals.

It was expected that the highest concentrations would be found among workers with direct contact with TCE. The estimated concentration of those with no contact with TCE (except from that due to presence in the same work area), however, was as high as 50% of that of directly exposed workers. Thus, most workers in an area where TCE is used are probably exposed, although factors such as the size of the room, the ventilation, and the work process influence the degree of exposure. In accordance with this finding, Grandjean et al. [1955] found that TCE concentrations in the center of ion and metal workshops were, on average, 74% of those close to the degreaser.

The available data on urinary TCA, combined with other occupational and job-specific information on individual workers, provide an opportunity to define a historical cohort of Danish workers exposed to TCE. The results of the present study can be used in exposure assessment for such a cohort, which can be followed up for the occurrence of cancer and other diseases to measure the potential long-term impact of TCE on human health.

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