Scand J Work Environ Health 1983;9(3):273-281

<https://doi.org/10.5271/sjweh.2409>

Issue date: Jun 1983

Biological monitoring of occupational exposure to tetrachloroethene.

by [Monster A](#), [Regouin-Peeters W](#), [van Schijndel A](#), [van der Tuin J](#)

This article in PubMed: www.ncbi.nlm.nih.gov/pubmed/6612269

This work is licensed under a [Creative Commons Attribution 4.0 International License](https://creativecommons.org/licenses/by/4.0/).

Biological monitoring of occupational exposure to tetrachloroethene

by Aart Monster, PhD,¹ Wilma Regouin-Peeters,¹ Anneke van Schijndel,¹ Jan van der Tuin²

MONSTER A, REGOUIN-PEETERS W, VAN SCHIJNDEL A, VAN DER TUIN J. Biological monitoring of occupational exposure to tetrachloroethene. *Scand j work environ health* 9 (1983) 273-281. In the breathing zone of 32 workers concentrations of tetrachloroethene were measured during five consecutive workdays. The feasibility of biological monitoring was tested by the measurement of the concentrations of tetrachloroethene in blood and exhaled air and the urinary excretion of trichloroacetic acid and trichloroethanol. The best parameter to estimate the time-weighted average exposure to tetrachloroethene over the whole workweek appears to be the concentration of both tetrachloroethene and trichloroacetic acid in blood 15-30 min after the end of the workday at the end of the workweek. Among the noninvasive methods the best parameter is the tetrachloroethene concentration in exhaled air 15-30 min after work at the end of the workweek, followed by the measurement of trichloroacetic acid in urine at the end of the workweek. In exposure to 2,050 μmol of tetrachloroethene/ m^3 (340 mg/m^3 , 50 ppm) the estimated values for the biological parameters are 13.2 μmol of tetrachloroethene/l of blood, 33 μmol of trichloroacetic acid/l of blood, 920 μmol of tetrachloroethene/ m^3 of exhaled air and 6.1 μmol of trichloroacetic acid/ mmol of creatinine in urine, respectively. With 95 % confidence it may be stated that an individual with a value for a biological parameter not exceeding 8.3 μmol of tetrachloroethene/l of blood, 20 μmol of trichloroacetic acid/l of blood, 515 μmol of tetrachloroethene/ m^3 of exhaled air and 3.0 μmol of trichloroacetic acid/ mmol of creatinine, respectively, had an exposure not exceeding 2,050 μmol of tetrachloroethene/ m^3 . The measurement of trichloroethanol in urine may be used for the estimation of the time-weighted average exposure over the previous 2 d. The concentration of tetrachloroethene in exhaled air 15-30 min after exposure had little value for the estimation of the time-weighted average exposure over the last 4 h. On Monday morning the concentration of tetrachloroethene in exhaled air is still about 15 % of the time-weighted average exposure concentration during the whole preceding workweek. The half-time of trichloroacetic acid in urine and blood during the weekend is about 65-90 h.

Key terms: metabolism, trichloroacetic acid, trichloroethanol.

Tetrachloroethene (tetrachloroethylene, perchloroethylene) is a volatile, non-flammable liquid widely used as a degreasing and drycleaning solvent. The uptake of tetrachloroethene by the lung is rather high (alveolar retention 60-80 %) (2, 8) because of its high solubility in blood and

adipose tissues. Only about 1-3 % of the amount absorbed is metabolized into trichloroacetic acid (2, 8) and probably even a smaller part into trichloroethanol (5). The concentration of tetrachloroethene in exhaled air or in blood and of trichloroacetic acid in urine or blood can be used as an indicator of occupational exposure.

In the present study we measured, by means of personal sampling, the tetrachloroethene concentration in inhaled air of workers during workhours over a normal workweek. In the same period biological monitoring was carried out by measuring the concentration of tetrachloroethene in blood and exhaled air, the concentration of trichloroacetic acid

¹ Coronel Laboratory of Occupational and Environmental Health, Faculty of Medicine, University of Amsterdam, Amsterdam, The Netherlands.

² TNO Research Institute for Environmental Hygiene, Indoor Air Pollution Division, Delft, The Netherlands.

Reprint requests to: Dr AC Monster, Coronel Laboratory, Faculty of Medicine, University of Amsterdam, PO Box 60.000, 1005 GA Amsterdam, The Netherlands.

in blood, and the concentration of trichloroacetic acid and trichloroethanol in urine. The objective of the study was to establish relationships between external exposure and the aforementioned biological parameters.

Material and methods

Subjects

Thirty-two subjects (3 females and 29 males), 16 to 59 years of age, who worked in four different workshops [three textile drycleaning shops (A, B, C) and one metal cleaning shop (D)], were studied. Body height ranged from 1.56 to 1.90 m and body weight from 48 to 100 kg. The deviation from the "ideal" body weight (height in cm - 100) varied between -20 and 22 kg with a mean of 0 (SD 10) kg (table 1).

Air sampling and analysis

Measurement of the concentrations of tetrachloroethene in air were performed during a 5-d workweek. Workroom air was collected from the breathing zone of the worker through charcoal sampling tubes with personal sampling pumps (Cassella) for two periods of about 4-6 h each day. Under these conditions the risk of tetrachloroethene passing through the charcoal tubes was very small. The level of risk was proved in the laboratory. Tetrachloroethene adsorbed on the charcoal was desorbed with dimethylformamide and analyzed by gas chromatography. A stainless steel column (length 2 m, internal diameter 3.2 mm) was used; the column was packed with 15 % tricresylphosphate on Chromosorb W AW, 80-100 mesh. The detector was a flame

ionization detector. The temperatures were as follows: oven 110°C, injector 125°C, detector 140°C. Nitrogen (30 ml/min) was used as the carrier gas.

The time-weighted average concentration was calculated for each subject from the individual 4- to 6-h samples. The total weekly work time varied from 37 to 54 h. Lunch and coffee breaks were included, except when the subject left the contaminated area. The calculated time-weighted average exposure was adjusted to a 40-h week in table 1.

Blood sample collection and analysis

Venous blood samples were obtained in a well-ventilated room on Monday morning before the subjects started work, on Wednesday and Friday at about 15-30 min after the end of the workday, and again Monday morning before work. The concentrations of tetrachloroethene and trichloroacetic acid (after methylation) in blood were determined with a head-space technique and by gas chromatography with a ^3H electron capture detector according to the method described for trichloroethylene by Monster & Boersma (6).

Exhaled air sample collection and analysis

Exhaled air samples were collected in duplicate about 1 min before the collection of the blood samples (Monday morning, Wednesday and Friday after the end of the workday, and again Monday morning before the start of work). The exhaled air was collected in a glass tube (length 20 cm, volume 65 cm³) each end of which (8 mm internal diameter) could be closed by means of caps. The caps had a predrilled hole for gas sampling; both caps had

Table 1. Number of workers, their age, sex and weight in respect to ideal weight, and the time-weighted average (TWA) exposure to tetrachloroethene (PERC) during the workweek.

Workshop	Number of workers		Age (years)	Weight in kg - (height in cm - 100) (range)	TWA (week) exposure per subject ($\mu\text{mol}/\text{m}^3$) ^a	
	Male	Female			Median	Range
A	4	1	16-46	-17-+22	300	190-520
B	8	1	23-59	-5-+10	1,900	1,410-2,700
C	8	1	24-51	-20-+22	2,150	1,200-6,600
D ^b	9	-	25-38	-10-+4	85	65-125

^a 1 $\mu\text{mol}/\text{m}^3$ = 0.166 mg/m³

^b Mixed exposure: 5% PERC and 95% 1,1,1-trichloroethane.

a silicon rubber liner and a teflon liner which sealed the glass tube, the latter to prevent absorption of tetrachloroethene into the silicon rubber. Alveolar air was obtained as follows: the subject inhaled deeply, held his breath for 5 s and exhaled through the sampling tube. Just before the expiration was finished, the tube was closed with the caps. Breathholding for 5 s had been checked to be sufficient to achieve at least 90 % of the alveolar equilibrium concentration. The tetrachloroethene concentration in the sampling tube was determined by gas chromatography as described for trichloroethylene by Monster & Boersma (6). The lower limit of detection (three times base level noise) was 0.1 mg/m³.

Urine sample collection and analysis

Urine samples were collected on Monday morning before the start of work, on Wednesday and Friday over the last 4 h of the workshift, and again on Monday morning. The volume, pH, and creatinine concentration of the urine samples were measured. The concentrations of trichloroacetic acid and trichloroethanol were determined by gas chromatography as described by Monster & Boersma (6). The trichloroacetic acid and trichloroethanol concentrations were corrected for the creatinine concentration.

Statistical methods

In order to estimate the time-weighted average exposure from the biological parameters, simple and multiple regression analyses were done with the (natural) logarithm of the biological parameters as the independent variable and the (natural) logarithm of the time-weighted average exposure as the dependent variable.

The significances of the increase of the coefficient of determination (R^2) was judged by the F-value. Calculated also was the geometrical residual error (Δ) as the exponential of the residual error of the regression equation.

For the estimation of a new value of a biological parameter resulting from tetrachloroethene exposure of 2,050 $\mu\text{mol/}$

m³ (240 mg/m³, 50 ppm), simple regression was used with the time-weighted average exposure as the independent variable. The same regression analysis was used to calculate the value of the biological parameter for which it may be stated with 95 % confidence that a subject with such a value or lower did not exceed the time-weighted average concentration of 2,050 $\mu\text{mol tetrachloroethene/m}^3$.

Results

Ambient air concentrations

The individual time-weighted average concentration of tetrachloroethene in the air varied from 65 to 6,600 $\mu\text{mol/m}^3$ over the whole workweek (table 1). For fifteen subjects, all working in workshops B and C, the level exceeded the present Dutch maximal acceptable concentration of 1,450 $\mu\text{mol/m}^3$ (240 mg/m³). About one-third of the 311 4-h samples exceeded 1,450 $\mu\text{mol/m}^3$, and 10 % exceeded 2,900 $\mu\text{mol/m}^3$ (480 mg/m³).

Tetrachloroethene concentrations in exhaled air and blood

Fig 1 presents the concentrations of tetrachloroethene in exhaled air 15–30 min after work on Wednesday and Friday in relation to the average concentration in the corresponding workroom air samples collected during the preceding 4 h.

Fig 2 shows the course of the relative (first Monday morning concentration taken as 100 %) concentrations of tetrachloroethene (geometrical mean and standard deviation) in blood and exhaled air during the workweek. The relative concentrations on Wednesday and Friday after work were higher by about a factor of four. On the second Monday morning the relative concentrations had returned again to about 100. The relative change in the concentration of tetrachloroethene in blood was very similar to that in exhaled air. This phenomenon is also expressed in the rather constant quotient between the concentration of tetrachloroethene in blood and in alveolar air (15.2 ± 2.6 , $N = 94$) simultaneously collected during the workweek.

The subjects were divided into two subgroups, one with body weights below

Fig 1. Relation between the time-weighted average (TWA) exposure to tetrachloroethene (PERC) over the last 4-h of a workday (Wednesday and Friday) and the concentration of PERC in exhaled air 15–30 min after the end of exposure. Indicated are the estimation of the concentration at an exposure of 2,050 μmol PERC/ m^3 (340 mg/m^3) and the value for which it may be stated (with 95 % confidence) that a new subject with such a value (or lower) did not exceed an exposure of 2,050 μmol PERC/ m^3 .

Fig 2. Course of the relative (first Monday morning concentration taken as 100 %) concentration of tetrachloroethene in blood and exhaled air (geometrical mean and SD) during the workweek (Monday morning, Wednesday and Friday evening and Monday morning).

Fig 3. Course of the relative (first Monday morning concentration taken as 100 %) concentration of trichloroacetic acid in blood and urine (geometrical mean and SD) during the workweek (Monday morning, Wednesday and Friday evening and Monday morning).

the "ideal" body weight (height in cm - 100) and the other with body weights above this level. The decrease in concentration in blood and exhaled air during the weekend was more pronounced in the slim subjects (N = 17) than in the obese ones (N = 12). In the slim subjects the decrease was a factor of 4.1 (1.5) for exhaled air (the geometrical standard deviation in parentheses) and 3.7 (1.4) for blood, and for the obese subjects the factors were 3.3 (1.5) and 3.0 (1.4), respectively.

Trichloroacetic acid concentrations in blood and urine

The concentrations of the metabolite trichloroacetic acid increased during the workweek in blood, as well as in urine. Fig 3 shows the course of the relative (first Monday morning concentration taken as 100 %) concentrations (geometrical mean and standard deviation) in blood and urine during the workweek. The relative concentrations on Wednesday and Friday after work were higher by about a factor of two than on Monday morning. The increase of the concentration in urine was more pronounced than that in blood. At the start of the following week the relative concentrations had returned to about 100 %.

Trichloroethanol concentration in urine

Small amounts of trichloroethanol (< 4 $\mu\text{mol}/\text{mmol}$ of creatinine) were detectable in the urine collected on Wednesday and Friday after work from subjects with a relatively high exposure (workshops B & C).

Estimation of the (individual) time-weighted average exposure from biological parameters

The data of a few workers had to be partly discarded because some workers did not work on Friday (N = 2) or had been already in contact with tetrachloroethene early on Monday morning before the measurements took place (N = 3). Among the measurements from workshop D only

the concentration of tetrachloroethene in blood and exhaled air could be used because in that workshop the metabolites trichloroacetic acid and trichloroethanol in blood and urine were for a greater part derived from exposure to 1,1,1-trichloroethane (see table 1). The metabolism of tetrachloroethene is so small that an increase or decrease in metabolism, possibly caused by the presence of 1,1,1-trichloroethane, will hardly have any influence on the concentration of tetrachloroethene.

The various biological parameters on Friday after work and on the second Monday morning before work correlated better with the time-weighted average exposure over the whole workweek than with the time-weighted average exposure over the preceding day. Table 2 shows various simple and multiple regression equations for the estimation of the individual time-weighted average exposure from biological parameters.

With one parameter the smallest residual error for estimating time-weighted average exposure over the whole workweek was obtained for the tetrachloroethene concentration in blood on Friday ($\Delta = 1.22$, see fig 4) followed by trichloroacetic acid in blood on Friday ($\Delta = 1.27$) and tetrachloroethene in exhaled air on Friday ($\Delta = 1.28$). A combination of the two parameters measured at the same time in blood or in excreta (tetrachloroethene in exhaled air and trichloroacetic acid in urine) with multiple regression analysis resulted in a somewhat smaller residual error in estimating the time-weighted average exposure than obtained from the single parameters (table 2). In the multiple regression the tetrachloroethene and trichloroacetic acid concentrations contributed about equally to the estimation of the time-weighted average exposure. The urinary excretion of trichloroethanol (in micromoles per millimole of creatinine) on Wednesday and Friday correlated better to the time-weighted average exposure of the two preceding days ($R^2 = 0.61$, $\Delta = 1.38$) than to the time-weighted average exposure of the preceding day ($R^2 = 0.32$, $\Delta = 1.91$) or preceding week. Table 3 presents the estimated value of the biological parameters in the case of tetrachloroethene exposure of $2,050 \mu\text{mol}/\text{m}^3$

Table 2. Regression equations for the estimation of individual time-weighted average (TWA) exposure to tetrachloroethene (PERC) ($\mu\text{mol}/\text{m}^3$)^a from the biological parameters: PERC in blood ($\mu\text{mol}/\text{l}$) and exhaled air ($\mu\text{mol}/\text{m}^3$), TCA in blood ($\mu\text{mol}/\text{l}$) and urine ($\mu\text{mol}/\text{mmol}$ creatinine), and TCE in urine ($\mu\text{mol}/\text{mmol}$ creatinine). (R^2 = coefficient of determination, Δ = geometrical residual error of regression equation, N = number of samples).

Medium	Time	TWA	Regression equation	R^2	Δ	N	F-value ^b
PERC in blood	Friday	Week	$\ln \text{TWA} = 5.66 + 0.756 \ln \text{PERC}$	0.953	1.22	21	7.3
TCA in blood	Friday	Week	$\ln \text{TWA} = 4.75$	0.933	1.27	21	17
PERC+TCA in blood	Friday	Week	$\ln \text{TWA} = 5.26 + 0.473 \ln \text{PERC} + 0.813 \ln \text{TCA}$	0.966	1.19	21	.
PERC in blood	Monday	Week	$\ln \text{TWA} = 6.15 + 0.941 \ln \text{PERC}$	0.786	1.48	19	32
TCA in blood	Monday	Week	$\ln \text{TWA} = 4.96$	0.843	1.40	19	20
PERC+TCA in blood	Monday	Week	$\ln \text{TWA} = 5.23 + 0.475 \ln \text{PERC} + 0.856 \ln \text{TCA}$	0.930	1.25	19	.
PERC in exhaled air	Friday	Week	$\ln \text{TWA} = 2.78 + 0.708 \ln \text{PERC}$	0.931	1.28	21	4.9
TCA in urine	Friday	Week	$\ln \text{TWA} = 6.41$	0.909	1.32	21	12
PERC+TCA in exhaled air and in urine	Friday	Week	$\ln \text{TWA} = 4.52 + 0.437 \ln \text{PERC} + 0.265 \ln \text{TCA}$	0.945	1.24	21	.
PERC in exhaled air	Monday	Week	$\ln \text{TWA} = 2.30 + 0.930 \ln \text{PERC}$	0.849	1.38	20	7.8
TCA in urine	Monday	Week	$\ln \text{TWA} = 6.77$	0.840	1.39	20	9.1
PERC+TCA in exhaled air and in urine	Monday	Week	$\ln \text{TWA} = 4.28 + 0.511 \ln \text{PERC} + 0.368 \ln \text{TCA}$	0.896	1.31	20	.
PERC in exhaled air	Wed + Fri	4 h ^c	$\ln \text{TWA} = 2.37 + 0.691 \ln \text{PERC}$	0.927	1.43	63	.
TCE in urine	Wed + Fri	1 d	$\ln \text{TWA} = 8.08 + 0.612 \ln \text{TCE}$	0.32	1.91	34	.
TCE in urine	Wed + Fri	2 d	$\ln \text{TWA} = 8.19 + 0.553 \ln \text{TCE}$	0.61	1.38	34	.

^a 1 μmol PERC/ m^3 = 0.166 mg PERC/ m^3 .

^b F-value for improvement (a value of 4.5 is significant at the 5 % level).

^c Afternoon.

Fig 4. Relation between the time-weighted average (TWA) exposure to tetrachloroethene (PERC) over the whole work-week (40 h) and the concentration of PERC in blood on Friday 15–30 min after the end of exposure. Indicated are the estimation of the concentration at an exposure of 2,050 μmol PERC/ m^3 (340 mg/ m^3) and the value for which it may be stated (with 95 % confidence) that a new subject with such a value (or lower) did not exceed an exposure of 2,050 μmol PERC/ m^3 .

(340 mg/ m^3 , 50 ppm, present threshold limit value, United States, and Maximale Arbeitsplatzkonzentration, Federal Republic of Germany). Furthermore it

contains the value of the biological parameters for which (with 95 % confidence) it may be stated that an individual having such a value (or lower) did not exceed

a tetrachloroethene exposure level of 2,050 $\mu\text{mol}/\text{m}^3$. For two parameters these values are also indicated in fig 1 and 4.

Discussion and conclusions

The concentration of tetrachloroethene in blood and exhaled air and of trichloroacetic acid in blood and urine were only slightly higher on the second Monday than on the first Monday morning. This finding implies that the exposure in the week of measurement was of the same magnitude or somewhat higher than in the preceding workweek(s).

Tetrachloroethene is metabolized only to a minor extent. The most important form of excretion is through exhalation. The quotient between the concentration of tetrachloroethene in blood and in alveolar air is rather constant [15.2 (SD 2.6)]. This finding corresponds well with the blood/gas partition coefficient of 13.1 measured by Sato & Nakajima (10). The olive oil/gas partition coefficient for tetrachloroethene is about 2,000 (1, 10). Correspondingly the solubility of tetrachloroethene in blood and body tissues is high, and consequently the rate of elimination is slow. The concentration of tetrachloroethene in exhaled air after the weekend was still about 15 % of the mean inhaled concentration in the previous workweek (table 3). This high percentage is caused by the lack of metabolism and the slow rate of elimination through the lungs. This percentage is higher than that predicted from the breath decay curves

developed from sedentary exposures for 7.5 h/d, 5 d/week, 4–6 % (4, 11). However, they did not take into account the higher uptake during occupational exposure caused by physical activity and presumably a higher degree of saturation of the body with tetrachloroethene due to repeated occupational exposure for months. The percentage is also higher than the level predicted from a mathematic model for the simulation of repeated exposure at rest (alveolar ventilation 7 l/min) for four weeks, 8 h/d, 5 d/week, about 5 % (3); the authors used a smaller partition coefficient, 9, for blood/gas and for oil/gas, 960. Therefore the rate of excretion of tetrachloroethene in this model will be faster than in a model with a higher partition coefficient and than in occupational exposure with a heavier work load.

The increase in concentrations in biological media (from Monday morning to Wednesday evening) and the decrease (from Friday evening to Monday morning) was more pronounced for the trichloroacetic acid concentration in urine than for the trichloroacetic acid concentration in blood. Monster et al (7) showed that during exposure to trichloroethylene (2,900 $\mu\text{mol}/\text{m}^3$, 4 h, 5 d) the amounts of trichloroacetic acid excreted in urine produced during the night were always lower than those excreted during the previous and following periods, whereas the trichloroacetic acid concentration in blood increased steadily. Therefore the concentrations of trichloroacetic acid measured in urine on the Monday mornings are relatively low and give rise to the

Table 3. Estimated concentrations in blood, alveolar air, and urine at the end of the workweek in subjects exposed to 2,050 μmol of tetrachloroethene (PERC)/ m^3 (340 mg/m^3 , 50 ppm) 8 h a day, 5 d a week, and the value for which it may be stated (with 95% confidence) that a new subject having such a value (or lower) did not exceed an exposure of 2,050 μmol PERC/ m^3 . (TCA = trichloroacetic acid, TCE = trichloroethanol).

Time after exposure	Period of time	Blood				Alveolar air		Urine			
		PERC ($\mu\text{mol}/\text{l}$)		TCA ($\mu\text{mol}/\text{l}$)		PERC ($\mu\text{mol}/\text{m}^3$)		TCA ($\mu\text{mol}/\text{mmol creatinine}$)		TCE ($\mu\text{mol}/\text{mmol creatinine}$)	
		Esti-mation	95% con-fidence limit	Esti-mation	95% con-fidence limit	Esti-mation	95% con-fidence limit	Esti-mation	95% con-fidence limit	Esti-mation	95% con-fidence limit
15–30 min	Week	13.2	8.3	33	20	920	515	6.1	3.0	.	.
60 h	Week	4.5	2.4	22	12	295	170	3.1	1.5	.	.
15–30 min	4 h ^a	.	.	.	.	1,755	805	.	.	.	.
15–30 min	2 d	.	.	.	.	.	.	.	.	0.46	0.21

^a Afternoon.

difference in the biological half-time for trichloroacetic acid in blood (90 h) and in urine (65 h) during the weekend of the present study because the half-times were calculated from the concentrations on Friday evening and on Monday morning.

In occupational exposure to tetrachloroethene Ikeda et al (5) measured urinary metabolites in 2-h samples at the end of the workday. From their curves the average excretion in exposure to 2,050 $\mu\text{mol}/\text{m}^3$ (340 mg/m^3) can be estimated to be about 285 μmol of trichloroacetic acid/l and about 200 μmol of trichloroethanol/l. These values are much higher than those measured in the present study (table 3). This difference may at least partly be explained by the difference in analysis. Ikeda et al (5) used a nonspecific spectrophotometric method (a modified Fujiwara-reaction), and in the present study a specific gas chromatographic method was used.

With a gas chromatographic method Weichard & Lindner (13) measured small concentrations of trichloroacetic acid and trichloroethanol in urine of workers exposed to tetrachloroethene. The time of sampling was not specified however. Extrapolation of the mean concentrations to exposure to 2,050 $\mu\text{mol}/\text{m}^3$ (340 mg/m^3) resulted in trichloroacetic acid and trichloroethanol concentrations of about 20 $\mu\text{mol}/\text{l}$ and about 5 $\mu\text{mol}/\text{l}$, respectively. In experimental exposure to pure tetrachloroethene no trichloroethanol was detected in urine (2, 4, 8).

On the basis of this study the best parameter to estimate the time-weighted average exposure to tetrachloroethene over the whole workweek appears to be measurement of the concentration of both tetrachloroethene and trichloroacetic acid in blood at the end of the workday on Friday (the smallest geometrical standard deviation). The second best parameter is measurement of only the concentration of tetrachloroethene in blood on Friday, followed by measurement of tetrachloroethene in exhaled air combined with trichloroacetic acid in urine on Friday. After single 4-h exposure to tetrachloroethene the best results in estimating exposure were also obtained from the concentrations in blood (9).

Among the single noninvasive methods the best method is tetrachloroethene in exhaled air on Friday after work, followed by trichloroacetic acid in urine on Monday morning.

For estimating the time-weighted average exposure over a shorter period than a week, trichloroethanol in urine may be used. With a biological half-time for trichloroethanol of 10–12 h (7) the exposure magnitude on the day before the last exposure will have influenced the trichloroethanol concentration in urine, especially when the magnitude of exposure on the day before the last exposure was high compared to exposure on the day on which trichloroethanol in urine was measured. Therefore, the best result was obtained by estimating time-weighted average exposure over the previous 2 d.

As expected, there was a high correlation ($R^2 = 0.93$) between the exposure concentration during the last 4 h and the concentration of tetrachloroethene in exhaled air 15–30 min after the end of exposure. However the confidence interval was rather large, an occurrence which makes estimation of the time-weighted average exposure of little value. The exhaled alveolar air concentration was high compared to the exposure concentration during the last 4 h of exposure. This high concentration can partly be explained by 1.5 (SD 0.8) ($N = 46$) times higher exposure concentrations during the morning than during the afternoon.

Estimation of individual time-weighted average exposure from the biological parameters can probably be improved when the following points can also be taken into account:

1. Physical activity during and after work. Moderate exercise during exposure increases the uptake and the postexposure tetrachloroethene concentrations in blood and exhaled air (4, 8). Because in the present study physical activity (respiratory minute volume) was not measured, this factor could not be taken into account in the estimation of the time-weighted average exposure from the biological parameters.

2. Influence of adipose tissue on uptake and, especially, excretion. This influence

was shown in the present study in the faster decrease of the tetrachloroethene concentrations in blood and exhaled air from Friday to Monday in slim subjects if compared to more obese subjects.

3. Skin absorption. Frequent immersion of the hands in liquid tetrachloroethene will result in substantial uptake through the skin (12). This aspect was not taken into account in the present study.

4. Peak exposure. When taking 4-h workroom samples there is insufficient insight into the variation of the exposure concentration and also into the influence of the variation on biological parameters.

5. In this study we did not measure the biological parameters on the next morning after exposure (before the next exposure). Probably such measurements may also be a reference point for estimating the time-weighted average exposure.

Acknowledgment

We wish to thank Mr H Sallé for his helpful advice concerning the statistical analysis.

This study was supported by grants from the Organization for Health Research TNO and the Ministry of Social Affairs and Employment.

References

1. Droz PO, Fernandez J. Solubility of organic solvents, pt-I: Gaschromatographic determination of oil-gas partition coefficients. *Helv chim acta* 60 (1977) 454-458.
2. Fernandez J, Gubéran E, Caperos J. Experimental human exposures to tetrachloroethylene vapor and elimination in breath after inhalation. *Am ind hyg assoc j* 37 (1976) 143-150.
3. Gubéran E, Fernández J. Control of

industrial exposure to tetrachloroethylene by measuring alveolar concentrations: Theoretical approach using a mathematical model. *Br j ind med* 31 (1974) 159-167.

4. Hake CL, Stewart RD. Human exposure to tetrachloroethylene, inhalation and skin contact. *Environ health perspect* 21 (1977) 231-238.
5. Ikeda M, Ohtsuji H, Imamura T, Komoike Y. Urinary excretion of total trichloro-compounds, trichloroethanol and trichloroacetic acid as a measure of exposure to trichloroethylene and tetrachloroethylene. *Br j ind med* 29 (1972) 328-333.
6. Monster AC, Boersma G. Simultaneous determination of trichloroethylene and metabolites in blood and exhaled air by gaschromatography. *Int arch occup environ health* 35 (1975) 155-163.
7. Monster AC, Boersma G, Duba WC. Pharmacokinetics of trichloroethylene in volunteers; influence of workload and exposure concentration. *Int arch occup environ health* 38 (1976) 87-102.
8. Monster AC, Boersma G, Steenweg H. Kinetics of tetrachloroethylene in volunteers; influence of exposure concentrations and work load. *Int arch occup environ health* 42 (1979) 303-309.
9. Monster AC, Houtkooper JM. Estimation of individual uptake of trichloroethylene, 1,1,1-trichloroethane and tetrachloroethylene from biological parameters. *Int arch occup environ health* 42 (1979) 319-323.
10. Sato A, Nakajima T. A structure-activity relationship of some chlorinated hydrocarbons. *Arch environ health* 34 (1979) 69-75.
11. Stewart RD, Baretta ED, Dodd HC, Torkelson TR. Experimental human exposure to tetrachloroethylene. *Arch environ health* 20 (1970) 224-229.
12. Stewart RD, Dodd HC. Absorption of carbon tetrachloride, trichloroethylene, tetrachloroethylene, methylene chloride and 1,1,1-trichloroethane through the human skin. *Am ind hyg assoc j* 25 (1964) 439-446.
13. Weichard H, Lindner J. Gesundheitsgefahren durch Perchloräthylen in Chemisch-Reinigungsbetrieben aus arbeitsmedizinisch-toxikologischer Sicht. *Staub Reinhalt Luft* 35 (1975) 416-420.

Received for publication: 8 November 1982