Scand J Work Environ Health 1976;2(4):212-219

<https://doi.org/10.5271/sjweh.2802>

Issue date: Dec 1976

Exposure to trichloroethylene II. Metabolites in blood and urine.

by [Vesterberg O](#), [Gorczak J](#), [Krasts M](#)

Key terms: [blood](#); [exposure](#); [metabolite](#); [trichloroacetic acid](#); [trichloroethanol](#); [trichloroethylene](#); [urine](#)

This article in PubMed: www.ncbi.nlm.nih.gov/pubmed/1019595

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

Exposure to trichloroethylene

II. Metabolites in blood and urine

by OLOF VESTERBERG, M.D., M.Sc., JADWIGA GORCZAK, M.Sc.,
and MUDITE KRASTIS, M.Sc.¹

VESTERBERG, O., GORCZAK, J. and KRASTIS, M. Exposure to trichloroethylene: II. Metabolites in blood and urine. *Scand. j. work environ. & health* 4 (1976) 212—219. Fifteen men were exposed to trichloroethylene (TRI) in three different ways with regard to the concentration of TRI in the air as well as exercise on a bicycle ergometer. The total amount of TRI supplied and taken up by each person was measured. The concentrations of trichloroethanol (TCE) and trichloroacetic acid (TCA) were determined in blood and urine. In spite of large differences in uptake, there were only small differences in the concentration of TCA in blood during the day of exposure. There was a large scatter for the values of TCA in urine within each group. The concentration of TCE in arterial blood increased during exposure. Thereafter the concentrations were almost constant for 2 h and differed among the groups. These results can be interpreted as being due to balanced rates of the formation and elimination of TCE. The levels mentioned were related to the uptake of TRI. The same was found for the rate of excretion of TCE in urine when calculations were made from the morning sample obtained the day after exposure.

Key words: trichloroethylene, exposure, trichloroethanol, trichloroacetic acid.

The metabolism (biotransformation) of trichloroethylene (TRI) has been studied previously in both animals and man (11, 15, 18). It is accepted that the metabolites are trichloroacetic acid (TCA) and trichloroethanol (TCE). The following pathway has been suggested:

¹ Chemical Division, Occupational Health Department, The National Board of Occupational Safety and Health, Stockholm, Sweden.

Reprint requests to: Dr. Olof Vesterberg, Chemical Division, Occupational Health Department, The National Board of Occupational Safety and Health, Fack, S-100 26 Stockholm 34, Sweden.

Several studies have shown that chloral hydrate is formed rapidly and is thereafter transformed to TCA and TCE (4, 6, 9). A review of the biotransformation of TRI has recently been published (8).

Both TCA and TCE can be found in the blood after exposure to TRI. TCA can be excreted directly in the urine, while most of the TCE is first converted to the

Fig. 1. The experimental exposure conditions, work load, and sampling times for blood and urine for the different groups.

corresponding glucuronide, which in turn is excreted in the urine. The concentration of TCA in the urine has been the accepted measure of exposure to TRI (3, 15). Several authors have attempted to establish the relationship between the concentrations of TCA and the concentration of TRI in the inhaled air (7, 16). Still other authors have suggested that the amount of TCA and the total TCE in the urine give the best estimates of TRI exposure (10, 20). It has recently been suggested that TCA and total TCE should be measured separately (16).

It seems as if earlier publications have not taken into account the fundamental relationship between the amount of TRI taken up and the rate of both the production and the excretion of the metabolites.

The uptake of a solvent is determined partially by the work load experienced, which in turn determines the amount of air inhaled (1). In addition there are substantial differences between individuals. Earlier publications are incomplete because the analysis of TCA and TCE in the blood as well as the accurate assessment of the amount of TRI taken up has been difficult. These problems indicated a need for a careful analysis of the TCA and TCE found in the blood and urine after exposure to TRI under varying work loads when the uptake of TRI is also determined.

MATERIALS AND METHODS

Experimental conditions

Fifteen healthy men were divided into three groups which inhaled different concentrations of TRI and worked at different work loads as described earlier (2). Each participant was exposed to TRI at rest and during exertion on a bicycle ergometer (fig. 1). During the course of the experiment blood samples were taken directly from an arterial catheter (from the arteria brachialis) into a test tube containing 0.1 ml of a citrate solution.² Each sampling consisted of double samples of seven drops of blood each. The exact amount of blood in each sample was determined by weighing. The day after exposure capillary blood samples were drawn from the subjects' fingertips. Fig. 1 gives the blood sampling schedule. Urine samples for the analysis of TCA and TCE were collected as shown in fig. 1. The rates of excretion of these metabolites were determined from the times given by the exposed persons.

² ACD solution: a water solution containing 0.48 % citric acid, 1.32 % sodium citrate and 1.47 % glucose.

Analytical methods

TCA and both TCE and TCE-G were analyzed in both blood and urine samples by gas chromatography according to a recently described method of Vesterberg et al. (21).

The concentration at each sampling is given as the average of the determinations in two blood samples and two urine samples, respectively.

RESULTS

Trichloroacetic acid in the blood

TCA was found in the blood after 30 min of exposure. The amount increased almost linearly for a considerable number of hours after exposure (table 1, fig. 2). The individual differences within each group were relatively small (table 1 and fig. 2).

By comparing data in fig. 2 and table 2, one can conclude that the greater the

exposure and the uptake, the faster the blood levels of TCA increase with time. The comparatively small differences between the groups indicate that even at the lowest exposure levels (group II), TCA approaches the maximal rate of production and elimination.

Trichloroacetic acid in the urine

The results of the TCA in the urine are shown in table 3. The variation within the groups is the least when the results are given as the amount excreted per minute because in this way the influence of individual differences in urine output per time unit is reduced. The TCA concentrations have also been corrected for the creatinine levels.

Trichloroethanol in the blood

TCE was found in the blood already after 30 min of exposure. The concentration then increased linearly with time until 30 min after the conclusion of exposure

Table 1. Concentrations of trichloroacetic acid in blood; averages of each group (n = 5) $\pm$ the standard error of the mean are given. (Fig. 1 shows information on intensity of exposure and work load.)

Time (min)	Group		
	I	II	III
0	0	0	0
30	0.4 $\pm$ 0.05	0.6 $\pm$ 0.09	0.7 $\pm$ 0.06
80	1.1 $\pm$ 0.12	1.4 $\pm$ 0.12	1.6 $\pm$ 0.12
110	1.7 $\pm$ 0.14	2.3 $\pm$ 0.09	2.3 $\pm$ 0.11
140	2.8 $\pm$ 0.28	3.0 $\pm$ 0.14	3.0 $\pm$ 0.16
170	3.6 $\pm$ 0.27	3.5 $\pm$ 0.17	3.9 $\pm$ 0.27
200	3.9 $\pm$ 0.32	3.7 $\pm$ 0.21	4.5 $\pm$ 0.28
230	4.5 $\pm$ 0.29	4.1 $\pm$ 0.31	5.3 $\pm$ 0.27
260	5.2 $\pm$ 0.52	4.5 $\pm$ 0.30	5.4 $\pm$ 0.38
1400	13.6 $\pm$ 2.22	13.3 $\pm$ 1.15	17.8 $\pm$ 1.29

Fig. 2. Concentrations of trichloroacetic acid (TCA) in blood during and after exposure to trichloroethylene; the average values of each group are shown. (Symbols: ☆ = group I, ○ = group II and ● = group III)

Table 2. Total amount of trichloroethylene supplied and taken up; averages of each group (n = 5) $\pm$ the standard error of the mean are given.

Group	Amount supplied (mg)	Amount taken up (mg)	Uptake in % of the amount supplied
I	1,681 $\pm$ 26	702 $\pm$ 31	45 $\pm$ 2
II	1,348 $\pm$ 41	565 $\pm$ 8	44 $\pm$ 1
III	3,907 $\pm$ 151	1,402 $\pm$ 307	42 $\pm$ 3

Table 3. Concentrations of trichloroethanol (TCA) and trichloroacetic acid (TCE) in urine and the excreted amount of TCA and TCE of the three groups; averages of each group (n = 5) $\pm$ the standard error of the mean are given.

Group	Time from beginning of exposure (h)	TCA			TCE		
		Concentration (mg/kg)	Excreted		Concentration (mg/kg)	Excreted	
			Amount (mg)	Amount (μ g/min)		Amount (mg)	Amount (μ g/kg)
I	0—5	4.3 $\pm$ 2.5	0.4 $\pm$ 0.0	1.5 $\pm$ 0.2	125.3 $\pm$ 39.9	20.2 $\pm$ 4.0	67.2 $\pm$ 12.9
	5—9	10.6 $\pm$ 2.8	1.8 $\pm$ 0.5	6.9 $\pm$ 1.6	236.2 $\pm$ 67.6	40.4 $\pm$ 8.1	154.1 $\pm$ 22.3
	9—13	22.2 $\pm$ 8.7	3.4 $\pm$ 1.0	13.6 $\pm$ 3.9	136.5 $\pm$ 36.3	24.0 $\pm$ 4.4	96.4 $\pm$ 16.6
	13—22 ^a	24.9 $\pm$ 8.1	5.5 $\pm$ 1.5	10.2 $\pm$ 3.1	131.2 $\pm$ 39.9	33.7 $\pm$ 6.6	61.3 $\pm$ 10.9
II	0—5	6.6 $\pm$ 2.2	1.4 $\pm$ 0.4	4.2 $\pm$ 1.3	157.5 $\pm$ 29.7	35.0 $\pm$ 7.8	106.1 $\pm$ 19.7
	5—9	14.2 $\pm$ 5.2	2.6 $\pm$ 1.6	12.1 $\pm$ 7.4	161.4 $\pm$ 11.2	25.4 $\pm$ 10.3	120.8 $\pm$ 45.3
	9—13	15.6 $\pm$ 6.3	4.1 $\pm$ 1.6	15.8 $\pm$ 7.2	79.7 $\pm$ 18.9	18.9 $\pm$ 5.0	67.3 $\pm$ 15.0
	13—22 ^a	21.1 $\pm$ 9.0	6.4 $\pm$ 2.6	12.2 $\pm$ 5.0	65.3 $\pm$ 8.4	20.2 $\pm$ 4.3	34.7 $\pm$ 8.5
III	0—5	3.0 $\pm$ 1.8	0.7 $\pm$ 0.4	2.3 $\pm$ 1.5	185.6 $\pm$ 83.2	51.2 $\pm$ 20.1	167.5 $\pm$ 59.6
	5—9	14.2 $\pm$ 7.4	5.2 $\pm$ 3.4	17.9 $\pm$ 9.7	258.3 $\pm$ 48.8	82.4 $\pm$ 17.9	316.6 $\pm$ 47.0
	9—13	22.9 $\pm$ 10.7	4.6 $\pm$ 1.6	21.3 $\pm$ 10.6	154.0 $\pm$ 31.2	36.6 $\pm$ 7.3	144.0 $\pm$ 22.2
	13—22 ^a	26.7 $\pm$ 12.8	11.8 $\pm$ 5.6	15.5 $\pm$ 8.1	167.5 $\pm$ 24.8	63.8 $\pm$ 7.9	113.4 $\pm$ 12.2

^a Night urine.

(table 4 and fig. 3). Each exposed person showed relatively constant TCE levels from the termination of the exposure until 2 h later; a plateau level was established. We regard this phenomenon as an important finding. The plateau can be interpreted as a balance between the rate of production and elimination.

As can be seen in fig. 3, the different groups had different angles of inclination of the plateau so that group II, which had the lowest uptake, had the steepest angle and the greatest tendency for TCE to decrease with time. This is a logical result, because the lower the uptake of TRI, the shorter the time necessary for the body to convert TRI and eliminate TCE.

For the determination of the differences between the groups with reference to blood levels of TCE after exposure, a t-test was made on the averages for each group at four time points on the plateau. The differences were significant to the 95 % level between groups I and II, and to the 99.9 % level of significance between groups II and III. This finding is in total agreement with the differences in the levels of uptake (table 2). As can be seen in fig. 4, a correlation exists between the average plateau values for TCE in the blood and the total uptake. These results indicate that it is possible to determine the

Table 4. Concentrations of trichloroethanol in blood; averages of each group (n = 5) $\pm$ the standard error of the mean are given.

Time (min)	Group		
	I	II	III
0	0	0	0
30	0.7 $\pm$ 0.05	0.8 $\pm$ 0.11	1.4 $\pm$ 0.10
80	1.9 $\pm$ 0.08	1.3 $\pm$ 0.08	2.2 $\pm$ 0.12
110	2.1 $\pm$ 0.11	2.2 $\pm$ 0.10	3.1 $\pm$ 0.25
140	3.0 $\pm$ 0.20	2.8 $\pm$ 0.14	3.9 $\pm$ 0.25
Exposure concluded			
170	3.3 $\pm$ 0.20	2.7 $\pm$ 0.11	4.5 $\pm$ 0.22
200	3.3 $\pm$ 0.20	2.6 $\pm$ 0.10	4.2 $\pm$ 0.28
230	3.2 $\pm$ 0.19	2.5 $\pm$ 0.13	4.4 $\pm$ 0.30
260	3.1 $\pm$ 0.13	2.4 $\pm$ 0.10	4.4 $\pm$ 0.29
1,400	1.0 $\pm$ 0.11	0.8 $\pm$ 0.06	1.6 $\pm$ 0.04

Fig. 3. Concentrations of trichloroethanol (TCE) in blood during and after exposure. (Symbols: $\star$ = group I, $\circ$ = group II and $\bullet$ = group III)

amount of TRI taken up during preceding hours with the analysis of TCE in the blood.

The samples taken the day after exposure showed lower levels than the plateau, and in those cases where two consecutive samples were taken for one person the

later value was always lower than the earlier one. The averages for the first sample in each group were 1.0, 0.8, and 1.6 mg of TCE/kg for groups I, II and III, respectively. Even with the variability between individuals within a group, it is possible to draw the conclusion that the TCE level in the blood 1 day after exposure is directly related to the amount of uptake and to state that the greater the uptake, the greater the concentration of TCE in the blood.

Fig. 4. Concentration of trichloroethanol (TCE) in blood as the average plateau values calculated for each individual as an average of four samples taken at intervals of 30 min during the time 30–120 min after the termination of exposure and in relation to the total uptake of trichloroethylene. The equation of the line is $y = 0.002x + 1.60$, and $r = 0.87$. (Symbols: ☆ = group I, ○ = group II and ● = group III)

Fig. 5. Rate of excretion of trichloroethanol (TCE) calculated from the morning sample (from 22:00 to 07:00) obtained the day after exposure in relation to the total uptake of trichloroethylene (TRI); average values of each group as well as the standard error of the mean is given. (Symbols: ☆ = group I, ○ = group II and ● = group III)

Total trichloroethanol in the urine

The results obtained for total TCE in the urine are shown in table 3. As with TCA in the urine, TCE in the urine varied from individual to individual within each group. The difference is not much accentuated if a correction is made for density (12). The correlation was relatively low between the total uptake of TRI and the concentration of TCE in the morning urine specimen the day after exposure. Using the correction milligrams of TCE per gram of creatinine reduces the individual differences and somewhat increases the differences between groups. However, there is a good correlation if the excretion of TCE is expressed as the excreted amount of TCE per time unit (fig. 5). The correlation between uptake of TCE in the urine seems to be valid even for the great uptake of group III.

As can be seen in fig. 6, a correlation was found between the TCE concentration in the blood after the termination of exposure (averages of the plateau values) and the rate of excretion of TCE in the urine in the morning sample taken on the day after the exposure.

Trichloroacetic acid and total trichloroethanol in the urine

The results of the TCA and the total TCE in the urine are shown in table 5. It is evident that TCE and, especially, TCA excretion continued even after the last sampling. It was already known that TCA can be found in the urine for more than 1 week after exposure (3, 9). There are large differences in the sum of TCA + TCE in relation to the uptake within the groups. Therefore using the sum of TCA +

TCE as a measure of exposure is questionable (10, 20). For the different groups practically the same percentage of the total uptake was excreted (table. 5). This result shows that the excretion is proportional to the uptake and therefore also speaks against using the sum of TCA + TCE as a measure of exposure.

DISCUSSION

The results showing higher TCA levels in the blood and urine the day after exposure indicate that production and excretion rates are relatively low. Therefore the metabolite can be expected to accumulate with continued exposure over several days, a result which has also been shown in earlier publications (9, 14) and which is important because, in this way, samples could show higher values at the end of the work week than at the beginning even though the actual exposure has been the

Fig. 6. Concentration of trichloroethanol (TCE) in blood after the termination of exposure as the average of the plateau for the time 30–120 min in relation to the rate of excretion of TCE in urine, calculated from the morning sample (from 22:00 to 07:00) obtained the day after exposure. (Symbols: ☆ = group I, ○ = group II and ● = group III)

Table 5. Excretion of trichloroethanol (TCE) and trichloroacetic acid (TCA) in urine for different periods of time during and after exposure to trichloroethylene (TRI). The average of the total uptake within each group is expressed in moles of TRI, as well as the excretion as the percentage of uptake. Averages of each series ($n = 5$) $\pm$ the standard error of the mean are given. (The individual variation was relatively large and the excretion was not yet concluded, especially in the case of TCA. The summations of the averages for each group have been made for the illustration of the rate of excretion.)

Group	Time from the beginning of exposure (h)	Time in min during which urine was collected	TCA (μ mol)	TCE (μ mol)	TCA + TCE (μ mol)	TRI uptake (μ mol)	Excretion in % of uptake
I	0—5	297 $\pm$ 3	3.0 $\pm$ 0.5	135 $\pm$ 27	138 $\pm$ 26	5,342	16.1
	5—9	255 $\pm$ 19	11 $\pm$ 3	271 $\pm$ 54	282 $\pm$ 56		
	9—13	247 $\pm$ 10	21 $\pm$ 7	161 $\pm$ 30	182 $\pm$ 32		
	13—22	547 $\pm$ 19	34 $\pm$ 9	226 $\pm$ 44	260 $\pm$ 45		
	Summation ^a	0—1,400	69	793	862		
II	0—5	318 $\pm$ 21	9 $\pm$ 3	235 $\pm$ 52	244 $\pm$ 54	4,300	17.6
	5—9	209 $\pm$ 10	16 $\pm$ 10	170 $\pm$ 69	186 $\pm$ 79		
	9—13	273 $\pm$ 27	26 $\pm$ 10	126 $\pm$ 34	152 $\pm$ 40		
	13—22	518 $\pm$ 29	40 $\pm$ 16	136 $\pm$ 29	176 $\pm$ 36		
	Summation ^a	0—1,400	91	667	758		
III	0—5	292 $\pm$ 26	4 $\pm$ 3	344 $\pm$ 135	348 $\pm$ 137	10,670	16.8
	5—9	258 $\pm$ 38	32 $\pm$ 21	553 $\pm$ 120	585 $\pm$ 137		
	9—13	258 $\pm$ 25	26 $\pm$ 11	246 $\pm$ 49	272 $\pm$ 53		
	13—22	558 $\pm$ 18	62 $\pm$ 30	428 $\pm$ 53	490 $\pm$ 81		
	Summation ^a	0—1,400	124	1,571	1,795		

^a Approximate.

same from day to day. The strong affinity of TCA for protein, i.e., albumin, may explain the tendency for accumulation and slow elimination. The fact that the variation between individuals increases with time indicates that the rate of production and/or elimination can demonstrate large individual differences. Earlier published data show that these individual differences tend to decrease if exposure to TRI is continued for several consecutive days (6, 7, 9, 14).

Toxicologically, TCE is the most important product resulting from TRI exposure because it can affect the central nervous system (5, 6, 13). For example, chloral hydrate, which has been used as a sleeping drug for many years, exerts its effects by conversion to TCE (6, 17). It has been proposed that the TCE blood levels are representative of the concentration in the central nervous system (6). There is possibly therefore a risk of accidents when TCE due to occupational exposure in the body exceeds a certain level. For the prevention of accidents the determination of TCE ought to be considered more important than the analysis of TRI in the inspired air as a method to assess the intensity of exposure, e.g., by measuring TRI in blood or alveolar air samples. Unfortunately no published value for a critical level of TCE in blood is available. However, according to Ertle et al. (6) the corresponding level for plasma seems to be below 6 $\mu\text{g/ml}$.

As noted earlier, the concentration of TCE in the blood immediately after the beginning of exposure, and for at least 2 h after that for each individual, is maintained at a relatively constant level, i.e., a plateau. The reason that this phenomenon has not been noted earlier may be that other workers used long time intervals between samplings. It can be shown by statistical analysis that the TCE in the blood measured at the plateau levels is positively correlated to the amount of both exposure and uptake. As pointed out earlier, we regard this finding as important. It has, for example, the practical consequence that fluctuations in the intensity of exposure, as well as time of sampling after terminated exposure, is not very critical. Earlier studies have shown that the levels of solvents in capillary blood correlate well with the levels in

arterial blood (1). It should be taken into consideration that TCE in blood can be present partially as TCE-G, which might make it difficult to use TCE as a measure of the uptake of TRI during occupational exposure.

In the light of the new observations, earlier proposals involving the estimation of exposure from the determination of the concentration of TCA in the urine (16, 18) or TCE+TCA (10, 20) now seems questionable. The explanation for the earlier proposals is to a great extent that a toxicodynamic approach has not been used. The results of this investigation are consistent with the recent reports of Ertle and co-workers (6) and Kimmerle and Eben (9), who have shown that the production, as well as the excretion rates, are very different for TCE and TCA. Therefore the accurate assessment of a urine analysis also requires specific information about the exposure to TRI. The exposure conditions for the week prior to TCA sampling must be considered and for the previous 24-h period for TCE. Standardization of the sampling time is highly desirable for TCE and TCA. The total amount or ratio of the metabolites (7, 10, 16) is difficult to interpret and may even be misleading because of previously mentioned facts. As TCE in the urine sample taken the morning after exposure seemed to give the best reflection of the exposure occurring on the preceding day and as it gives information about the level of TCE in the blood, such a measurement appears to be a valuable analysis. However, there are some practical difficulties, e.g., getting exposed persons to provide accurate data on the time of urine collection, since inaccurate data might make calculations of the TCE excretion rate uncertain in some cases. The results presented in this study do not preclude evaluation of conditions that would be present during repeated exposure over several consecutive days. Although such studies have been made (6, 9, 14, 19), it is not easy to compare published data on TCA and TCE in urine partly because widely different exposure conditions have been used.

REFERENCES

1. ASTRAND, I. Uptake of solvents in the blood and tissues of man: A review. *Scand.*

- j. work environ. & health* 1 (1975) 199—218.
2. ÅSTRAND, I. and ÖVRUM, P. Exposure to trichloroethylene: I. Uptake and distribution in man. *Scand. j. work environ. & health* 4 (1976) 199—211.
3. AHLMARK, A. and FORSSMAN, S. Evaluating trichloroethylene exposures by urine analyses for trichloroacetic acid. *Arch. ind. hyg. occup. med.* 3 (1951) 386—398.
4. BREIMER, D. D., KETELAARS, H. C. J. and ROSSUM, J. M. VAN. Gas chromatographic determination of chloral hydrate, trichloroethanol and trichloroacetic acid in blood and in urine employing Head-Space analysis. *J. chromatogr.* 88 (1974) 55—63.
5. ELSTER, I., KONIETZKO, H., VETTER, K. and WEICHARDT, H. Telemetrische EEG-Überwachung bei Lösungsmittelarbeitern an Trichloräthylen-Waschanlagen. *Zentrabl. Arbeitsmed. Arbeitsschutz* 23 (1973) 129—133.
6. ERTLE, T., HENSCHLER, D., MÜLLER, G. and SPASSOWSKI, M. Originalarbeiten. Metabolism of trichloroethylene in man. *Arch. toxicol.* 29 (1972) 171—188.
7. IKEDA, M., OHTSUJI, H., IMAMURA, T. and 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.
8. JAKOBSON, I. *Biotransformationen av trikloretalen*. (Undersökningsrapport AMMT 102/75). Arbetskyddsstyrelsen, Stockholm 1975.
9. KIMMERLE, G. and EBEN, A. Metabolism, excretion and toxicology of trichloroethylene after inhalation. *Arch. toxicol.* 30 (1973) 127—138.
10. KUNDIG, S. and HÖGGER, D. Die Bedeutung der Tri- und Perchloräthylenmetaboliten im Urin. *Int. Arch. Arbeitsmed.* 26 (1970) 306—315.
11. LEIBMAN, K. and MC ALLISTER, W. J. Metabolism of trichloroethylene in liver microsomes. *J. pharmacol. exp. ther.* 157 (1967) 574—580.
12. LEVINE, L. and FAHY, J. P. Evaluation of urinary lead determination. *J. ind. hyg. toxicol.* 27 (1945) 217—223.
13. MIKISKOVA, H. and MIKISKA, A. Trichloroethanol in trichloroethylene poisoning. *Br. j. med.* 23 (1966) 116—125.
14. MÜLLER, G., SPASSOVSKI, M. and HENSCHLER, D. Trichloroethylene exposure and trichloroethylene metabolites in urine and blood. *Arch. toxicol.* 29 (1972) 335—340.
15. NATIONAL INSTITUTE FOR OCCUPATIONAL SAFETY AND HEALTH. Occupational exposure to trichloroethylene. In: *Criteria for a recommended standard*. U.S. Department of Health, Education and Welfare, Public Health Service, Cincinnati, Ohio 1973, p. 102.
16. OGATA, M., TAKATSUKA, Y. and TOMOKUNI, K. Excretion of organic chlorine compounds in the urine of persons exposed to vapours of trichloroethylene and tetrachloroethylene. *Br. j. ind. med.* 28 (1971) 386—391.
17. OWENS, A. H., MARSHALL, E. K., BROWN, G. O., et al. A comparative evaluation of the hypnotic potency of chloral hydrate and trichloroethanol. *Bull. hopkins hosp.* 96 (1955) 71—83.
18. SMITH, G. F. Trichloroethylene: A review. *Br. j. ind. med.* 23 (1966) 249—262.
19. STEWART, R. D., DODD, H. C., GAY, H. H. and ERLEY, D. S. Experimental human exposure to trichloroethylene. *Arch. environ. health* 20 (1970) 64—71.
20. TANAKA, S. and IKEDA, M. A method for determination of trichloroethanol and trichloroacetic acid in urine. *Br. j. ind. med.* 25 (1968) 214—219.
21. VESTERBERG, O., GORCZAK, J. and KRASTS, M. Methods for measuring trichloroethanol and trichloroacetic acid in blood and urine after exposure to trichloroethylene. *Scand. j. work environ. & health* 1 (1975) 243—248.

Received for publication: 1976-07-02