URINARY METABOLITES FROM CONTROLLED EXPOSURES OF HUMANS TO TRICHLOROETHYLENE

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16. Abstracts

The urinary metabolites of trichloroethylene (TCE) (79016), trichloroethanol (115208) and trichloroacetic acid (76039), were measured after humans had been exposed for controlled periods of time to either 20, 100 or 200ppm of TCE vapor for 5 days per week. The quantity and concentration of each metabolite varied widely during the daily exposures of identical magnitudes. If the excretion of either of these metabolites, or their sum, is to be considered as a measure of exposure, it must be remembered that at the current TLV, and at higher exposures, both the concentration and quantity are affected by previous recent exposures. At the lowest level of exposure studied the effect was lessened, indicating a better clearance of the metabolites on a daily basis. It is the conclusion that the measurement of urinary metabolites is not an ideal method of predicting the magnitude of a human exposure to the vapors of TCE, particularily if the exposure was near or greater than the current TLV.

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Trichloroethylene is widely used throughout the world as an industrial solvent. One of its primary industrial uses is that of "degreasing", and unless the operation is in a completely closed system, industrial workers are not infrequently exposed to its vapors. It is well known that trichloroethylene is metabolized to both trichloroethanol and trichloroacetic acid in the human, with excretion in the urine, the former as its glucuronide, urochloralic acid. The measurement of these metabolites in the urine of humans, both after industrial and controlled exposures, has been used to assess the magnitude of exposure to the trichloroethylene [1,2,3,4,5,6,7,8,9,10,11,12]. Unfortunately, there is a great individual variation in the concentration and total excretion of these metabolites in the urine of persons exposed to almost identical vapor levels of the compound. In addition, there has been considerable variation between laboratories in reported levels of excretion.

Papers on the subject of trichloroethylene metabolites excretion have generally reported the use of a quantitative method of analysis based upon the "Fujiwara" reaction, a non-specific color reaction for highly chlorinated compounds. Slight variations of conditions under which the reaction is carried out can cause significant differences in the quantity and quality of the color produced. For these reasons, it was decided to investigate gas chromatographic methods for the analysis of these metabolites in urine.

This report covers the gas chromatographic methods used to assay the metabolites of trichloroethylene in the urine, and the quantity of these

metabolites in 24-hour urine samples obtained from subjects exposed to varying magnitudes of trichloroethylene vapor. Other papers discuss the breath and blood analyses, and the responses of the humans exposed[13,14,15,16].

EXPERIMENTAL PROCEDURES

Exposures:

Ten young adult, male subjects were divided into three groups. Group I, consisting of four subjects, was exposed to the vapors of trichloroethylene (TCE) for $7\frac{1}{2}$ hours per day, 5 days per week; Group II, consisting of three subjects, was exposed for 3 hours daily; while Group III, also consisting of three subjects, was exposed for 1 hour daily. During the first week, Monday through Friday, the male subjects were exposed to a stable TCE vapor concentration of 20 ppm, during the second week to a stable TCE vapor concentration of 100 ppm, during the third week to a fluctuating TCE vapor concentration of from 50 to 200 ppm with a daily time-weighted average concentration of 100 ppm, and during the fourth week to a stable TCE vapor concentration of 200 ppm. Ten female subjects, also divided into 3 groups, were exposed to a stable TCE vapor concentration of 100 ppm on five consecutive days during one week. See Table I for a summary of these exposures. The chamber used for these exposures, and the methodology used for determining concentrations of trichloroethylene in the chamber, have been described[13]. Subjects were generally sedentary during the exposures, with the exception of 5 to 15

minutes daily exercise periods. They were encouraged not to drink alcohol to excess during the weeks of exposure, however, despite this encouragement, most males imbibed in from light to heavy consumption several evenings during each week of the study. When one male subject developed "degreasers flush" the evening following the fifth day of exposure to a fluctuating concentration of 100 ppm TCE (third week), additional studies to elicit this phenomenon were carried out during the last week of exposures of male subjects [17].

Urine Collection:

Daily urine collections were begun just prior to exposure and were concluded with the urinalysis sample the following day. Each collection represented a 24-hour sample, with the exception of the Friday to Saturday morning sample from Group III subjects, where it represented an 18-hour collection. Subjects voided into a 4-liter plastic jar with a large screw cap, and the jar was contained in an ice-cooled foam-type bucket. Volume measurements were made prior to sampling. Subjects were alerted to note any missed voids.

Samples were frozen for creatinine, trichloroacetic acid and trichloroethanol determination.

Creatinine:

Creatinine determinations were carried out on previously frozen urine samples using the Autoanalyzer® at the rate of sixty per hour. Values

reported in mg% were converted to g/24 hours by multiplying by measured urine volumes.

Trichloroacetic Acid:

A Varian Aerograph Model 204 research gas chromatograph with a hydrogen flame ionization detector was used to separate the trichloroacetic acid (TCA) peak. The column was a 1' x 1/8" O. D. stainless steel column packed with 25% Apiezon on Chromosorb W, 45/60 mesh. It was conditioned at 200°C for at least 12 hours prior to each day's use; column temperature during use was 85 - 90°C. The aliquots (all 1.0 μl in volume) of the urine samples were injected without treatment directly into the injection port. The flow rate of the N_2 carrier gas was adjusted so that the TCA peak was recorded within sixty to ninety seconds after injection. Standards at three concentrations to bracket the unknown levels were prepared by diluting with control urine a stock standard of TCA (Fisher, Certified ACS) in water. Standards were refrigerated when not in use. Peak heights of unknowns were compared to standard curves run at least twice daily. Interference studies with ethanol, monochloroacetic acid, and trichloroethanol were carried out.

Trichloroethanol:

The trichloroethanol (TCEt) was released from urochloralic acid by enzymatic hydrolysis with β-glucuronidase (Sigma, Type II: Crude Bacterial Powder). The β-glucuronidase was dissolved (approximately 500 units/ml) in 0.15 M phosphate buffer (pH 6.0) and checked for enzymatic activity by

the phenolphthalein glucuronide method [18]. One ml of the β-glucuronidase solution was added to 1 ml of urine and the solution was incubated at 37° for 1 hour. A Varian Aerograph Model 2740 research gas chromatograph with a hydrogen flame detector was used for TCEt assay. An identical column to that used for the TCA assay was employed, however, to obtain the comparable retention time, the column temperature was raised to 175°C. Standards of TCE (Eastman 2,2,2-trichloroethanol) were prepared in urine by dilution, carrying them through the enzymatic hydrolysis step in an identical manner to the unknown. Peak heights of unknowns were compared to standards run on the same day.

RESULTS

The 24-hour creatinine excretion values varied considerably between subjects. Because several values were available for each subject, an average of the normal values was used to calculate corrected urine volumes for the 24-hour collections with abnormal values. Table II lists the normal creatinine excretion value and range for each subject, and the number of 24-hour collections falling within and outside the normal range.

The gas chromatographic method for the direct assay of trichloroacetic acid in urine proved to be very satisfactory for the rapid determination of this metabolite. Of the probable interfering compounds in the urine, ethanol peaked almost immediately after the aqueous solvent peak under the

conditions used, while trichloroethanol peaked approximately five minutes after the trichloroacetic acid peak. However, the trichloroethanol presented no baseline problem because it was present as its glucuronide, urochloralic acid. Monochloroacetic acid, a minor metabolite of trichloroethylene, caused no chromatographic peak at levels as high as 1.28 mg/ml. Therefore, no gross interference from the metabolic products of trichloroethylene was observed. The precision of this method was fairly good. One set of 10 urines analyzed one week apart had a mean difference of 12.5%. The most disturbing problem was a carryover (echo) in the trichloroacetic acid peak from one sample to the next when the column had been in use several hours without additional conditioning at a higher temperature. This reduced the overall precision. Sensitivity was a problem at the lowest exposure level (20 ppm). The limit of sensitivity was 0.02 mg/ml, and dilution of the urine with increased fluid intake magnified the sensitivity problem. However, it should be noted that the gas chromatograph used was over six years old; the newer models are more sensitive.

There was complete hydrolysis of the urochloralic acid upon incubation with β-glucuronidase for one hour as shown by a lack of increase in trichloroethanol assayed upon additional incubation. The trichloroethanol elution from the column was complete after each sample, probably because of the higher column temperature. The trichloroacetic acid peak appeared with the aqueous solvent peak at this temperature. Sensitivity was no particular problem because all samples, with the exception of the third post-exposure

day following the last week of exposure, were assayed on a new gas chromatograph. As little as 0.005 mg/ml caused a peak height twice the background noise. Trichloroethanol gives a two-fold higher peak than does an equivalent concentration of trichloroacetic acid.

The mean and the range of values for trichloroacetic acid and trichloroethanol excreted in the urine for the 24-hour period during and after exposure of humans to three levels of trichloroethylene vapor are presented in Table III. The mean values listed represent at least 2 of 3 or 3 of 4 values for each day. All exposures approximated the planned magnitude of exposure with the exception of day 1, Experiment 3. There was no exposure of the 1-hour subjects on that day, and the $7\frac{1}{2}$-hour subjects were exposed for only $5\frac{1}{2}$ hours. Where all, 2 of 3, or 3 of 4 values were below the sensitivity of the gas chromatograph used, the values was noted as $<$ the average.

It was of interest to rank each Group I subject according to the magnitude of daily trichloroethanol excretion for his group. This can be seen in Figure 1. Of the four males in Group I, subject number 82 excreted the largest (or equal to the largest) amount of trichloroethanol on 13 of the 21 days, while subject number 81 excreted the least amount on 13 of the 21 days. Subject number 82 had the highest urine volume on 14 of 21 days, and subject number 81 had the lowest on 17 of 21 days. However, the correlation between urine volume and rank of trichloroethanol excretion was not absolute.

Table IV lists the urinary concentrations in mg/L of trichloroacetic acid, trichloroethanol, and their combined values for males and females

exposed daily for $7\frac{1}{2}$ hours to 100 ppm trichloroethylene vapor.

For the results of the other parameters measured in this study, such as breath analysis, health effects, and performance, please see the papers previously cited.

DISCUSSION

Many studies have been reported concerning the value of measuring trichloroethylene metabolites in the urine of humans as a function of their exposure to this compound. Most of the studies were undertaken in actual industrial settings where the measurement of the magnitude of the exposure was difficult and of some doubtful accuracy. In other studies, where the measurement of inhaled vapors was of greater accuracy and the studies were well controlled, the exposures were not repeated on a daily, 5 days per week, basis. Usually they were single exposures of less than 8 hours duration. The one exception to these controlled studies was the study by Stewart, et al[19], in which human subjects were exposed on five successive days for 7 hours per day to 200 ppm of trichloroethylene vapor. The study reported in this paper is complementary to this previous work by Stewart, et al. It adds several magnitudes of exposure to the study, and adds the influence of alcohol at the level of exposure previously reported.

The use of the pyridine-alkali "Fujiwara" method for measuring trichloroethylene metabolites is a valuable method in the hands of skilled

chemists who have developed the "art" of carrying out this sensitive color reaction. The gas chromatographic methods for trichloroethanol and trichloroacetic acid reported in this paper, add another type of assay methodology which should prove useful to laboratories where this instrument is used routinely. Again, the analyst must be skilled, this time in the "art" of gas chromatography, for "echo" peaking in successive samples can only be corrected by a skilled analyst. The problem of sensitivity in the trichloroacetic acid assay noted in this study can be overcome by the use of the newer instruments. It is also very probable that both trichloroacetic acid and trichloroethanol could be assayed from one urine sample in a sensitive chromatograph with a programmed temperature oven.

When the results of this study are compared to those of the previous study by Stewart, et al, it is evident that the daily urinary metabolite levels, especially that of trichloroethanol, found during and after a $7\frac{1}{2}$-hour daily exposure to 200 ppm were usually 20 to 50% higher in the present study. Several explanations seem possible, the most logical being a combination of carryover from the previous week's exposure to 100 ppm trichloroethylene (this study) and the possible effect of alcohol consumption increasing the excretion (this study). In addition, the subjects in this study were exposed for 30 minutes longer each day, although this 7% increase in exposure time would not be expected to increase the daily metabolite excretion 20 to 50%. It is also of interest that the urinary excretion of trichloroacetic acid, though almost doubled in this study on day 1, was almost identical to the previous

study level by day 5. From this, and the values from other magnitudes of exposure, it appears that the average excretion of trichloroacetic acid on the fifth exposure day of a 5-day work-week may be the best indicator of the exposure magnitude during the previous five days. However, as seen from Figures 2 and 3, where the average daily values for the 3- and 7-hour subjects are graphed, this value is not always consistent for identical time-weighted exposures.

In general, this study confirms the previous observations on the excretion of metabolites of trichloroethylene: (1) trichloroethanol appears in greater amounts more rapidly than trichloroacetic acid, and (2) trichloroethanol levels decrease more rapidly after discontinuance of daily exposure. It also demonstrates the daily carryover of trichloroacetic acid excretion at the current TLV, as this compound almost always was excreted in greater amounts through day 4 of each 100 and 200 ppm exposure week. Trichloroethanol excretion, on the other hand, often peaked on the third successive day of exposure in a 5-day week. The daily increase or leveling off of urinary metabolites adds to the problem of their use for predicting the magnitude of a specific exposure. This affect of a daily carryover of excretion was not observed at an exposure level of 20 ppm, indicating a more complete daily clearance of these metabolites after exposure to this vapor level of trichloroethylene.

It was of interest to compare the metabolite excretions between males and females in industrial exposures to trichloroethylene. Nomiyama and Nomiyama [10] reported that females excreted 2 - 3 times more trichloroacetic acid than males during the first 24 hours after exposure. In our study, the excretion of trichloroacetic acid over a 24-hour period including exposure was surprisingly consistent between males and females (see Figure 4 for comparison of $7\frac{1}{2}$-hour exposures to 100 ppm). We did observe a tendency toward greater excretion of trichloroethanol by the male subjects, especially for $7\frac{1}{2}$- and 3-hour subjects, as reported in the same paper. However, this finding was not consistent in a comparison of the 1-hour male and female subjects.

It is of interest to compare the average urinary creatinine excretion values in g/24 hours to the weight of each subject. These data are plotted in Figure 5. Only one subject, a female and the only obese individual in the entire study, fell considerably outside the straight line defining the best fit of points.

Nomiyama [9] has published a table of "coefficient (c) for estimating environmental trichloroethylene by urinary total trichloro-compounds (E) when a worker exposed to trichloroethylene at a same concentration for same hours in successive t days." In order to obtain E, Nomiyama used spot samples of urine collected during work. Using the Nomiyama coefficients for each successive day of exposure to 100 ppm for $7\frac{1}{2}$ hours, and the combined trichloroethanol and trichloroacetic acid concentration in mg/L, the predicted

exposure was calculated. The results are listed in Table III. It is obvious that the Nomiyama coefficients predicted a low exposure by a factor of 2 to 3. However, it must be remembered that in our study the subjects were relatively sedate during the $7\frac{1}{2}$-hour exposure, and our urine values represented concentrations of 24-hour collections rather than samples excreted during exposure. The possibility also exists that the actual time-weighted-average exposure of the workers from whom Nomiyama obtained his data was higher than was calculated. From this comparison, it is obvious that many factors need to be considered before an assumption of the magnitude of exposure can be made by using metabolite excretion data. Ikeda, et al[12], report that the concentration of total trichloro-compounds in the urine after the work day exposures to 100 ppm trichloroethylene should be 730 mg/L. The highest average level that our subjects excreted while exposed to 100 ppm was 666 mg/L on the fifth exposure day of the first week. The average did not excede this level the following week after the subjects had two days of non-exposure on the weekend. It is conceivable, however, that workers who are physically more active than our subjects would obtain the level quoted by Ikeda, et al. A rule of thumb for correlating trichloroacetic acid excretion with trichloroethylene exposure was made by Grandjean, et al[5], who concluded "that the mean allowable concentration for trichloroethylene should be fixed below 40 ppm, and that the mean allowable concentration for trichloroacetic acid should be fixed below 96 mg/L." All of our subjects exposed to 100 ppm trichloroethylene for $7\frac{1}{2}$ hours excreted less than 96 mg/L trichloroacetic acid prior to

the third consecutive day of exposure in experiment 2 (males) and 5 (females). In experiment 3, the second consecutive week of exposure to 100 ppm, the males exceeded this level on the second day. Again, it is obvious that exposure and excretion of metabolites are difficult to correlate.

CONCLUSIONS

The urinary metabolites of trichloroethylene, trichloroethanol and trichloroacetic acid, were measured after humans had been exposed for controlled periods of time to either 20, 100 or 200 ppm of trichloroethylene vapor for 5 days per week. The quantity and concentration of each metabolite varied widely during the daily exposures of identical magnitudes. If the excretion of either of these metabolites, or their sum, is to be considered as a measure of exposure, it must be remembered that at the current TLV, and at higher exposures, both the concentration and quantity are affected by previous recent exposures. At the lowest level of exposure studied (20 ppm) the affect was lessened, indicating a better clearance of the metabolites on a daily basis. It is our conclusion that the measurement of urinary metabolites is not an ideal method of predicting the magnitude of a human exposure to the vapors of trichloroethylene, particularly if the exposure was near or greater than the current TLV.

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TABLE I

EXPOSURE OF HUMAN SUBJECTS TO VARIOUS LEVELS OF TRICHLOROETHYLENE

Experiment No.	No. & Gender of Subj.	Planned Exposures ppm	Group, Hrs. & No. of Subjects	Actual Exposures - TWA ppm (± S.D.) Day 1	Day 2	Day 3	Day 4	Day 5
1	10 Male	20, Stable	I - $7\frac{1}{2}$ - 4	20.4±1.8	20.6±2.3	20.0±2.2	20.8±1.8	19.9±7.9
			II - 3 - 3	20.8±2.3	20.2±1.9	20.8±3.0	21.2±2.3	19.3±1.4[a]
			III - 1 - 3	20.7±1.4	21.1±2.2	18.8±1.3	19.9±0.8	19.5±1.1[b]
2	10 Male	100, Stable	I - $7\frac{1}{2}$ - 4	99.2±7.2	98.0±3.8	98.1±5.0	99.8±6.8	100.9±8.2
			II - 3 - 3	97.7±11.1	95.6±3.5	98.4±4.6	97.8±7.8	100.8±5.5
			III - 1 - 3	99.1±1.6	98.4±1.6	97.5±2.0[c]	96.9±5.9	95.6±17.7[d]
3	10 Male	100, Fluctuating	I - $7\frac{1}{2}$ - 4	91.7±53.1[e]	101.9±55.1[f]	100.6±51.4	99.73±51.1	100.6±51.2[i]
			II - 3 - 3	104.3±60.0	100.9±59.3[g]	100.4±56.4	93.7±51.9[h]	98.5±55.5
			III - 1 - 3	no exposure	114.4±64.1	100.9±58.3	104.7±56.1	104.2±52.4
4	10 Male	200, Stable	I - $7\frac{1}{2}$ - 4	200.9±7.4	197.1±5.6	198.3±8.3	198.8±4.9	199.9±6.7
			II - 3 - 3	200.1±7.2	194.0±5.5	200.4±8.0	198.5±5.8	198.6±7.8
			III - 1 - 3	195.3±8.0	200.2±5.2	193.0±10.3[j]	198.6±3.7	201.2±5.5[k]
5	10 Female	100, Stable	I - $7\frac{1}{2}$ - 4	100.0±3.3	100.0±2.8	100.0±3.2	100.0±4.8	100.0±3.5
			II - 3 - 3	99.1±3.8	99.4±3.2	100.0±3.7	99.9±4.0	99.6±2.8
			III - 1 - 3	100.1±2.2	99.8±2.0	98.9±2.5[l]	97.9±2.6	97.7±3.2

a 1 subject absent
b 1 subject's exposure was 19.3±1.3ppm
c 1 subject's exposure was 93.5±3.5 ppm
d 1 subject exposed for $6\frac{1}{2}$ hrs. to 101.7±8.4 ppm
e all 4 subjects exposed $5\frac{1}{2}$ hrs.
f 1 subject exposed for 5hrs to 113.2±59.0 ppm
g 1 subject exposed to 104.7±56.9 ppm
h 1 subject absent
i 1 subject exposed for $5\frac{1}{2}$ hrs. to 113.1±52.9 ppm & 1 subject for 4 hrs. to 107.3±48.1 ppm
j 1 subject exposed to 203.7±3.2 ppm
k 1 subject exposed for 6 hrs. to 200.6±6.7 ppm
l 1 subject absent

TABLE III

URINARY CREATININE EXCRETION

Subject No.	Gender	Mean of Normals g/24 hours	Range of Normals g/24 hours	No. Normal	No. Abnormal	Weight (kg)
55	M	1.629	(1.080 - 2.052)	17	3	72.5
81	M	1.183	(1.006 - 1.393)	14	7	62.0
82	M	1.601	(1.057 - 2.085)	19	2	80.0
83	M	1.278	(1.009 - 1.547)	12	9	72.6
84	M	1.742	(1.234 - 2.016)	20	1	76.0
85	M	2.024	(1.548 - 2.331)	21	0	88.4
86	M	1.441	(1.128 - 2.286)	16	4	66.4
87	M	1.751	(1.302 - 2.180)	20	1	77.5
88	M	1.333	(1.039 - 2.089)	14	5	61.0
89	M	1.509	(1.015 - 1.972)	15	5	81.8
94	F	0.917	(0.863 - 0.970)	4	1	48.0
95	F	1.165	(1.040 - 1.247)	3	2	60.3
96	F	1.178	(1.123 - 1.229)	3	2	61.5
97	F	1.292	(1.264 - 1.311)	3	2	62.0
98	F	1.045	(1.022 - 1.078)	4	1	89.7
99	F	0.847	(0.825 - 0.874)	4	1	50.2
100	F	1.182	(1.038 - 1.420)	3	2	64.0
101	F	0.7000	(0.632 - 0.768)	2	2	41.1
115	F	0.7635	(0.673 - 0.952)	4	0	58.4
116	F	1.110	(1.085 - 1.132)	3	2	62.1

TABLE III

Experiment No.	No. & Gender of Subj.	Planned Exposures* ppm	Hrs./Day & No. of Subjects	Mean° and Range of 24-Hour Excretion of TCA and TCEt										Day 3 Post
				Day 1		Day 2		Day 3		Day 4		Day 5		
				TCA	TCEt	TCA	TCEt	TCA	TCEt	TCA	TCEt	TCA	TCEt	TCA
1	10 Male	20 Stable 5 Days	7½ - 4	<22	37 28-55	<30	52 45-68	<20	49 39-60	<32	48 38-55	<40	43 42-43	
			3 - 3	<33	24 17-32	<25	44 22-84	<22	26 18-28	<33	19 17-20	<31	26 18-33	
			1 - 3	<16	8 1-14	<14	18 8-27	<15	14 7-19	<20	16 11-24	<24	11 5-21	
2	10 Male	100 Stable 5 Days	7½ - 4	51 30-62	135 12-189	121 51-238	409 263-541	175 111-295	487 340-672	214 105-320	450 309-634	253 123-372	523 409-690	
			3 - 3	<29	105 68-153	48 26-75	195 173-209	81 65-112	186 117-239	126 105-163	220 193-257	111 88-155	174 146-204	
			1 - 3	<32	40 13-56	<18	51 42-59	21 11-27	64 43-78	<27	61 51-66	<35	84 33-134	
3	10 Male	100 Fluctuating 5 Days	7½ - 4	165** 61-176	198** 148-276	158 108-238	365 290-440	226 79-329	404 346-537	241 97-538	370 257-497	197 121-235	220 200-259	
			3 - 3	64 36-95	159 140-186	81 43-119	233 177-285	115 75-176	252 185-341	140 77-242	216 199-233	110 47-190	298 210-452	
			1 - 3	no exposure		<21	75 58-102	28 24-32	68 50-85	34 15-72	56 28-77	23 13-37	104 92-115	
4	10 Male	200 Stable 5 Days	7½ - 4	175 44-353	450 119-858	244 71-483	508 295-722	283 145-552	528 440-573	356 158-725	860 699-1060	390 128-684	894 703-1083	215 102-301
			3 - 3	98 67-155	362 327-397	118 52-189	403 263-543	170 90-262	548 506-601	195 117-243	556 328-848	180 102-312	429 348-490	145 88-178
			1 - 3	<16	97 86-106	22 19-26	97 49-144	35 21-58	143 131-155	40 11-84	118 111-129	35 22-56	126 81-167	<29
5	10 Female	100 Stable 5 Days	7½ - 4	28 10-40	211 183-241	81 67-100	291 258-324	184 133-194	341 293-388	225 203-236	294 250-334	241 204-260	296 256-330	
			3 - 3	<25	118 86-160	36 27-44	102 87-118	64 41-84	134 125-140	74 44-100	99 86-113	84 81-86	113 67-143	
			1 - 3	<26	39 25-63	23 13-32	64 22-92	<27	156 78-233	22 13-31	51 20-93	32 27-40	58 32-95	

° mean of at least 2 of 3 or 3 of 4 subj. * Actual expo. approx. planned expo. except where noted in table ** The expo. time for this day was 5½ hrs.

TABLE IV

URINARY METABOLITE CONCENTRATION* (MG/L) AFTER 7½ HOUR DAILY EXPOSURE TO 100 PPM TRICHLOROETHYLENE VAPOR

Day	MALES a TCA	b TCEt	a + b Comb.	Exposure Predicted° ppm	FEMALES a TCA	b TCEt	a + b Comb.	Exposure Predicted° ppm
1	48	153	201	34	30	203	233	39
2	75	306	381	40	63	230	293	30
3	138	358	496	43	118	257	375	31
4	165	368	533	41	193	254	447	33
5	210	456	666	49	233	283	516	36

* Average of 4 values.

° By use of (a + b) x coefficient c found in Nomiyama [9].

INDIVIDUAL VALUES FOR URINARY EXCRETION OF TRICHLOROETHANOL DURING AND AFTER EXPOSURE TO VARYING LEVELS OF TRICHLOROETHYLENE FOR 7 1/2 HOURS PER DAY

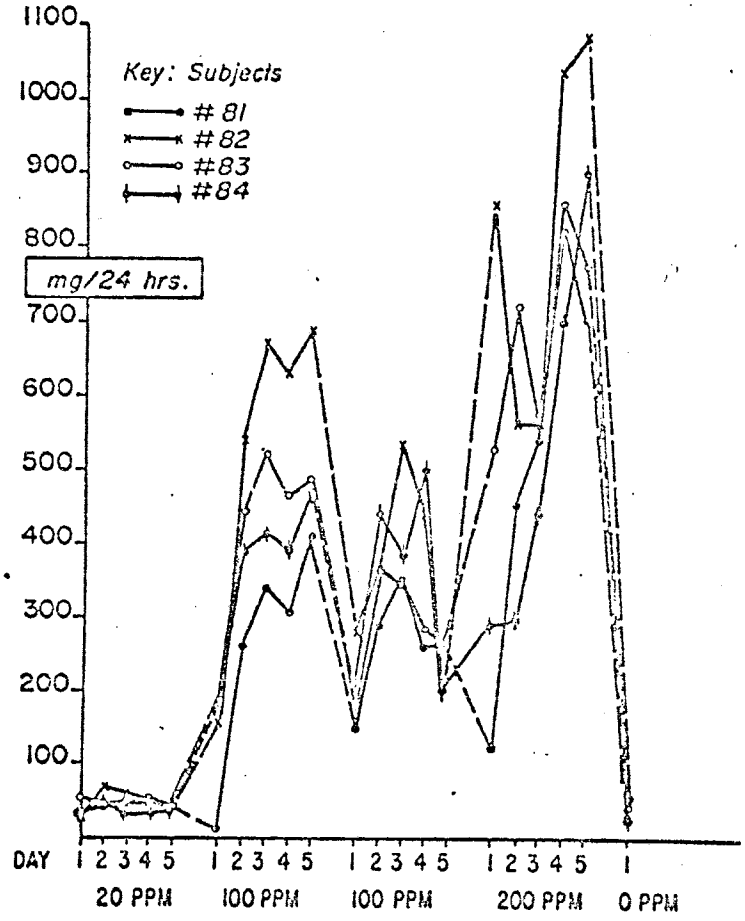


FIGURE 1

URINARY EXCRETION OF TRICHLOROACETIC ACID (TCA) AND TRICHLOROETHANOL (TCEt) IN MALE SUBJECTS DURING AND AFTER VAPOR EXPOSURE TO VARYING CONCENTRATIONS OF TRICHLOROETHYLENE DAILY FOR 3 HOURS

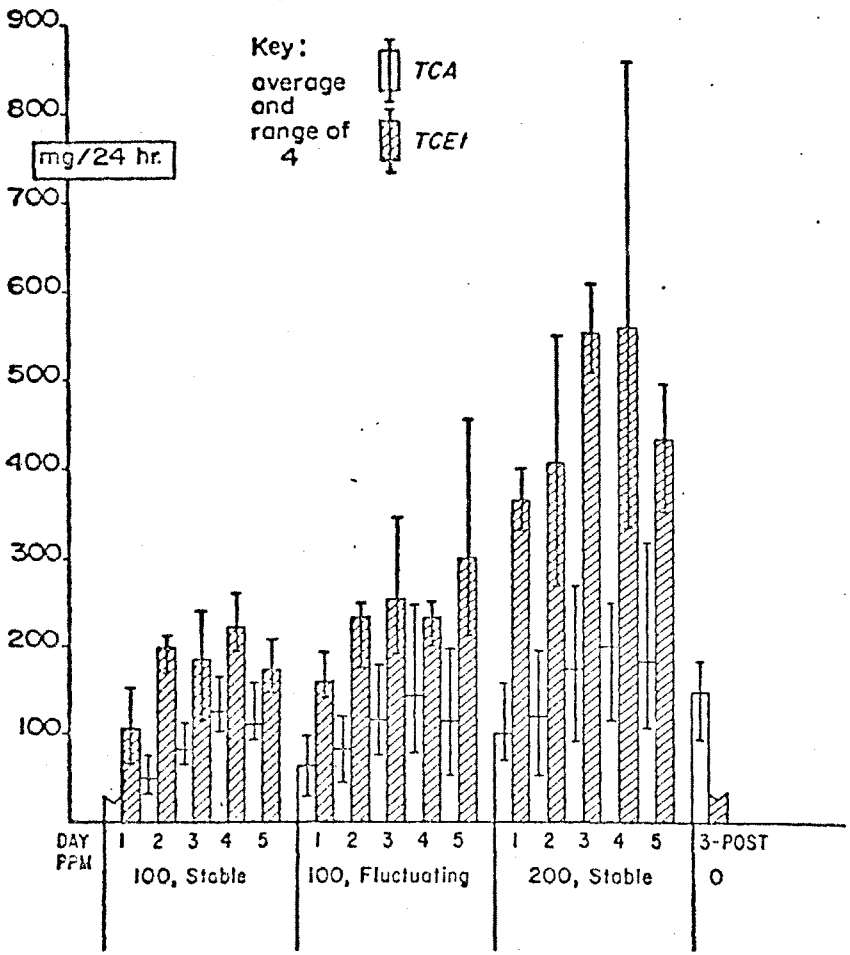


FIGURE 2

URINARY EXCRETION OF TRICHLOROACETIC ACID (TCA) AND TRICHLOROETHANOL (TCEt) IN MALE SUBJECTS DURING AND AFTER VAPOR EXPOSURE TO VARYING CONCENTRATIONS OF TRICHLOROETHYLENE DAILY FOR 7 1/2 HOURS

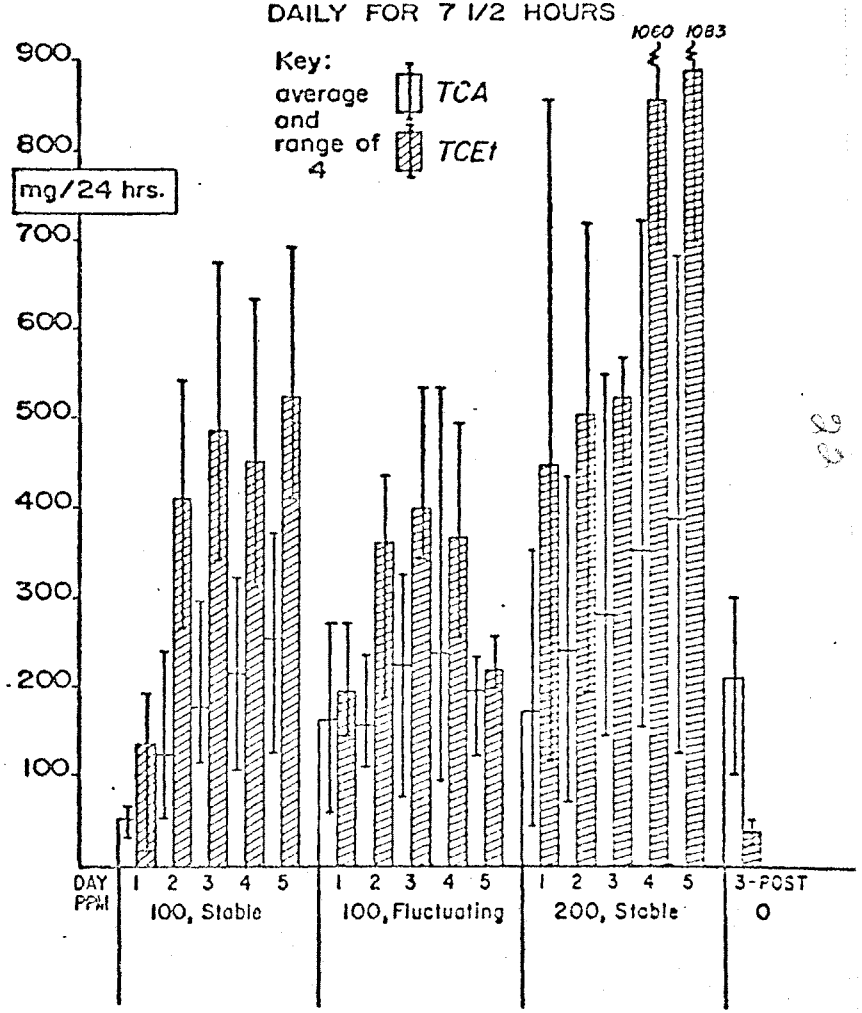


FIGURE 3

URINARY EXCRETION OF TRICHLOROACETIC ACID (TCA) AND TRICHLOROETHANOL (TCET) IN MALES AND FEMALES DURING AND AFTER VAPOR EXPOSURE TO 100 PPM TRICHLOROETHYLENE DAILY FOR 7 1/2 HOURS

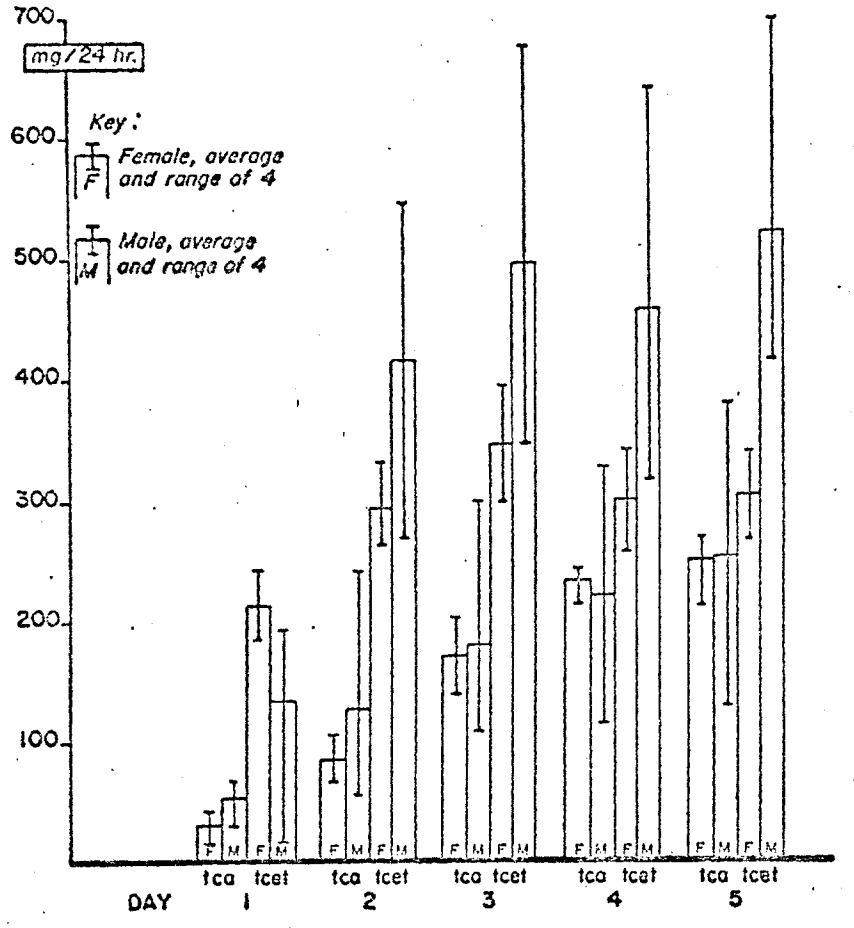
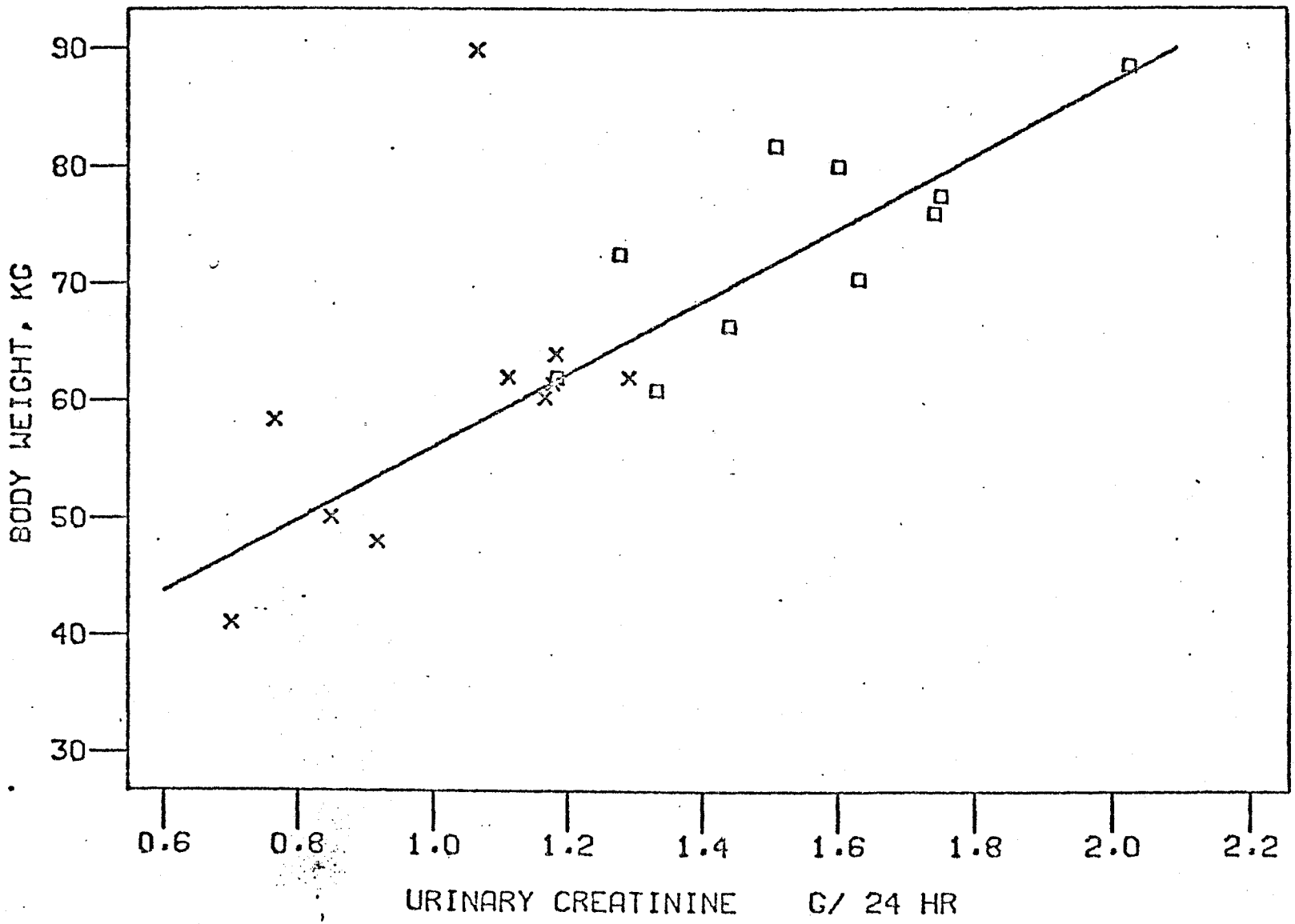


FIGURE 4

AVERAGE URINARY CREATININE EXCRETION AND BODY WEIGHT

OF MALE (□) AND FEMALE (X) SUBJECTS



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