Subjective Symptom Increase Among Dry-Cleaning Workers Exposed to Tetrachloroethylene Vapor

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Abstract: Subjective symptoms, hematology, serum biochemistry and other clinical signs were investigated in 56 dry-cleaning workers exposed to tetrachloroethylene at 20 ppm (as a geometric mean of 8-hr time-weighted average), and the results were compared with the findings in 69 non-exposed controls from the same factories. There were exposure-related increases in the prevalence of subjective symptoms during the work as well as in the past 3 month period, whereas there was no significant changes in hematology. Effects of the exposure on liver and kidney functions were also negative as judged by emission enzyme activities, BUN and creatinine in the serum.

Key words: Hematology—Liver function—Kidney function—Occupational exposure—Subjective symptoms—Tetrachloroethylene

INTRODUCTION

Tetrachloroethylene (TETRA, or perchloroethylene) has been used in industries primarily as a degreaser, especially for dry cleaning of cloth. Despite the fact that this chemical is carcinogenic at least to experimental animals¹⁾ and might have reproductive toxicity,²⁾ cases of environmental pollution has also being reported³⁻⁶⁾ because of its popular use in close contact with general population. The reports on the possible health effects after chronic occupational exposure to

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this widely used solvent are however relatively scarce in literature.⁷⁾ A factory survey was conducted in this study to examine if there is any positive evidence of effects on the central nervous system (CNS) and liver functions among those who were occupationally exposed to this solvent as dry-cleaning workers.

The relation of TETRA vapor exposure with urinary excretion of metabolites has been described in a separate paper.⁸⁾ The possible effects on sister chromatid exchange in peripheral lymphocytes of the workers were also studied.⁹⁾

MATERIALS AND METHODS

Workers studied

The factory survey (Table 1) was conducted in the second half of a working week, although this consideration for the maximum internal exposure¹⁰⁾ may not be necessary because TETRA has a long biological half-time of over one hundred hours.¹¹⁾ In total, 56 TETRA-exposed workers were examined, who had been serving in 3 dry-dcleaning workshops for several years (Table 1). Because TETRA exposure intensity was almost the same in the 3 dry-cleaning workshops, 56 workers (29 men and 27 women) as a whole were pooled to make up a TETRA-exposed group. The nonexposed control workers of similar ages (32 men and 37 women; Table 1) were recruited from the same factories but in workshops with no solvent exposure.

Table 1. Age and service duration of the exposed workers and the non-exposed controls

Sex	Exposed			Non-exposed		
	No.	Age	Service	No.	Age	Service
Men	29	33.8 (17-55)	39.3 (2-120)	32	37.9 (22-65)	72.5 (1-436)
Women	27	36.4 (18-51)	33.1 (1-83)	37	31.5 (19-52)	42.8 (1-198)
Total	56	35.1 (17-55)	36.3 (1-120)	69	34.5 (19-65)	56.6 (1-436)

Except for number of subjects (No.), values in the table are arithmetic mean (minimum-maximum) of the ages (in years) and service duration (in months).

Exposure measurements

The time-weighted average exposure intensity was monitored by means of diffusive sampling with carbon cloth KF-1500 (Toyobo Co., Osaka, Japan) as absorbent.^{12,13)}

Subjective symptom survey

The subjective symptom questionnaire set employed was originally designed by Inoue¹⁴⁾ in Japanese, and subsequently modified and translated into both English and Chinese by the present study group.^{15,16)} The survey was conducted in a clinical interview by a doctor, asking all the questions in the set verbally. There are 12 questions in Part 1 (i.e., the symptoms during work), and 57 for men or

59 for women in Part 2 (i.e., those in past 3 month period).

The rate of subjective symptom prevalence is defined as

$$\frac{\text{Number of affirmative answers}}{(\text{Number of subjects}) \times (\text{Number of questions in the Part})}.$$

Clinical examination

The clinical examination included palpation, auscultation, skin observation and tendon reflex examination, with foci on neurology and possible liver damage.

Evaluation of hematology and serum biochemistry

Hematology and serum biochemistry were conducted by conventional methods under strict quality control. In evaluating the results, log-normal distribution was assumed for enzymic parameters taking the clinically established normal range as a $4 \times \text{GSD}$ (geometric standard deviation) range, whereas normal distribution was considered for non-enzymic ones taking the normal range as $4 \times \text{ASD}$ (arithmetic standard deviation) range. Thus the lower and upper limits of the borderline range (i.e., the line between the borderline and abnormal values) were set at $\text{GM}/(\text{GSD})^3$ and $\text{GM} \times (\text{GSD})^3$ respectively for the formers, and at $\text{AM} - 4\text{ASD}$ and $\text{AM} + 4\text{ASD}$ respectively for the latters (except for WBC counts), where GM and AM are geometric and arithmetic means. The values thus set (see Tables 6 and 7 for examples) agree well with the evaluation in clinical practice. In the case of WBC counts, 3000 cells/mm³ was selected as the lower borderline limit based on the clinical experience. When ASAT and ALAT, or ALP and LAP were evaluated in pair, the case was classified as *normal* when both enzyme activities (i.e., ASAT and ALAT, for example) stayed in normal ranges, and as *abnormal* when one of the two parameters was in the borderline or abnormal range and the other was in the abnormal range. Other cases were classified as *borderline*.

Statistical analysis

The difference in prevalence between the groups were examined by chi-square test.

RESULTS

Characteristics of the exposed and the controls, and the exposure

The age and service duration of the exposed and non-exposed subjects are summarized in Table 1. Ages were comparable between two sexes and also between the exposed and the non-exposed. Service duration was also essentially the same between the two sexes. Although the mean service duration was longer in the exposed than in the non-exposed, no further consideration was made for the possible difference because of wide ranges in the distributions. The time-weighted average intensity of exposure was such that the concentration was close

to 100 ppm in a few cases, but mostly much lower than that, so that the GM was about 20 ppm in both sexes and therefore in the combination of the two sexes (Table 2).

Increase in subjective symptom prevalence after TETRA exposure

Subjective symptom prevalence (for definition, see MATERIALS AND METHODS) was calculated for the comparison between the TETRA-exposed workers and the controls. It was found that there was an increase ($p < 0.001$) in the rate both in Part 1 and Part 2 of the questionnaires among the exposed regardless of sexes (and therefore the two sexes combined) as compared with the rates among the corresponding controls (Table 3). Further break-down of the exposed group into 3 dose (i.e., < 10 , 10–20, and > 20 ppm) subgroups of a comparable size (5 to 12 men or women, or 11–23 subjects of either sex) and comparison of the rates, however, failed to detect any note-worthy dose-response relationship in Part 1 symptoms (Table 3). In Part 2 symptoms, there was an increase in the 10–20 ppm subgroup as well as in the over 20 ppm subgroup in some cases, but the rates in the over 20 ppm subgroup were not significantly higher than the rates in the 10–20 ppm subgroup.

To identify the symptoms with a significant increase after exposure, the prevalence of each symptom in Part 1 and 2 was compared between the exposed and the non-exposed controls. Symptoms with a significant increase are listed in Table 4 (those during work, i.e., Part 1) and Table 5 (those in past 3 month period, i.e., Part 2), respectively. The Part 1 symptoms thus listed included several CNS-related symptoms such as dizziness, floating sensation, drunken feeling and heavy feeling in head among the exposed group. Headache also showed an increase but only with bare significance. Nasal irritation and sore throat may reflect the local effects of TETRA. The analyses of Part 2 symptoms (Table 4) revealed that some complaints such as heavy feeling in head and drunken feeling are essentially reproducible when asked about its presence in past 3 months period. In addition, some long-term effects such as forgetfulness, rough skin and frequent cough are also complained. Loss in hearing capacity (as a subjective judgement with no objective measurement) might be associated with

Table 2. Exposure to TETRA in three workshops

Workshop	TETRA (ppm)								
	Men			Women			Total		
	No.	GM	Min. –Max.	No.	GM	Min. –Max.	No.	GM	Min. –Max.
1	11	23.4	7.1–92.8	10	21.7	7.7–75.9	21	22.6	7.1–92.8
2	9	27.3	11.7–60.7	12	15.5	4.5–51.5	21	19.8	4.5–60.7
3	9	12.5	3.8–51.7	5	25.1	10.7–94.4	14	16.0	3.8–94.4
Total	29	21.2	3.8–92.8	27	19.6	4.5–94.4	56	19.9	3.8–94.4

Except for number of subjects (No.), values in the table are geometric mean (minimum-maximum) of the concentrations.

Table 3. Comparison of subjective symptom prevalence between the exposed workers and the non-exposed controls

Subjective symptom	Sex	Non-exposed			Exposed			Rate by TETRA exposure (ppm) ^c		
		No.	Aff. ^a	Rate ^b	No.	Aff.	Rate	< 10	10-20	> 20
Part 1	Men	32	19	0.049	29	72	0.207***	5 (0.200)	12 (0.236)	12 (0.181)
	Women	37	26	0.059	27	56	0.173***	6 (0.083)	10 (0.242)**	11 (0.159)
	Total	69	45	0.054	56	128	0.190***	11 (0.136)	22 (0.239)*†	23 (0.170)
Part 2	Men	32	85	0.047	29	227	0.137***	5 (0.119)	12 (0.133)	12 (0.145)
	Women	37	212	0.097	27	210	0.132***	6 (0.051)	10 (0.181)***†	11 (0.139)***
	Total	69	297	0.074	56	437	0.135***	11 (0.081)	22 (0.155)***	23 (0.142)***

The asterisks show that the difference in the prevalence from the control group or from the < 10 ppm-exposed subgroup is statistically significant (***, ** and * for $p < 0.001$, 0.01 and 0.05, respectively). The daggers show that the difference between the 10-20 ppm subgroup and the > 20 ppm subgroup is significant († for $p < 0.05$).

^a Number of affirmative answers.

^b The rate of subjective symptom prevalence is defined as

$$\frac{\text{Number of affirmative answers}}{(\text{Number of subjects}) \times (\text{Number of questions in the Part})}.$$

There are 12 questions in Part 1, and 57 for men (59 in women) in Part 2.

^c Classified by intensity of exposure to TETRA (ppm). The values are the number of subjects and the rate of subjective symptom prevalence parentheses.

rather noisy working environments.

Serum biochemistry, hematology, and clinical signs

Serum biochemistry results (Table 6) showed that there was no exposure-related increase in the prevalence of borderline or abnormal cases in ASAT/ALAT, γ -GTP, ALP/LAP nor total bilirubin, suggesting that the exposure to TETRA did not result in liver function disturbances. Such was also the case for kidney functions as examined by BUN and creatinine levels.

Hematological changes were also negative as examined in terms of RBC counts, hemoglobin concentration, hematocrit value and WBC counts. The results of hemoglobin concentration and WBC counts analyses are summarized in Table 7 as examples in hematology studies. Clinical examinations including auscultation, abdominal palpation and tendon reflex examination were also not informative; examples are shown in Table 8.

DISCUSSION

The present study on possible neurotoxicity, hematotoxicity, hepato-renal toxicity and local irritation effects of TETRA in chronically exposed workers showed that symptoms related to the CNS effects and local effects on mucous membrane and skin are increased in the workers exposed to TETRA. The CNS-related symptoms during work (i.e., Part 1 symptoms) included dizziness, floating sensation and drunken feeling, and possibly headache also (Table 4). Similar symptoms as well as forgetfulness, rough skin and frequent cough were complained off

Table 4. Prevalence of subjective symptoms during work: Comparison of the exposed workers with the non-exposed controls

Symptom ^a	Exposed	Non-exposed
	No. (%)	No. (%)
3. Nasal irritation	16 (28.6)**	5 (7.2)
4. Unusual smell	11 (19.6)***	0 (0.0)
5. Sore throat	11 (19.6)	6 (8.7)
7. Face flashing	5 (8.9)*	0 (0.0)
8. Dizziness	25 (44.6)***	8 (11.6)
9. Floating sensation	13 (23.2)**	4 (5.8)
10. Drunken feeling	10 (17.9)***	0 (0.0)
11. Heavy feeling in head	11 (19.6)***	1 (1.4)
12. Headache	13 (23.2)	8 (11.6)

The number of subjects studied is 56 in the TETRA-exposed group, and 69 in the control group. The asterisks show that the difference in the prevalence from the control group is statistically significant (***, ** and * indicates $p < 0.001$, 0.01 , and 0.05 , respectively). Only symptoms with significant difference in the prevalence are described; sore throat and headache are with bare significance ($0.10 < p < 0.05$) and are shown for references.

^a Part 1 symptoms during work in the questionnaire set.

Table 5. Prevalence of subjective symptoms in recent 3 months: Comparison of the exposed workers with the non-exposed controls

Symptom ^a	Exposed	Non-exposed
	No. (%)	No. (%)
1. Heavy feeling in head	9 (16.1)**	1 (1.4)
11. Drunken feeling	6 (10.7)*	0 (0.0)
13. Forgetfulness	22 (39.3)**	10 (14.5)
18. Fainting after sudden standing up	20 (35.7)**	10 (14.5)
23. Dullness in extremities	15 (26.8)*	8 (11.6)
24. Poor appetite	15 (26.8)**	4 (5.8)
32. Changes in perspiration pattern	10 (17.9)**	1 (1.4)
38. Loss in hearing capacity	11 (19.6)***	1 (1.4)
43. Joint pain	8 (14.3)**	0 (0.0)
50. Rough skin	8 (14.3)**	0 (0.0)
52. Frequent cough	8 (14.3)*	2 (2.9)
59. Frequent flatus	12 (21.4)***	1 (1.4)

The asterisks show that the difference in the prevalence from the control group is statistically significant (***, ** and * indicates $p < 0.001$, 0.01, and 0.05, respectively).

^a Part 2 symptoms in the post 3 months; only those with significant difference are shown.

Table 6. Abnormal liver and kidney function prevalence: Comparison between the exposed workers and the non-exposed controls

Serum biochemistry item	[EC No.]	Unit	Normal range	Upper border line	Exposed	Non-exposed
					Abn./Bor./Nor. ^a	Abn./Bor./Nor.
ASAT	[2. 6. 1. 1.]	KU	8-23	29.9		
ALAT	[2. 6. 1. 2.]	KU	3-20	32.1	2/2/52	1/3/61
γ -GTP	[2. 3. 2. 1.]	IU/l	2-39	62.5	0/1/55	0/0/65
ALP	[3. 1. 3. 1.]	KAU	2.6-10.0	14.0		
LAR	[3. 4. 1. 1.]	GRU	100-170	194.1	0/8/48	0/6/59
Total bilirubin		mg/100 ml	0.3-1.1	1.5	1/1/54	1/4/60
BUN		mg/100 ml	9-20	25.5	0/2/54	0/7/58
Creatinine		mg/100 ml	0.6-1.2	1.5	0/0/56	0/1/64

The number of subjects examined is 56 (29 men and 27 women) in the exposed group and 65 (30 men and 35 women) in the control group. The difference from the number shown in Table 1 is due to inavailability of blood samples. There was no ($p > 0.10$) significant difference in the prevalence between the exposed and the controls.

^a Number of cases with an abnormal value/borderline value/normal value in the item studied. For definition of abnormal and borderline values, see MATERIALS AND METHODS section. ASAT and ALAT, and ALP and LAP were evaluated in pair. For details of evaluation procedure, see Materials and Methods.

Table 7. Abnormal hematology prevalence: Comparison between the exposed workers and the non-exposed controls

Hematology item	Unit	Sex	Normal range	Lower border line	Exposed	Non-exposed
					Abn./Bor./Nor. ^a	Abn./Bor./Nor.
Hemoglobin concentration	g/100 ml	Men	13, 7-17, 4	11, 9	0/5/51	1/ 7/57
		Women	11, 3-14, 5	9, 5		
WBC counts	x10 ³ /mm ³	Men	4, 1-6, 1	3, 0	0/1/55	0/1/65
		Women	3, 9-6, 3	3, 0		

The number of subjects examined is 56 (29 men and 27 women) in the exposed group and 65 (30 men and 35 women) in the non-exposed control group. The difference from the number shown in Table 1 is due to inavailability of blood samples. There was no significant ($p > 0.10$) difference in the prevalence between the exposed workers and the non-exposed controls.

^a Number of cases with an abnormal value/ borderline value/ normal value in the item studied. For definition of abnormal and borderline values, and for details of evaluation procedure, see MATERIALS AND METHODS.

Table 8. Clinical signs: Comparison between the exposed workers and the non-exposed controls

Symptom ^a	Exposed		Non-exposed	
	NO. ^a	(%)	No.	(%)
Abnormal ankle jerk reflex	2	(3, 6)	6	(8, 7)
Liver enlargement	0	(0, 0)	2	(2, 9)
Tenderness of liver	0	(0, 0)	2	(2, 9)
Petechial hemorrhage of skin	1	(1, 8)	0	(0, 0)
Heart murmur	2	(3, 6)	2	(2, 9)

The number of subjects examined is 56 (29 men and 27 women) in the exposed group, and 69 (32 men and 37 women) in the non-exposed control group. There was no significant ($p > 0.10$) difference in the prevalence between the exposed and non-exposed groups.

^a Number of cases with an abnormal sign in the item studied.

the work in past 3 month period (Table 5). The CNS-depressing effects of this chlorinated solvent after acute intensive exposure has been well documented.¹⁷⁻¹⁹⁾

The observation is in a general agreement with the findings in the previous studies from this study group.^{15, 16, 20, 21)} For example, dizziness and headache were among the most common symptoms in those exposed to benzene or toluene,¹⁵⁾ and the symptoms very similar to the present findings were common among the workers exposed to toluene.^{20, 21)} Of particular interest is the fact that the workers exposed to trichloroethylene, a TETRA congener, had almost identical complaints.¹⁶⁾ In addition to such CNS effects, rough skin and frequent cough are typical local effects of TETRA (Table 5). In literature, Chmielewski *et al.*²²⁾ also described in their study on TETRA-exposed Polish workers that drawsiness, fatigue, headache and dizziness are among the most frequently complained CNS-related symptoms and that coughing and irritation in throat are also common among the workers of 1 to 10-year service history.

Whereas the present negative findings in hematology is in a good agreement

with the general opinion that TETRA at occupational dose is not toxic to the hematopoietic system,²³⁾ possible hepato-renal toxicity of this compound may deserve discussion. The early observation by Franke and Eggeling²⁴⁾ and the recent findings by Gluszcowa²⁵⁾ are in a close agreement with each other in that the effects of the occupational exposure to TETRA in dry-cleaning facilities to elevate ASAT and ALAT in serum is very minute, if present. In the cases of accidental high-dose exposure to TETRA, most authors observed no²⁶⁾ or minimal and transient effect^{27,28)} on the liver. In a statistical review of cases, McCarthy and Jones²⁹⁾ also reported that the involvement of the liver is rather rare in the industrial gassing cases. In contrast, Meckler and Phelps³⁰⁾ described a case of woman who was heavily exposed to TETRA during cleaning and maintenance work of dry-cleaning machines and subsequently showed liver enlargement, jaundice and remarkable increases in serum ASAT. The liver biopsy, made immediately before discharge from the hospital in 2 months, disclosed significant changes in the histology. The present negative observation on liver function (Table 6) is in the support of the observation by Franke and Eggeling²⁴⁾ and Gluszcowa.²⁵⁾ Effect on kidney in the present study was also negative as judged by BUN and creatinine in serum (Table 6). No serious attention was paid on kidney function changes in the above-cited accidental cases,^{26,28,30)} except that Saland²⁷⁾ observed one case each of transient microscopic hematuria and albuminuria among 9 firemen after heavy TETRA exposure during the fight against fire in a cellar. Although subtle changes might occur in kidney function after occupational TETRA exposure,³¹⁾ it appears likely that the kidney involvement may not be very severe in occupational circumstances.

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