

Kinetics of Tetrachloroethylene in Volunteers; Influence of Exposure Concentration and Work Load

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Summary. Six male volunteers were exposed for 4 h to 72 ppm tetrachloroethylene (PERC) at rest, to 144 ppm PERC at rest, and to 142 ppm PERC at rest with work load (2 times 30 min., 100 W). Minute volume and concentrations in exhaled air were measured to estimate the uptake. Concentrations of PERC and trichloroacetic acid (TCA) were determined in blood. Exhaled air was analysed for PERC; urine for TCA.

The uptake/min decreased in the course of the exposure to 60 % of the initial uptake. The total uptake was influenced more by (lean) body mass than by respiratory minute volume or adipose tissue. During work load the uptake and minute volume increased to 3 fold the value at rest. In the post exposure period the quotient of the bloodconcentrations and exhaled air concentrations of PERC remained nearly constant at 23. Following exposure about 80–100 % of the uptake was excreted unchanged by the lungs, whereas till 70 h after exposure the amount of TCA excreted in urine represented about 1 % of the uptake.

Key words: Tetrachloroethylene – Trichloroacetic acid – Toxicokinetics – Work load

The kinetics of tetrachloroethylene (perchloroethylene, PERC) in humans has been studied only to a limited extent. It has been established that PERC is mainly eliminated through the respiratory tract. After exposure of volunteers to PERC, Hake et al. (1976), Fernandez et al. (1976) and Ogata et al. (1971) measured trace amounts of trichloroacetic acid (TCA) in urine, whereas Ikeda et al. (1972 a, 1972 b) also detected trichloroethanol (TCE) in urine of workers exposed to PERC.

Considerably less is even known about uptake during exposure and the influence of work load on uptake and metabolism. The purpose of our experiments is to explore quantitatively the absorption, concentrations in blood, and excretion in volunteers exposed to PERC.

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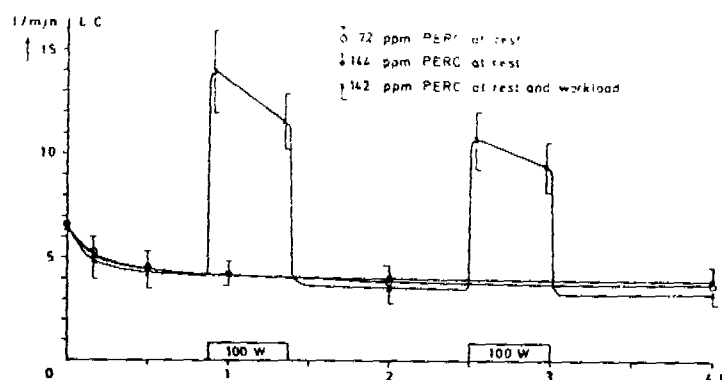


Fig. 1. Lung clearance (LC) during exposure to tetrachloroethylene (PERC) for 4 h. Each point represents the mean $\pm$ s. d. of 6 subjects

Table 1. Estimated uptake of 6 subjects exposed for 4 h to 72 and 144 ppm PERC at rest and to 142 ppm PERC at rest combined with 2 x 1/2 h 100 W work load, the coefficient of variation in each condition (c. v.) and anthropometric data of the subjects

Subject	uptake in mg			body mass kg	lean body mass kg	minute volume at rest l/min
	72 ppm at rest	144 ppm at rest	142 ppm at rest + work load			
A	370	670	1060	70	62	7.6
B	490	940	1500	82	71	11.6
C	530	1000	1400	82	71	10.0
D	500	1210	1510	86	74	11.3
E	390	880	1320	67	61	12.3
F	450	970	1120	77	61	8.8
c. v.	14 %	19 %	14 %			

Material and Methods

Six healthy male volunteers (aged 27–34 years) were exposed to 72 ± 2 ppm PERC ($488 \mu\text{g/l}$) at rest, to 144 ± 7 ppm at rest and to 142 ± 6 ppm at rest combined with 2 x 1/2 h 100 W work load on a bicycle ergometer. Duration of exposure was 4 h. Between the exposure sessions of the same subject was an interval of two weeks.

The design of these experiments was the same as in the methylchloroform exposure study. For detailed information see Monster et al. (1978).

Tetrachloroethylene was obtained from BDH Chemicals Ltd. product no. 30693.

For analysis of blood and exhaled air the gaschromatographic technique described by Monster and Boersma (1975) for trichloroethylene, TCE and TCA was applied: in 2 ml blood PERC and TCA were determined simultaneously by means of head space technique; PERC in exhaled air was analysed under the same gaschromatographic conditions. TCA in urine was measured according to Ogata et al. (1974)

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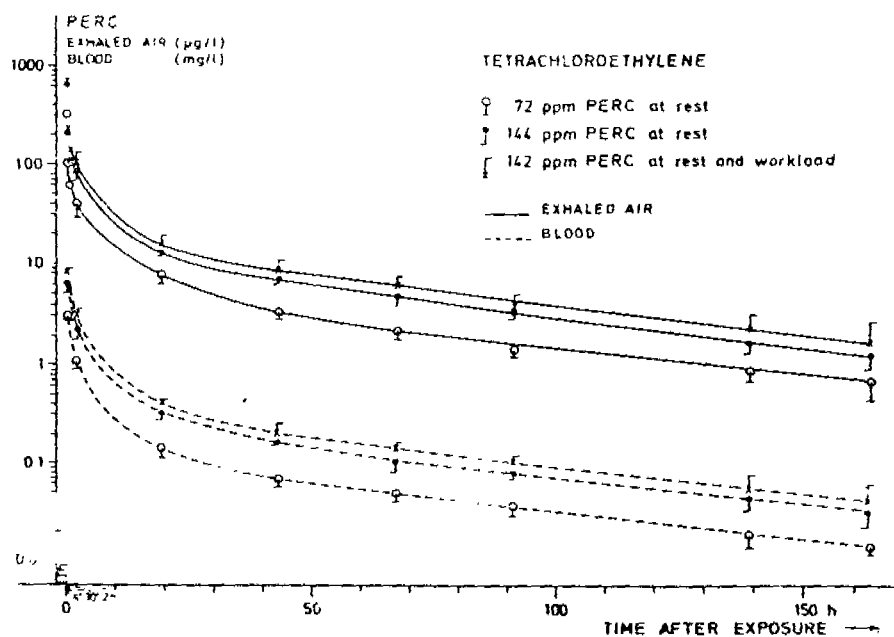


Fig. 2. Tetrachloroethylene (PERC) in blood and exhaled air following exposure to PERC for 4 h. Each point represents the geometric mean $\pm$ s. d. of 6 subjects

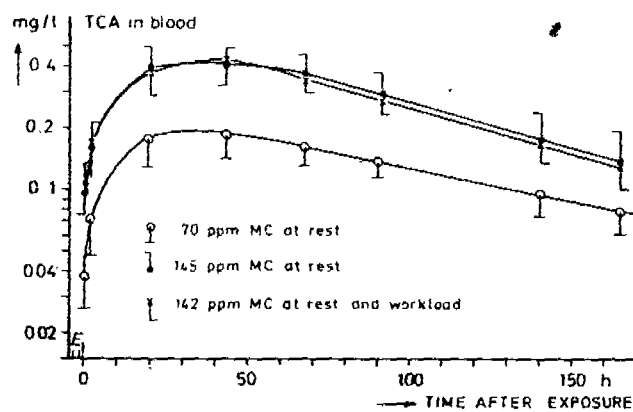


Fig. 3. Trichloroacetic acid (TCA) in blood following exposure to tetrachloroethylene (PERC) for 4 h. Each point represents the geometric mean $\pm$ s. d. of 6 subjects

Results

Uptake

The uptake/min and lung clearance were calculated as in the methylchloroform exposure study (Monster et al., 1979).

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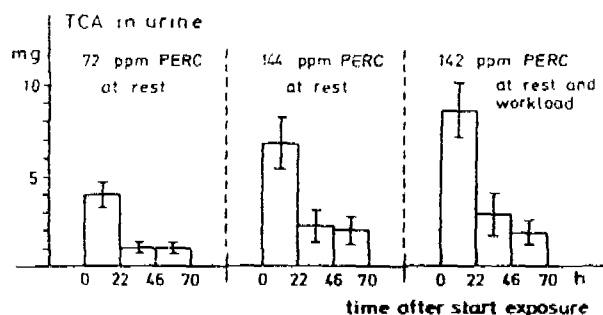


Fig. 4. Urinary excretion of trichloroacetic acid following exposure to tetrachloroethylene (PERC) for 4 h. Each point represents the mean $\pm$ s. d. of 6 subjects.

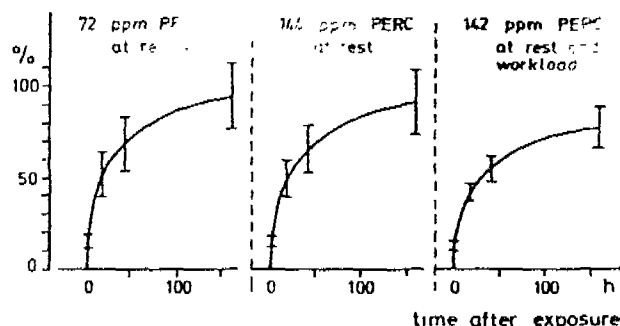


Fig. 5. Cumulative excretion of tetrachloroethylene (PERC) by the lung as percentage of the uptake following exposure to tetrachloroethylene for 4 h. Each point represents the mean $\pm$ s. d. of 6 subjects.

During exposure to PERC at rest lung clearance decreased slowly from 6.7 l/min initially to 5 l/min at 10 min, to 4.2 l/min at 1 h and to 3.8 l/min at 4 h. The mean minute volume of the subjects at rest was 10.3 l/min (range 7.6–12.3). The minute volume seems to be rather high. This is caused by the dead space of the gasmask (0.15 l). With the usual frequency of respiratory ventilation of 14/min and a total dead space of 0.3 l (0.15 l physiological dead space and 0.15 l of the gasmask) an alveolar retention can be calculated of about 60% at the end of exposure. During work load (100 W) minute volume increased threefold to 29.8 l/min (range 25–35) and lung clearance also increased threefold (range 2.5–3.5) the values at rest. The mean lung clearance during rest and work load is presented in Fig. 1. During work load the retention decreased. This resulted in decrease of lung clearance during work load. During the second work load the mean retention was about 20% (range 10–30) lower than during the first work load; this must be due to a higher saturation of tissues.

For each subject the total uptake in each condition was estimated (Table 1). The individual total uptake was increased 40% (range 15–60) by the extra 2 x 1/2 h 100 W

Kinetics of trichloroethylene (TCE) work load. The mean concentration was higher than at 72 ppm PERC.

PERC in Blood and Urine

The mean PERC concentrations in blood and urine are shown in Fig. 3. The concentration in blood was higher at 30 min and 2 h after exposure than at 5 min after the end of exposure.

In the post-exposure period the air concentration was 72 ppm PERC.

The slope of the concentration-time curve at 100 h after exposure was about 55 h⁻¹.

Trichloroacetic Acid (TCA) in Urine

The concentration of TCA in urine after exposure was higher than before exposure. From the concentration-time curve a half-life of about 70 h after exposure was calculated for the subjects.

Recovery

The amounts of TCA excreted in urine and the concentration of PERC in blood and urine were measured until 2, 18, 42, and 70 h after exposure (Fig. 5). At 16 h after exposure TCA excreted in urine was 14 mg PERC and represented 10% of the uptake.

Discussion

Uptake

The uptake of PERC during the first and last exposure was 100 W.

The course of the concentration-time curve (1976), assuming a half-life of 70 h.

The mean concentration of PERC in blood (Table 1). To subjects, the mean concentration of PERC in blood was 1.5 mg/l.

work load. The individual uptake at 144 ppm at rest was 2.1 (range 1.9- 2.4) times higher than at 72 ppm at rest.

PERC in Blood and Exhaled Air

The mean PERC concentrations in blood and exhaled air after each exposure condition are shown in Fig. 2. The concentration in blood at 2 h after exposure was about 37 % of the concentration just before the end of exposure. The concentration in exhaled air at 30 min and 2 h after exposure was 60 % and 44 % respectively of the concentration 5 min after the end of exposure.

In the post exposure period the quotient of the blood concentration and exhaled air concentration remained nearly constant at 23 ± 4 .

The slope of the concentration curve of PERC in blood and exhaled air at 20, 50 and 100 h after exposure corresponded with a half life of PERC of 12-16 h, 30-40 h and about 55 h respectively.

Trichloroacetic Acid in Blood and Urine

The concentration of TCA in blood continued to increase until 20 h after the end of exposure. From about 60 h after exposure the concentration decreased exponentially with a half life of 75-80 h (Fig. 3). Figure 4 shows the amounts of TCA excreted until 70 h after start of exposure. A base level of 0.6 mg TCA/day, measured in urine of the subjects before exposure, was subtracted from the mean.

Recovery

The amounts of PERC excreted in exhaled air after exposure were estimated from the concentration curves in exhaled air after exposure and multiplied by the mean individual minute volume as measured during exposure at rest. The amounts of PERC excreted until 2, 18, 42 and 162 h after exposure were expressed as percentage of the uptake (Fig. 5). At 162 h the recovery represented 80-100 % of the uptake. The amounts of TCA excreted within 70 h after the start of exposure were recalculated to amounts PERC and represented about 1 % of the uptake.

Discussion

Uptake

The uptake/min decreased in the course of the exposure due to a decrease in retention. During the first exposure hour at rest the uptake was about 25 % higher than during the last exposure hour.

The course of the lung clearance at rest in our experiments agree with the course of the concentration in alveolar air during exposure, as obtained by Fernandez et al. (1976), assuming an alveolar minute volume of about 6 l/min.

The mean coefficient of inter-individual variation in uptake at rest was 17 % (Table 1). To determine the relation between uptake and physical characteristics of subjects, the individual uptake was divided by mean minute volume at rest, body weight, lean body mass and amounts adipose tissue. The mean coefficients of inter-

This decrease was significant (1963). In the condition where the use of PERC and TCA were avoided, as the uptake was 40% higher in recovery after work loss.

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2. stimulation of an u
3. excretion of PERC

We do not have reason to

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This decrease was significant ($p < 0.05$, a significance test for linear ranks, Page 1963). In the condition with work load the mean concentration and amounts excreted of PERC and TCA were about 20% higher than in the condition with only rest, whereas the uptake was 40% higher. The following hypothetical possibilities for the decrease in recovery after work load may be considered:

1. overestimation of uptake during work load
2. stimulation of an unknown metabolic pathway during work load
3. excretion of PERC by another route during work load

We do not have reason to prefer one of these possibilities.

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