*Original article*

Scand J Work Environ Health 1984;10(5):317-320

doi:10.5271/sjweh.2323

**Skin absorption as a source of error in biological monitoring.**

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Print ISSN: 0355-3140 Electronic ISSN: 1795-990X Copyright (c) Scandinavian Journal of Work, Environment & Health

*Scand J Work Environ Health* 10 (1984) 317—320

# Skin absorption as a source of error in biological monitoring

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AITIO A, PEKARI K, JÄRVISALO J. Skin absorption as a source of error in biological monitoring. *Scand J Work Environ Health* 10 (1984) 317—320. Concentrations of toluene, tetrachloroethylene, and 1,1,1-trichloroethane were determined in blood collected from both forearms of subjects after one of their hands was soaked for 5 min in the corresponding solvent or in a thinner containing toluene, as a simulation of the washing of hands with solvent after work. The concentrations of toluene, tetrachloroethylene, and 1,1,1-trichloroethane on the soaked side were high, maximally 5.4, 9.0, and 4.0 μmol/l, respectively, and 20-, 130-, and 35-fold, respectively, compared to the contralateral side. Intraindividual differences were very marked, and dramatic changes were detected within a short period of time. It was not until after 3 h with toluene and 5 h with the chlorinated solvents that the difference between the two arms vanished. It is concluded that analyses of solvents in blood specimens drawn during or immediately after the workday may lead to markedly erroneous estimations of exposure.

*Key terms:* organic solvents, tetrachloroethylene, toluene, 1,1,1-trichloroethane.

Absorption of a variety of different organic chemicals through intact skin is well documented (6, 7, 10, 14), and it is generally regarded as one of the reasons why one should use biological monitoring of exposure to chemicals. Concentrations of chemicals in the air need not bear any correlation to the amounts absorbed through the skin. However, it is seldom realized that skin absorption may also represent a source of error for biological monitoring (2). The organic chemical concentrations in blood collected from the forearm may not represent those in other parts of the body, but only the local concentrations at the venipuncture site. A prerequisite for this kind of error is that concentrations of the chemical itself — not a metabolite (the majority of which are primarily generated in the liver) — is measured in the blood. In our laboratory, we perform biological monitoring of toluene, tetrachloroethylene, and 1,1,1-trichloroethane routinely by analyzing the solvent concentrations of blood and have therefore studied the possible error ensuing from skin absorption.

## Subjects, materials and methods

The studies were performed on two (in case of toluene, three) volunteers. In order to simulate the widely practiced habit of painters who wash their hands after the workday with a solvent, we decided to use a short exposure time of 5 min. We soaked one hand, emerged to the wrist, in a solvent [tetrachloroethylene (pa) or 1,1,1-trichloroethane (pa) or toluene (pa) or Dicco® thinner containing 65 % toluene]. In order to minimize exposure by inhalation, the vessel containing the solvent was kept in a fume hood closed with a plastic cover with a small hole for the arm. After the exposure, the hand was washed with soap and water. Blood specimens were drawn through indwelling cannulas (one volunteer, chlorinated solvents) or repeated venipunctures (all other experiments).

Blood was collected in glass vials containing heparin, carefully mixed, and either analyzed immediately (specimens collected during the first 2 h) or stored in a refrigerator and analyzed on the following day. Under these conditions of storage no loss of the solvents could be detected.

1,1,1-Trichloroethane and tetrachloroethylene concentrations in the blood were determined with capillary gas chromatography using electron capture detection after hexane extraction, as has been described earlier (11, 12); toluene was analyzed with headspace gas chromatography (5) using *o*-xylene as the internal standard.

## Results and discussion

Skin absorption of toluene was studied with the use of pure (pa) toluene and a thinner (Dicco) containing 65 % toluene, 30 % butylacetate, and 5 % butyl alcohol (figure 1). In both cases the difference between the toluene concentrations in the blood drawn from the two arms was marked, the maximal differences being 7-, 13- and 20-fold for the three persons studied. The highest concentrations of toluene reached were 2.0, 2.6, and 5.4 μmol/l. In experi-

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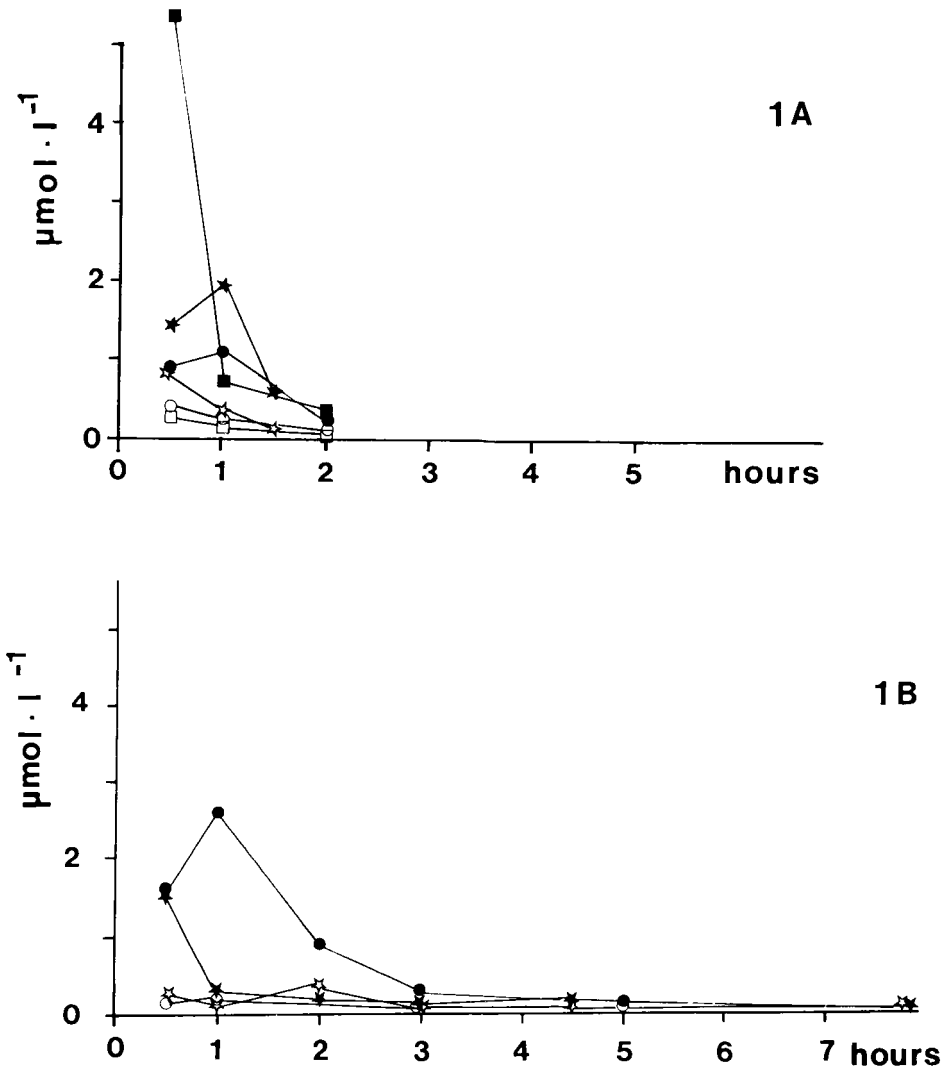


**Figure 1.** Toluene concentrations in blood drawn from volunteers who exposed one hand to toluene (A) and Dicco® thinner containing 65 % toluene (B). (closed symbols: ipsilateral arm, open symbols: contralateral arm)

mental inhalation exposure to 100 ppm of toluene at rest, the concentration of toluene in blood was 4.3—4.9 µmol/l (1, 14); during light work a concentration of 14.6 µmol/l was detected (1). In line with the latter finding, a blood concentration of toluene of 12.5 µmol/l, may be extrapolated from the data of Apostoli et al (4) for work during exposure to 100 ppm; the corresponding value for the figures of Angerer & Behling (3) is 19.0 µmol/l. After 3 h the difference between the two arms disappeared; thus the practical solution to toluene exposure estimation from blood toluene concentrations is the collection of specimens in the morning before exposure.

The highest blood concentrations of tetrachloroethylene found in blood drawn from the ipsilateral arm after exposure of the hand to the liquid solvent were 9 and 3.5 µmol/l in the two volunteers; those for 1,1,1-trichloroethane were 4.0 and 0.7 µmol/l. These values are in line with the findings of Stewart & Dodd (14) that there is a marked interindividual variation in the skin absorption of 1,1,1-trichloroethane. With these chlorinated solvents the error that skin absorption may cause in the estimation of exposure was even more marked than in the case of toluene; the maximal difference between the arms was 17- and 130-fold for tetrachloroethylene and 11- and 35-fold for 1,1,1-trichloroethane.

The data on concentrations of chlorinated solvents in blood in inhalation exposure is scanty. Monster (9) reported that continuous exposure (8 h/d, 5 d/week) to 50 ppm of 1,1,1-trichloroethane caused a blood concentration (5—15 min after exposure) of 6.7 µmol/l, while Savolainen and co-workers (13) detected a concentration of 16.5 µmol/l of 1,1,1-trichloroethane in

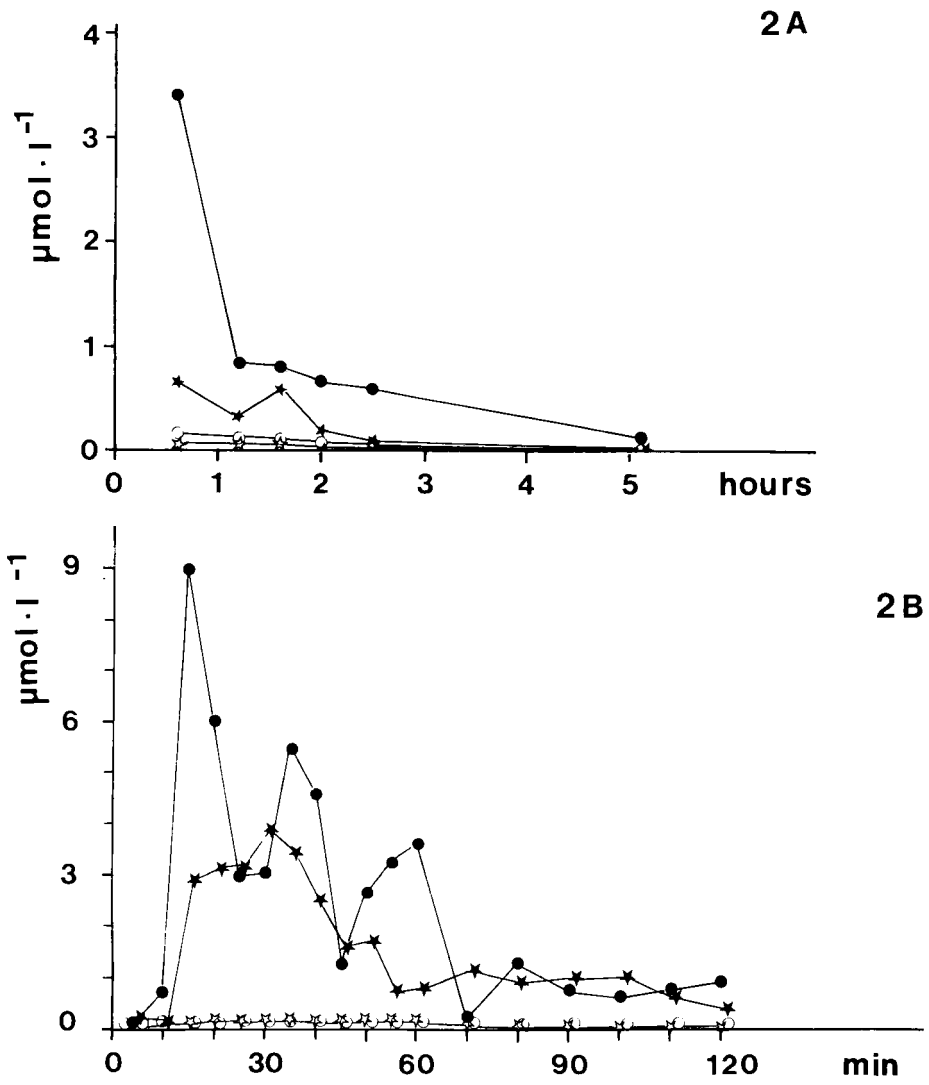


**Figure 2.** Blood concentrations of 1,1,1-trichloroethane (★, ☆) and tetrachloroethylene (●, ○) in two volunteers (A & B) who exposed one hand to the corresponding solvent. (closed symbols: ipsilateral arm, open symbols: contralateral arm)

blood after 4 h of exposure to 200 ppm at rest. Continuous exposure (8 h/d, 5 d/week) to 50 ppm of tetrachloroethylene was calculated to result in a blood concentration of 14 μmol/l 5—15 min after the exposure (8).

The concentrations of chlorinated solvents, especially that of tetrachloroethylene, showed marked fluctuations within a short time interval (figure 2). This phenomenon can probably be explained by physical activity of the arms. Movement causes a flush-out of venous blood with a concomitant decrease in the solvent concentration, whereas immobility results in stagnation of venous blood and a build-up of the solvent concentration. These rapid changes add to the uncertainty of exposure estimation. The differences between the chlorinated solvent concentrations in blood from different arms were the most marked immediately after the exposure, but they did not vanish until several hours later (figure 2A).

In conclusion, toluene, tetrachloroethylene, and 1,1,1-trichloroethylene, under conditions that probably exist in the workplace, are absorbed through the skin to such an extent that biological monitoring of exposure, based on solvent concentrations in blood specimens drawn during or up to 5 h after the exposure, may be remarkably erroneous. Correct estimations of exposure may be obtained from specimens drawn in the morning on the day after the exposure.

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Received for publication: 27 September 1984