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Markers of Occupational Exposure to Pentachlorophenol

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Pentachlorophenol (PCP) is a versatile biocide used for industrial and home applications. Industrial uses include leather tanning, wood manufacture and treatment, paper and cellulose industry, and paint production. Occupational exposure to PCP occurs during its manufacture and uses (World Health Organisation 1987). General population may be exposed to PCP: in fact, PCP can be released into the environment from treated materials such as wood, leather or unproperly disposed wastes; several studies have documented an increase of PCP levels in blood and urine in occupants of log homes (C.D.C., Centres for Disease Control 1980; Maroni 1987).

The technical-grade PCP formulations often contain other chlorophenols, furans and chlorinated dioxins as contaminants. Chronic exposure to PCP formulations may give rise to adverse effects, such as chloracne, altered porphyrin metabolism, liver toxicity, induction of microsomal enzymes and disorders of the immune system (World Health Organisation 1987). Some of these toxic effects have been attributed to the contaminants rather than to PCP itself (World Health Organisation 1987).

PCP is easily absorbed through the lungs, skin and gastrointestinal tract. The elimination kinetics of PCP in human beings are a controversial subject. Following a single oral administration of PCP sodium salt, the compound is excreted almost completely (86% of the dose) within 7 days, mainly in the urine, as phenol and its glucuronide conjugate (74% and 12% respectively of the original dose); the half lives of unmodified and conjugated PCP are 33.1 $\pm$ 5.4 and 12.7 $\pm$ 5.4 hrs respectively (Braun 1979). Following a single oral administration of PCP dissolved in ethanol a urine elimination half life of 17 days was found (Uhl, 1986). In case of long-term occupational exposure, toxicokinetics of PCP seem characterised by a prolonged urinary excretion (Casarett, 1969), however the elimination pattern of the compound is not clear (Kalman, 1983). These data make difficult to define protocols for biological monitoring of occupational exposure to PCP. ACGIH suggests to measure the compound in urine collected prior to the work shift of the last day of the week or in plasma collected at the end of the work shift (ACGIH, 1992).

This study was carried out to validate a protocol for biological monitoring of exposure to PCP.

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MATERIALS AND METHODS

The investigation was carried out at a wood factory located in Northern Italy, where PCP dissolved in solvents was used to preserve wood surfaces by brush application; three groups of subjects were selected, as follows:
- a group of 11 male-workers (age 22-56 yrs) directly exposed to PCP because they were engaged in the wood treatments (Group 1);
- a group of 8 male-workers (age 26-49 yrs) only indirectly exposed to PCP (Group 2). These subjects handled the wood after the treatment;
- five adult males (age 25-45 yrs) not exposed to PCP were selected as control group (Group 3).

During their activity the workers of group 1 and 2 wore gloves (rubber or leather made) and protective clothing.

Sampling was performed the fourth working day of the week. Workers of the groups 1 and 2 were investigated for total (free and conjugated) PCP concentration in plasma and urine and PCP hand skin contamination. Blood and urine samples were collected from the workers of the groups 1 and 2 at 8.00 a.m. (beginning of the work) and 5.00 p.m. (end of the work shift) of the same day. Plasma and urine samples were kept frozen at -20°C until analysis. The hands of the workers were washed with a 0.1 M K_2CO_3 solution at the end of the work shift. Washings were collected and kept frozen until analysis. PCP was also measured in samples of leather and rubber gloves. Only one blood and urine sample was collected from subjects of group 3 at 8.00 a.m.

PCP extraction from hand washing liquid was performed according to Gebefugi (1978) and from plasma, urine and gloves samples according to Needham (1981). Aliquots of 1 μL of n-hexane extracts were analysed by isothermal gas chromatography at 165°C, using a HRGC chromatograph (Carlo Erba) equipped with an electron capture detector and a 30 m capillary column packed with SE-30 phase (0.25 μm thickness, J&W). Helium was used as carrier gas at a flow rate of 1.8 mL/min. The make up gas was a mixture of argon and methane (v/v 9:1), flow rate of 33 mL/min. Detection limit was 1 μg/L.

Plasma and urine PCP values were expressed as total (free and conjugated) PCP in μg/L, while values of hand washings were expressed as $\mu g/dm^2$. Urine values were also evaluated as ratio to creatinine concentration. PCP concentration in gloves samples were expressed in ppm.

Data were processed by means of the SPSS package; logarithmic conversion of values was performed where the data were not normally distributed. Groups were compared with T-test or Mann-Withney test; correlations between different variables were done with the Pearson coefficient. A p value less than or equal to 0.05 was chosen as significance level.

RESULTS AND DISCUSSION

Figure 1 shows gas chromatograms of extracts of urine collected from a worker directly exposed to PCP and a control subject.
Table 1 shows the results of the biological monitoring.

Gloves were impregnated with PCP (leather gloves 13,045 ppm; rubber gloves 3,523 ppm) and did not prevent the exposure. Table 2 shows the

amount of PCP, detected at the end of the work shift, on the skin of the hands of groups 1 and 2. Adequate protection can be achieved by means of nitril rubber or latex/neoprene gloves (Silkowsky, 1984).

Table 1. PCP concentrations in the plasma and urine samples collected before and after the workshift. (Plasma values as μg/L; urine values as μg/g creatinine; N.D. = Not determined)

	Group 1 Directly exposed (n = 11)		**Group 2** Indirectly exposed (n = 8)		**Group 3** Reference group (n = 5)	
	Mean	Range	Mean	Range	Mean	Range
Plasma PCP at 8.00	742	137 - 1694	124	41 - 272	< 1	< 1
Plasma PCP at 17.00	703	171 - 1554	129	41 - 274	N.D.	N.D.
Urine PCP at 8.00	175	36 - 346	28	16 - 71	3.2	1.4 - 8.1
Urine PCP at 17.00	106	20 - 298	18.6	4.3 - 42	N.D.	N.D.

Table 2 - PCP concentration on the skin of the hands of the two groups of workers. (Values as $\mu g/dm^2$)

	Group 1 Directly exposed (n = 11)	**Group 2** Indirectly exposed (n = 8)
PCP concentration	627 ± 475	23 ± 14

Correlations between plasma and urine PCP concentrations, respectively determined in morning and evening samples, are depicted in figures 2 and 3. PCP concentrations in body fluids of occupationally exposed groups were within the limits proposed by ACGIH (1992); plasma and urine PCP concentrations were significantly higher in group 1 than in group 2. Within each group of workers, PCP concentrations in morning urine samples were significantly higher than in evening samples: this observation could be explained by considering the half-life of the compound (Braun 1979).
Evaluation of urine PCP values as ratio to creatinine concentration showed results in the same ratio as with the original concentrations as μg/L. PCP plasma concentrations were significantly higher in group 1 when compared to group 2. PCP concentrations in morning and evening samples of each group were not significantly different. As PCP is distributed to tissues such as liver and kidney (World Health Organisation 1987), the plasma concentration is in equilibrium with that of these tissues.

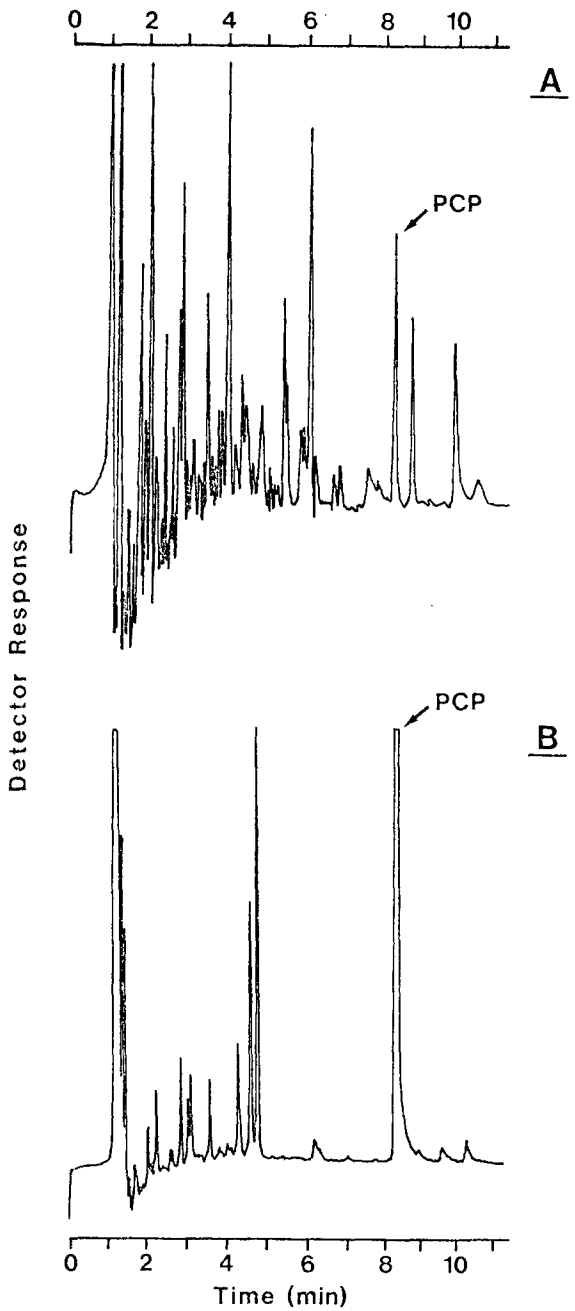

Figure 1. Gaschromatograms of urine extracts. A) Control subject; B) PCP directly exposed worker. The detector response is plotted against time. The detector response is in arbitrary units. The peaks corresponding to PCP are indicated by arrows.

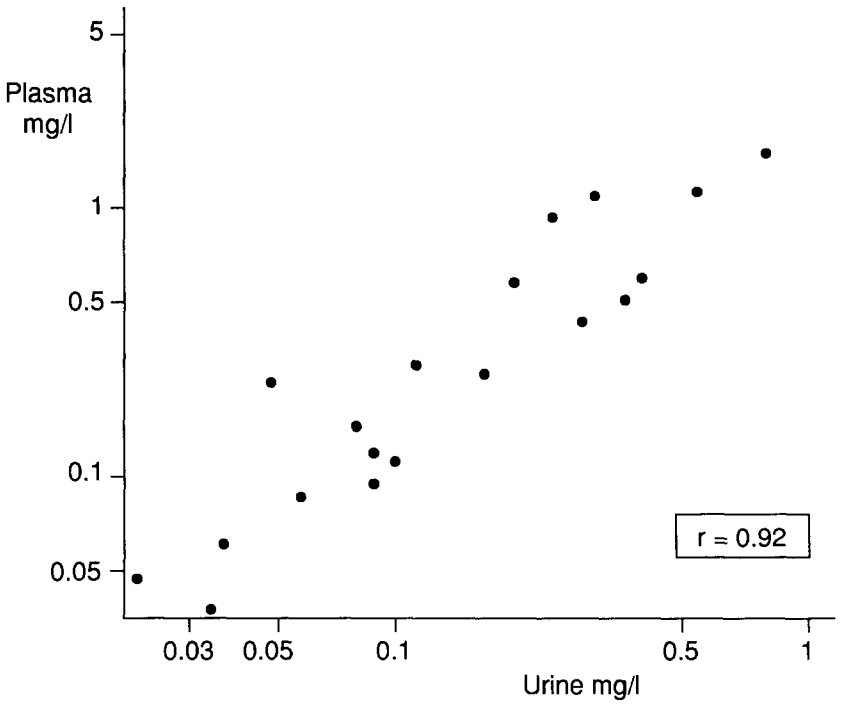

Figure 2. Correlation between plasma and urine PCP concentrations in morning samples.

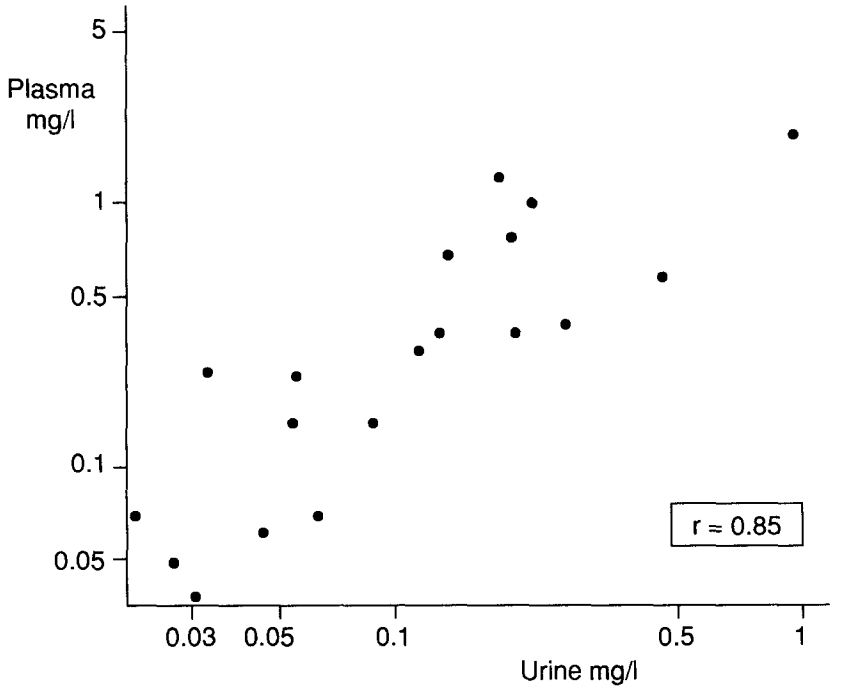

Figure 3. Correlation between plasma and urine PCP concentrations in evening samples.

Plasma PCP concentrations in the control group were below the detection limit and the urine values ranged from 1.4 to 8.1 μg/g of creatinine (4 to 14 μg/L). Plasma and urine values of control subjects were always significantly lower than the corresponding values of the groups 1 and 2. These findings are in agreement with other investigations ((World Health Organisation 1987; Cline RE 1989) and suggest that the general population of Italy is exposed to low levels of PCP, in the same way as the general population of other comparable countries (World Health Organisation 1987).

High levels of correlation were observed between dermal PCP values and urine concentration ($r=0.92$) and between dermal PCP values and plasma concentration ($r=0.84$). These findings indicate the relevance of dermal absorption in occupational exposure to PCP. High levels of correlation were also observed between plasma and urine values in morning samples ($r=0.92$) and in afternoon samples ($r=0.85$) (Figures 2 and 3). Thus, both plasma and urine PCP concentrations are suitable biological indicators of exposure to the compound.

Our findings suggest that biological monitoring may be performed, after few days of exposure, by the determination of urine or plasma PCP concentration. Urine should be collected before the work shift, according to ACGIH suggestions, while plasma can be sampled at any time of the day; because of the greater practicality of sampling and analytical procedures, we suggest the use of urine total PCP concentration as biomarker of exposure to PCP.

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