A Survey of Pentachlorophenol Content in Human Urine

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Introduction

Pentachlorophenol (PCP), its salts and derivatives, are widely used for such diverse applications as a contact herbicide and defoliant, as a control for termites, powder post beetles and other wood boring insects, for the control of microbial attack in the manufacture of cellulosic products, adhesives, and paints, and as a fermentation inhibitor for non-edible materials. The spectrum and mode of usage of this material provide ample opportunity for human exposure as a direct occupational occurrence, as an incidental contact or from residues in products treated with PCP. Domestic animals and wildlife are also potentially subject to exposure. An extensive review of PCP which discusses its uses, properties, methods of analysis and toxicological implications is in press (1).

This research was supported by the Pesticides Program, National Communicable Disease Center, Bureau of Disease Prevention and Environmental Control, Public Health Service, Department of Health, Education, and Welfare under Contract No. PH-86-65-79. Views expressed are those of the investigators and do not necessarily reflect official views of the Public Health Service.

Bulletin of Environmental Contamination & Toxicology,
Vol. 2, No. 6, 1967, published by Springer-Verlag New York Inc.

PCP has become of special interest to the Community Studies on Pesticides in Hawaii because of its extensive local use, particularly in the treatment of wood products, and because of its apparent ubiquitous appearance in the enviroment. Usage of PCP in the Oahu community appears to be extensive as judged from questionnaire data and levels of PCP found in urine samples. Occupational use and probable exposure appear to be quite high among commercial pest control operators.

The present paper is confined to some observed relationships between reported exposures to PCP and urinary excretion patterns. A continued, selective survey of PCP usage, direct and incidental exposure, and measurement of PCP residues in the general environment as well as the human system should provide a more complete correlative study.

Methods

Urinary levels of PCP were measured and related questionnaire data were collected on 541 people (mostly males) residing in Honolulu or adjacent rural areas of the island of Oahu. Of these people, 130 were pest control operators employed by 30 different commercial firms. Another 117 were State or City and County pest control operators, office workers, or from randomly selected households. An additional 294 people were drawn from a large cohort under study by the Honolulu Heart Program as an "intramural study of the National Heart Institute"; the latter group represents a wide diversity of employment and socio-economic levels. A further categorization of all groups, according to occupational exposure to PCP, was made for interpretive purposes. Although this categorization was based in part on inadequate and sometimes conflicting questionnaire data, it is a reasonable approximation

of exposure.

One to five samples of urine were collected from each individual, at sampling intervals ranging from 1 to 115 days. All samples were analyzed for PCP by the method described by Bevenue et al. (2). Essentially this entailed acidification with concentrated H_2SO_4, extraction with petroleum ether, reaction with diazomethane, and measurement on a gas chromatograph employing a column containing 5% QF-1 on Gas Chrom Q (100/200 mesh), electron capture detection, and preset inlet, column and detector temperatures.

Results

Table I summarizes all groups by number of individuals sampled, total number of urine samples analyzed from each group, and the high, low, and mean levels of PCP in parts per billion (ppb) found in the urine. Despite variability in the levels of PCP, definite differences occurred among the groups of people sampled. The PCP levels in people classified as occupationally exposed (Group A and part of Group C, Table I) were usually much higher than those in people with no apparent occupational exposure. Mean urinary PCP values for the 30 different employer firms (Group A) varied widely, suggesting different degrees of occupational exposure. An analysis of variance (Table II) indicated a highly significant difference among these firms. The error term in this analysis was based both upon variation among individuals within employment

Table I.

Ranges and means for urine concentrations of PCP, in 541 people classified according to occupational and non-occupational exposure to PCP.

Group classification		No. of people	Total analyses	PCP in urine (ppb) Low	High	Mean
Group A. Occupationally exposed pest control operators in 30 different commercial firms.						
Firm No.	1	19	20	3	234	64
	2	15	33	10	35700	1885
	3	12	42	40	16600	2203
	4	12	12	40	1160	286
	5	11	17	34	6440	1497
	6	5	7	17	280	108
	7	5	5	52	7200	1733
	8	5	5	29	188	98
	9	4	9	16	3420	451
	10	4	4	10	2750	698
	11	3	6	34	4200	821
	12	3	5	780	27490	12990
	13	3	5	110	1380	419
	14	3	3	96	200	135
	15	3	3	21	310	127
	16	3	3	12	100	64
	17	2	7	600	6240	3429
	18	2	4	2400	15400	7160
	19	2	2	610	11700	6155
	20	2	2	262	6826	3544
	21	2	2	31	436	234
	22	2	2	70	75	73
	23	1	3	2576	12000	6192
	24	1	3	2000	3800	3009
	25	1	1			1600
	26	1	1			1040
	27	1	1			528
	28	1	1			264
	29	1	1			120
	30	1	1			28
	Overall	130	210	3	35700	1802

(continued)

Table I (Continued)

Group classification	No. of people	Total analyses	PCP in urine (ppb) Low	High	Mean
Group B. Non-occupationally exposed individuals representing miscellaneous groups, as indicated.					
Households	32	32	7	65	31
Mosquito Control*	23	114	5	444	33
Office Workers	18	19	10	43	21
Orchid Growers	12	43	ND**	112	26
Rodent Control*	10	32	3	34	14
Hawaii Housing Authority	10	14	8	1840	186
State Dept. of Agriculture	5	5	36	164	78
City & County Honolulu	4	4	21	372	169
Division of Forestry	3	3	22	150	77
Overall	117	267	ND	1840	40
Group C. Mixed exposure; individuals from a Honolulu Heart Program cohort.					
1. Occupationally exposed	121	121	3	38642	465
2. Non-occupationally exposed	173	173	3	570	44
Overall	294	294	3	38642	217
Overall for Groups A, B, and C	541	771	ND	38642	587

* Separate groups of the State Dept. of Health.
** ND = not detected.

Table II.

Analysis of variance (one way classification) of urinary levels of PCP in individuals from 30 different pest control firms.

Source of variation	Degrees of freedom	Mean square	F test
Among employment firms	29	37,003,120	2.51*
Error	180	14,755,828	

* $p < 0.01$.

firms and among sampling periods for individuals, where repeat determinations for PCP were made. A further analysis of variance on data from selected people (with analyses of triplicate urine samples collected at the same

three sampling periods) indicated significant variability only among individuals and not among sampling periods even though these were spread over an interval of 10 months. A logarithmic conversion and re-analysis of these data diminished the difference among individuals to borderline significance.

Considerable variation in urinary content of PCP also occurred among people classified as non-occupationally exposed (Group B and part of Group C, Table I), although levels in general were relatively low. A statistical analysis of the data from some of the sub-groups revealed significant variation either among individuals or among different, replicate sampling periods, or both. Illustrative data, showing significant variability among mean values for individuals and sampling periods, are shown in Table III.

Table III.

Variation in urinary levels of pentachlorophenol among individuals of an orchid grower cohort, for four different sampling periods arranged in decreasing order of mean values.

Individuals	Sampling period				Mean	HSD*
	April (1)	May (2)	March (3)	February (4)		
	ppb					
1	44	112	41	27	56.0	
2	69	48	23	19	39.8	
3	40	57	18	20	33.8	
4	52	28	28	11	29.8	
5	37	36	18	9	25.0	
6	40	25	6	13	21.0	
7	26	20	9	24	19.8	
8	38	9	11	3	15.3	
9	29	17	5	3	13.5	
Mean	41.7	39.1	17.7	14.3	28.2	
HSD*						

*Honestly significant difference between any two means (3). Any two means not underscored or joined by a parallel bar are significantly different at the 95% confidence level.

Questionnaire and analytical data were examined for a meaningful relationship of PCP levels with age. It was anticipated that such a relationship, if found, might in turn be related to the length of time workers had been handling pesticides. A histographic illustration of this examination is presented in Figure 1. Although there are areas of uncertainty in such a presentation, it is clear that there is a progressively intense exposure during the early phases of the work experience and a reduced exposure probability for those with many years of experience. Not unexpectedly, there is a general qualitative similarity of years of pesticide experience and age of the workers, particularly at the ends of the distribution. It should be pointed out that there is a greater likelihood of error in establishing the previous experience for those in the intermediate range of the distributions.

Other questionnaire data such as smoking, eating and drinking habits were less readily subject to similar analysis. No clear trends have been noted at this stage of the study. Because of the inherently less quantitative nature of such information, detailed follow-up inquiries and an expansion of the numbers of people involved are considered necessary to determine any possible correlations with these parameters.

Sequential urinary levels were examined partly to identify exposure probabilities among workers and partly to identify individual variation in excretion patterns. There were some instances in which samples were taken 24 to 48 hours apart. Taking each pair of samples (7 pairs) one of which was known to have been immediately preceded by an exposure, a mean daily rate of decrement in urinary PCP was calculated. Repeat samples taken over longer periods of time were similarly grouped and

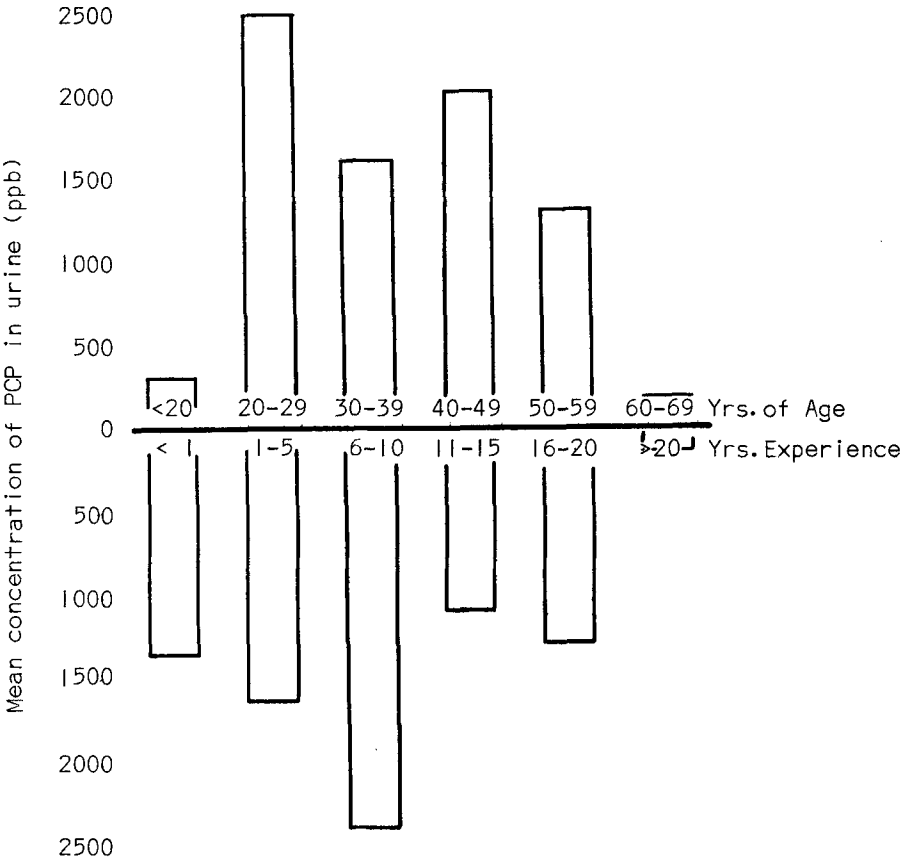

Figure 1. Relation of age and years of experience to PCP in urine.

evaluated. A summary of the data obtained is presented in Table IV. It is clear that urinary PCP decreased more rapidly at shorter intervals after presumed exposure than at longer intervals of time.

Table IV.

Summary of mean decrements in urinary pentachlorophenol.

Time interval (days)	No. of values	Mean decrement (%/day) ± S.D.
1-2	7	34.7 ± 4.3
3-9	No data available	
10-23	9	3.3 ± 1.9
24-63	No data available	
64-115	17	0.85 ± 0.23

These excretion data can be represented in another way, as in Figure 2, by plotting the log of the rate of urinary decrease of PCP against the time interval between which the decrement occurred. The values presented have been calculated from all of the available instances to date in which there has been a decrement in urinary PCP from one sampling period to another. Although a smooth curve has been drawn, two single straight lines can also be drawn because the data can as readily be represented as a combination of two exponential functions. This suggests the possibility of two different excretion rates.

In a further examination of the data, there seemed to be a partially independent relation between the amount in the initial sample and the rate of decrease of PCP levels in the urine. This relationship is shown in Figure 3. Despite a few aberrant points, it appears that the rate of excretion is higher when the body burden is sufficiently

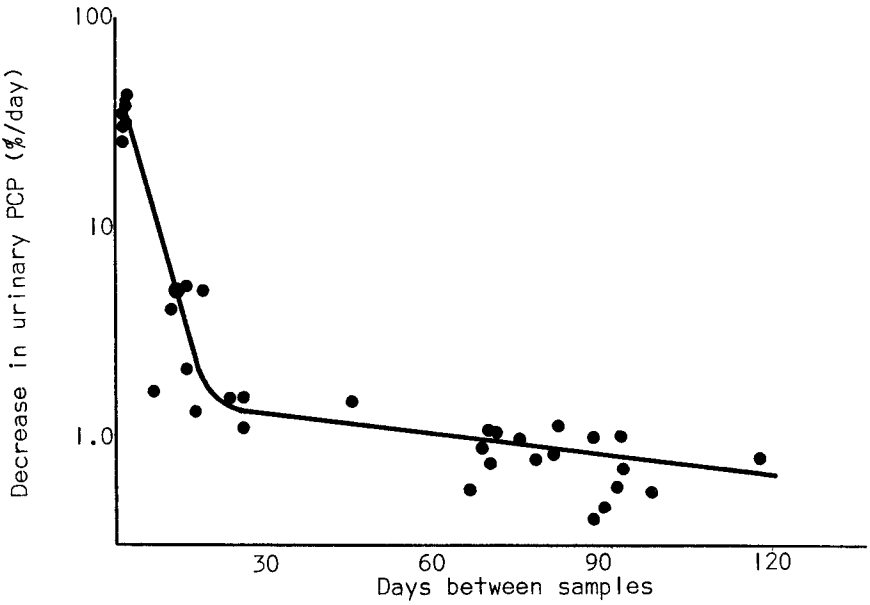

Figure 2. Change of urinary PCP with time.

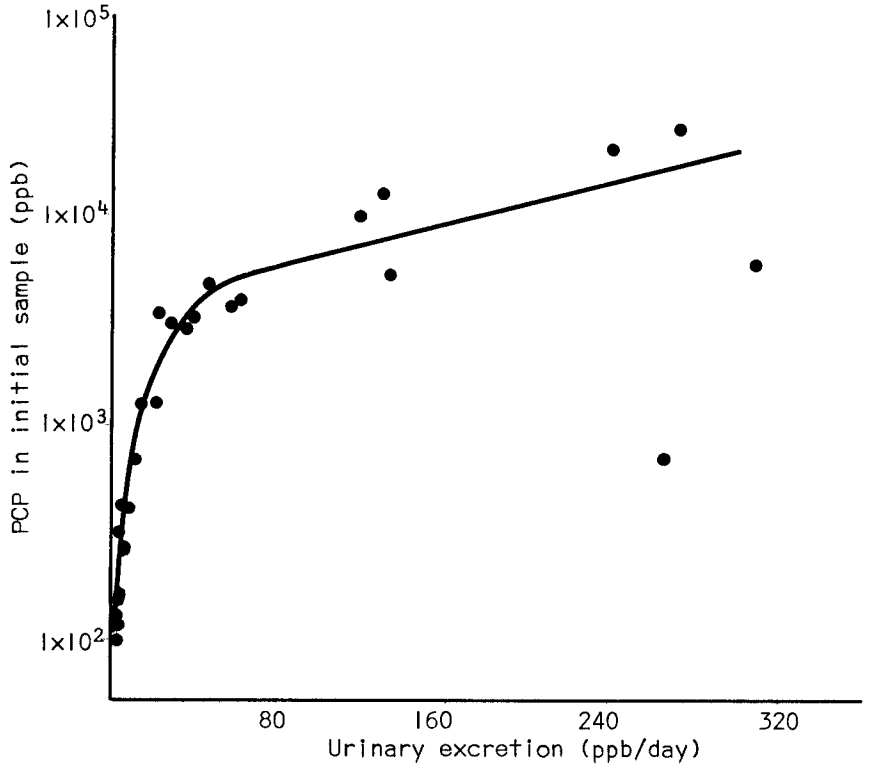

Figure 3. Relation of excretion rate with concentration.

high to result in an excretion level greater than about three to five thousand ppb in the "initial" sample. The curve presented in Figure 3 also implies the possibility of more than one excretion rate.

Discussion

Variable levels of PCP are detectable in a cross-section of the local population. As might be expected, those involved in commercial operations (Table I, Groups A and C-1) have relatively high PCP levels in the urine reflecting a higher level of expsoure than other groups. It was less predictable that those not occupationally exposed would have a measurable content of PCP in urine (Groups B and C-2). Clearly, there is a source of exposure by the general public to PCP. Additional investigation is required to assess all sources of the exposure.

It might be suggested that, in many samples, a low analytical baseline was measured rather than urinary PCP, particularly in groups showing low levels of PCP. Although reagents and other analytical factors contribute slightly to the measurement of PCP, it has been demonstrated that the level of detectability of PCP is about 3 ppb (4). Even if one assumes a substantially larger analytical baseline (e. g., 10 ppb), those individuals not occupationally exposed (Groups B and C-2, Table I) show a reasonably well established mean of 40-44 ppb. This suggests that there is, indeed a low level of PCP in the population apart from any analytical contribution or occupational exposure. An obvious extension of this conclusion is that there is a low level exposure in a population not using the material directly. Although such a conclusion is consistent with the wide use to which PCP has been put locally, the source(s) of exposure are still conjectural.

The relationship of age and pesticide experience to PCP exposure as suggested by urinary PCP content is, in retrospect at least, not surprising. At early periods of a working experience (1-5 years) one might suspect the increasing exposure to be the result of one or more possible causes. Inexperience in handling the materials or with use of protective gear might be one causal feature but one would then expect to find higher levels in the "beginners" (less than 1 year). On the other hand, a laxity in the proper use of protective gear arising from a few years of experience might be another reason for elevated levels in the intermediate years. A more clearly related point is that those with the shorter intervals of experience (1-10 years) are most likely to be engaged in tasks more directly connected with preparation, mixing and application of the chemical. Conversely, those who have been employed for longer times (15-20 years) are more likely to be in supervisory positions and be remote from exposure potential.

The variation of mean PCP levels at different sample times is of some interest although the explanation is obscure. The patterns of variation in sampling time among the groups was random in nature so that a trend of analytical error or variance is not a reasonable explanation. Those with a history of occupational exposure (Group A, Table I) showed no such pattern of variability with sampling time. Therefore, one would expect to find a seasonal or time-dependent variable in the "non-users" either in their employment or in the home. There are not yet sufficient data to point to any particular causal relation.

Little is known about the kinetics of human excretion of PCP. Animal studies have indicated that urinary excretion is relatively rapid.

Deichmann et al. (5) have reported that rats excrete about 13 percent of an intraperitoneal dose in 24 hours. For rabbits, following oral administration, urinary excretion varied from about 37 to 70 percent of the dose in 24 hours (5). The values found and calculated in this study cannot be translated directly and quantitatively into terms of body burden or dose; nor can it be assumed that human excretion is the same as that found for animals. It is, however, a reasonable assumption that the amount or rate of excretion reflects the dose or level of exposure.

If the amount of PCP in the urine is a reflection of the body content, then there appears to be a more rapid excretion when the exposure is such as to have elevated urine level above several thousand ppb (Figure 3). Further, at lower urine levels (possibly reflecting lower body content) the rate of excretion is changed. Thus, one might postulate the existence of at least two rate-limiting excretion processes. Similarly, in Figure 2, the data as presented are consistent with a dual rate of excretion dependent on time. If one could assume that the time between samples was the interval following a single exposure, the conclusion that there are two rates of excretion might be justified. However, there is no way to eliminate the possibility that intermittent exposures had occurred in most of the individuals represented by Figure 2. Such exposures could explain at least part of the apparent change of rate, and might even be the entire explanation. If such a relationship is confirmed, one might be able to assess exposure by the degree of deviation from an established excretion curve.

In at least a few instances, multiple values from individuals were obtained over relatively short intervals of time (up to 11 days). No data were obtained, however, for individuals at short intervals of time beyond the area of inflection of the curve (about 20 days). Data of this kind would be necessary to support the suspicion of a "threshold" above which there is a higher excretion rate and below which there is a slower rate.

Additional information is needed to confirm the excretory patterns. To test the possibility of a dual rate, one should relate the urinary output with known dosage conditions with a minimal opportunity for extraneous exposure. Within the limitations of the current program, studies are planned to provide more definitive information about this question.

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