Metabolites of Pyrethroid Insecticides in Urine Specimens: Current Exposure in an Urban Population in Germany

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Pyrethroids are important insecticides used in agriculture, forestry, horticulture, and in the home. In humans, they are rapidly metabolized and renally eliminated. In numerous studies, pyrethroid metabolites have been detected in urine after occupational exposure to insecticides. In this study, we used a new, reliable, easy, and sensitive analytical method to assess the internal pyrethroid exposure of an urban population without exposure to pyrethoids at home or at work (children and adults). A total of 1,177 persons took part in this investigation, including 331 children under 6 years of age and 247 children between 6 and 12 years of age. None of them reported exposure to pyrethroids at home or at work. Accordingly, the levels of permethrin found in household dust from their homes were lower than expected (median < limit of detection; 95th percentile, 4.8 mg/kg; maximum value, 19 mg/kg). Urine specimens were analyzed for *cis*-3-(2,2-dibromo-vinyl)-2,2-dimethylcyclopropanecarboxylic acid (Br_2CA), *cis*- and *trans*-3-(2,2-dichlorovinyl)-2,2-dimethylcyclopropane-carboxylic acid (*cis*-Cl_2CA and *trans*-Cl_2CA), and 4-fluoro-3-phenoxybenzoic acid (F-PBA) using a gas chromatographic method with mass-selective detection. The limit of detection for pyrethroid metabolites was between 0.1 and 0.2 µg/L. *trans*-Cl_2CA was detected in 65% of the urine specimens tested, *cis*-Cl_2CA was detected in 30%, and Br_2CA and F-PBA were found in 19% and 16%, respectively, of the urine specimens. The urinary metabolite levels in children did not differ from those in adults, and there was no correlation between the levels of metabolites and indoor exposure to permethrin in household dust. Moreover, no seasonal correlations could be found. The 95th percentile levels in urine specimens were as follows: Br_2CA, 0.30 µg/L; *cis*-Cl_2CA, 0.51 µg/L; *trans*-Cl_2CA, 1.43 µg/L; F-PBA, 0.27 µg/L. Background exposure to pyrethroids was found in the general population; it seems to be caused by the uptake of pyrethroids with the diet. This hypothesis needs to be tested in duplicate diet studies combined with biomonitoring. As long as representative data are lacking, however, the rounded 95th percentile values obtained in our study may be used as reference values for pyrethroid metabolites in urine samples from the population in Germany; 95th percentile values for children and adults are as follows: Br_2CA, 0.3 µg/L; *cis*-Cl_2CA, 0.5 µg/L; *trans*-Cl_2CA, 1.5 µg/L; and F-PBA, 0.3 µg/L. *Key words*: biomonitoring, *cis*-3-(2,2-dibromovinyl)-2,2-dimethylcyclopropanecarboxylic acid, *cis*- and *trans*-3-(2,2-dichlorovinyl)-2,2-dimethylcyclopropanecarboxylic acid, 4-fluoro-3-phenoxy-benzoic acid, permethrin, pyrethroids, urinary metabolites. *Environ Health Perspect* 109:213–217 (2001). [Online 14 February 2001] *http://ehpnet1.niehs.nih.gov/docs/2001/109p213-217heudorf/abstract.html*

Pesticides are widely used throughout the world in agriculture to protect crops and in public health to control diseases transmitted by vectors or intermediate hosts. Up to the 1960s organochlorines such as DDT were used intensively, but due to their accumulation in the environment and in humans their use was prohibited in the 1970s in many industrialized countries. Carbamates, organophosphates, and pyrethroids were subsequently developed and used extensively.

Today, pyrethroids are among the most frequently used pesticides. They are used in agriculture, forestry, horticulture, public health (e.g., hospitals), and homes, as well as for the protection of textiles, such as carpets. Because natural pyrethrins, derivatives of chrysanthemums, are unstable in sunlight, efforts were undertaken to modify the chemical structures of natural pyrethrins to obtain substances with improved physical and chemical properties and greater biological activity. The pyrethroids commercially available include permethrin, cypermethrin, cyfluthrin, deltamethrin, and fenvalerate.

Exposure to pyrethroids of the general population is thought to occur mainly via residues in the diet. Residue levels in crops grown according to good agricultural practice are generally low. The resulting exposure of the general population is expected to be low, but precise data in the form of total-diet studies are lacking (*1*).

Additional exposure via inhalation or ingestion of contaminated household dust may occur after the indoor application of pesticides. Because of their low volatility, pyrethroids are detected in indoor air only in very small concentrations up to the lower nanogram range, or are not detectable. Therefore, the assessment of indoor exposure is usually carried out by analyzing household dust. In Germany, representative data for pesticide contamination in household dust were obtained in 1985 and 1990–1991. Of the eight different pyrethroids analyzed (cyfluthrin, cyhalothrin, cypermethrin, α-cypermethrin, deltamethrin, empenthrin, δ-phenothrin, and permethrin), only permethrin was detected regularly, whereas the other substances were found only very rarely [< 2% > limit of detection (LOD)]. In 1990–1991 permethrin was detected in 91% of the samples, with a 98th percentile of 30.5 mg/kg and maximum value of 267 mg/kg (*2*). Comparable results were obtained in other epidemiologic studies in Germany (*3*,*4*): permethrin was the main pyrethroid used in the home, and other pyrethroids were hardly ever detected.

In humans, pyrethroids are rapidly metabolized by esterases, mainly in the liver. The detoxified metabolites are renally eliminated, with the elimination half time ($t_{1/2}$) for the metabolites being about 6 hr (*5*). In recent years, methods for determining pyrethroid metabolites in urine have been developed that are sensitive enough for biomonitoring.

In this paper we report data on the internal pyrethroid exposure of an urban population in Germany not known to have been exposed to pyrethroids. All the persons included in the study lived on the former U.S. Forces housing estates in Frankfurt am Main, where polycyclic aromatic hydrocarbons and some pesticides, such as DDT and chlorpyrifos, were detected in 1997. In all flats and houses, household dust was analyzed for these substances, and redevelopment measures were performed when elevated levels were detected.

Household dust from about 300 homes was also analyzed for different pyrethroids; only permethrin was found, and the mean and maximum levels were well below the levels of the representative data (median < LOD; 95th

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percentile, 4.8 mg/kg; maximum level, 19 mg/kg). The results were in accordance with information from the U.S. Army that chlorpyrifos and pyrethrum were previously used as indoor insecticides, but no other pyrethroids, including permethrin, had been used.

The residents were offered the opportunity of participating in biomonitoring tests to determine their internal exposure to the substances of interest (i.e., polycyclic aromatic hydrocarbons, DDT, and chlorpyrifos) (*6*,*7*). Although we found no evidence of indoor exposure to pyrethroids, we also analyzed pyrethroid metabolites in the urine samples to assess background exposure to these substances.

Methods

Collective. The residents were first offered the opportunity to receive consultation and take part in biomonitoring tests at an information evening organized after a first meeting of the experts, on 5 February 1998 in Frankfurt am Main. In addition, the residents were informed via the mass media and the distribution of leaflets. All residents of the former U.S. housing estates—flats and houses—were invited to take part in the tests, without any preclusion criteria. Most of them attended the consultation meetings between March and August 1998. Only a few people came later, so that by the end of December these special consultation meetings were brought to a close.

A total of 9,548 persons inhabited the former U.S. housing estates at the time of the investigation. Urine samples from 1,177 persons were tested for pyrethroid metabolites; this represents urine specimens from 13% of the total residents of the former American Forces housing estates in Frankfurt. Considered according to age group, 24% of the children younger than 6 years of age, 16.6% of older children and teenagers, and 8% of adults older than 20 years of age were tested for pyrethroid metabolites in urine.

The study population was a self-administered random sample. Though participation in this study was voluntary, there were no hints for selection bias with regard to pyrethroid exposure because these substances were not in the focus of interest of the people.

Biomonitoring. The urine samples were frozen until anaylsis for the following four pyrethroid metabolites: *cis*-3-(2,2-dibromovinyl)-2,2-dimethylcyclopropanecarboxylic acid (Br_2CA), *cis*- and *trans*-3-(2,2-dichlorovinyl)-2,2-dimethylcyclopropanecarboxylic acid (*cis*-Cl_2CA and *trans*-Cl_2CA), and 4-fluoro-3-phenoxybenzoic acid (F-PBA) (Figure 1). Analyses were carried out using a sensitive and selective capillary gas chromatographic procedure with mass-spectrometric detection (GC/MS). Briefly, after hydrolysis using sulfuric acid, the urinary solution was drawn through a C18 column on which the pyrethroid metabolites were enriched. After elution the metabolites were converted to their derivatives using methanol/sulfuric acid. 2-Phenoxybenzoic acid served as an internal standard. The calibration was carried out using pooled urine to which known amounts of pyrethroid metabolites were added and which was processed and analyzed in the same manner as the samples. Curves were linear between 1 and 200 µg/L of each of the metabolites. The between-day imprecision for the determination of the above-mentioned analytes was between 6.2 and 8.7% at a concentration of 10 µg/L urine. The LOD was in the range of 0.1–0.2 µg/L urine. For each of the analytes, two or three fragment ions were scanned (*cis*/*trans*-Cl_2CA M/e: 163, 187, 222; Br_2CA M/e: 231, 253, 312; F-PBA M/e: 215, 246) (*8*). The method has been proven for its analytical reliability from the analytical chemistry working group of the "senatcommission for the investigation of health hazard of chemical compounds in the work area" of the Deutsche Forschungsgemeinschaft (*9*). To ensure the reliability of our data, we regularly and successfully take part in the German external quality assurance system for the analyses of toxic substances in human body fluid. For internal quality assurance, we used urine samples which were spiked with the pyrethroid metabolites to concentrations between 6 and 8 µg/L. The between-day imprecision during this study was between 5 and 7%. Because the LOD for the determination of 3-phenoxybenzoid acid (3-PBA) is higher by a factor of about 5, we did not determine this metabolite in this study. Environmental medicine requires a lower LOD. Moreover, our analytes are more specific for the individual pyrethroids than 3-PBA. We used the SPSS program, version 8 (SPSS GmbH Software, München, Germany) for statistical analysis.

Results

Tables 1 and 2 show the results for Br_2CA, *cis*-Cl_2CA, *trans*-Cl_2CA, and F-PBA in all 1,177 urine samples, listed according to different age groups (Table 1 µg/L; Table 2 µg/g creatinine). The levels of *trans*-Cl_2CA were above the LOD in 65% of the urine samples; *cis*-Cl_2CA was detected in 29% of the urine specimens. The levels of Br_2CA and F-PBA were above the detection limit in 19% and 16% of all urine samples, respectively (Table 3). No significant correlation was found between the levels of pyrethroid metabolites in urine and the age of the persons tested. A significant seasonal variation in the excretion of pyrethroid metabolites in urine was not found either, but in the relatively small group of 38 persons tested between October and December 1998, there was a tendency for the concentrations of *trans*-Cl_2CA in urine to be lower (Table 4). The correlation coefficients for the relationship between the permethrin contamination in household dust and the specific metabolites in the urine samples of the inhabitants were low and insignificant (Spearman rank correlations two-tailed; $p >> 0.5$).

Discussion

All synthetic pyrethroids are rapidly metabolized by hydrolytic cleavage to form their corresponding metabolites, Br_2CA or *cis*-Cl_2CA and *trans*-Cl_2CA. The alcohol moiety is oxidized to F-PBA or 3-PBA. *Cis*- and *trans*-Cl_2CA are the specific metabolites of permethrin, cypermethrin, and cyfluthrin,

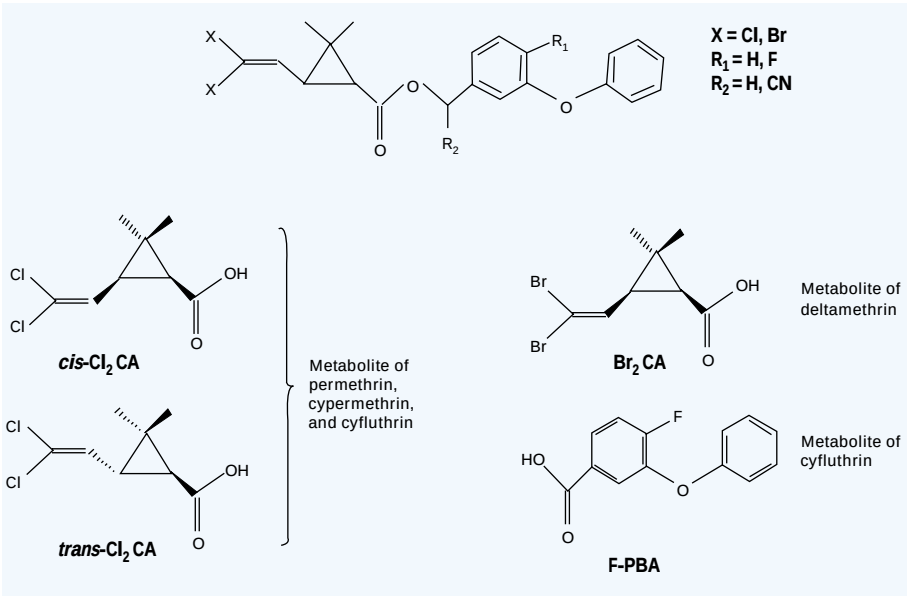

Figure 1. Metabolites of the most important pyrethroids.

whereas deltamethrin is transformed to Br_2CA. Most pyrethroids are metabolized to form 3-PBA, but some fluoro-substituted pyrethroids such as cyfluthrin are transformed to F-PBA. Pyrethroids may produce markedly different metabolite patterns after oral and dermal administration. After dermal administration of cypermethrin, the ratio of *trans*:*cis* cyclopropane acids is approximately 1:1, compared to 2:1 after oral administration (*10*). After inhalation exposure of volunteers to cyfluthrin, the ratio of *trans*:*cis*-cyclopropane was approximately 2:1 (*5*).

Almost 20 years ago, the first study of permethrin metabolites in urine was carried out with samples from occupationally exposed forestry workers in Sweden (*11*). In all but one person the levels of permethrin metabolites were below the LOD of the method (i.e., < 0.5–0.1 mg/L urine). The person subjected to the highest level of exposure (85 $\mu g/m^3$) excreted 0.26 mg permethrin metabolite/L urine the following morning, but in the afternoon the amount excreted was < 0.5 mg/L urine (*11*). In several later studies with field workers and greenhouse workers exposed to permethrin and cypermethrin, the urinary metabolite Cl_2CA was analyzed (*1,11,12*). Br_2CA was found in the urine of workers exposed to deltamethrin by inhalation and dermal contact (*13–16*). In 2 of 10 greenhouse workers exposed to deltamethrin, 3-PBA was detected, with a range of < 2–52 µg/L (*17*). Analyses of the levels of pyrethroids excreted by pest control workers using a method with an improved LOD (0.5–1 µg/L urine) showed the pyrethroid levels in urine samples to be in the range of < 0.5–277 µg/L (*18*). The metabolites were detectable in urine for up to 3.5 days after exposure to cyfluthrin (*19*). Data on occupational exposure are, however, scarce, as are data from the biomonitoring of pyrethroid exposure in the population (i.e., in an environmental setting).

In our environmental, population-based study we used an improved method with an LOD of 0.1–0.2 µg metabolite/L urine. A total of 1,177 urine samples from persons who had stated that they were neither occupationally exposed nor had used pyrethroids in their homes were tested for F-PBA, Br_2CA, and the Cl_2CA-isomers. *trans*-Cl_2CA was detected in > 60% of the urine samples, and *cis*-Cl_2CA was found in about 30%. The *trans*:*cis* ratio was about 2:1. This ratio indicated oral or inhalation exposure, with no evidence of dermal uptake. The other metabolites were detected in < 20% of the urine samples. Although *trans*-Cl_2CA was found in the highest amounts, in some cases Br_2CA and F-PBA were excreted in high concentrations as well. There was no correlation between the excretion of pyrethroid metabolites and age; the levels of pyrethroid metabolites in the urine of adults did not differ from those in children.

Our data may be compared with two other recently published studies. In 1998, Butte et al. (*20*) published data on the levels of Cl_2CA and 3-PBA in 254 urine specimens from healthy adults from Schleswig-Holstein, in the northern part of Germany. Due to a

Table 1. Pyrethroid metabolites in urine samples (µg/L) listed according to age group.

Metabolite/ age (years)	No.	Mean ± SD	Range	Percentile 25th	50th	75th	95th
Br_2CA							
< 6	331	0.08 ± 0.55	< LOD–9.19	< LOD	< LOD	< LOD	0.25
6 to < 12	247	0.09 ± 0.65	< LOD–9.19	< LOD	< LOD	< LOD	0.32
12 to < 20	108	0.14 ± 0.67	< LOD–6.14	< LOD	< LOD	0.10	0.50
≥ 20	483	0.07 ± 0.32	< LOD–4.76	< LOD	< LOD	< LOD	0.29
All (0–65)	1,177	0.08 ± 0.50	< LOD–9.19	< LOD	< LOD	< LOD	0.30
cis-Cl_2CA							
< 6	331	0.06 ± 0.17	< LOD–1.16	< LOD	< LOD	0.10	0.39
6 to < 12	247	0.11 ± 0.29	< LOD–2.67	< LOD	< LOD	0.10	0.53
12 to < 20	108	0.13 ± 0.27	< LOD–1.51	< LOD	< LOD	0.22	0.48
≥ 20	483	0.14 ± 0.57	< LOD–9.76	< LOD	< LOD	0.10	0.65
All (0–65)	1,177	0.11 ± 0.41	< LOD–9.76	< LOD	< LOD	0.10	0.51
trans-Cl_2CA							
< 6	331	0.31 ± 0.50	< LOD–3.40	< LOD	0.21	0.38	1.07
6 to < 12	247	0.41 ± 0.69	< LOD–6.15	< LOD	0.26	0.51	1.27
12 to < 20	108	0.48 ± 0.63	< LOD–3.99	0.10	0.31	0.61	1.52
≥ 20	483	0.47 ± 1.37	< LOD–17.82	< LOD	0.23	0.45	1.67
All (0–65)	1,177	0.41 ± 0.99	< LOD–17.82	< LOD	0.24	0.46	1.43
F-PBA							
< 6	331	0.05 ± 0.15	< LOD–1.04	< LOD	< LOD	< LOD	0.39
6 to < 12	247	0.04 ± 0.14	< LOD–1.35	< LOD	< LOD	< LOD	0.27
12 to < 20	108	0.06 ± 0.19	< LOD–1.73	< LOD	< LOD	< LOD	0.37
≥ 20	483	0.05 ± 0.33	< LOD–5.11	< LOD	< LOD	< LOD	0.10
All (0–65)	1,177	0.05 ± 0.24	< LOD–5.11	< LOD	< LOD	< LOD	0.27
All pyrethroids, sum							
< 6	331	0.51 ± 0.94	< LOD–10.33	< LOD	0.31	0.51	1.85
6 to < 12	247	0.66 ± 1.30	< LOD–10.43	< LOD	0.35	0.68	2.23
12 to < 20	108	0.82 ± 1.10	< LOD–6.83	0.23	0.52	1.01	2.87
≥ 20	483	0.74 ± 2.10	< LOD–24.22	< LOD	0.29	0.67	2.53
All (0–65)	1,177	0.66 ± 1.59	< LOD–24.22	< LOD	0.32	0.68	2.23

The age of eight participants was not known.

Table 2. Pyrethroid metabolites in urine samples (µg/g creatinine) listed according to age group.

Metabolite/ age (years)	No.	Mean ± SD	Range	Percentile 25th	50th	75th	95th
Br_2CA							
< 6	331	0.10 ± 0.45	< LOD–6.56	< LOD	< LOD	< LOD	0.51
6 to < 12	247	0.08 ± 0.57	< LOD–7.18	< LOD	< LOD	< LOD	0.22
12 to < 20	108	0.10 ± 0.41	< LOD–3.57	< LOD	< LOD	0.05	0.39
≥ 20	483	0.06 ± 0.24	< LOD–2.26	< LOD	< LOD	< LOD	0.29
All (0–65)	1,177	0.08 ± 0.40	< LOD–7.18	< LOD	< LOD	< LOD	0.35
cis-Cl_2CA							
< 6	331	0.11 ± 0.32	< LOD–4.0	< LOD	< LOD	0.09	0.60
6 to < 12	247	0.11 ± 0.32	< LOD–3.34	< LOD	< LOD	0.10	0.61
12 to < 20	108	0.10 ± 0.19	< LOD–0.98	< LOD	< LOD	0.12	0.59
≥ 20	483	0.14 ± 0.61	< LOD–9.06	< LOD	< LOD	0.07	0.53
All (0–65)	1,177	0.12 ± 0.45	< LOD–9.06	< LOD	< LOD	0.09	0.58
trans-Cl_2CA							
< 6	331	0.47 ± 0.98	< LOD–14.70	< LOD	0.30	0.55	1.82
6 to < 12	247	0.40 ± 0.66	< LOD–6.47	< LOD	0.23	0.50	1.44
12 to < 20	108	0.32 ± 0.36	< LOD–1.86	0.05	0.26	0.44	1.11
≥ 20	483	0.42 ± 1.22	< LOD–17.13	< LOD	0.17	0.39	1.28
All (0–65)	1,177	0.42 ± 0.99	< LOD–17.13	< LOD	0.22	0.47	1.40
F-PBA							
< 6	331	0.09 ± 0.24	< LOD–1.96	< LOD	< LOD	< LOD	0.61
6 to < 12	247	0.04 ± 0.13	< LOD–1.17	< LOD	< LOD	< LOD	0.27
12 to < 20	108	0.05 ± 0.15	< LOD–1.23	< LOD	< LOD	< LOD	0.32
≥ 20	483	0.07 ± 0.43	< LOD–5.74	< LOD	< LOD	< LOD	0.20
All (0–65)	1,177	0.07 ± 0.32	< LOD–5.74	< LOD	< LOD	< LOD	0.40
All pyrethroids, sum							
< 6	331	0.79 ± 1.44	< LOD–18.17	< LOD	0.42	0.93	3.12
6 to < 12	247	0.63 ± 1.28	< LOD–12.08	< LOD	0.31	0.61	2.06
12 to < 20	108	0.57 ± 0.67	< LOD–3.77	0.14	0.36	0.78	2.22
≥ 20	483	0.69 ± 1.95	< LOD–20.92	< LOD	0.27	0.61	2.04
All (0–65)	1,177	0.69 ± 1.59	< LOD–20.92	< LOD	0.32	0.73	2.30

The age of eight participants was not known.

different analytical method, they were not able to differentiate between the *cis*- and *trans*- isomers of Cl_2CA. The median, maximum, and 95th percentile values for Cl_2CA in the urine tested were below the LOD (0.2 µg/L), 11.5 µg/L, and 0.51 µg/L, respectively, and thus lower than in our study. The differences may be due to differences in the analytical approach or may be caused by different external exposure in different regions in Germany. Because we did not find seasonal differences in the levels of pyrethroid metabolites determined in urine, the time of urine sampling can be excluded as an influencing factor.

In the study conducted by Hardt et al. (*21*), 45 adult volunteers who were not occupationally exposed to pyrethroids were studied in the same laboratory as in our study, using the same analytical method, so that methodologic differences may be disregarded. The data on the excretion of Cl_2CA was comparable to our data from more than 1,000 persons, but the levels of Br_2CA and F-PBA excreted were lower (*21*). To date, there are no other data available on the pyrethroid metabolites excreted in the urine of children.

The indoor exposure of our study area, calculated on the basis of the pyrethroid levels in household dust, was lower than the general exposure evaluated in the representative environmental survey in Germany, 1990–1991. No correlations were detected in our study between the indoor exposure (permethrin in household dust or cupboard dust) and the levels of pyrethroid metabolites excreted in the urine of the inhabitants. This is also true for the study published by Butte et al. (*20*), although rather high permethrin levels were found in household dust (95th percentile, 73 mg/kg). It may be concluded, therefore, that the internal pyrethroid exposure detected in the general population in Germany for children and adults is mainly caused by dietary exposure. To test this hypothesis, duplicate diet studies combined with biomonitoring should be conducted, preferably with a representative design.

Toxicologic evaluations have been drawn up for several synthetic pyrethroids by the Food and Agriculture Organization of the United Nations/World Health Organization Joint Meeting on Pesticide Residues (*22*). The acceptable daily intake (ADI) has been estimated for various synthetic pyrethroids. The ADI values are in the range of 10 µg/kg body weight (e.g., deltamethrin) up to 50 µg/kg body weight (e.g., permethrin, cypermethrin) (*22*). The level of background exposure reported here is therefore orders of magnitude lower than the ADI values.

Table 3. Percentage of urine samples in which pyrethroid metabolites were detected.

Age (years)	Urine samples (*n*)	(% > LOD) Br_2CA	*cis*-Cl_2CA	*trans*-Cl_2CA	F-PBA
< 6	331	16.6	21.0	51.3	16.1
6 to < 12	247	14.8	26.9	59.7	12.7
12 to < 20	108	25.6	36.4	68.6	18.2
≥ 20	483	16.8	28.0	61.7	13.3
All	1,177	19.3	29.4	65.3	16.4

Table 4. Pyrethroid metabolites found in urine specimens (µg/L) in different months of 1998.

Metabolite/ months	No.	Mean ± SD	Range	Percentile 25th	50th	75th	95th
Br_2CA							
Feb–March	537	0.07 ± 0.27	< LOD–4.03	< LOD	< LOD	< LOD	0.34
April–May	286	0.12 ± 0.88	< LOD–9.19	< LOD	< LOD	< LOD	0.27
June–July	227	0.07 ± 0.34	< LOD–4.76	< LOD	< LOD	< LOD	0.26
Aug–Sept	88	0.09 ± 0.40	< LOD–2.88	< LOD	< LOD	< LOD	0.84
Oct–Dec	38	0.08 ± 0.06	< LOD–0.30	< LOD	0.10	0.10	0.11
cis-Cl_2CA							
Feb–March	537	0.10 ± 0.31	< LOD–3.94	< LOD	< LOD	0.10	0.51
April–May	286	0.13 ± 0.62	< LOD–9.76	< LOD	< LOD	0.15	0.63
June–July	227	0.12 ± 0.40	< LOD–5.01	< LOD	< LOD	0.10	0.59
Aug–Sept	88	0.05 ± 0.13	< LOD–0.55	< LOD	< LOD	< LOD	0.39
Oct–Dec	38	0.08 ± 0.06	< LOD–0.25	< LOD	0.10	0.10	0.23
trans-Cl_2CA							
Feb–March	537	0.43 ± 1.00	< LOD–17.82	< LOD	0.25	0.46	1.52
April–May	286	0.46 ± 1.05	< LOD–14.27	< LOD	0.27	0.57	1.47
June–July	227	0.40 ± 1.11	< LOD–14.45	< LOD	0.21	0.40	1.39
Aug–Sept	88	0.31 ± 0.40	< LOD–1.78	< LOD	0.24	0.48	1.23
Oct–Dec	38	0.23 ± 0.27	< LOD–1.26	0.10	0.10	0.26	1.26
F-PBA							
Feb–March	537	0.08 ± 0.33	< LOD–5.11	< LOD	< LOD	< LOD	0.48
April–May	286	0.03 ± 0.18	< LOD–1.83	< LOD	< LOD	< LOD	0.10
June–July	227	0.02 ± 0.05	< LOD–0.43	< LOD	< LOD	< LOD	0.10
Aug–Sept	88	0.02 ± 0.15	< LOD–1.37	< LOD	< LOD	< LOD	0.10
Oct–Dec	38	0.07 ± 0.04	< LOD–0.10	< LOD	0.10	0.10	0.10
Pyrethroids, sum							
Feb–March	537	0.68 ± 1.48	< LOD–21.76	< LOD	0.36	0.72	2.36
April–May	286	0.76 ± 1.89	< LOD–24.03	< LOD	0.32	0.69	2.81
June–July	227	0.61 ± 1.80	< LOD–24.22	< LOD	0.26	0.63	2.00
Aug–Sept	88	0.49 ± 0.75	< LOD–4.52	< LOD	0.25	0.61	2.10
Oct–Dec	38	0.47 ± 0.34	< LOD–1.69	0.40	0.40	0.54	1.29

Summary

In this study, spot urine samples from 1,177 persons with neither occupational nor recent indoor exposure were analyzed using a method shown to be precise, accurate, specific, sensitive, and suitable for routine analysis. With this method, the most important pyrethroid metabolites can be determined in one run. Background exposure to pyrethroids was found in the general population: *trans*-Cl_2CA was detected in 60% of the urine samples tested, *cis*-Cl_2CA was detected in 30%, and Br_2CA and F-PBA were detected in 16–19%. The urinary metabolite concentrations in children did not differ from those in adults, and there was no correlation with the indoor exposure, assessed by determining the levels of permethrin in household dust. The month in which the urine samples were taken had no influence on the levels of pyrethroids in urine. As long as representative data are lacking, the rounded 95th percentile values obtained in our study may be used as reference values in the population, for both children and adults: Br_2CA, 0.3 µg/L; *cis*-Cl_2CA, 0.5 µg/L; *trans*-Cl_2CA, 1.5 µg/L; and F-PBA, 0.3 µg/L.

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