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# Biomonitoring of Persons Exposed to Insecticides Used in Residences

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**Pesticides used indoors inevitably result in some unintentional and unavoidable exposures of residents. Measured dosages of residents are well below toxic levels. Exposures (μg/kg-day) are substantially less and occur over a longer time than suggested by unvalidated estimates derived from previous extreme, conservative default assumptions based solely on environmental residues. Human chlorpyrifos exposures were monitored following three different types of applications: fogger, broadcast, and crack-and-crevice. Persistence of total residue on carpet was substantially greater than the persistence of transferable residue (μg/cm²). Low-level (μg/kg) exposures of family members persisted for periods of weeks to a month after pesticide use. Although few children who resided with their parents in pest-protected homes have been monitored, they eliminated more biomarker than their parents on a kg body weight-day basis when absorbed dosages (μg/kg-day) were derived from spot urine specimens corrected for volume by an age-specific creatinine correction. Ultimately environmental residues may become useful elements of predictive residential exposure models, but their potential contribution to indirect exposure assessments must include careful determination of residue availability for contact transfer to clothing or skin and biological validation. When environmental data from monitoring studies reported here were used to estimate residential exposure according to Residential Exposure Assessment Standard Operating Procedures (SAP meeting, 1997), measured exposures were substantially less than assessments. Experimental and situational monitoring of exposed persons is essential for meaningful and responsible predictive resident exposure model building.** 

*Keywords:* pesticide; residential exposure; biomonitoring; absorbed dosage; chlorpyrifos

## INTRODUCTION

Protection of residences using insecticides and other pesticides creates opportunities for human chemical exposures. The products used by both homeowners and professional applicators contain active ingredients that are usually semi-volatile (vapor pressure $<10^{-4}$ mm Hg) and form deposits on indoor surfaces (Table 1). The persistence of these chemicals is longer indoors than in agricultural environments due to diminished or filtered sunlight, reduced moisture and air movement, surface area, and lack of soil microorganisms. Measurable dermal, oral, and inha-

Table 1. Surface deposition levels of chlorpyrifos (μg/cm²) following discharge from fogger canisters for two residences in Riverside, CA

| Room # | Amount of chlorpyrifos on deposition coupons (μg/cm²) | |
|---|---|---|
| | Poly[a] | Riverside[b] |
| A | 0.9 | 13.5 |
| B | 2.2 | 14.3 |
| C | 1.3 | 17.3 |
| D | 2.8 | NS |
| E | 1.0 | NS |
| F | 1.5 | NS |
| Ave | 1.6 | 15.0 |

[a]Poly study include foil deposition coupons from each of the six rooms that were treated

[b]Riverside study included deposition coupons from three rooms that were treated

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lation exposure occurs over a period of weeks to months. When used as directed, the systemic exposure levels are well below toxic thresholds based upon the normal experience of consumers.

During the contemporary risk characterization process, the experimental Lowest Observed Adverse Effect Level (LOAEL; mg/kg) is reduced many fold as the toxicology reference point cascades downwards to no effect levels of regulatory significance but of uncertain biological relevance: No Observed Adverse Effect Level (NOAEL), No Observed Effect Level (NOEL), Reference Dosage (RfD), and acute Population Adjusted Dose (aPAD). Adverse effects often attributed to indoor insecticide use (Berteau *et al*., 1989) in all likelihood result from adverse responses to sensory stimuli rather than from absorption of toxic amounts (Krieger and Ross, unpublished). Such responses are important health effects or nuisances in some cases. Those amounts of exposure would be even less than the absorbed doses described in this paper.

Our goal was to measure the extent of exposure of persons residing in homes where pesticides have been used. Chlorpyrifos products were utilized to study the human exposure potential of a variety of residential human activities. This particular active ingredient is a very well characterized model semi-volatile, organophosphate insecticide of moderate toxicity. The stable biomarker, trichloropyridinol, produced by chlorpyrifos hydrolysis (Nolan *et al*., 1984) has a half-life of 27 h and at least 70% of oral and dermal doses are eliminated in urine. The dialkyl phosphate metabolites are also rapidly eliminated, but their limits of detection are nearly an order of magnitude higher than TCP.

Exposure data for evaluation of predictive models and standard regulatory operating procedures were acquired using two approaches. Situational exposure monitoring was urine biomonitoring of persons who lived in residences where occupants themselves or a pest control operator applied pesticides. The second approach included biomonitoring of family members and limited indoor sampling after a research application of chlorpyrifos. Each approach produced similar exposure data, but situational studies include more uncertainties since residents rather than investigators direct the work.

In this paper, an experimental study that examines the issue of pesticide residue persistence and availability will be presented as well as situational monitoring of three post-application exposure scenarios including fogger, broadcast, and crack-and-crevice (Table 2). Post-application residential exposure assessments will be assessed according to Residential Exposure Assessment Standard Operating Procedures of the US Environmental Protection Agency (SOPs; USEPA, 1997b). These SOPs are intended for use in the absence of or as a supplement to chemical and/or site-specific data and are included in default methods for developing assessments for handlers (operators) and post-application exposures (USEPA, 1997a). The results will also be matched with indirect measures of residential exposure in the literature that have been important in the development of present US regulatory policy (Berteau *et al*., 1989; Fenske *et al*., 1990; Gurunathan *et al*., 1998).

## METHODS

### *Experimental exposure studies*

'Highland I and II' experimental studies consisted of two successive fogger applications in a 2000 $ft^2$ (186 $m^2$) residence approximately a year apart from each other in accord with a protocol approved by the Human Subjects Review Committee, University of California, Riverside. Both studies were conducted by biomonitoring a family (8 members in Highland I and 7 members of the same family in Highland II) in Highland, CA following treatment of a nylon-carpeted, 2-story home. Foggers were discharged into six primary unobstructed areas including bedrooms (2), a home office, living room, dining room and master bedroom with KRID™ Roach and Flea Foggers (EPA reg. No.11715-137-46515) containing chlorpyrifos (1.000%), pyrethrins (0.050%), technical piperonyl butoxide (0.100%), and MGK 264 (0.166%) and inert ingredients (98.684%). The home was ventilated after 2 h and the occupants reentered later in the day.

The Highland I study included mother 55 and father 54, grandmother aged 88, an aunt aged 49, and four daughters aged 24, 23, 22, and 18 while the Highland II study consisted of the same family members except for the 22 year-old daughter who lived elsewhere at that time. Pretreatment urine specimens were collected beginning 24 h before the fogging in the Highland I study (day -1). Subsequently, 24-h urine collections occurred on days 1, 2, 3 and 30 after application (Fig. 2). In the Highland II study, morning urine voids were collected prior to fogging (day -1) and were continued on days 1, 2, 3, 4, 5, 6, 7, 11, 15 and 22 after application (Fig. 2).

### *Situational exposure monitoring*

The three post-application situational monitoring studies were done based upon the interest and cooperation of family, friends or acquaintances who were familiar with exposure studies of this research group. Their homes were treated by the residents themselves as part of normal pest management activities. Monitoring of the crack-and-crevice application followed chlorpyrifos use by a commercial pest management firm. The 'Poly Fogger' study was conducted by biomonitoring a family of four residing in an 1800 $ft^2$ (167 $m^2$) nylon-carpeted home in Riverside, CA. A bedroom, home office, living room, dining room and master bedroom were treated for cockroaches and fleas with ACE Indoor Foggers (EPA reg.

Table 2. Chlorpyrifos exposures from situational biomonitoring studies

| Subject | Age | Daily dosage (μg CP/kg body weight)[a,b] Pre-spray | Post-spray |
|---|---|---|---|
| Poly fogger discharge | | | |
| Father | 54 | 0.03 | 0.1 |
| Mother | 51 | 0.04 | 0.6 |
| Female teenager | 19 | 0.1 | 1.5 |
| Male child | 8 | 0.1 | 2.9 |
| Riverside broadcast spray | | | |
| Father | 45 | 0.6 | 1.0 |
| Mother | 37 | 0.1 | 0.6 |
| Male child (A) | 12 | 0.4 | 3.4 |
| Female child (B) | 10 | 0.6 | 2.0 |
| Female child (C) | 4 | 0.4 | 1.4 |
| Corona crack-and-crevice | | | |
| Mother | 30 | 0.3 | 1.7 |
| Female teenager (A) | 17 | 0.4 | 1.1 |
| Male teenager (B) | 19 | 0.4 | 1.1 |
| Male teenager (C) | 16 | 0.4 | 0.8 |
| Male toddler | 2 | 2.1 | 5.3 |

[a]Average daily clearance of TCP reported as chlorpyrifos equivalences: Number of days biomonitored after insecticide application; Poly (10) Riverside (5), and Corona (10)
[b]Daily dosage was estimated from adjusted daily TCP clearance using a creatinine correction (1 g creatinine/day for female adults; 1.7 g creatinine/day for male adults; 0.08 g creatinine/day/year of age x age for male and female children; ICRP, 1994) and transformed to chlorpyrifos equivalents using the following equation:

$$\text{chlorpyrifos (CP) equivalents} = \frac{\mu\text{g TCP}}{\text{ml urine}} \times \frac{\text{ml urine}}{\text{g creatinine}} \times \frac{\text{g creatinine cleared}}{\text{day (adult female)}} \times \frac{\text{formula wt CP}}{\text{formula wt TCP}}$$

No. 9688-63) containing chlorpyrifos (0.50%), d-trans allethrin (0.05%), and inert ingredients (99.45%). The family ventilated the house after 3 h and reentered later in the day. The family consisted of a father and mother, one teenage girl and an 8-year old male child. Urine collection began the morning of the application prior to fogger discharge (day 0) and was continued on days 1, 2, 3, 4, 5, 6, 7, 9, 11, and 13 after application.

The 'Riverside Broadcast' situational monitoring of a family of five was conducted following treatment of the residence for houseflies and unspecified nuisance insects. Bedrooms (2), family room, dining space, kitchen and master bedroom were treated with a broadcast application of diluted aqueous suspension of Spectracide Dursban® Indoor and Outdoor Insect Control (EPA reg. No. 8845-30) containing chlorpyrifos (6%) and inert ingredients (94.0%) and was applied using a hand held pressurized tank and wand. Outside areas were also sprayed to reduce the fly population that was attracted to a nearby livestock pen. The family consisted of a father and mother, and three children aged 12, 10 and 4. Urine collection began the morning of application prior to insecticide spraying (day 0) and was continued on days 1, 2, 3, 4, and 7 after application.

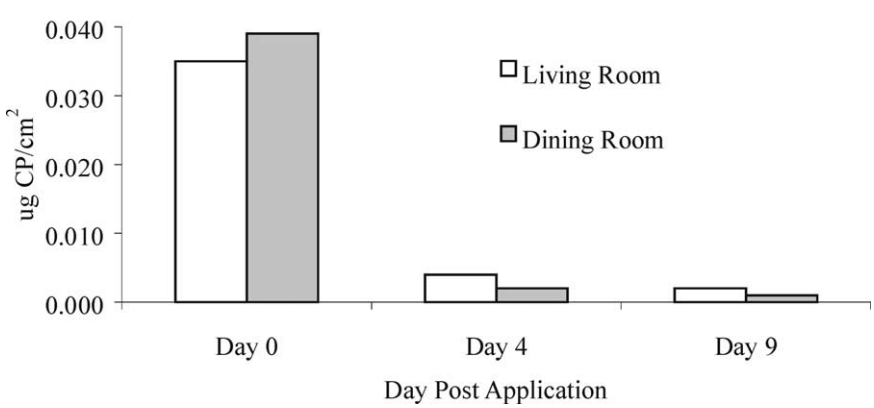


Fig. 1. The amount of chlorpyrifos surface residue transferred at the Poly residence from carpet to cotton cloth using the CDFA method (Ross *et al*., 1990).

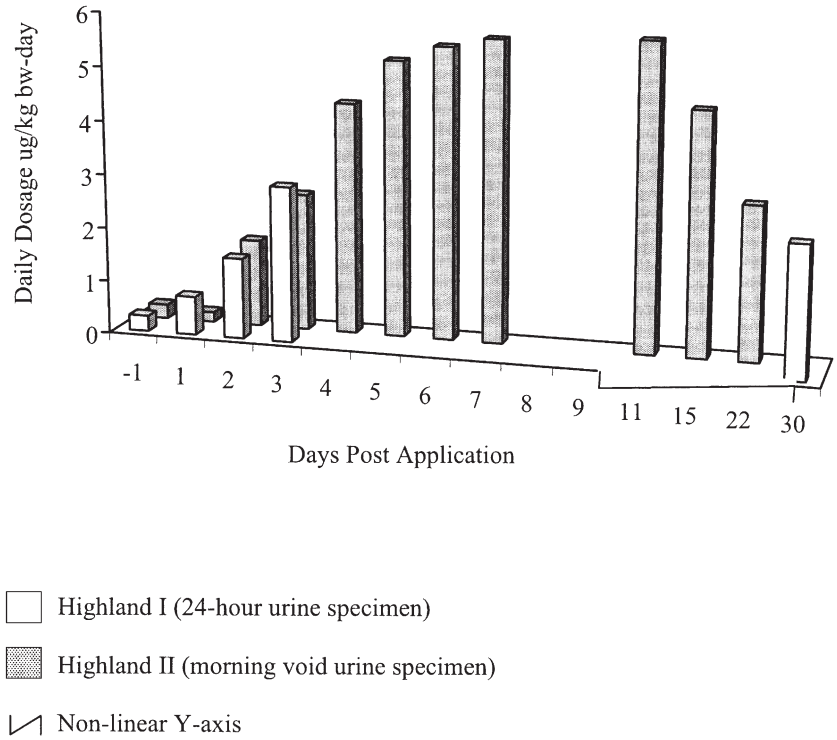


Fig. 2. The Highland I and Highland II experimental monitoring studies showing daily elimination of chlorpyrifos equivalents through urine of 8 (I) or 7 (II) adults.

The 'Corona Crack-and-Crevice' study was conducted by biomonitoring a family of five living in Corona, CA that had a certified pesticide applicator apply a diluted aqueous suspension of Dursban Pro® (EPA reg. No. 62719-166) containing chlorpyrifos (23.7%) and inert ingredients (76.3%) to bedrooms (2), family room, dining space, kitchen and master bedroom (total 167 $m^2$). The family consisted of a mother, three teenagers and a 2 year-old child. Urine collection for the older persons included pre-exposure specimens from the day prior to insecticide spraying and the morning of application prior to exposure and was continued on days 1, 2, 3, 4, 5, 7, 9, 11, 13, and 15 after insecticide application. The parent obtained several spot urine specimens from her child as the child was being prepared for bathing.

*Urine specimen collection*

In 'Highland I' all samples were complete 24-h voids and no adjustment was made for urine volume. In all other studies only first or 'morning' voids were used. Participants had a general familiarity with urine collection procedures in clinical settings and a certified physicians assistant gave additional instruction in the experimental studies. Urine specimens were provided before and after chlorpyrifos use. No adjustments were made for TCP in the specimens provided before chlorpyrifos use. Participants were provided a variety of collection vessels, but most reported using a small polyethylene cup to collect urine. Samples of 25–30 ml were transferred to pre-labeled 35 ml polyethylene tubes and each was stored frozen without delay prior to TCP analysis. TCP was analyzed in less than one month of the first collection, in each unpublished studies (Bernard and Krieger) affirm stability of the analyte.

*Analysis*

Conjugated and free 3,5,6-trichloro-2-pyridinol (TCP) was analyzed after acid hydrolysis of urine. Stable isotope labeled TCP ($^{13}C_2{}^{15}N$-TCP) and concentrated HCl were added to urine specimens and held overnight at 60°C. TCP was extracted with 1-chlorobutane and derivatized in an auto-sample vial with N-methyl-N-(tert-butyldimethyl-dimethylsilyl)-trifluoroacetamide reagent to produce tert-butyldimethylsilyl derivatives of 3,5,6-TCP and the internal standard. The sample was then analyzed by gas chromatography with mass selective detection in the selective ion-monitoring (SIM) mode. The limit of quantification using this method was approximately 5 ppb TCP in urine. TCP was reported as chlorpyifos equivalents. Daily urine volume was estimated using a creatinine correction (1.7 and 1.0 g creatinine/day for adult males and females, respectively) (Rowland and Tozer, 1980; ICRP, 1994). Creatinine levels were assigned to children assuming 0.08 g creatinine/day for each year of age 2–12 yr (ICRP, 1994). TCP (μg/g

creatinine) was transformed to chlorpyrifos equivalents using the following equation:

$$\text{chlorpyrifos (CP) equivalents} = \frac{\mu\text{g TCP}}{\text{ml urine}} \times \frac{\text{ml urine}}{\text{g creatinine}} \times \frac{\text{g creatinine cleared}}{\text{day}} \times \frac{\text{formula wt CP}}{\text{formula wt TCP}}$$

When residential monitoring was performed, environmental samples were obtained as foil deposition coupons and/or cotton sheet dosimeters pressed against treated carpet with a 30 lb roller (Ross *et al*., 1991). The coupons and cotton dosimeters were extracted using ethyl acetate. Volume was reduced, if necessary, by heating at 45°C in a fume hood. The extracts were analyzed by gas chromatography with a flame photometric detector (FPD). The HP 5890 GLC was equipped with a 30 m×0.32 mm HP-5 crosslinked 5% diphenyl- and 95% dimethypolysiloxane chromatography column with a film thickness of 0.25 μm. Following sample injection, the oven was held at an initial temperature of 50°C for 1 minute and was increased thereafter at 20°C/min until a final temperature of 300°C was obtained and held for 3 min. The flow rate for the He carrier gas was 2 ml/min. Extraction efficiency was about 95% based upon spiked blanks.

## RESULTS

*Experimental human exposure monitoring*

Insecticide availability and the duration of exposure were addressed in studies conducted during two successive years in a single-family residence in Highland, CA. The same chlorpyrifos product was used each year at virtually the same place in the home. Results are shown in Fig. 2. Continuing exposure and partial elimination of the absorbed dose was clearly evident from measurements of TCP elimination during the first year's monitoring using serial 24-h urine specimens. The following year the monitoring period for collection of morning voids was lengthened to 23 days. Fogging produced a residue, which produced low-level exposures (relative to toxic dosages), over a substantially longer period than predicted by our previous environmental monitoring (Ross *et al*., 1990, 1991).

It is important to note the similarity of the exposure estimates between the 2 Highland studies (Fig. 2). In the first year 24-h specimens were used to estimate the chlorpyrifos exposure of eight persons. In the second year, after more monitoring experience was obtained, only morning voids were provided by seven of the same family members. The correspondence of the exposure profiles contributes to confidence that morning voids represent daily TCP elimination when creatinine is used to adjust daily urine volume.

*Indoor surface monitoring*

Previous studies of residential pesticide deposition and residue transferability predict rapid decline in residue transferability within a few hours of application (Fenske *et al*., 1990; Ross *et al*., 1990). Very limited measurements of residential residues were made during experimental studies at Highland I and II, and situational monitoring at the Poly, Riverside, and Corona homes to determine the amount of insecticide which may be transferred and absorbed by humans. In the Poly study, foil deposition coupons in each fogged room captured an average of 1.6 μg chlorpyrifos/cm$^2$ (Table 1). The Riverside Broadcast study included foils in three of six treated rooms that retained an average of 15.0 μg chlorpyrifos/cm$^2$ (Table 1).

Cotton cloth dosimeters were rolled about 4 h after fogger discharge as well as on days 4 and 9 post-application in the living and dining rooms of the Poly residence (Fig. 1). Transferred chlorpyrifos from carpet after 4 h was 2.3% of that on deposition foils. On days 4 and 9, the amount transferred was 0.2% and 0.1% of that on the foil. The amount residue transferred from carpet to cotton cloth using the roller at about 4 h in the Riverside monitoring was about 0.25% of that deposited on deposition foils.

*Situational exposure biomonitoring*

Before chlorpyrifos application morning urine specimens (adjusted to daily levels using creatinine; ICRP, 1994) ranged from 0.03 to 0.1, 0.1 to 0.6, and 0.3 to 2.1 μg chlorpyrifos equivalents/kg body weight-day for the Poly, Riverside and Corona studies, respectively (Table 2). In a recently published report (Krieger *et al*., 2000) pre-study chlorpyrifos equivalents among 34 persons ranged from 4 to 81 μg (mean 19±15 μg equivalents chlorpyrifos). The background level of 4–81 μg equivalents/day would be associated with a dosage of 0.1–1 μg/kg-day.

During the 13-day monitoring period of the Poly and Corona studies, daily TCP elimination averaged 0.1–2.9 μg chlorpyrifos equivalents/kg-day (Poly) and 0.8–5.3 μg chlorpyrifos equivalents/kg-day (Corona) (Table 2). The daily average dosage for the Riverside residents following broadcast spraying ranged from 0.6 to 3.4 μg chlorpyrifos equivalents/kg-day. Chlorpyrifos equivalents represent aggregate TCP elimination. If corrected for TCP background the average TCP elimination ranged from 0.07 to 2.8 μg chlorpyrifos equivalents/kg-day (Poly), 0.4–3.2 μg chlorpyrifos equivalents/kg-day (Corona), and 0.3–3.0 μg chlorpyrifos equivalents/kg-day (Riverside).

*Indirect exposure estimates*

Assessments of human exposure may be developed from environmental sampling data used with standard regulatory operating procedures (USEPA, 1997b).

For instance, the published USEPA regulatory default for an exposure assessment is 50% transfer of the deposited surface residue to skin and 100% absorption of that dose using an empirical transfer coefficient of 43 000 $cm^2$/h and duration of exposure of 8 h/day. This would result in a hypothetical dermal absorbed daily dosage (ADD) for the father from the Riverside study on the day of insecticide application of approximately 32 mg/kg (15.0 μg/$cm^2$×50% available deposition ×8 h×43 000 $cm^2$/h÷80 kg=32 250~μg/kg bw−day) (Table 3). The USEPA chlorpyrifos Registration Eligibility Document lists dermal absorption of chlorpyrifos at 3%, which would reduce the hypothetical ADD to 1 mg/kg.

In a similar manner, estimates of exposure may also be generated using measurements of transferable residue (CDFA roller) in conjunction with the indoor residential standard operating procedure (USEPA, 1997b). The transferable residue from the Poly study averaged 0.037 μg/$cm^2$ (Fig. 1) 4 h following application. Using these transferable residue data and assuming a 0.1 clothing penetration factor and 0.1 dermal absorption/day (in this case until bathing the next morning), the estimated ADD for an 80 kg female would be about 1.6 μg/kg [(0.037 μg/$cm^2$ × 8h × 43 000 $cm^2$/h ÷ 80 kg) × 0.1 × 0.1=1.6 μg/kg-day) (Table 3). In this estimate, exposures via hands, face, and neck are not included in the algorithm. Those factors would serve to further increase the estimate of exposure which already is similar to the measured ADD (1–2.2 μg/kg-day, Bernard and Krieger, unpublished).

## DISCUSSION

The overall goal of this continuing research is clarification of the magnitude and determinants of residential chemical exposure resulting from indoor pesticide use. Additional studies of this type make it possible to evaluate regulatory algorithms used for residential exposure assessment. The strength of the studies is derived from assessment of aggregate human exposure under normal conditions of pesticide use in natural residential settings. Limitations include the incompleteness of urine collections and uncertainties related to urine as a route of elimination. Suitable pharmacokinetic data for TCP elimination following low dermal exposures of the whole body is lacking. The exposure estimates here at low dermal and inhaled dosages assume that complete elimination occurs via urine.

Residential uses of insecticides include structural, area treatments using broadcast sprays and foggers, crack-and-crevice sprays, as well as outdoor turf and home perimeter pest management which may result in indoor exposures. In the work reported here, chlorpyrifos is a model semi-volatile insecticide that is easily linked to an extensive human database concerning exposure. Those studies have facilitated experimental and situational monitoring, but the results of this work were not intended to directly contribute to the regulation of residential use of chlorpyrifos or any other products.

Exposure monitoring studies have shown that similar, very low chlorpyrifos exposures (relative to toxic amounts) occur following broadcast, fogger, and crack-and-crevice applications. Differences related to application method are not as large as predicted by regulatory SOPs (USEPA, 1997b), probably because the standard regulatory defaults are screening level estimates based upon indirect measurements from multiple pathways of human exposure. Among families, friends, and acquaintances that have participated in this work, children have eliminated more TCP

Table 3. Estimated absorbed daily dosage using the USEPA Standard Operating Procedure for dermal exposure and environmental sampling at the Riverside and Poly residences

| Subject | Body weight (kg) | Estimated absorbed daily dosage (μg CP/kg body weight-day) | |
|---|---|---|---|
| | | Foil deposition[a] | Transferable residue[b] |
| Poly fogger discharge | | | |
| Father | 175 | 1600 | 0.7 |
| Mother | 80 | 3400 | 1.6 |
| Female teenager | 50 | 5500 | 2.5 |
| Male child | 35 | 7900 | 3.6 |
| Riverside broadcast spray | | | |
| Father | 80 | 32 000 | 1.6 |
| Mother | 91 | 28 000 | 1.4 |
| Male child (A) | 55 | 47 000 | 2.3 |
| Female child (B) | 36 | 72 000 | 3.5 |
| Female child (C) | 16 | 161 000 | 8.0 |

[a]Derived using the US EPA SOP algorithm: deposition (μg/$cm^2$)×50% transfer×duration of exposure (8 h)×transfer coefficient (43 000 $cm^2$/h)÷body weight (kg)=Absorbed Daily Dosage (μg/kg)

[b]Derived using the following algorithm: dislodgeable residue (μg/$cm^2$)×duration of exposure (8 h)×transfer coefficient (43 000 $cm^2$/h)×10% (clothing penetration)×10% (dermal absorption)÷body weight (kg)=Absorbed Daily Dosage (μg/kg); Based on a measured dislodgeable residue in both the Poly and Riverside of 0.037 μg/$cm^2$ approximately 4 h post-application

(μg/kg-day) than their parents (Bernard and Krieger, unpublished), however, the magnitude of the difference is usually less than the 10× intrapersonal uncertainty factor that is routinely used in risk characterization. The duration of exposure indicated by elevated urine TCP levels is longer than predicted by whole body dosimetry (Ross *et al*., 1990). Urinary TCP may remain above pretreatment urine TCP levels of residents for about 1 month following thorough fogging of a home (Fig. 2). It is important to note that the exposures listed in Table 2 and presented in Fig. 2 represent exposures of populations of users of chlorpyrifos products rather than the general population. Among the user population, measurable exposures greater than background levels (usually less than 0.4 μg/kg-day) could be expected for at least one month afterwards due to insecticide persistence in residences. Measurements of transferable residue (as oppose to total amounts detected) are critical to the establishment of reliable exposure estimates (Fig. 1).

Limited epidemiological data are available concerning TCP elimination from the general population (Hill *et al*., 1995). The use of chlorpyrifos equivalents, rather than TCP itself, potentially overestimates the exposure since TCP may result from other exposures, notably TCP as a food residue and a trace (molecular) environmental contaminant. Aggregate chlorpyrifos equivalents eliminated as TCP ranged from nondetectable to 2 μg/kg-day (Hill *et al*., 1995). Measurable levels were evident in 82% of the samples, which is similar to the 100% positive specimens in our continuing studies (e.g., Krieger *et al*., 2000). This exposure range represents a population of 1000 persons that is a valuable point of reference for situational and experimental monitoring and the reported values are orders of magnitude less than previous hypothetical estimates.

Other studies detailed in the literature include estimates of residential non-dietary exposures. For example, Berteau *et al*. (1989) developed estimates of exposure to the insecticides propoxur, DDVP, and chlorpyrifos based on a contact–transfer, worst-case scenario. Default assumptions concerning inhalation exposure, the extent of surface residue contact, the spatial distribution of the pesticide, availability of the insecticide, and dermal absorption resulted in extreme estimates of exposure (mg/kg body weight-day dosages). Using more reasonable default assumptions, particularly with respect to dermal absorption and hand-to-mouth contact, Fenske *et al*. (1990) developed hypothetical exposure assessments with major amounts of exposure attributed to inhalation that were more than an order of magnitude less than those offered by Berteau *et al*. (1989). Lioy and colleagues (Gurunathan *et al*., 1998) attributed more than half of children's exposure to hand-to-mouth activity in their forecasted exposures from indoor insecticide use. These unvalidated estimates of dose have had substantial impact over a 10-year period on present USEPA regulatory policy, particularly policy-driven actions concerning children.

In response to uncertainty and the extreme estimates of insecticide exposures of children (Berteau *et al*., 1989), an experimental approach for the study of pesticide contact–transfer was developed at the California Department of Food and Agriculture (Ross *et al*., 1990; Krieger *et al*., 2000). Volunteers wore whole body cotton dosimeters during a 20-min intensive period of structured activity to represent extreme daily dermal exposure to carpets treated with chlorpyrifos-allethrin. Follow-up studies include measurements of exposure determined by biomonitoring (Krieger *et al*., 2000). The absorbed dosage of persons who wore whole body dosimeters was 1.9±2.3 μg/kg (corrected for 10% clothing penetration). The absorbed dosage for persons who wore only swim suits was 3.3±3.3 μg/kg. Much of the variability probably results from uneven application of insecticide delivered by the foggers (Bernard, Williams and Krieger, unpublished).

The values obtained from the structured activity studies may be used in conjunction with regulatory SOPs to estimate exposure (Table 3; USEPA, 1997b). For instance, the USEPA regulatory default for dermal exposure assessment is 50% of the available surface deposit and 100% absorption of that dose using a transfer factor of 43 000 $cm^2/h$ and duration of exposure of 8 h/day. Using these defaults, estimated absorbed dosage (ADD) of the father from the Riverside study on the day of insecticide application of approximately 32 mg/kg (15.0 $\mu g/cm^2 \times 50\% \times 8$ h $\times$ 43 000 $cm^2/h \div 80$ kg = 32 250 μg/kg). The USEPA chlorpyrifos Registration Eligibility Document lists dermal absorption of chlorpyrifos at 3%, which would reduce the ADD to 1 mg/kg. The measured dosage was 1 μg/kg-day (Table 2).

In a similar manner, estimates of exposure may also be generated using measurements of transferable residue (CDFA roller) in conjunction with the indoor residential standard operating procedure (USEPA, 1997b). The transferable residue in the Poly study averaged 0.037 $\mu g/cm^2$ (Fig. 1) 4 h following application. Using these transferable residue data and assuming a 0.1 clothing penetration factor and 0.1 dermal absorption/day (in this case until bathing the next morning), the estimated ADD for an 80 kg female would be about 1.6 μg/kg [(0.037 $\mu g/cm^2 \times 8$ h $\times$ 43 000 $cm^2/h \div 80$ kg) $\times 0.1_{penetration} \times 0.1_{absorption}$ = 1.6 μg/kg-day)] (Table 3). In this estimate, exposures via hands, face, and neck are not included in the algorithm. Those factors would serve to further increase the estimate of exposure which already is similar to the measured ADD (1–2.2 μg/kg-day; Bernard and Krieger, unpublished).

The measured dosage by biomonitoring was 0.6 μg CP equivalents/kg-day (Table 2). In each of these examples based upon biomonitoring and limited environmental measurements, exposures based upon

default estimates were 2 to 3 orders of magnitude greater than measured levels (Table 3).

The USEPA Standard Operating Procedures (USEPA, 1997b) also call for estimating residential inhalation exposure. The inhalation route is more difficult to assess since very small amounts are normally absorbed via inhalation when there is opportunity for absorption by other routes, particularly dermal. At very low exposure levels the percent contributed by inhalation will be larger than at proportionally higher dosages. The algorithm for estimating residential exposure via inhalation takes the following form:

$$PDR = C_a \times IR$$

where:

| | |
|---|---|
| PDR | potential dose rate (mg/day) |
| $C_a$ | pesticide air concentration (mg/m$^3$) |
| IR | average daily inhalation rate (m$^3$/day). |

If 70% of the inhaled vapor and small particles (<10 microns) is retained in the lung (minute volume), 100% is assumed to be absorbed as the inhaled dose. With semivolatile chemicals (vapor pressure ca. $10^{-4}$ or less mm Hg) such as chlorpyrifos, air sampling was not routinely conducted in our experimental and situational exposure monitoring studies due to its comparatively small exposure potential when there is opportunity for dermal contact–transfer (Table 2). Air normally makes a negligible contribution to absorbed dose under conditions of relatively high source strength on treated surfaces (Krieger *et al*., 2000). It is axiomatic inhalation will contribute more substantially to exposure when contact–transfer and dermal absorption are very low, but such circumstances will also be coupled with a low body burden of the chemical. Air normally makes a negligible contribution to absorbed dose under conditions of relatively high source strength on treated surfaces (Krieger *et al*., 2000). Airborne concentrations decline rapidly during the several hours following pesticide application, but surface exposure potential persists considerably longer (Fig. 3). Since the total residue likely persists longer than transferable residue, indirect exposure assessments based upon indoor residue is likely to substantially overestimate potential dermal dose.

An experimental indoor air level of 6.5 μg chlorpyrifos/m$^3$ was measured several hours following discharge of a fogger in a hotel room with a volume of 51.8 m$^3$ (Ross *et al*., 1990). The lack of furnishings in that room would support the conclusion that the measured air levels are high end or extreme. Assuming a mean inhalation rate of 13.3 m$^3$/day (USEPA, 1997b) and 100% absorption of 70% of the inhaled material, an 80 kg adult female from the Poly study would absorb less than the default dosage of 0.8 μg/kg body weight-day (0.0065 mg/m$^3$ × 13.3 m$^3$/day × 0.7 ÷ 80 kg = 0.0008 mg/day). The default inhaled level was similar to the average *aggregate* absorbed dosage of 0.6 μg/kg-day. When exposure levels are low, the inhalation pathway may contribute proportionally more to ADD than during the times that contact–transfer predominates.

Since pesticide biomonitoring is usually based upon collection of urine specimens, it is convenient to utilize spot samples rather than 24-h voids. This practice is justified for short-lived biomarkers ($t_{1/2}$< 48 h) that are eliminated in urine. Situational and experimental monitoring studies can utilize spot or convenience urine specimens when chemicals with a short half-life (<48 h) such as chlorpyrifos are being studied. The need to correct urine specimens for volume is also strongly evident in other situational monitoring (Bernard and Krieger, unpublished) as well as in this report (Table 2). In several cases in which urine specimen volume rather than creatinine has been used to estimate elimination, uncertain estimates of exposures have been reported.

Three studies (Moses, unpublished; Esteban *et al*., 1996; Loewenherz *et al*., 1997) included organophosphate insecticide exposure estimates for children, which were normalized to μg analyte/day/g creatinine. In each case, age-dependent elimination was not considered. This procedure inevitably results in an apparent higher exposure for 1-year olds (0.08 g creatinine/day) relative to 5-year olds (0.4 g creatinine/day) when both are normalized to g creatinine/day used in studies with adults. For example, adults who cleared 25 μg p-nitrophenol/kg/day were compared with children (*N*=6) who cleared 147 μg PNP/g creatinine (Esteban *et al*., 1996). However, mean creatinine elimination of 1- to 3-year-olds is markedly less (0.08g/day/year of age) in children. Correcting the children's exposure estimates for their lower creatinine clearance and body weight results in a children's dosage of about 1.6 μg PNP/kg compared to the adult dosage of about 0.4 μg PNP/kg. The estimated dosage of 1- to 3-year-olds is low relative to the acute human LOAEL of 7500 μg/kg for cholinesterase inhibition (plasma, RBC, brain) and nerve demylination or the 30-day human NOEL of 310 μg/kg-day (CDPR, 1999). The possibility that aggregated exposures of either adults or children contributed to adverse experiences resulting from methyl parathion exposure seems remote. Similar uncertainty results from consideration of the Moses report (unpublished) concerning urinary dialkyl phosphate levels of children of farmworkers in Florida, and again in the frequently cited studies of dimethyl (thio)phosphate elimination in Wenatchee, Washington, children (Loewenherz *et al*., 1997). To compare pesticide exposures of young children and older ones when 24-h urine specimens are not available, age-dependent differences in daily creatinine clearance must be considered when the creatinine volume adjustment is used (ICRP, 1994).

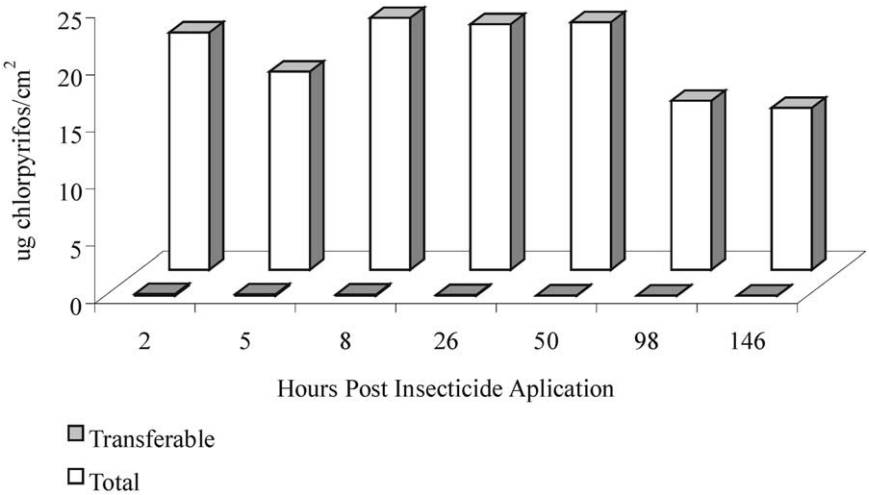


Fig. 3. Chlorpyrifos extracted from carpet swatches using soxhlet extraction (total) and residue transferred (CDFA roller method) from a carpet surface that was applied with a uniform application using a mobile linear spray cart (Bernard and Krieger, unpublished).

Biomonitoring experience to date includes many additional lessons related to determination of the extent and duration of human exposure resulting from indoor pesticide use. Most of the lessons learned are not ready to be cast as guidance, but exposure assessments based upon biological monitoring clearly must have a central place in risk management and risk communication. Table 4 contains a list of four general considerations that may contribute to future progress.

First, urine biomonitoring used to establish aggregate exposure potential following normal use of familiar chemicals such as chlorpyrifos (clarify dose and dosage, duration of availability, critical human activities) can reduce the need for default assumptions that inevitably inflate exposure assessments. The downside of this suggestion is that few pesticides are as completely studied as chlorpyrifos. Development of biological exposure indices (Table 4) to record the normal elimination of pesticides or their metabolites to which humans are exposed could serve at least two important functions; (1) to bring more physicians into the risk characterization and risk management processes, and, (2) to encourage use of a broader range of human experience and exposure data (manufacturing, occupational, personal) in the risk management process. In cases where exposure itself continues to be considered a disease, persons will have difficulty with biological exposure indices and some may demand 'zero' exposure. Continued advances in environmental and biological chemistry must be nurtured and vigorously pursued so the scientific health community can address present and future health concerns about the complex of chemicals in the molecular environment.

Secondly, the study of critical pathways and routes of exposure (contact, inhalation, clothing protection, human activity patterns, etc.) can contribute to building reliable, predictive models and to serve as foundation for future environmental monitoring. Structured activity exposure studies with chlorpyrifos make it very clear that dermal exposure can contribute substantially to residential exposures (Krieger *et al*., 2000). Similar recent studies in this laboratory have successfully forecasted the fate of cyfluthrin (Table 5). In work on critical exposure pathways, the most useful studies to improve the quality of the risk assessment process will be investigations that directly couple environmental monitoring and human exposure assessment.

Table 4. Measuring and assessing indoor chemical exposures of children and adults from surface deposition and dermal contact

| | |
|---|---|
| 1 | Use urine biomonitoring for establishing aggregate exposure potential following normal use of familiar chemicals (clarify dose and dosage, duration of availability, critical human activities). |
| 2 | Study critical pathways and routes of exposure (contact, inhalation, protective clothing, human activity patterns) as foundation for specific monitoring studies (lots of a little is still a little). |
| 3 | Develop exposure models based upon biological exposure indices (exposure aggregation under normal conditions of use). |
| 4 | Experimentally evaluate critical components of model and reference to biochemical exposure indices to important indoor environmental data for risk assessment, risk management, and risk communication. |

Table 5. Environmental and biological monitoring of humans following fogger and area sprays

| Chemical | Chlorpyrifos[a] | Chlorpyrifos[e] | Cyfluthrin[i] |
|---|---|---|---|
| Method of application | Fogger | Broadcast | Broadcast |
| Sample type | | Measurement | |
| Total residue on foils (μg/cm$^2$) | 3.6±2.8[b] | 34±12[f] | 7.3±0.8[j] |
| Transferable: carpet to cotton cloth (CDFA roller) (μg/cm$^2$) | 0.27±0.30[c] | 0.34±0.29[g] | 0.07±0.005[k] |
| Biomonitoring (μg/kg-day) | 3.3±3.3[d] | 1.3±0.7[h] | 0.16±0.10[l] |

[a]Krieger *et al*. (2000)
[b]Average amount of chlorpyrifos deposited on foil deposition coupons (*N*=12)
[c]Average amount of residue transferred from carpet to cotton cloth (*N*=12) that was pressed with a CDFA roller
[d]Average absorbed dosage of 20 participants that wore swimsuits and performed 2–20 min structured activity on carpet about 3 h after fogging
[e]Bernard *et al*. (unpublished) Exposure of persons performing a structured activity program on carpet treated with chlorpyrifos on three different days following a broadcast application
[f]Average amount of chlorpyrifos deposited on foil deposition coupons (*N*=6)
[g]Average amount of residue transferred from carpet to cotton cloth (*N*=2) that was pressed with a CDFA roller at about three hours following a broadcast application
[h]Average absorbed dosage of participants (*N*=15) that wore exercise-suits and performed a 20 min structured activity on carpet about 3 h after broadcast spraying
[i]R.L. Williams. Unpublished Masters thesis: determinants of indoor human exposure to cyfluthrin following a structured activity program. University of California, Riverside, 2000
[j]Average amount of chlorpyrifos deposited on foil deposition coupons (*N*=5)
[k]Average amount of residue transferred from carpet to cotton cloth (*N*=3) that was pressed with a CDFA roller about 24 h following a broadcast application
[l]Average absorbed dosage of participants (*N*=7) that wore exercise-suits and performed a 20 min structured activity on carpet about 24 h following a broadcast application

## CONCLUSIONS

Models are not an adequate substitute for experimental evaluation of critical components of exposure assessment models and reference biochemical exposure indices to important indoor environmental data, which are determinants of exposure for risk assessment, risk management, and risk communication. The ambitious tasks listed in Table 4 are likely to contribute to improved and innovative exposure assessments of residents who use indoor pesticides.

The need for accurate and responsible residential exposure assessments remains. Ott and Roberts (1998) in a review, suggested, 'Armed with a better understanding of toxic substances found in common products and in other sources at home, people could then make their own informed choice.' It is easy to concur with the goal of their concluding statement, but public understanding remains poor. In part, the difficulties result from the regulatory practice of designating and listing chemicals as *toxic substances*. The vast majority of human chemical exposures are doubtless too small to measure and far too small to have adverse consequences. Residential chemical exposures of greater extent and magnitude should be better studied.

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