Analysis of Environmental and Biologic Methyl Parathion Data to Improve Future Data Collection

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The Agency for Toxic Substances and Disease Registry analyzed concurrently collected data on environmental methyl parathion (MP) and urinary *p*-nitrophenol (PNP) at the request of the U.S. Environmental Protection Agency (U.S. EPA). The purpose of the analysis was to assess whether individuals' age or level of residential MP contamination might predict their urinary PNP level. Unlicensed pesticide applicators had sprayed residences in Mississippi with MP, which is approved as a pesticide only for outdoor agricultural use. Data were received from Mississippi for MP wipe sample levels for 409 homes and urinary PNP levels for 929 residents of the residences sampled. In addition to descriptive and bivariate analyses, ordinal logistic regression was performed after categorizing the data. Interpretation of results was limited by several identified data gaps and pre-existing data-quality issues. On the basis of the lessons learned from identified data gaps, specific recommendations were made to the U.S. EPA for improving future data collection methods for more meaningful exposure assessment in similar environmental contaminations. The recommended changes were successfully incorporated in subsequent data collected by other states that had experienced similar residential MP spraying. ***Key words:*** **biologic and environmental data, correlation analysis, methyl parathion.** ***Environ Health Perspect*** **110(suppl 6):1071–1074 (2002).** ***http://ehpnet1.niehs.nih.gov/docs/2002/suppl-6/1071-1074imtiaz/abstract.html***

In 1996, two unlicensed pesticide applicators sprayed approximately 5,000 homes and businesses in Mississippi with varying concentrations of methyl parathion (MP), an organophosphate pesticide that was approved for outdoor, non-food-crop applications only. The Mississippi State Department of Health (MSDH) and the Agency for Toxic Substances and Disease Registry (ATSDR) conducted a mass public education campaign to make area residents aware of the potential adverse health effects of exposure to MP and to encourage them to call a hotline if they experienced any of the signs and symptoms of MP toxicity. After the campaign, a large number of residents called to report symptoms of severe headaches, vomiting, diarrhea, and respiratory problems (Brackin 2001), which were consistent with health effects caused by organophosphate pesticide toxicity.

Because of the misapplication of the pesticide and the adverse health effects noted in people who lived in the residences that had been sprayed, the U.S. Environmental Protection Agency (U.S. EPA) determined that some residents should be relocated until their homes could be decontaminated.

By January 1997, 1,270 persons (420 of whom were children) had been relocated, and environmental samples were collected from approximately 1,100 buildings (93% of which were private residences). Approximately 50% of the residences tested had MP levels warranting decontamination according to existing guidelines (Clark MJ, unpublished data). Urine samples were obtained from 1,300 individuals and analyzed for *p*-nitrophenol (PNP), a metabolite of MP, at the National Center for Environmental Health, Centers for Disease Control and Prevention (CDC), in Atlanta, Georgia (Barr et al. unpublished data.).

In February 1997, at the request of U.S. EPA Region 4, the ATSDR Division of Health Studies agreed to analyze environmental MP and urinary PNP data that had been collected concurrently (but in a nonsystematic manner) in Mississippi to determine the extent of the relationship between an individual's age and urinary PNP level and the MP level in the individual's residence. The purpose of the analysis was to evaluate whether an individual's age and the level of environmental MP found in the residence could accurately predict his/her urinary PNP level. The environmental MP data were collected by U.S. EPA for remediation purposes to identify the most contaminated residential structures, whereas the urinary PNP data were collected by the MSDH to determine individual exposures in residents of the households that were sprayed. ATSDR was not part of the original data collection by either the U.S. EPA or MSDH. Also, at the time of data collection, any future possible use of the data sets (other than for agency purposes stated above) was not considered. Data were not collected to test any study hypotheses.

Methods

Data files and data conversions. ATSDR received two data files from MSDH. The first file contained environmental wipe sampling data for MP from 409 households. The second contained information on urinary PNP levels for 929 individuals living, at the time of urine sampling, in the 409 households sampled. Unique identifiers were recorded for households and for urine samples, but personal identifiers were omitted. After editing the data files for typing and coding errors, the two data sets were merged to create one file with one record per individual. Three of the households were deleted from this file because the numbers of children and their ages listed indicated that the locations were day care centers, not residences. The final analysis file included 406 households and 858 residents. The maximum number of individuals with urinary PNP values from the same household included in this analysis was three (five households): 72% of the 406 households contributed one individual urinary PNP to the data set.

Household environmental measures of MP. Environmental sampling for MP was conducted by the U.S. EPA using wet-wipe samples of a 100-cm^2 area of surfaces in several locations within a given household; however, these wipe sample locations were not consistent from house to house. The environmental wipe samples were analyzed for MP by the U.S. EPA using gas chromatography with thermionic-specific detection and mass spectrometry confirmation (Hill et al. 1995).

For analysis, three environmental measures were considered: *a*) The *kitchen composite* consisted of several wipe samples taken in the kitchen in areas other than that of the kitchen sink area; these samples were then analyzed collectively in the lab. The total MP value for the collective sample was then divided by the number of wipe samples taken for that sample to arrive at the kitchen composite measure. *b*) An *arithmetic average* was obtained from all samples from a household (including the kitchen area). *c*) *Sink* was the sampled value of MP in and around the kitchen sink. This measure was considered for analysis because it was thought that the kitchen sink area might represent the most heavily sprayed area in the house. In addition, because most of these

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houses were built for lower socioeconomic communities and had a smaller constructed area, children were likely to crawl around the cooler kitchen sink area. Environmental MP was measured in micrograms per 100 cm^2.

Biologic sampling. Individual, spot urine samples were taken from the residents of the sampled households and analyzed at CDC for PNP levels and adjusted for creatinine levels. We used creatinine-adjusted urinary PNP values in our analysis (microgram per gram creatinine). Information on the time that urine sample was voided and on other individual risk-related behaviors was not available. The urine samples were collected from residents while they were still living in the sprayed houses.

Data Analysis

Descriptive analysis. The distribution of urinary PNP levels, age, and the three environmental values for household MP (average, composite, and sink) were evaluated.

Bivariate analysis. To examine the relationship between age of participant and their urinary PNP levels, age was grouped into six categories and urinary PNP was dichotomized into levels below the detection limit of 25 µg/g and levels above the detection limit (Table 1).

Ordinal logistic regression. Rather than treating urinary PNP levels as a continuous variable and excluding the levels below 25 µg/g, they were categorized into five groups. The first group consisted of urinary PNP levels below the detection limit (<25 µg/g). The next four groups consisted of quartiles of the levels of urinary PNP detected. Table 2 shows these five groups and the relationship between groups of individual urinary PNP levels and levels of average household MP.

Results

Descriptive analysis. Four hundred and twenty-six (49.7%) of the urinary PNP levels were below the detection limit (25 µg/g). Four hundred and thirty-two (50.3%) of the participants had PNP levels ranging from 25 to 1,100 µg/g, with a median of 25 µg/g. Age was not recorded for 84 (9.8%) of the participants. For the remainder, age ranged from 1 month to 96 years, with a mean of 14.7 years and a median of 9 years. Because of issues related to risk, MSDH had targeted younger people and pregnant women for urine testing. Of the participants whose age was known, 82.9% were younger than 20 years. The three environmental measures of household MP were all skewed to the right. The average MP level was the only one of the three measures that was recorded for all 406 households. The kitchen composite MP level was missing for 29 households, and the kitchen sink level was missing for 15 households.

Table 1. Age distribution for participants with urine PNP ≥ 25 µg/g and with urine PNP < 25 µg/g.[a]

Age groups (years)	Urine PNP ≥ 25 µg/g [*n* (%)]	Urine PNP < 25 µg/g [*n* (%)]	Total (%)
0–4	93 (50.5)	91 (49.5)	184
5–9	123 (54.9)	101 (45.1)	224
10–19	122 (52.1)	112 (47.9)	234
20–29	18 (47.4)	20 (52.6)	38
30–44	7 (31.8)	15 (68.2)	22
≥45	33 (45.8)	39 (54.2)	72
Total	396	378	774
Age not recorded[b]	36	48	84

[a]The limit of detection was 25 µg/g of creatinine. [b]Missing ages are not included in the column totals.

Bivariate analysis. For the 396 participants with both a recorded age value and a detected urinary PNP level, a scatter plot of age versus urinary PNP suggested no relationships, as expected. Because the average MP level was available for all households, it was selected as the environmental MP sampling measure for all remaining analyses.

A major drawback of linear regression was the inability to use the nondetectable levels that made up nearly half the urinary PNP data. An analytic approach that retained these data was needed; hence, ordinal logistic regression was used.

Ordinal logistic regression. Table 2 shows the distribution of the individuals with urinary PNP levels below detection limits across quartiles of average MP levels; 37.3% of these nondetectable urinary PNP levels are in the first quartile of average MP levels, and only 17.8% of the nondetectable values were in the highest average MP quartile. The three middle groups of urinary PNP, which represent the first three quartiles of the detected PNP levels, all exhibit somewhat similar distributions across the levels of average MP, with fairly equal weighting. The highest group of urinary PNP levels has only 6.6% in the lowest quartile of average MP. The percentage increases as average MP levels increase, with more than half (50.9%) falling in the highest group of average MP levels.

In fitting the ordinal logistic regression model of the urinary PNP categories, average MP level was statistically significant ($p = 0.0001$). Parameter estimates from the ordinal regression model can be used to predict probabilities of being in a particular urinary PNP group given a particular average MP value. The middle three urinary PNP groups had very similar predicted probabilities, so we decided to fit another model with these three groups collapsed into one. The new groupings, shown in Table 3, revealed the same associations across the rows and columns as did those in Table 2. Once again, the statistics testing ordinal association were positive and significant (chi-square = 101.8, $p < 0.0001$; Spearman's rank correlation = 0.3058, $p < 0.0001$). In fitting this model, average MP level is once again statistically significant ($p = 0.0001$), and the graph of predicted probabilities is easier to interpret because of fewer groups (Figure 1). For example, if an average MP value of 200 µg/100 cm^2 is selected, the model predicts that the probability of being in the nondetected urinary PNP group is about 46%, the probability of being in the middle urinary PNP group is about 41%, and the probability of being in the highest urinary PNP group is 13%. Also, at the average MP value of 545 µg/100 cm^2, there is an equal probability of the urinary PNP level being nondetectable or falling in the highest group (91–1,100 µg/g).

The overall interpretation of the data shown in Figure 1 is that the relationship between average MP and urinary PNP levels is such that the average MP level cannot predict the corresponding urinary PNP level with high probability. Individuals from

Table 2. Groups of urinary PNP by groups of average MP [*n* (%)].

Groups of urinary PNP (µg/g)	Groups of average MP (µg/100 cm^2) 5–28	29–81	82–220	221–1,208	Total
<25	159 (37.3)	110 (25.8)	81 (19.1)	76 (17.8)	426 (100)
25–37	25 (22.7)	30 (27.3)	32 (29.1)	23 (20.9)	110 (100)
38–56	18 (17.0)	26 (24.5)	37 (34.9)	25 (23.6)	106 (100)
57–90	19 (17.3)	25 (22.7)	36 (32.7)	30 (27.3)	110 (100)
91–1,100	7 (6.6)	12 (11.3)	33 (31.2)	54 (50.9)	106 (100)
Total	228	203	219	208	858

Table 3. Groups of urinary PNP (collapsed) by groups of average MP [*n* (%)].

Groups of urinary PNP (µg/g)	Groups of average MP (µg/100 cm^2) 5–28	29–81	82–220	221–1,208	Total
<25	159 (37.3)	110 (25.8)	81 (19.1)	76 (17.8)	426 (100)
25–90	62 (19.0)	81 (24.8)	105 (32.3)	78 (23.9)	326 (100)
91–1,100	7 (6.6)	12 (11.3)	33 (31.2)	54 (50.9)	106 (100)
Total	228	203	219	208	858

households with any level of average MP have a reasonable probability of being in any of the three urinary PNP groups. A high average household MP value (>1,000) does indicate that a participant is more likely to be in the highest urinary PNP group, but it is still reasonable (probability = 10%) that the participant could be in the group having a nondetectable urinary PNP level.

Data Limitations

- Quality assurance and quality control procedures related to data collection and entry were questionable. For example, how was a household defined? Did duplicate ages on discrete urine samples within the same household represent twins, two families sharing a dwelling, or multiple urine samples from the same individual?
- Environmental sampling was not based on residents' exposure patterns but rather on finding the highest contamination level for cleanup purposes according to the U.S. EPA mandate.
- There did not appear to be a standard format for collecting environmental samples from similar sites within each household.
- The methods of deriving the values for the kitchen composite and household average MP samples were not clearly defined and appeared inconsistent.
- Frequency and duration of individual exposures were not documented, especially relative to household areas that were sampled.
- There was no information on multiple exposures for children attending day care centers and living in houses that had both been sprayed.

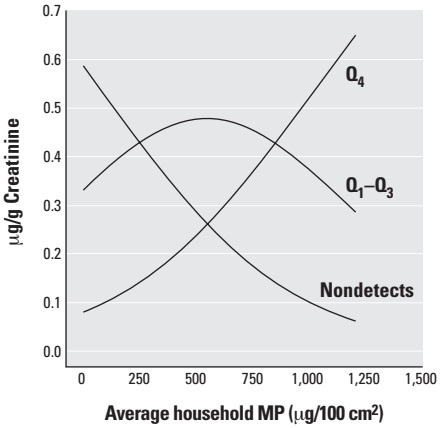

Figure 1. Predicted probabilities for urinary PNP groups by average MP levels using ordinal logistic regression. Urinary PNP values are creatinine adjusted and reported as micrograms per gram of creatinine. Urinary PNP values were divided into three groups: all values below the detection limit of 25 (n = 426); the first three quartiles of all values above the detection limit, Q_1–Q_3 (25–90, n = 326); and the fourth quartile, Q_4 (91–1,100, n = 106).

- Date and time of environmental and urine sample collection were not known.
- Occupational histories were not known.

Discussion

These data were collected by two different agencies for their own distinct purposes to immediately address issues related to urgent public health response. The U.S. EPA collected environmental data to identify structures with the highest levels of contamination to determine which structures would need decontamination. MSDH collected urinary PNP data to identify residents with significant exposures so they could be relocated. The correlation request to ATSDR came much later when the need to identify at-risk residents superseded the need to identify contaminated structures. In addition, the U.S. EPA (requesting agency) expected the analysis to better predict the exposure levels of residents of sprayed dwellings.

Despite the data limitations, the analysis showed some association between urinary PNP values at the low and high ends, and the average MP levels, but the association was not significant for the middle groups where relocation was an issue. It was felt that for any meaningful predictive correlation to exist between urinary PNP values and household wipe samples for MP, the area that was sampled would have to be the major source of exposure immediately before the collection of the urine samples. This additional information would have permitted the analysis to better define the associations for the middle groups of PNP values and average household MP levels.

The levels of urinary PNP reflect the total exposure from all routes of exposure to MP, environmental PNP, and degradation products of other, similar compounds. PNP has a short half-life in the body, with 100% excretion within 24 hr of dosing (Morgan et al. 1977). If urine PNP is elevated, this may indicate numerous recent contacts with MP (and other, similar compounds that were not tested for in this investigation) from different sources, and this may confound interpretation of the data. Low urine PNP levels may indicate either low exposure before urine collection or urine collection well after (>12 hr) exposure, but it does not exclude past exposure or the risk of future exposures from existing household contamination.

The analysis presented here provided useful information to the requesting agency despite several data limitations, including the absence of detectable levels of PNP in almost half the urine samples that were available (this was overcome by grouping data for ordinal regression, as detailed in "Methods"). The identification and communication of data limitations to the U.S. EPA and the MSDH made this analysis worthwhile. It clearly pointed out the gaps that exist between knowledge, public health policy, and practice (application of available knowledge). Natural experiments such as this massive misapplication provide us with a unique opportunity to review public health practice. The opportunity to work on these two large but disconnected data sets revealed critical issues related to the collection of exposure data. Key public health policy decisions such as relocation criteria were initially based on these exposure data. Provision of additional information such as concurrent measures of environmental PNP, air sampling, behavioral information of residents before giving urine samples, and indoor breakdown rates for environmental MP would have led to much better correlations and predictive probabilities.

This experience also underscores the importance of bridging the gap between ongoing environmental research in academic settings and public health policy at various levels of the government (regulators). Although improved exposure assessment methods have since been developed for pesticide exposures (Adgate et al. 2000, 2001), they are not necessarily incorporated and translated into public health practice. After this analysis and discussions with involved agencies, ATSDR organized a workshop with invited experts from various academic and government institutions to address this major issue (ATSDR, 1997).

The results of this analysis helped to bring data quality and planning issues to the forefront, and as indoor MP spraying was later identified in Chicago, Tennessee, Alabama, and Louisiana, standard changes were made by all concerned agencies and state health departments to improve data collection.

Recommendations

- The results of this data analysis must be interpreted and applied with reservation because of the data limitations listed previously.
- Similar future investigations may benefit by clearly defining the objectives of data uses before collection. A protocol for the collection of environmental and biologic samples and individual exposure-related behavioral information should then be designed with the coordinated input from all concerned agencies before data collection begins.
- Individual information that may help define personal exposure (and therefore strengthen analysis) needs to be collected through standard questionnaires. Examples of such information include occupation of adult residents, time of use of sampled household areas, other sources of exposures, and gender.

Testing should be done to identify all exposures from similar compounds and

breakdown products in the environment that may affect biomonitoring results. For example, in the case of this analysis, it would have helped to have concurrent measures of environmental PNP that could also have been excreted in the urine of tested residents but has minimal biologic activity. Correction for environmental PNP, if available, might have improved the association between the levels of average household MP and urinary PNP.

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