Introduction—The Methyl Parathion Story: A Chronicle of Misuse and Preventable Human Exposure

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In the fall of 1994, Lorain County, Ohio, became the site of the first investigation of several large-scale incidences in which the organophosphate pesticide methyl parathion was illegally applied to private residences. The extent of potential human exposure to this pesticide led the Ohio Department of Health to formally request technical assistance from the Centers for Disease Control and Prevention (CDC). This article describes the initial investigation of 64 homes in Ohio and introduces the method of using both biological markers of exposure (*p*-nitrophenol levels in human urine samples) and environmental markers of contamination in dust and air samples when making public health decisions about the cleanup of homes sprayed with methyl parathion. The results of the CDC rapid investigation led the U.S. Environmental Protection Agency to declare the contaminated homes in Lorain County a Superfund cleanup site. Seven years after the Lorain incident, and after subsequent Superfund actions had been implemented in Illinois and Mississippi, researchers participated in an expanded session devoted to methyl parathion at the 11th Annual Meeting of the International Society of Exposure Analysis held in Charleston, South Carolina, in the fall of 2001. The articles included in this monograph are based on presentations at that meeting. They report previously unpublished data that tell the methyl parathion story from different perspectives, each providing in-depth information about separate aspects of this multistate, multiagency, and multimillion dollar chemical exposure. This monograph is the methyl parathion story. *Key words:* methyl parathion, pesticide, *p*-nitrophenol, organophosphate. *Environ Health Perspect* 110(suppl 6):1037–1040 (2002).

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In the late 1980s, an elderly man in Lorain County, Ohio, provided low-cost pest control treatment for people who lived in roach-infested homes. Stories of the success of his service spread from one satisfied customer to another, and during a 5- to 7-year period, he applied pesticide chemicals to hundreds of homes. The applicator gave inconsistent verbal instructions about when residents should return to their homes, and he did not leave any written information about the chemical that he had sprayed. In the fall of 1994, a Lorain County resident contacted the Ohio Department of Agriculture (ODA) about a persistent chemical odor that had forced his family to move out of their home after pest control treatment. The ODA technicians sampled the home and identified the pesticide methyl parathion in dust wipe samples. In late November, ODA notified the Ohio Department of Health (ODH) that an organophosphate licensed only for agricultural application had apparently been used in a Lorain County home. State and county officials went to the home of the applicator and found large quantities of highly concentrated methyl parathion. The extent of potential human exposure to this pesticide led ODH to formally request technical assistance from the Centers for Disease Control and Prevention (CDC). This article describes the initial investigation in Ohio and supports the importance of using both biological markers of exposure (*1,2*) and environmental markers of contamination (*3*) when making public health decisions about the cleanup of methyl parathion-sprayed homes.

The results of the CDC rapid investigation led the U.S. Environmental Protection Agency (U.S. EPA) to declare the contaminated homes in Lorain County as a Superfund cleanup site. During the multiyear evaluation and remediation of the homes, CDC conducted a study of health effects among residents (*4*) as well as a case–control investigation of the potential relationship between unexplained infant death and residential exposure to methyl parathion (*5*). Unfortunately, this apparently isolated incident in Ohio turned out to be the first of several contamination sites. Even before the cleanup in Lorain County was completed, reports of residential exposure to methyl parathion surfaced in Illinois and Mississippi. In an effort to reassess cleanup criteria and actions, the Agency for Toxic Substances and Disease Registry (ATSDR) convened an expert review panel (Appendix 1) and began a follow-up study of neurological health effects among children exposed to methyl parathion (*6*).

The response to this widespread illegal use of the pesticide methyl parathion in residential dwellings eventually involved dozens of local, state, and federal agencies collaborating in ascertaining exposure, adverse health effects, and remediation steps for thousands of people who were inadvertently exposed to this highly toxic chemical. Ultimately, this misuse of methyl parathion can be viewed as a tragic natural experiment; it is important that we use the circumstances to learn as much as possible about the relationship between human health and nonoccupational exposure to organophosphate pesticides. The articles included in this monograph tell the methyl parathion story from different perspectives, each elucidating separate aspects of this multistate, multiagency, and multimillion dollar chemical exposure.

Methyl Parathion: What We Knew About the Chemical in 1994

Methyl parathion is an organophosphate pesticide intended only for outdoor use and is classified in U.S. EPA Toxicity Category I (i.e., most toxic). Methyl parathion is used primarily on field crops such as cotton. When used according to the manufacturer's directions, the chemical is degraded by water, sunlight, and bacteria found in soil and water, and workers can re-enter a treated field 2 days after aerial application (*7*). In 1994 only one company manufactured methyl parathion, and its product was not formulated to include a dye or olfactory agent that would discourage illegal indoor use. Isolated incidents of human exposure that resulted in severe illness and death occurred when small amounts of occupationally formulated methyl parathion were taken from the workplace for personal use (*8,9*). However, these exposure case reports were considered unique (e.g., involved very confined space, direct contamination of drinking water supply) rather than representative of how the chemical might be predicted to behave in a typical indoor setting. Several deaths were also attributed to intentional ingestion (*10*).

This article is part of the monograph *The Methyl Parathion Story: A Chronicle of Misuse and Preventable Human Exposure.*

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In 1994, when the first Lorain County home was identified as contaminated, we suspected that such indoor application would result in a slower but predictable series of degradation steps of the organophosphate. Methyl parathion is metabolized to methyl paraoxon, then detoxified to dimethyl phosphate and *p*-nitrophenol (PNP). The latter metabolite often produces a characteristic yellow stain on indoor surfaces such as wallboard and carpets where the parent chemical has been directly applied. The PNP metabolite is excreted in urine, and detection of PNP in urine is considered evidence of recent human exposure. Investigators assumed that the first identified home represented the most recent spraying and the worst exposure scenario. It was anticipated that homes sprayed in previous months or years might exhibit some PNP staining but that the pesticide itself would not be detected, nor would PNP be found in urine samples collected from residents.

Immediate Response to the Lorain County Discovery

When ODA and ODH investigators went to the home of the unlicensed Lorain County pesticide applicator, they found large amounts of methyl parathion in a basement area that appeared to be the site for the mixing and storing of the chemical, which had been purchased in bulk quantities. Apparently, the applicator did not use standard protocols for dilution nor did he report using consistent dilution techniques. Although there were no systematic records available, the investigators did recover scraps of papers that recorded some client names and application dates. This evidence suggested the potential for more widespread human exposure and prompted ODH to request technical assistance from the National Center for Environmental Health (NCEH) at CDC. The day after the applicator's home was visited, an epidemiologist and a laboratory scientist from CDC joined city (Lorain and Elyria) and county (Lorain) public health officials in assembling a list of potentially exposed people. A hotline was established, and public service announcements were distributed via newspaper, radio, and television, and through local religious organizations. Within days, almost 200 residents reported having contracted the services of the unlicensed applicator. Initial interviews determined that the applicator had used varying spray protocols, including spraying into heating ducts, spraying dishes in kitchen cabinets, and spraying childrens' beds and play areas. Teams from the local health departments and CDC visited 64 of the homes, concentrating initially on those homes most recently sprayed. In each home, air samples and surface wipe samples were collected to ascertain environmental contamination, and urine samples were collected from residents to evaluate personal exposure.

Before the 1994 Lorain County incident, scientists at NCEH laboratories had developed the methodology to measure various pesticide metabolites in human urine (*11*). The test was extremely sensitive and specific but labor intensive and slow. Because the analysis had been used to define pesticide levels in samples originally collected as part of the Third National Health and Nutrition Examination Survey (NHANES III), there were reference range population values of PNP for comparison with the Lorain County samples (*12*). Levels detected in the reference population varied from 0 to 63 ppb PNP; mean, 1.6 ppb; and median, < 1.0 ppb.

The very first urine sample analyzed from Lorain County revealed a level > 4,000 ppb PNP. The 142 urine samples collected from the first 64 homes ranged from less than the detection limit of 1.0 ppb to > 4,800 ppb. Figure 1 demonstrates the distribution of the reference range samples compared with the Lorain County samples. These bar charts dramatically demonstrate the importance of having baseline data that can be used to provide perspective regarding human exposure that occurs in nonoccupational misuse situations such as that in Lorain County. Although many Lorain County residents had nondetectable PNP levels, Figure 1 shows that a great number of residents exceeded the 16 ppb 99th percentile level reported in the reference population.

As expected, PNP levels in urine of residents exposed in this incident as well as PNP levels in dust wipe and air samples decreased over time (*13*). However, the number of days since the self-reported spray date was not always predictive of urinary PNP level. Figure 2 shows detectable PNP levels measured in people who reported that more than 3 years had passed since their homes were sprayed with methyl parathion. Of the eight urine samples collected from peoples whose homes were sprayed more than 1,080 days previously, six of the samples had detectible PNP levels. During the initial response and analysis, 5 of the 11 people with detectable levels more than a year after their spray date were children less than 5 years of age.

The evidence of unprecedented human exposure to methyl parathion was presented to the U.S. EPA, and the contaminated homes

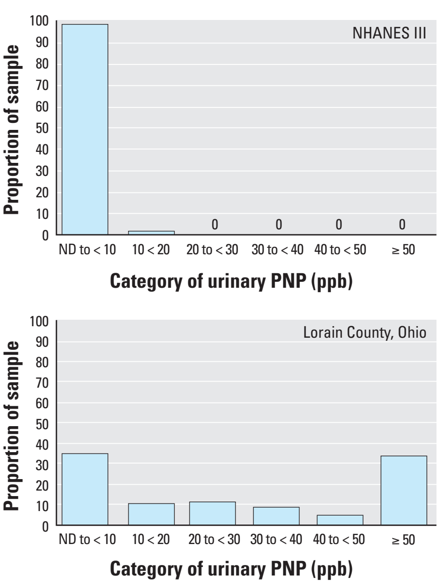

Figure 1. Bar chart depictions of the distribution of PNP levels in parts per billion (ppb) among a reference population of 1,000 adults from whom urine samples had been collected between 1988 and 1994 during the Third National Health and Nutrition Examination Survey (NHANES III) and 142 PNP levels measured in urine samples collected from 64 residents in Lorain County, Ohio, during November 1994. ND, below the limit of detection.

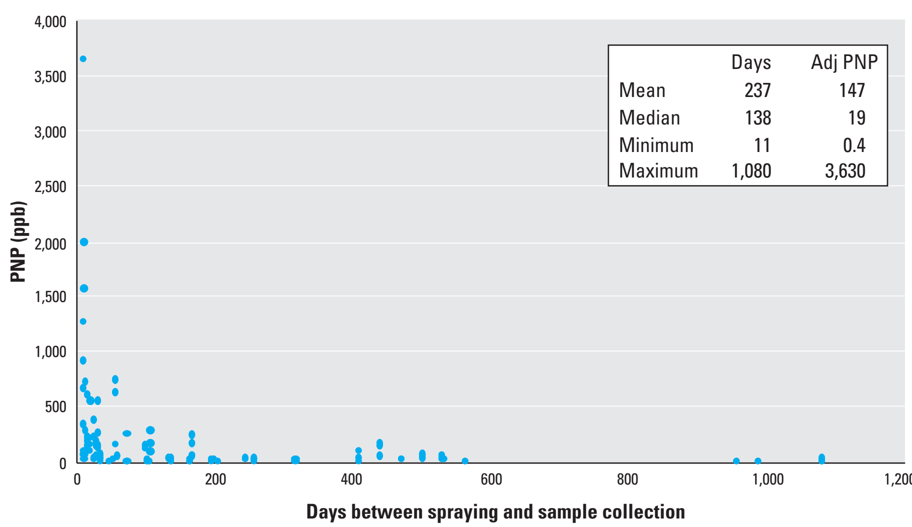

Figure 2. Scatter plot of creatinine-adjusted PNP levels in urine samples collected from the 124 people with a reported spray date and living in Lorain County, Ohio, homes. The levels are plotted by number of days since reported spraying of methyl parathion.

were designated as a Superfund cleanup site in January 1995. As will be discussed later in this monograph (*3*), the cleanup of the homes presented a challenge for all the agencies involved. Many of the homes had to have wallboard, carpeting, and baseboards removed when repeated surface cleaning failed to remove trace amounts of methyl parathion. Residents had to be temporarily relocated, personal items replaced, and transportation to schools and workplaces provided. In early 1995, several units in a large apartment complex in Lorain County were identified as meeting the highest priority criteria for cleanup. This finding required evaluation of the entire complex and suggested the possibility that residents living in units having common walls with contaminated units might also require evacuation and cleanup.

Exposure Extends Beyond Ohio

As the Lorain County work progressed, reports of similar large-scale incidents of residential contamination were beginning to come in from other states, including Illinois, Mississippi, New York, and Arkansas. As the number of potentially contaminated residences grew, the number of dust and air samples and urine samples requiring rapid analyses exceeded the capacity of existing laboratory methods. Preliminary analysis of the initial 64 homes suggested that urine PNP levels were the most sensitive indicator of exposure in vulnerable groups such as children or pregnant women, but existing laboratory methods were too slow to meet the demand placed upon them. Development of new methods became necessary.

By the fall of 1996, the focus had shifted from Ohio to Mississippi, where more than 5,000 homes had been evaluated for methyl parathion contamination; another 1,000 homes in Chicago were evaluated during spring of 1997. Activation of Superfund designates ATSDR as the lead agency for the Department of Health and Human Services, and in the spring of 1997, ATSDR convened an expert panel to review the data and the decisions that had been made in Ohio and Mississippi, with the goal of identifying data gaps and learning from the previous response activities (*14,15*).

Lessons Learned

Within 5 years, the initial case report of persistent and unpleasant chemical odor in a single home became a multimillion dollar cleanup activity with undefined long-term human health ramifications. It is important that the details of the various investigations be recorded and that the scientific data and the decision-making process be presented and reviewed so that we can learn from this experience. As a result of these investigations, methyl parathion is no longer produced in a formula that can be so easily misused indoors. Methyl parathion has been reformulated by adding a stenching agent (*16*), and special valves that permit use only with agricultural sprayers have replaced conventional caps. Bar codes have also been added to permit tracking sale and distribution (*17*). However, methyl parathion is only one

Appendix 1: Methyl Parathion Expert Panel Report*

The Agency for Toxic Substances and Disease Registry (ATSDR) convened an expert panel workshop on 24–25 April 1997 in Atlanta, Georgia, for assistance in addressing key issues of science, public health practices, and risk management related to the indoor use of methyl parathion (MP). Guidance on these issues was essential to the agencies (U.S. EPA, state and local governments, and ATSDR) that were preparing a public health response to the illegal residential spraying. This appendix is a summary of the findings of the expert panel.

Panel members were D.O. Hryhorczuk; C. Chess; J.E. Chambers; L. Claudio; M.A. O'Malley; J. Riviere; V.S. Roth; S. Schuman; and S. Wagner. The opinions and recommendation of the panel were based on a time-limited review of material and data as well as on personal expertise and experience during an ongoing public health response.

The expert panel addressed eight key issues: environmental fate and degradation products of MP in indoor settings, environmental sampling protocols, biomarkers of exposure and effect, correlation of environmental and biological data, susceptible populations, appropriateness of relocation criteria, health education, and risk communication strategies.

The expert panel developed a public health intervention and risk management protocol to manage decisions on whether or not to relocate residents. Investigators can use this protocol to evaluate a combination of environmental sampling data and human biomarker data to make decisions that range from relocation of residents to no further action. The protocol focuses on protecting susceptible populations (pregnant women, infants, children). To ensure protection for residents whose homes were contaminated at levels below those required for relocation, periodic biomonitoring was recommended. Implementation of this protocol led to a more accurate assessment of the public health risks associated with the exposure and a more effective use of resources.

In addition to the protocol for relocation decisions, the expert panel made six recommendations to fill data gaps related to the indoor use of MP.

1) Conduct a 7-day study with concurrent environmental sampling and measurements of daily morning and evening PNP levels. The purpose of this study would be to determine the variability of spot urine samples, the usefulness of individual exposure questionnaire data in selecting optimal sampling times, and the efficacy of adjustment for urinary creatinine.
2) Plan and conduct dermal absorption studies. The expert panel recommended that human volunteer and animal dermal absorption mass balance studies be conducted to correlate MP dermal dose with urine PNP excretion patterns.
3) Conduct a pilot study of urinary PNP and blood red blood cell (RBC) cholinesterase monitoring in a representative sample of MP-exposed residents to determine whether chronic low-dose MP exposure depresses RBC cholinesterase. Experience with occupationally exposed agricultural workers shows that depression of RBC cholinesterase is unlikely to occur at urinary PNP levels < 2 mg/L.
4) Plan a cohort study of the neurobehavioral effects in children exposed to MP *in utero* and in early childhood. In animal studies of MP exposure, neurobehavioral effects were noted. Low levels of xenobiotic-metabolizing enzymes and lower renal clearance rates might make children more sensitive than adults to the effects of MP. In addition, little is known about the normal development of the enzymes involved in neurotransmission or in the degradation of MP and its metabolites.
5) Further study the correlation of environmental and biological data. Correlation of these data has shown only a general association between extent of environmental contamination and urinary PNP and very limited ability of the model to predict urinary PNP. Exposure questionnaires can be developed to n improving the predictive capability of future regression models. Variables representing the selection of appropriate environmental samples and the timing of the urine samples might improve the predictive capability of the models.
6) Integrate education and communication planning with risk management decisions. Recommendations included proactive planning, involvement of communication specialists in policy decision making, and integration of the technical message with the communication.

The expert panel's most important output was to develop the science-based framework for risk management of this large public health emergency. This process and the protocol developed can serve as a model if similar public health emergencies occur. Several of the expert panel's research recommendations have been implemented. Subsequent studies have been conducted to assess the variability of spot urinalysis (recommendation 1), measure dermal absorption (recommendation 2), and examine the neurobehavioral effects in children (recommendation 4).

*Co-authors: S.W. Metcalf and P.S. Wigington, ATSDR of many agricultural chemicals that may be used—either accidentally or intentionally—in situations vulnerable human populations are exposed.

The various locations and dates of the identification of the methyl parathion contamination sites meant that primary investigators and decision makers were almost always different for each new incident and that there was only minimal overlap of personnel dedicated to the investigation. Nonetheless, each exposure event presented similar challenges that required concerted public health action, and the continuous involvement of several federal agencies increased the likelihood that each event was a learning experience. To facilitate the compiling of experience gained from the various incidents, this monograph comprises papers that were presented during an expanded session devoted to methyl parathion at the 11th Annual Meeting of the International Society of Exposure Analysis that was held in Charleston, South Carolina, in the fall of 2001. This monograph brings all the circumstances of each event, including the laboratory data and the health status information, together for the first time.

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