Public Health Decisions: The Laboratory's Role in the Lorain County, Ohio, Investigation

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In 1994 officials from the Ohio Department of Health reported that some residents of Lorain County, Ohio, possibly had been exposed to methyl parathion (MP), a highly toxic restricted-use pesticide. The U.S. Centers for Disease Control and Prevention (CDC) assisted in the investigation by providing epidemiologic and laboratory support to the state and local health departments. Although the initial investigation found MP inside the homes, it was unclear if the residents were exposed. CDC used a new biological monitoring method to measure urinary *p*-nitrophenol (PNP), the metabolite of MP. This biological monitoring measures the internal dose from exposure to toxic chemicals from all routes. Laboratory analyses demonstrated that the urine of residents contained moderate to high levels of PNP, with median, mean, and highest reported concentrations of 28, 240, and 4,800 µg/L, respectively, thus confirming exposure of the residents. Almost 80% of the residents had urinary PNP concentrations above the 95th percentile of the reference range concentrations. This information, combined with other analytical results of air and wipe tests, guided public health officials' decisions about the potential risk in each household. In this article we illustrate the laboratory's role in providing information to assist in making these public health decisions. Furthermore, it illustrates how a multidisciplinary team from various governmental agencies worked together to protect the public's health. *Key words:* biological monitoring, exposure, laboratory, methyl parathion, pesticide, *p*-nitrophenol, public health, reference range concentrations, urinary analyses. *Environ Health Perspect* 110(suppl 6):1057–1059 (2002).

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In late 1994 public health officials in Lorain County, Ohio (near Cleveland), discovered through complaints from some residents that homes had been treated with a highly toxic, dangerous organophosphate pesticide—methyl parathion (MP) (Esteban et al. 1995; Hill et al. 1995a; Clark et al. 1995). This restricted-use pesticide is licensed for outdoor use only on crop cotton, soy beans, and vegetables (ATSDR 1996) and has long been recognized as the cause of occupational exposures and acute poisonings (Arteberry et al. 1961; Durham et al. 1972; Davies et al. 1966; Roan et al. 1969). Outdoor application requires observance of field reentry standards: workers cannot reenter a field for a specific length of time, usually at least 48 hr. Concern existed among the public and pubic health officials, particularly because residents included people who are especially susceptible to adverse health effects from toxic chemicals—young children, expectant mothers, and elderly people (NRC 1993; Ottoboni 1997; Sherman 1988).

Investigation revealed that the pesticide was applied by an unlicensed applicator who provided a relatively inexpensive service to many low-income families who could not otherwise have afforded these pesticide applications. Because his applications were highly effective in eliminating pests, his business rapidly expanded to include approximately 200 homes in Lorain County. In November 1994, in response to a request by state public health officials, the U.S. Centers for Disease Control and Prevention (CDC) sent an epidemiologic team to work with the local and state health departments. The CDC also used its laboratory resources at the National Center for Environmental Health to complement the on-site investigation.

The CDC laboratory specializes in developing and applying biological monitoring methods to analyze samples with state-of-the-art technology. Biological monitoring evaluates exposure to toxic chemicals in the environment or workplace by measuring that chemical or its metabolite in a biologic sample (e.g., blood, serum, urine, tissue) from the people exposed. Biological monitoring methods provide a means of examining the uptake of a toxic chemical that reflects the overall dose from all routes of exposure. In Lorain County, at least three possible routes of exposure existed: through the air (inhalation), through the skin, or through inadvertent ingestion. Some young children could have been exposed by hand-to-mouth activities around MP-contaminated areas. Biological monitoring quantitatively measures concentrations and relates these concentrations to the extent of exposure to the toxic chemical. These methods can be powerful tools in public health or occupational health investigations because they document exposure and estimate the extent of exposure from all routes—the internal dose. Biological monitoring, combined with other environmental measurements such as air or wipe samples, can be used to make public health decisions (Esteban et al. 1996; Clark et al. 1995).

We describe here the laboratory's role as an important team member in providing information for data-driven public health decisions. The Lorain County investigation also is a splendid example of how collaboration among agencies protected the public's health. Although in this article we focus on the laboratory's contribution, the investigation was a multidisciplinary, multiagency effort, and each group complemented the others to produce a result that no one group could have accomplished alone.

Methods

We measured the urinary metabolite of MP, *p*-nitrophenol (PNP), using the method of Hill et al. (1995b), which involved the use of an isotopically labeled internal standard with tandem mass spectrometry, a technique known as isotope dilution. Urine samples were spiked with the carbon-13 internal standard, hydrolyzed with enzyme, extracted, derivatized, concentrated, and finally analyzed using capillary gas chromatography with tandem mass spectrometry. The retention times and selected daughter ions from decomposition of parent ions made this method highly selective and sensitive. All sample runs had blind quality-control samples that met rigid quality criteria, including relative retention time and ion ratios. Quality-control samples were prepared from sterile urine spiked with PNP, aliquoted into small vials, and stored frozen at –78°C. This method was highly selective and sensitive with a detection limit of 1 µg/L (1 ppb) for a 10-mL urine sample.

Results

The early investigation revealed that households had been sprayed with MP, a fact confirmed by air and wipe sampling (Clark et al. 1995). However, because residents did not exhibit symptoms of classic organophosphate pesticide exposure, the exposure to MP was

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questioned. The results of urine samples from Lorain County residents are shown in Table 1.

Reference range concentrations were observed in the general population that had no reported exposure to a given contaminant (Hill et al. 1995c, 1996). Reference range concentrations for PNP (Table 1) were determined from urine samples of a subset from the Third National Health and Nutrition Examination Survey (Hill et al. 1995c). They were analogous with normal clinical values reported for various biomedical measurements in a clinical laboratory, except they were for toxic chemicals or metabolites not naturally found in the body in high concentrations. Additionally, previous reports of PNP concentrations among MP and parathion pesticide workers and among victims of MP and parathion poisonings are shown in Table 1 as yet another basis of comparison. Comparison with the reference range concentrations clearly demonstrates that many residents had been exposed. In fact 78% of the Lorain County residents had urinary PNP concentrations greater than the 95th percentile of the reference range concentrations. One family had PNP concentrations ≥4,000 µg/L, including a child with a urinary concentration of 4,800 µg/L, 1,000 times greater than the 95th percentile. Residents in the upper 5% of this group had PNP concentrations in the same range as observed in occupational pesticide exposures and poisonings. The concerns of the public health officials were validated with these results.

Discussion

Before 1994, laboratories at CDC's National Center for Environmental Health had been actively involved in the forefront of assessing exposures to toxic chemicals using biological monitoring or biomonitoring. A component of this biological monitoring program was to develop a highly sensitive, selective, and accurate method to measure 12 urinary analytes, including PNP, representing potential exposures to 35 pesticides (Hill et al. 1995b). This method was then used to measure the reference range concentrations of these analytes in a subgroup of the general U.S. population (Hill et al. 1995c). When the Lorain County investigation began, the same method was used to measure PNP among the Lorain County residents. PNP is the metabolite of MP and is also the metabolite of ethyl parathion, EPN, and nitrobenzene (Hill et al. 1995c). PNP was selected for monitoring MP exposure for the following reasons: *a*) MP was confirmed to be present, and no other PNP-producing compounds were suspected or found to be present (Esteban et al. 1996); therefore, the urinary PNP observed was due to exposure to MP or to PNP itself as a decomposition product of MP in the household. *b*) Urine samples are relatively easy to acquire, especially in investigations involving children. *c*) Urinary PNP reference values for unexposed people were available to serve as a basis for comparison (Hill et al. 1995c).

The results of the urine analyses demonstrated that concern was valid for the residents, especially the young children and elderly. The urinary PNP analytical results combined with the results of air and wipe samples were used to make important public health decisions (Esteban et al. 1996). On the basis of these results, the homes contaminated with MP were declared a Superfund cleanup site (Esteban et al. 1995). This analytical information was used to make decisions about the priority of cleanup and the time at which the homes needed to be evacuated (Clark et al. 1995; Hill et al. 1996; Esteban et al. 1996). The decision tree used to make these public health decisions were based on the extent of exposure:

- Priority 1: On the basis of exposure information, residents were immediately removed until the home could be decontaminated.
- Priority 2: On the basis of exposure information, decontamination of the home was required, but residents could remain until decontamination began.
- Priority 3: On the basis of exposure information, residents had only low-level exposure and could remain without further assistance.
- Priority 4: No exposure.

Several key elements in the laboratory helped this investigation succeed. In addition, the laboratory adapted its procedures to deal with this special problem as it expanded.

- The laboratory recognized the need to develop biological monitoring methods to assess exposures to a variety of toxic chemicals, including pesticides such as MP. It was prepared to provide assistance for this investigation because it had recently developed a method for 12 analytes, including PNP (Hill et al. 1995b), and was operational at the initial investigation. A quality-control program was already in place for this method, so the reliability of the data could be ensured.
- The laboratory had developed the method with high sensitivity (i.e., 1 µg/L or 1 ppb), so low concentrations of PNP (and other analytes) could be measured. This sensitivity allowed measurement of the urinary PNP concentrations among 86% of the samples collected in Lorain County. Older methods would have detected only about 20% of the PNP concentrations, and results would have been much more difficult to interpret. These older methods did not have the selectivity or sensitivity of the new method and could detect only down to 100 ppb of PNP (Arteberry et al. 1961; Durham et al. 1972; Davies et al. 1966; Roan et al. 1969).
- The laboratory had used this same method to measure and establish reference range concentrations, so a basis of comparison was available to demonstrate that the Lorain County residents had been exposed (Hill et al. 1995c, 1996). The sensitivity of the method allowed meaningful results to be obtained in the reference range study; that is, 41% of the population had measurable PNP concentrations (Hill et al. 1995c). Older methods would not have detected any of these values (detection limit of 100 ppb), and interpretation of the Lorain County results would not have been possible.
- As the investigation progressed, the method for 12 analytes needed to change to meet the demand of the sample load. This method was labor intensive and usually took about a week to produce results. The laboratory used new technology to develop an improved single-analyte method for PNP with greatly increased sample throughput to support the rapid response needed to make public health decisions for the investigation (Barr et al. 2002).

The Lorain County investigation illustrates how biological monitoring played a key role in public health decisions. The availability of sensitive, selective methodology and supporting data for interpretation (reference

Table 1. Urinary *p*-nitrophenol concentrations from Lorain County, Ohio, residents, reference range population, selected occupational pesticide exposures, and poisonings.

Measurements	Lorain County	Reference range	Pesticide workers	Poisonings
Mean	240 µg/L	1.6 µg/L	1,200–1,600 µg/L[a]	10,800 µg/L[b]
			800–900 µg/L[b]	1,000–8,400 µg/L[a]
			4,300 µg/L[b]	40,300 µg/L[b]
			400–12,300 µg/L[c]	
Median	28 µg/L	< 1.0 µg/L		
95th percentile	910 µg/L	16 µg/L		
Highest observed	4,800 µg/L	63 µg/L	8,000 µg/L[a]	22,000 µg/L[b]
			2,400 µg/L[d]	32,200 µg/L[a]
			11,300 µg/L[a]	122,000 µg/L[b]
Detection limit	1 µg/L	1 µg/L	100 µg/L	100 µg/L
Number in group	131	974	7–43[a–d]	9–14[a–c]
% Detection	86	41		

[a]Arteberry et al. (1961). [b]Davies et al. (1966). [c]Roan et al. (1969). [d]Durham et al. (1972).

range concentrations) was essential to the success of the investigation. Biological monitoring is a critical element in evaluating exposures to toxic chemicals and contaminants because it provides direct evidence of exposure and extent of exposure. Biological monitoring will continue to provide information that will allow public health officials to make data-driven decisions. As technology advances, the CDC laboratory will continue to improve its methods, providing even better methods that help assess exposures to toxic chemicals, provide critically needed data for risk assessments, and enable public health officials to more quickly make decisions based on scientific data.

Although the laboratory's contribution was an essential part of this effort, the Lorain County investigation and cleanup succeeded because of the multidisciplinary teamwork approach of many agencies: the Lorain County Department of Health, the Ohio State Department of Health, the CDC, the U.S. Environmental Protection Agency, and the Agency for Toxic Substances and Disease Registry. It required the talents and efforts of epidemiologists, physicians, scientists, laboratory workers, industrial hygienists, field workers, public health officials, and agency leadership. This is a good example of how the public's health and welfare were protected and served by its government.

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