Characterizing Exposures to Nonpersistent Pesticides during Pregnancy and Early Childhood in the National Children’s Study: A Review of Monitoring and Measurement Methodologies

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Pesticide use is widespread in the United States. A billion pounds or more of conventional pesticides are used annually, and 85% of households store at least one pesticide in their homes (Adgate et al. 2000; Kiely et al. 2004). Approximately 78% of conventional pesticide use is for agriculture, 10% is used in the home and garden, and the remainder is for government, commercial building, and industrial use. Recent biologic monitoring studies indicate that pesticide exposures are ubiquitous, including among women of childbearing age, pregnant women, children, and fetuses (Adgate et al. 2001; Barr et al. 2004; Berkowitz et al. 2003; Bradman et al. 2003; Lu et al. 2000; Whyatt and Barr 2001; Whyatt et al. 2003). To test the hypothesis that exposures to nonpersistent pesticides in utero and postnatally increase the risk of neurobehavioral and cognitive exams during infancy and early childhood. Characterization of exposures will be challenging. Nonpersistent pesticides include many chemicals with biologic half-lives on the order of hours or days. Exposures can occur through multiple pathways (e.g., food and residential or agriculture pesticide use) and by multiple routes (inhalation, ingestion, dermal). Effects may depend on the developmental stage when exposure occurs. Sequential sampling is likely to be required and may involve a combination of environmental and biologic monitoring as well as collection of questionnaire data. In this article we review measurements that can be used to characterize exposures. These include biologic markers, personal and indoor air sampling techniques, collection of dust, surface and dermal wipe samples, and dietary assessment tools. Criteria for sample selection will necessitate evaluation of the time frame of exposure captured by the measurement in relation to critical windows of susceptibility, the cost and validity of the measurements, participant burden, and variability in exposure routes across populations and at different age periods. Key words: biomonitoring, early childhood, environment, exposure assessment, in utero, National Children’s Study, pesticides. Environ Health Perspect 113:1092–1099 (2005). doi:10.1289/ehp.7769 available via http://dx.doi.org/[Online 12 May 2005]

Exposure assessment will be challenging. Nonpersistent pesticides do not accumulate in the body and are generally excreted within hours and days, often via water-soluble metabolites in urine. Biologic exposure markers tend to reflect low-level, transient exposures that are highly variable. Further, the pesticides often degrade rapidly in the ambient environment. Although persistence in the indoor environment appears longer (Gurunathan et al. 1998; Lewis et al. 1994; Whyatt et al. 2004a), indoor levels can be highly variable depending on use patterns. Pesticide exposures can also vary by season (Berkowitz et al. 2003; Whyatt et al. 2003), and exposures can occur through multiple pathways and routes. Diet may be a significant source for some children (Clayton et al. 2003). Dermal exposure and non-intentional ingestion as well as inhalation may all be important routes for pesticides used in the home (Clayton et al. 2003; Fenske et al. 1990; Gurunathan et al. 1998; Lewis et al. 1994; Pang et al. 2002; Whitmore et al. 1994; Whyatt et al. 2003). In addition, effects of the pesticides may depend on the developmental stage when exposure occurs (Slootkin 1999). Experimental data for OPs indicate that the developing brain could be vulnerable to exposures from early embryonic life into childhood (Eskenazi et al. 1999; Garcia et al. 2003; Slootkin 1999). Thus, sampling to characterize exposure will need to be intensive and multimedia and will require repeat assessments during pregnancy and early childhood. A combination of environmental and biologic monitoring, as well as collection of questionnaire data, will likely be involved.

Tables 1 and 2 present the sampling framework proposed by the Exposure to Chemical Agents Working Group of the NCS for assessing exposures to nonpersistent pesticides. Details on the NCS and the role of the Exposure to Chemical Agents Work Group are provided in the accompanying article by Needham et al. (2005). A review of monitoring and measurement methods for assessing pesticide exposure is detailed below. Barr et al. (2005a) provide an additional overview of biologic monitoring. 

Biologic Monitoring

Biomonitoring has the advantage over environmental monitoring of providing integrating dosimeters summing exposures from all routes and may more accurately reflect the dose to the target tissue. However, biologic half-lives of nonpersistent pesticides are short, and thus, biomarkers generally provide only...
transient dosimeters. Therefore, repeat sampling designs will be necessary to characterize exposure.

**Urinary monitoring.** The measurement of pesticide metabolites in urine offers advantages over other potential exposure biomarkers. Urine is easy and noninvasive to collect, and laboratory methods are available to measure many different pesticide- and class-specific metabolites. Collection from adults is straightforward, and pediatric urine bags can be used with very young children. In one study approximately 90% of 6-month-old infants provided samples during assessments (Fenske et al. 2005). However, urine is an unregulated body fluid and varies from void to void in volume and in the concentration of endogenous and exogenous chemicals (Barr et al. 2005b; Wessels et al. 2003). This may not be true for very young children (e.g., < 12 months) because they feed and urinate frequently, but variability in urinary dilution has not been evaluated for this age group. Creatinine adjustment of urinary metabolites has been the standard method for accounting for urine dilution. However, urinary creatinine levels vary by age, sex, race/ethnicity, and body mass index (Barr et al. 2005b). Adjustments of urinary pesticide levels by creatinine may not be appropriate, therefore, in pregnant women and children. A recent study suggests that for multiple regression analyses in health outcome studies, the analyte concentration unadjusted for creatinine should be included in the model, with urinary creatinine added as a separate independent variable (Barr et al. 2005b).

Spot urine samples are easiest to collect, but no studies have assessed whether single or serial spot urine samples can be used to classify daily or chronic pesticide exposures. Several recent studies indicate that pesticide metabolites in children’s spot urine samples exhibit high intrindividual variability (Adgate et al. 2001; Koch et al. 2002). In addition, analyses have not been conducted to evaluate whether 24-hr urine samples can be used to classify chronic exposures. It is important to note that a number of urinary validation studies are under way and should be published within the next 2 years. One recent study suggests that first morning void samples may more accurately represent total daily exposure (Kissel et al. 2005). Existing literature evaluating spot versus 24-hr urine samples for nutrients, renal function measures, and some toxicants is mixed (Boeniger et al. 1993; Chitalia et al. 2001; Evans et al. 2000; Hinwood et al. 2002; Kawakami et al. 1982; Kieler et al. 2003; Lee et al. 1996; Luft et al. 1983; Neirhardt et al. 2002; Tsai et al. 1991; Woods et al. 1998).

An additional concern that has recently been raised about urinary biomarkers is that the metabolites in urine may reflect exposure to the metabolites themselves in the environment rather than to the parent compound (Duggan et al. 2003; Wilson et al. 2003). For example, 3,5,6-trichloro-2-pyridinol (TCPy), the specific metabolite for chlorpyrifos, and several dialkyl phosphates, the class-specific metabolites for many OPs, have been found in food samples (Lu et al. 2005; Wilson et al. 2003).

**Blood monitoring.** Blood monitoring has advantages over urinary measurements in that the parent compound, instead of a metabolite, can be directly monitored (Barr et al. 2002). Pesticide concentrations in blood may more accurately reflect the absorbed dose and the dose available to the target tissue because the measured dose has not yet been eliminated from the body. Whyatt et al. (2004b) recently showed a significant inverse association between chlorpyrifos levels in umbilical cord blood and both birth weight and length, whereas no association was seen between chlorpyrifos in maternal personal air samples measured during pregnancy and either parameter of fetal growth. These results suggest that the biomarker may better reflect exposure from all routes and the amount of insecticides absorbed by the mother as well as the amount of the absorbed dose that has been transferred to the developing fetus (Fenske et al. 2005). Further, unlike urinary levels, no corrections for dilution are necessary when quantifying contaminant levels in blood (Barr et al. 2002). Additionally, it has recently been hypothesized that blood levels may provide a better dosimeter than urinary levels for steady-state exposures (Needham 2005). However, this hypothesis has yet to be validated. The Centers for Disease Control and Prevention (CDC) has developed a sensitive and accurate analytical method for quantifying 29 contemporary-use pesticides in human serum or plasma (Barr et al. 2002). However, laboratory methods are not available for many OPs and other pesticides in blood, including many without specific- or class-specific metabolites in urine. Finally, blood is invasive to collect, although collection can be timed to coincide with medically scheduled blood collections, such as during the pregnancy glucose tolerance test (at 26 weeks gestational age), delivery, and during 12- and 24-month lead screens (Eskenazi et al. 2003; Fenske et al. 2005).

**Other biologic monitoring.** Laboratory methods are also under development for pesticides in saliva, meconium, and amniotic fluid, although validated methods are available for only a few compounds. Pesticides in saliva should reflect blood plasma levels (depending on the protein-binding capacity) and therefore recent exposure (Lu et al. 1997, 1998). Current saliva collection methods, which use a cotton sponge, could pose a choking hazard to very young children. Meconium, the first bowel void of the newborn, is a concentrated mixture of swallowed amniotic fluid, cells, bile, and other materials and likely accumulates in the third trimester. Measurement of pesticides in meconium could provide an integrated dosimeter for assessment of fetal exposure in the third trimester (Whyatt and Barr 2001). However, this hypothesis has not been validated. Measurement of pesticide metabolites in amniotic fluid is feasible (Bradman et al. 2003), but amniosentesis poses risks to the fetus and therefore can be conducted only when medically indicated. Thus, population-wide sampling is not possible.

Few data are available on levels of nonpersistent pesticides in breast milk. Many nonpersistent pesticides are soluble in water and therefore may partition to the water fraction of breast milk. Furthermore, the log of the octanol-water coefficient (log $K_{ow}$)—a measure of fat solubility—suggests that some

### Table 1. Recommended preconception, pregnancy, and perinatal sample collection for nonpersistent pesticide analysis.

<table>
<thead>
<tr>
<th>Samples</th>
<th>Preconception</th>
<th>First Trimester</th>
<th>Second Trimester</th>
<th>Third Trimester</th>
<th>Perinatal period</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maternal urine&lt;sup&gt;a&lt;/sup&gt;&lt;b&gt;</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Maternal blood&lt;sup&gt;a&lt;/sup&gt;&lt;b&gt;</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Cord blood&lt;sup&gt;a&lt;/sup&gt;&lt;b&gt;</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Meconium</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Colostrum/breast milk&lt;sup&gt;c&lt;/sup&gt;&lt;sup&gt;e&lt;/sup&gt;</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Maternal saliva&lt;sup&gt;c&lt;/sup&gt;</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Dietary assessment&lt;sup&gt;f&lt;/sup&gt;</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Home/personal air sample&lt;sup&gt;b&lt;/sup&gt;&lt;sup&gt;d&lt;/sup&gt;</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Home composite dust/wipe&lt;sup&gt;b&lt;/sup&gt;&lt;sup&gt;d&lt;/sup&gt;</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Other home samples&lt;sup&gt;b&lt;/sup&gt;&lt;sup&gt;g&lt;/sup&gt;</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Outdoor samples&lt;sup&gt;e&lt;/sup&gt;</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Questionnaire&lt;sup&gt;e&lt;/sup&gt;</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Ecologic analysis (e.g., GIS)&lt;sup&gt;a&lt;/sup&gt;</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
</tbody>
</table>

✓, sample collection recommended.

<sup>a</sup>Metrics that have been used in prior epidemiologic studies. <sup>b</sup>Media with existing laboratory methods for likely target pesticides (e.g., urine, dust, air, food). <sup>c</sup>Blood collection should coincide with glucose tolerance test. <sup>d</sup>Blood collection that is normative for medical care. <sup>e</sup>Blood samples crucial for paraoxonase status and acetylcholinesterase activity. <sup>f</sup>Metrics that are more experimental or costly. <sup>g</sup>Duplicate diet sampling, food frequency questionnaire, or other method (see text). <sup>h</sup>We recommend that air and/or composite dust or wipe samples be collected for each home lived in during pregnancy. Other environmental samples should be considered for special studies of selected participants. <sup>i</sup>For example, clothing dosimeters or hand wipes.
nonpersistent OPs such as malathion (log $K_{ow} = 4.5$) could partition into the lipid fraction of breast milk. Parathion, malathion, fenchlorphos, and chlorpyrifos have been detected in breast milk in studies from central Asia and India (Lederman 1996; Sanghi et al. 2003). Fumonos and diazinon have been detected in cows’ milk or butter fat after acute exposure (Cook and Carson 1985; Spradbery and Tozer 1996). These data suggest that OP and possibly other nonpersistent pesticides may be found in breast milk, although available data are extremely limited. The CDC and the Center for Children’s Environmental Health at the University of California, Berkeley, are conducting a study to develop laboratory methods to measure nonpersistent pesticides in human breast milk. Results for several OPs, carbamates, pyrethroids, phthalates, fungicides, and dicarboximides are promising. Numerous research studies indicate that persistent organic pollutants [e.g., 1,1,1-trichloro-2-(o-chlorophenyl)-2,2-(p-chlorophenyl)ethane (DDE), polychlorinated biphenyls (PCBs), and polybrominated diphenyl ethers] bioaccumulate in fat and are transferred to breast milk, thereby exposing breast-feeding infants (Ladrič et al. 2002).

**Environmental Monitoring**

Measurements of pesticides in environmental media can be used to augment biomonitoring and, additionally, can provide information about routes of exposure. In cases when no biomarker is available, the environmental measure may provide the only dosimeter of exposure. For example, no laboratory methods are available for measuring either the parent compound or chemical-specific metabolite of the OP oximevin methyl in biologic media.

**Air monitoring**. Many pesticides are semivolatile (Lewis 2001; Lewis et al. 2001) and are readily detectable in indoor and personal air samples. These include the OPs and carbamate insecticides; many of the older organochlorine compounds; herbicides such as alachlor, atrazine, 2,4-dichlorophenoxyacetic acid (2,4-D) and dicamba; and several fungicides (e.g., folpet and o-phenylphenol) (Geno et al. 1995; Hau et al. 1988). The pyrethroids are less volatile, and some of the newer insecticides (e.g., abamectin) are basically nonvolatile. Air sampling may thus not be the best protocol for these less volatile compounds; however, both semi- and nonvolatile pesticides can be resuspended into air on particles by human and pet activity (Lewis et al. 2001; Nishioka et al. 1999, 2001). Pesticides can reach indoor air as a result of volatilization off of treated surfaces within the home or from pesticides tracked into the house from outdoor uses or from occupational take-home exposures (Lewis et al. 2001; Lu et al. 2000; Nishioka et al. 2001; Simcox et al. 1995). There have been numerous prior studies of pesticide levels in indoor air (Clayton et al. 2003; Estean et al. 1996; Fenske et al. 1990; Lewis et al. 1994, 2001; Pang et al. 2002; Whitmore et al. 1994) and personal air (Clayton et al. 2003; Whitmore et al. 1994; Whyatt et al. 2002, 2003). Indoor air sampling has been conducted over hours to weeks at flow rates ranging from 0.5 to 4 L/min. Sampler height needs to be considered, as pesticide air concentrations may vary with height, being greatest near the floor after indoor application (Fenske et al. 1991; Lewis et al. 1994). Because of participant burden, personal air samples have generally been collected over shorter time periods (24–48 hr) at the higher flow rates (e.g., 4 L/min). However, a recent study collected 6-day integrated average personal air samples at a flow rate of 1.25 L/min from 74 children in Minnesota (Clayton et al. 2003; Quackenbush et al. 2000). Pesticide detection limits depend on the analytical technique and amount of air sampled but are generally in the low nanogram per cubic meter range (Clayton et al. 2003; Whitmore et al. 1994; Whyatt et al. 2003).

Prior studies have shown that inhalation exposure to semivolatile pesticides in indoor air can be substantial and may be a primary route of exposure after residential use among homes using insecticides (Fenske et al. 1990; Whitmore et al. 1994; Whyatt et al. 2002, 2003). However, for any given pesticide/exposure scenario, the primary route of exposure (inhalation vs. ingestion or dermal) will depend both on use patterns and on the volatility of the pesticides. For example, an aggregate exposure assessment of chlorpyrifos found that inhalation exposures accounted for approximately 85% of total daily dose (Pang et al. 2002). Similarly, results from the U.S. Environmental Protection Agency (EPA) Nonoccupational Pesticide Exposure Study indicate that 85% of the total daily exposure of adults to airborne pesticides is from breathing air inside the home (Whitmore et al. 1994). By contrast, a recent assessment of children’s exposure to chlorpyrifos, diazinon, malathion, and atrazine determined that ingestion rather than inhalation was the dominant route (Clayton et al. 2003). Indoor air pesticides levels have been shown to be considerably higher than outdoor air levels.

**Dust monitoring**. Several researchers have concluded that the majority of household pesticides are better detected by dust sampling than by air sampling (Butte and Heinzow 2002; Fenske et al. 2002b; Roberts et al. 1991; Whitmore et al. 1994). Multiple organic chemicals (both persistent and nonpersistent) can be measured in a single house dust sample, and samples without detectable pesticides are rare. For example, laboratory methods are available for measuring pesticides (both semivolatile and nonvolatile), PCBs and other organochlorine compounds, dioxin, dibenzofurans, polycyclic aromatic hydrocarbons, and phthalates in house dust (Butte and Heinzow 2002; Chuang et al. 1995; Lewis et al. 1999; Moate et al. 2002; Rudel et al. 2003). Studies designed to characterize children’s exposure to pesticides indicate that the largest number of pesticides and the highest concentrations are found in household dust compared with air, soil, and food (Lewis et al. 1994; Simcox et al. 1995). Finally, whereas air levels of semivolatile pesticides decline rapidly after use, residues are more constant in house dust and can still be detected for months or years after use (Lewis et al. 1994; Roinestad et al. 1993; Rudel et al. 2003). Because of hand-to-mouth activities, house dust may be a significant pesticide exposure pathway for young children.

**Table 2. Recommended sample collection for nonpersistent pesticide analysis during early childhood.**

<table>
<thead>
<tr>
<th>Samples</th>
<th>Months</th>
<th>Years</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>3</td>
<td>6</td>
</tr>
<tr>
<td>Uring</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Blood</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Breast milk</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Saliva</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Dietary assessment</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Home air sample</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Home dust or wipe samples</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Other home samples</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Outdoor samples</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Questionnaire✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Ecologic analysis (e.g., GIS)✓</td>
<td>✓</td>
<td>✓</td>
</tr>
</tbody>
</table>

✓: sample collection recommended.

*Metrics that have been used in prior epidemiologic studies.*

*Pediatric urine bag or diaper sample for non-toilet-trained children. If not diaper, spot samples or multiple spots. Methods to measure pesticides in diapers under development.*

*Media with existing laboratory methods for likely target pesticides (e.g., urine, dust, air).*

*Blood collection at young ages should coincide with CDC-recommended lead screen at 12 and 24 months. Ongoing research has also established that blood collection at 4-5 years of age is feasible.*

*Metrics that are more experimental or costly.*

*Choking hazard for saliva.*

*Smaller sample size due to lower concentration.*

*High priority for sample collection.*

*Sample collection more readily available.*

*Sample collection may not be feasible.*

*Sample collection may be dangerous due to potential exposure.*

*Sample collection may not be feasible due to cost.*

*Sample collection may not be feasible due to technical difficulties.*

*Sample collection may not be feasible due to biological limitations.*

*Sample collection may not be feasible due to logistical constraints.*

*Sample collection may not be feasible due to ethical considerations.*

*Sample collection may not be feasible due to legal restrictions.*

*Sample collection may not be feasible due to funding limitations.*

*Sample collection may not be feasible due to equipment limitations.*

*Sample collection may not be feasible due to personnel limitations.*

*Sample collection may not be feasible due to space limitations.*

*Sample collection may not be feasible due to time limitations.*

*Sample collection may not be feasible due to other limitations.*

*Sample collection may not be feasible due to additional limitations.*

*Sample collection may not be feasible due to multiple limitations.*
Most prior studies have collected a sample of house dust from carpets or rugs with the high-volume, small-surface HVS-3 sampler (Cascade Stamp Sampling Systems, Bend, OR) (Lewis et al. 1994; Roberts and Dickey 1995; Simcox et al. 1995). Dust has also been collected using other vacuuming devices (Thompson et al. 2003), and several studies have sampled uncarpeted areas, although dust loading levels are much lower. In all cases, the protocols are labor intensive because they require that the sample be collected by the study team. Studies have also collected dust samples by asking the participants themselves to save the bag from a vacuum cleaner (Roinestad et al. 1993). Colt et al. (1998) compared levels of pesticides and other compounds in dust obtained from used vacuum cleaner bags with those collected by the HVS-3 among 15 homes and found reasonably comparable results. This approach has the advantage of relatively low cost of sample collection. However, disadvantages include the fact that participation is limited to those subjects who own a vacuum cleaner. Further, although the protocol allows determination of contaminant concentrations per gram of dust, pesticide loading (amount of pesticide/floor area) cannot be assessed. A limitation of dust sampling is that the timing of application is not known, and levels in the dust may reflect use months to years before the sampling. Also, dust on hard surfaces may be readily available to transfer to children’s skin and result in nondietary ingestion or dermal exposures, whereas dust lodged deeply in carpets may not be available to children. Carpet dust and dust from other surfaces may function as a reservoir for household pesticide contamination, recontaminating surfaces and air after cleaning depending on the physical and chemical properties (“fugacity”) of the specific compounds. Additionally, studies on the interrelationships of environmental and personal exposures can be difficult to interpret. Wipe samples. Initial attempts to look at direct child exposures have included the use of hand wipes to collect pesticides directly from children’s hands. These methods include wiping the child’s hand with sterile gauze dressing pads that have been moistened with propanol or asking the child to place his/her hand in a bag containing propanol (Bradman et al. 1997; Geno et al. 1996; Lioy et al. 2000). Gordon et al. (1999) found excellent correlations between chlorpyrifos in indoor air and corresponding dermal wipes but poor correlations between chlorpyrifos in dust and dermal wipes. Another study reported a weak association between concentrations of OP pesticides in house dust, loadings in house dust, and concentration on hands, hand surface area, and urinary levels of OP metabolites (Shalat et al. 2003). However, hand loadings of OP pesticides were more strongly associated with urinary OP metabolite levels. This finding suggests that on a cross-sectional basis, pesticides on hands may be more strongly correlated with exposure biomarkers. On a longitudinal basis, however, the dust measure may provide better classification of potential and actual exposure. Dust wipe samples have also been collected using the Edwards and Lioy (EL) press sampler and the Lioy, Wainman, and Weisel (LWW) surface wipe sampler (Lioy et al. 2000). The EL sampler has been designed to collect surface concentrations of dust and pesticides that are representative of those adhering to the human hand (Edwards and Lioy 1999). A significant correlation was seen between chlorpyrifos levels in EL surface and carpet samplers (Lioy et al. 2000). The LWW sampler has been used to obtain dust samples from smooth surfaces in the home (Lioy et al. 2000). A protocol that is currently being validated involves mailing study participants an alcohol wipe with instruction for wiping dust on the top of a specified doorknob. The sample is then placed in a Zipploc bag and mailed back to the study team. Advantages include low cost of sample collection and low participant burden. However, research is currently ongoing to determine detection limits and detection frequencies using this method. Other techniques include use of clothing dosimeters such as cotton gloves, union suits, and socks, as well as alternative surface wipe techniques, to quantify exposures (Fenske 1993; Lewis 2005).

Dietary sampling. Diet is a potentially significant pathway of exposure to pesticides for children (Clayton et al. 2003; Fenske et al. 2002a; National Academy of Sciences 1993). Numerous studies have detected OP and organochlorine insecticides and herbicides in food, including chlorpyrifos, malathion, dichlorodiphenyldichloroethylene (DDE), diazinon, and atrazine (Clayton et al. 2003; MacIntosh et al. 2001; Pang et al. 2002). Market-basket surveys by the U.S. Department of Agriculture (USDA) indicate that most food types contain some pesticide residues (USDA 2002). For example, 65 and 82% of conventionally grown vegetables and fresh fruits tested by the USDA Pesticide Data Program (PDP) from 1994 through 1999 contained one or more pesticide residues (Baker et al. 2002). However, pesticide concentrations vary significantly across foods (Gunderson 1995). Low detection frequencies, combined with highly variable individual diets, make it difficult to estimate individual dietary exposures using food consumption questionnaires (MacIntosh et al. 2001). Instead, studies have generally estimated dietary exposures by measuring pesticides in duplicate diet samples, in which study participants prepare and collect duplicate portions of all foods and beverages consumed (Quackenboss et al. 2000; Wilson et al. 2004). Pesticide exposure assessment for the National Children’s Study

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1,2-dichloropropane, 2,4-D, atrazine, oxamyl have been detected in surface water statewide. Diazinon, dimethoate, chlor- were all below 1%, including bentazon, diazi-

Detection frequencies for other compounds lachlor oxanilic acid (OA) was detected in Simazine was detected in 15% of samples (con-

 limits in the part-per-trillion range; 297 sam-

pounds have been detected in surface and well

waters, available data suggest that contamina-
tion of drinking water by herbicides may
 contribute to chronic exposures in some parts
 of the United States. Although other com-
 pounds have been detected in surface and well
 waters, available data suggest that contamina-
tion is limited to isolated communities or
 households and does not result in population-
wide exposures. Although the core NCS
 hypotheses do not focus on nonpersistent her-
bicides, laboratory methods for measuring
herbicides in biologic samples are available for
future studies of archived material.

**Questionnaire Data and Ecologic Analyses**

It is unlikely that questionnaires alone will
prove adequate data for pesticide exposure
classification (Sexton et al. 2003). However,
questionnaires can provide an important sup-
plement to environmental and biologic moni-
toring. For example, results from ongoing
studies by the Children’s Environmental
Health Centers funded by the U.S. EPA and
National Institute of Environmental Health
Sciences have found that questionnaires are
able to provide information about residential
use habits but are rarely able to obtain more
detailed information on specific chemicals
(Fenske et al. 2005). In preliminary analyses
of questionnaires administered by the Columbia
Center for Children’s Environmental Health,
women provided a pesticide product name for
fewer than half the pest control methods
reported to be used in the home during preg-
nancy and, in particular, were rarely able to
identify the pesticide products used by an
exterminator (Fenske et al. 2005). Further,
pesticide products can have the same brand
name but contain different active ingredients,
and, in particular, were rarely able to
identify the pesticide products used by an
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Discussion
Quantifying exposure to nonpersistent pesticides in the NCS will be challenging (Needham et al. 2005). Exposures are likely to be variable, can occur simultaneously from multiple routes (dietary and nonintentional ingestion, inhalation, and dermal absorption), and can vary dramatically within a particular group or across populations depending on use patterns. These circumstances will require intensive sampling and a repeat-measurement design and will likely necessitate use of a combination of both environmental and biologic monitoring supported by questionnaire information. Özkaynak et al. (2005) provide an overview of the steps necessary in selecting appropriate exposure assessment methods in the NCS. The framework presented in Tables 1 and 2 outlines assessment methods specific for characterizing pesticide exposures for a longitudinal epidemiologic study of neurodevelopmental outcomes in children. Experimental evidence indicates that the window of susceptibility for neurotoxic pesticides is likely during nervous system development (Slotkin 1999). Thus, the prenatal and early postnatal periods are the key critical life stages during which pesticide exposure must be carefully assessed. The initial step in selecting the exposure assessment methods will include an evaluation of whether the exposure at the critical life stage can be reliably estimated using questionnaire data alone or another indirect low-cost, low-burden measure of exposure. In most instances these measurements alone will not provide reliable dosimeters for pesticide exposures and will need to be supplemented by other methods. However, the survey instruments will be useful to assess household information directly related to pesticide exposures, including household practices such as home pesticide use, food consumption trends, address changes, and so forth. Where feasible, GIS and other ecologic methods should be used. At the very least, the latitude and longitude coordinates of each home should be determined for future studies of pesticides or other environmental exposures. It is also important that questionnaires and other indirect exposure measurements be validated against more direct measures (e.g., biologic or environmental monitoring).

In selecting the direct measurements, the researcher must decide whether to collect a biologic or an environmental sample, or some combination of both. Given the complexity of assessing exposure to nonpersistent pesticides, it is likely that both environmental and biologic sampling will be needed for many compounds. It is important to realize, however, that although efforts to assess children’s pesticide exposures have increased dramatically in the last decade, most exposure assessment methods are not fully validated for use in an epidemiologic study. Despite these limitations, a strong case can be made for collecting biologic and environmental samples to characterize children’s exposure for the NCS. Tables 1 and 2 include the primary media we believe should be collected to assess pesticide exposures: a) urine from mothers and children, b) maternal and child blood with blood collection linked to scheduled medical tests, c) cord blood, and d) air and/or house dust or wipe samples. Meconium, breast milk, and saliva should also be collected and stored for future use. Validation studies are currently underway that will provide key information about pesticide exposure assessment methods (Bradman et al. 2003; Fenske et al. 2005; Kieszak et al. 2002; Kissel et al. 2005; Whyatt and Barr 2001; Whyatt et al. 2003). Additionally, several birth cohort studies have successfully used blood and urinary metabolite exposure markers to assess relationships between nonpersistent pesticide exposure and adverse health outcomes in newborns (Berkowitz et al. 2004; Eskenazi et al. 2004b). In some cases the findings of these studies are not consistent. However, these studies have demonstrated the feasibility of collecting environmental and biologic samples, including blood and urine, for large cohort studies. Finally, each project has also stored a variety of samples that will ultimately allow replication of each study and direct assessment of key criteria necessary to judge causal relationships. Planning for the NCS should be forward-looking and include resources to bank a variety of sample types to ensure that new or improved laboratory methods can be applied when they become available. Other exposure assessment methods should be considered for specialized exposure or health outcome studies that involve a subset of participants. These methods could include measuring pesticides in duplicate diet or breast milk samples, or other media (reviewed above). Information from new validation studies should be continuously monitored to improve exposure assessment protocols for this long-term prospective study. For example, exploratory studies of semipermeable membranes that absorb pesticides or wipe and settled dust-sampling techniques may provide less expensive strategies to assess exposure (Roberson et al. 2003). Participant incentives should also be carefully chosen to maintain retention and encourage cooperation. For example, some participants could be provided with vacuum samplers to collect house dust. Participant burden will be a key factor to consider when choosing exposure assessment methods. Initial pilot studies for the NCS should determine what is feasible for participants and tailor protocols to accommodate participant needs. Recent birth cohort studies have implemented protocols approximating the sampling framework presented in Tables 1 and 2. These efforts, however, require intensive staff time to collect the information and samples and to maintain retention. They also require a major time commitment by participants and are logistically challenging, especially when different visit types (e.g., prenatal, delivery, child) with different women are occurring simultaneously.

References


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