Contemporary-Use Pesticides in Personal Air Samples during Pregnancy and Blood Samples at Delivery among Urban Minority Mothers and Newborns

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We have measured 29 pesticides in plasma samples collected at birth between 1998 and 2001 from 230 mother and newborn pairs enrolled in the Columbia Center for Children's Environmental Health prospective cohort study. Our prior research has shown widespread pesticide use during pregnancy among this urban minority cohort from New York City. We also measured eight pesticides in 48-hr personal air samples collected from the mothers during pregnancy. The following seven pesticides were detected in 48–83% of plasma samples (range, 1–270 pg/g): the organophosphates chlorpyrifos and diazinon, the carbamates bendiocarb and 2-isopropoxyphenol (metabolite of propoxur), and the fungicides dicloran, phthalimide (metabolite of folpet and captan), and tetrahydrophthalimide (metabolite of captan and captafol). Maternal and cord plasma levels were similar and, except for phthalimide, were highly correlated ($p < 0.001$). Chlorpyrifos, diazinon, and propoxur were detected in 100% of personal air samples (range, 0.7–6,010 ng/m^3). Diazinon and propoxur levels were significantly higher in the personal air of women reporting use of an exterminator, can sprays, and/or pest bombs during pregnancy compared with women reporting no pesticide use or use of lower toxicity methods only. A significant correlation was seen between personal air level of chlorpyrifos, diazinon, and propoxur and levels of these insecticides or their metabolites in plasma samples (maternal and/or cord, $p < 0.05$). The fungicide *ortho*-phenylphenol was also detected in 100% of air samples but was not measured in plasma. The remaining 22 pesticides were detected in 0–45% of air or plasma samples. Chlorpyrifos, diazinon, propoxur, and bendiocarb levels in air and/or plasma decreased significantly between 1998 and 2001. Findings indicate that pesticide exposures are frequent but decreasing and that the pesticides are readily transferred to the developing fetus during pregnancy.
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Residential pesticide use is widespread in the United States, with approximately 80–90% of American households using pesticides (Landrigan et al. 1999). Contemporary-use pesticides include the organophosphates, carbamates, and pyrethroids, which have replaced the older organochlorines for residential insect control (Landrigan et al. 1999). Commonly detected pesticides in house dust and indoor air of U.S. homes include the organophosphates chlorpyrifos and diazinon, the pyrethroids *cis*-permethrin and *trans*-permethrin, the carbamates propoxur and bendiocarb, and the fungicide/disinfectant *ortho*-phenylphenol (Camann et al. 2000; Lewis et al. 1994; Whitmore et al. 1994). It is likely that indoor levels of chlorpyrifos and diazinon will decline as a result of the recent regulatory action by the U.S. Environmental Protection Agency (U.S. EPA) to phase out their residential uses (U.S. EPA 2000a, 2001). Little is known about residential pesticide exposures among minority populations or about exposures during pregnancy. The lack of data regarding prenatal exposures is of concern because experimental studies have shown a link between exposures to several organophosphates during gestation, or the early postnatal period, and adverse neurodevelopmental sequelae in the offspring (reviewed in Eskenazi et al. 1999). The validation of biomarkers of prenatal pesticide exposure is an important area of research (Whyatt and Barr 2001).

Most prior biomonitoring for contemporary-use pesticides has involved measurements of metabolites in urine. Urinary measures have the advantage over blood measures in that pesticide concentrations in urine are usually orders of magnitude higher than in blood (Barr et al. 2002). Urine is also a plentiful matrix and easy to obtain. Associations between urinary pesticide levels and measures of external exposure have been seen in prior studies of both adults and children (Aprea et al. 2000; Azaroff 1999; Loewenherz et al. 1997; Lu et al. 2001). However, blood measures have advantages over urinary measures in that the parent compound, instead of a metabolite, can be directly monitored (Barr et al. 2002). Further, 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. In addition, no corrections for dilution are necessary when quantifying contaminant levels in blood (Barr et al. 2002).

The U.S. Centers for Disease Control and Prevention (CDC) has developed a sensitive and accurate analytic method for quantifying contemporary-use pesticides in human serum or plasma (Barr et al. 2002). The method has detection limits in the low picogram/gram range and coefficients of variation of typically less than 20% (Barr et al. 2002). We have used the method to measure pesticide levels in plasma samples collected at birth from African-American and Dominican mothers and newborns enrolled in the prospective cohort study being conducted by the Columbia Center for Children's Environmental Health (CCCEH). Our prior data show widespread use of pest control during pregnancy among this minority cohort (Whyatt et al. 2002). Specifically, 266 (85%) of the 314 women questioned reported that some form of pest control was used during pregnancy: 35% reported using an exterminator, and 50% reported using other forms of pest control (Whyatt et al. 2002). The pesticides detected with the greatest frequency in personal air samples collected from the mothers during pregnancy were the organophosphates chlorpyrifos and diazinon, the carbamate propoxur, and the fungicide/disinfectant *ortho*-phenylphenol (Whyatt et al. 2002).

Methods

The women in this study are part of an ongoing prospective cohort study of minority

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mothers and their newborns being conducted by the CCCEH. The CCCEH study was initiated in 1997 to evaluate the effects of prenatal exposures to ambient and indoor pollutants on birth outcomes, neurocognitive development, and procarcinogenic damage among a cohort of mothers and newborns from minority communities in New York City. In 1998, the study began to gather information on prenatal pesticide use in response to growing concerns over the extent of residential insecticide use in New York City (Thier et al. 1998). To date, pesticide levels in personal air samples collected over 48 hr during pregnancy and in blood samples (maternal and/or umbilical cord) collected at delivery have been measured on 230 mother–newborn pairs in the cohort. These 230 mothers and newborns are the subjects of the present study. Study protocols including eligibility requirements and comparability between women who agreed to participate and those who refused have been described in detail previously (Whyatt et al. 2002; Perera et al. 2003). Women were initially recruited into the study during pregnancy through the prenatal clinics at New York Presbyterian and Harlem Hospitals and were considered fully enrolled once the prenatal monitorings and questionnaires had been completed and blood samples (from the mother and/or newborn) had been collected at delivery (Whyatt et al. 2002). The study was restricted to women 18–35 years old who self-identified as African American or Dominican and had resided in northern Manhattan (Central Harlem or Washington Heights/Inwood) or the South Bronx for ≥ 1 year before pregnancy. Women were excluded if they smoked cigarettes or used other tobacco products during pregnancy; used illicit drugs; had diabetes, hypertension, or known HIV infection; or had their first prenatal visit after the 20th week of pregnancy. The study was approved by the Institutional Review Board of Columbia University, and informed consent was obtained from all study subjects.

Questionnaire data. A 45-min questionnaire was administered to each woman in her home by a trained research worker during the third trimester of pregnancy that included information on demographics, home characteristics, lifetime residential history, history of active and passive smoking, occupational history, alcohol and drug use during pregnancy, and history of residential pesticide use. Women were also asked whether any pest control measures were used during pregnancy by an exterminator or by others (the woman, other household member, or the apartment superintendent). If pest control measures were used, women were asked about the following specific types of methods: sticky traps, bait traps, boric acid, gels, spray by an exterminator, can sprays, pest bombs and any other methods (Whyatt et al. 2002). Information on the brand was also collected, if known.

Personal ambient air samples. During pregnancy, women in the cohort were asked to wear a small backpack holding a personal ambient air monitor during the daytime hours for 2 consecutive days and to place the monitor near the bed at night. The personal air sampling pumps operated continuously at 4 L/min over this period, collecting particles of ≤ 2.5 μm in diameter on a precleaned quartz microfiber filter and collecting semivolatile vapors and aerosols on a polyurethane foam cartridge backup. An average of 11.5 m^3 of air was drawn through the sampler. The 230 women who are the subjects of the present study were monitored between September 1998 and May 2001, with all but two women monitored after 1998. The monitoring took place 6.4 ± 3.5 weeks before delivery; 27% of the subjects were monitored within 1 month of delivery.

For quality control, each personal monitoring was coded as to accuracy in flow rate, time, and completeness of documentation. A code of 0–1 indicated no or minor problems; 2, greater concern; and 3, unacceptable and not analyzed. Three samples received a code of 3 and are not included in results presented here. Five of the 230 women had personal air monitoring results with a quality control code of 2; we performed statistical analyses both including and excluding these subjects. Results were essentially unchanged from those we present here for all 230 women.

Within several hours of collection, the air monitoring samples were brought to the molecular epidemiologic laboratory at the Mailman School of Public Health, inventoried, and frozen at approximately –15°C. Once each month, air samples were shipped on ice to Southwest Research Institute and stored at –12°C. Within 10 days of arrival, the polyurethane foam plug and filter were placed in a Soxhlet extractor (Corning, Corning, NY), spiked with terphenyl-d_{14} as a recovery surrogate, and extracted with 6% diethyl ether in hexanes for 16 hr. The extract was then concentrated to 1 mL and frozen at –12°C before analysis. The pesticides are stable under these conditions (Ortiz et al. 2000). The extracts were analyzed in batches during November 1999 (72 samples), August–September 2000 (94 samples), and June–July 2001 (94 samples). The nine pesticides selected for analysis were chosen based on prior results of pesticides found in house dust and indoor air of homes in the United States (Lewis et al. 1994; Whitmore et al. 1994). Pesticides were analyzed by gas chromatography–mass spectrometry essentially as described previously (Whyatt et al. 2002). For some samples, interfering compounds coeluted with the analyte and elevated the detection limit. Results for these samples were flagged. In cases in which the interfering peak raised the detection limit but no analyte was detected, analytic results were considered to be below the limit of detection only if the quantified peak was within 4-fold of the true detection limit for that analyte. If the interfering peak raised the detection limit > 4-fold for that analyte, results were coded as missing. This approach was considered appropriate because the laboratory methodology was adequately sensitive to detect the analyte at 25% of the interference peak in all cases. In cases in which both the analyte and an interfering compound coeluted, the entire peak was quantified and the quantified amount was reduced by 50% to estimate the true analyte amount. This adjustment was made in 30 of 1,821 (1.6%) of the sample results.

Blood samples. A sample of umbilical cord blood was collected as close to delivery as possible by syringing the blood into a heparinized syringe to avoid clotting. A sample of maternal blood was obtained within 2 days postpartum into a heparinized vacutainer tube by the hospital staff. Of the 230 mother–newborn pairs in the present study, blood samples from both the mother and newborn were available for 180 pairs (78%); a maternal blood sample only was available for 19 mothers (8%), and a cord blood sample only for 31 newborns (14%). There was no difference in maternal self-reported pesticide use between mother–newborn pairs with blood samples collected from both the mothers and newborns compared with mother–newborn pairs with blood samples collected from the mother or newborn but not both ($\chi^2 = 0.5$, $p = 0.9$). In total, blood pesticide levels were available for 199 maternal blood samples and 211 umbilical cord blood samples. The deliveries took place between November 1998 and May 2001, with all but one taking place after 1998. Within 12 hr of collection, the cord and maternal blood were transferred to a centrifuge tube and spun for 15 min at 1,500 rpm. The plasma was collected and stored at –70°C before shipment to the CDC on dry ice. At the CDC, the plasma samples were thawed and a 4 g aliquot was taken for analysis. The plasma was spiked with stable isotopically labeled internal standards and then extracted using a mixed-phase Oasis solid-phase extraction cartridge (Waters Corp., Milford, MA). The cartridge was eluted with dichloromethane, and the eluent was dried over anhydrous sodium sulfate. The eluent was concentrated to 10 μL. We analyzed and quantified 1 μL of the concentrated extract using isotope-dilution gas chromatography–high-resolution mass spectrometry. Details on the laboratory assay, including quality control, reproducibility, and limits of detection, have been published previously (Barr et al. 2002).

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Recoveries ranged from 13 to 91%; however, the added isotopically labeled standards were used to internally correct for analyte recoveries in each of the individual samples (Barr et al. 2002). Relative recoveries ranged from 94 to 104%. The 29 pesticides selected for analysis include pesticides used for residential pest control as well as in agriculture (Barr et al. 2002).

Statistical analysis. Before statistical analyses, the range of pesticide concentrations in personal air and plasma samples, median levels, and the percentage of samples with levels above the detection limit were calculated. Arithmetic means and standard deviations (SDs) were additionally calculated for the pesticides detected in > 45% of the air or plasma samples (range, 48–100%). Statistical analyses were restricted to these pesticides. Pesticide levels were log-transformed before statistical analyses to normalize positively skewed distributions. Spearman rank was used to examine correlations between pesticide levels in paired maternal and newborn plasma samples. Spearman rank was also used to examine correlations between pesticide levels in air and plasma samples. Multiple linear regression was used to examine associations between pesticide levels (in air and plasma) and ethnicity and neighborhood of residence. Models of insecticide levels additionally controlled for the level of housing disrepair reported. As described previously, housing disrepair was defined as the total number of adverse indoor housing problems reported by the woman, each indicator being counted as present (1) or absent (0) (Rauh et al. 2002; Whyatt et al. 2002). The indicators were holes in ceilings or walls, peeling or flaking paint, water damage, visible mold, and leaking pipes. Analysis of variance (ANOVA) was used to test whether pesticide levels varied significantly among the following groups: *a*) women not using any pest control methods; *b*) women using nonspray methods only (sticky traps, bait traps, boric acid, and gels); *c*) women using can sprays and pest bombs (with or without nonspray methods); and *d*) women using exterminators (with or without the other methods). If levels differed significantly among the groups, the least significant difference test was used to determine which groups varied significantly. ANOVA was also used to test whether pesticide levels changed significantly by the year of the personal monitoring or birth (from 1999 to 2001) and to test for linearity in the change, if any, over the 3 years. The two women who were monitored or gave birth at the end of 1998 were included in the 1999 group. Because the detection limit for chlorpyrifos and diazinon in plasma samples varied (from 0.5 to 1.5 pg/g plasma) depending on the year that the laboratory analysis was undertaken, the detection limit for these two insecticides was set at one-half the average detection limit over the course of study. ANOVA was also used to test whether pesticide levels varied by season of the personal monitoring or birth. Geometric means are presented showing the differences in pesticide levels among groups (Flanders et al. 1992). Results were considered statistically significant at $p < 0.05$ (two-sided).

Results

Table 1 presents demographics for the 230 women and shows the number of women who reported using pest control measures in the home during pregnancy. Consistent with our prior results (Whyatt et al. 2002), 85% of the women reported using some form of pest control, and 37% reported using an exterminator.

Table 1. Demographics and the number of women using pest control during pregnancy (n = 230).

Age	24.8 ± 5.1
Ethnicity	
African American	103 (45)
Dominican	127 (55)
Community[a]	
Harlem	103 (45)
Washington Heights	78 (34)
South Bronx	48 (21)
Marital status[a]	
Never married	153 (67)
Married[b]	52 (23)
Separated, widowed, divorced	24 (10)
Medical recipient	206 (90)
Education[a]	
< High school	70 (31)
High school diploma or GED	97 (42)
Some college (< 4 years)	51 (22)
College degree (4 year)	11 (5)
Income[a]	
< $10,000	96 (43)
$10,000–30,000	92 (42)
> $30,000	33 (15)
Total number using pest control[a]	193 (85)[a]
By an exterminator only	17 (8)
By exterminator plus others[c]	67 (29)
By others[c] only	109 (48)

Maternal age is reported as mean ± SD; the other items report number of subjects (%) in each category.
[a]Missing values: maternal age (n = 1), community (n = 1), marital status (n = 1), education (n = 1), income (n = 9), pest control (n = 2). [b]Includes women living as married with same partner > 7 years. [c]The woman herself, other household member, or the apartment superintendent.

Table 2. Levels of 29 pesticides and/or their metabolites[a] (pg/g) in maternal plasma samples collected at delivery between 1998 and 2001 from African-American and Dominican women residing in northern Manhattan and the South Bronx (n = 199).

Pesticide	LOD	No. > LOD	Percent	Median	Mean ± SD[b]	Range
Organophosphates						
Chlorpyrifos	0.5–1	148	74	3.1	4.8 ± 5.5	ND–35.0
Diazinon	0.5–1.5	99	50	0.8	1.2 ± 2.1	ND–25.0
Dichlorvos	1–3	4	2	ND	NC	ND–2.4
Fonophos	1	1	0.5	ND	NC	ND–2.7
Malathion	12–40	2	1	ND	NC	ND–24
Methyl parathion	2–10	2	1	ND	NC	ND–5.0
Parathion	1–5	1	0.5	ND	NC	ND–2.5
Phorate	1	0	0	—	—	—
Terbufos	1–5	3	1.5	ND	NC	ND–92.0
Carbamates						
Bendiocarb	5	97	49	ND	4.7 ± 3.6	ND–34.0
Carbofuran	1	89	45	ND	NC	ND–46.6
Carbofuranphenol[a]	1	0	0	—	—	—
1-Naphthol[a]	20	42	21	ND	NC	ND–613
Propoxur	1–2	7	3.5	ND	NC	ND–140
2-Isopropoxyphenol[a]	3	90	45	ND	NC	ND–16.0
Pyrethroids						
trans-Permethrin	1	14	7	ND	NC	ND–27.0
cis-Permethrin	1	20	10	ND	NC	ND–11.4
Herbicides						
Acetochlor	1	17	9	ND	NC	ND–11.2
Alachlor	1	6	3	ND	NC	ND–3.3
Atrazine	1	45	23	ND	NC	ND–13.0
Chlorthal-dimethyl	1	71	36	ND	NC	ND–4.6
Metolachlor	1	9	5	ND	NC	ND–4.7
Trifluralin	1	14	7	ND	NC	ND–5.2
Fungicides						
Chlorothalonil	5–10	28	14	ND	NC	ND–102
Dicloran	1	154	77	2.2	3.1 ± 3.5	ND–29
Metalaxyl	5	20	10	ND	NC	ND–28.0
Phthalimide[a]	20	153	77	25.2	29.2 ± 24.3	ND–270
Tetrahydrophthalimide[a]	1	99	50	ND	2.3 ± 4.5	ND–43.0
Repellant						
Diethyltoluamide	1–10	60	30	ND	NC	ND–21.0

Abbreviations: LOD, limit of detection; NC, not calculated; ND, not detected.
[a]Metabolites measured [corresponding parent compound(s)]: carbofuranphenol (carbofuran/carbosulfan), 2-isopropoxyphenol (propoxur), 1-naphthol (carbaryl/naphthalene), phthalimide (folpet, phosmet, captan), tetrahydrophthalimide (captan/captafol). [b]Calculated if the pesticide was detected in > 45% of samples; levels in samples without detections were set at one-half of the detection limit.

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Tables 2 and 3 present levels of the 29 pesticides in maternal and umbilical cord plasma samples. Seven pesticides were detected in > 45% of samples (range, 48–83%). These were the organophosphates chlorpyrifos and diazinon, the carbamates bendiocarb and 2-isopropoxyphenol (metabolite of propoxur) and the fungicides dicloran, phthalimide (metabolite of the fungicides folpet and captan, as well as the organophosphate phosmet), and tetrahydrophthalimide (metabolite of the fungicides captan and captafol). Table 4 shows the correlation between levels of these seven pesticides in paired maternal and cord plasma samples. Paired levels were similar and, except for phthalimide, were significantly correlated ($p < 0.001$).

Table 5 presents levels of nine pesticides measured in personal air samples collected from the mothers over 48 hr during the third trimester of pregnancy. Eight of these pesticides were also measured in plasma samples. Chlorpyrifos, diazinon, and propoxur were detected in 100% of air samples. In addition, the fungicide/disinfectant *ortho*-phenylphenol was measured in a subset of air samples ($n = 140$) but was not measured in plasma samples. It was detected in 100% of air samples. The remaining five pesticides were detected in < 30% of personal air samples.

Table 6 shows the correlation between levels of chlorpyrifos, diazinon, and propoxur in maternal personal air samples during pregnancy and levels of these insecticides or their metabolites in plasma samples at delivery (maternal and cord). Data are presented both for the total cohort and also after stratifying by the amount of time in months that had elapsed between the personal monitoring and delivery. Among the total cohort, weak but significant correlations were seen between levels of all three insecticides in personal air and blood samples (maternal and/or cord). The correlations were generally stronger when analyses were restricted to the mother–newborn pairs with an elapsed time of 1 month or less between the personal monitoring and delivery. However, they were significant only for chlorpyrifos among this subset ($r = 0.30–0.45$, $p < 0.05$).

Table 7 provides results of the multiple linear regression analyses of the associations among pesticide levels (in personal air and plasma), ethnicity, and neighborhood of residence. African Americans had higher levels of most pesticides than did Dominicans; the difference was significant for *a*) propoxur in personal air samples, *b*) chlorpyrifos in maternal plasma and cord plasma, *c*) dicloran in maternal and cord plasma, and *d*) phthalimide in cord plasma. With controlling for ethnicity and housing disrepair (for insecticides), residents of Washington Heights had significantly higher levels than did residents of Harlem of *a*) propoxur in personal air, *b*) chlorpyrifos in maternal plasma, and *c*) diazinon in maternal plasma. With controlling for ethnicity, women residing in the South Bronx had significantly higher levels of dicloran in plasma samples than did residents of Harlem. No significant associations were seen between the level of housing disrepair reported and insecticide levels in either personal air or plasma samples.

Figure 1 shows geometric mean personal air levels of chlorpyrifos, diazinon, and propoxur among women who reported that pest control measures were not used during pregnancy compared with women who reported use of *a*) nonspray pest control methods only, *b*) can sprays and/or pest bombs, and *c*) spraying by an exterminator. Air levels of diazinon and propoxur but not chlorpyrifos varied significantly among these

Table 3. Levels of pesticides and/or their metabolites[a] (pg/g) in umbilical cord plasma samples collected between 1998 and 2001 from African-American and Dominican newborns residing in northern Manhattan and the South Bronx ($n = 211$).

	LOD	No. > LOD	Percent	Median	Mean ± SD[b]	Range
Organophosphates						
Chlorpyrifos	0.5–1	150	71	2.6	4.7 ± 6.5	ND–63
Diazinon	0.5–1.5	103	49	ND	1.2 ± 1.5	ND–13
Dichlorvos	1–3	9	4	ND	NC	ND–4.8
Fonophos	1	2	0.9	ND	NC	ND–9.2
Malathion	12–40	3	1	ND	NC	ND–47
Methyl parathion	2–10	5	2	ND	NC	ND–16
Parathion	1–5	5	2	ND	NC	ND–4.4
Phorate	1	1	0.5	ND	NC	ND–10
Terbufos	1–5	4	2	ND	NC	ND–69
Carbamates						
Bendiocarb	5	77	36	ND	NC	ND–31
Carbofuran	1	94	45	ND	NC	ND–48
Carbofuranphenol	1	1	0.5	ND	NC	ND–15
1-Naphthol[a]	20	36	17	ND	NC	ND–158
Propoxur	1–2	20	9	ND	NC	ND–650
2-Isopropoxyphenol[a]	3	101	48	1.5	3.3 ± 3.0	ND–23
Pyrethroids						
trans-Permethrin	1	15	7	ND	NC	ND–4.9
cis-Permethrin	1	28	13	ND	NC	ND–4.2
Herbicides						
Acetochlor	1	6	3	ND	NC	ND–9.3
Alachlor	1	7	3	ND	NC	ND–15
Atrazine	1	43	20	ND	NC	ND–12
Chlorthal-dimethyl	1	81	38	ND	NC	ND–6.7
Metolachlor	1	21	10	ND	NC	ND–11
Trifluralin	1	25	12	ND	NC	ND–5.1
Fungicides						
Chlorothalonil	5–10	30	14	ND	NC	ND–191
Dicloran	1	175	83	2.2	3.3 ± 3.7	ND–32
Metalaxyl	5	39	18	ND	NC	ND–250
Phthalimide[a]	20	148	70	24	24.0 ± 14.6	ND–110
Tetrahydrophthalimide[a]	1	92	44	ND	NC	ND–37
Repellent						
Diethyltoluamide	1–10	69	33	ND	NC	ND–33

Abbreviations: LOD, limit of detection; NC, not calculated; ND, not detected.
[a]Metabolites measured [corresponding parent compound(s)]: carbofuranphenol (carbofuran/carbosulfan), 2-isopropoxyphenol (propoxur), 1-naphthol (carbaryl/naphthalene), phthalimide (folpet, phosmet, captan), tetrahydrophthalimide (captan/captafol). [b]Calculated if the pesticide was detected in > 45% of samples; levels in samples without detections were set at one-half of the detection limit.

Table 4. Correlation between levels of pesticides or their metabolites[a] in paired maternal and umbilical cord blood samples[b] ($n = 180$ pairs).

	Maternal blood levels (mean ± SD)	Cord blood levels (mean ± SD)	Spearman rank correlation
Bendiocarb	4.4 ± 3.0	3.7 ± 2.5	$r = 0.51$, $p < 0.001$
Chlorpyrifos	4.1 ± 4.5	4.0 ± 6.5	$r = 0.76$, $p < 0.001$
Diazinon	1.3 ± 2.2	1.1 ± 1.5	$r = 0.57$, $p < 0.001$
Dicloran	3.1 ± 3.5	3.3 ± 3.8	$r = 0.78$, $p < 0.001$
2-Isopropoxyphenol[a]	3.0 ± 2.5	3.4 ± 3.2	$r = 0.39$, $p < 0.001$
Phthalimide[a]	29.0 ± 24.7	25.3 ± 14.3	$r = 0.13$, $p < 0.10$
Tetrahydrophthalimide[a]	2.1 ± 3.8	1.9 ± 3.8	$r = 0.33$, $p < 0.001$

[a]Metabolites measured [corresponding parent compound(s)]: 2-isopropoxyphenol (propoxur), tetrahydrophthalimide (captan/captafol), phthalimide (folpet, captan, phosmet).
[b]Analyses restricted to the seven pesticides detected in > 45% of maternal and/or cord blood samples.

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groups ($p \leq 0.01$, ANOVA). Specifically, diazinon levels were significantly higher among women reporting use of can sprays and/or pest bombs ($p = 0.007$) or an exterminator ($p = 0.005$) compared with levels among women who reported that pest control was not used. Propoxur levels in personal air samples were significantly higher among women reporting use of can sprays and/or pest bombs compared with women reporting using no pest control ($p = 0.007$), women using nonspray methods only ($p = 0.001$), or women using an exterminator ($p = 0.002$). There was no significant difference in levels of chlorpyrifos, diazinon, 2-isopropoxyphenol, or bendiocarb in maternal and/or cord plasma levels among the groups based on self-reported pesticide use by the mother during pregnancy ($p \geq 0.05$, data not shown).

Table 8 shows geometric mean insecticide levels in the personal air samples by the year that the monitoring was conducted and in plasma samples by the year that the baby was delivered. A significant linear decrease over time was seen in personal air levels of diazinon ($p = 0.03$) and propoxur ($p < 0.001$). Specifically, diazinon levels were significantly lower among women monitored in 2001 compared with women monitored in both 1999 ($p = 0.01$) and 2000 ($p = 0.04$). Propoxur levels were significantly lower among women monitored in both 2001 and 2000 compared with 1999 ($p < 0.001$). Propoxur levels were also significantly lower in women monitored in 2001 compared with 2000 ($p = 0.004$).

Levels of the insecticides in maternal and/or cord plasma also decreased significantly over time. The test for linearity and the differences between the groups were significant for chlorpyrifos in both maternal and cord plasma samples ($p < 0.001$), bendiocarb in maternal plasma samples ($p < 0.001$) and diazinon and 2-isopropoxyphenol in cord plasma samples ($p < 0.01$). There was also some variability in fungicide levels in plasma samples by year of birth (data not shown). Specifically, dicloran and tetrahydrophthalimide levels in maternal and/or cord plasma samples were significantly lower in subjects who delivered in 2001 compared with those who delivered in 1999 or 2000 ($p < 0.01$). By contrast, phthalimide levels were significantly higher in cord plasma samples of infants born in 2001 and 2000 compared with those born in 1999 ($p \leq 0.02$; data not shown).

We also assessed whether pesticide levels in personal air or plasma samples varied by the season of the monitoring or season of birth. Levels of the pesticides tended to be highest in the summer (July–September), although this was not always the case. Levels of dicloran, tetrahydrophthalimide, and bendiocarb in maternal plasma samples and levels of dicloran and 2-isopropoxyphenol in cord plasma samples were significantly higher in summer compared with levels in any of the other three seasons ($p < 0.05$). Chlorpyrifos levels in maternal personal air samples were also significantly higher in the summer compared with spring or fall, and chlorpyrifos levels in cord plasma levels were significantly higher in summer compared with winter and fall ($p < 0.05$). By contrast, diazinon levels in plasma samples were highest in the fall and spring. Specifically, among the maternal plasma samples, diazinon levels were significantly higher among women who delivered in the fall compared with winter or spring ($p < 0.05$). Among the cord blood samples, diazinon levels were significantly higher among infants delivered in the fall compared with winter and were significantly higher among infants who delivered in the spring compared with summer or winter ($p < 0.05$).

Table 5. Air concentrations (nanograms per cubic meter) of nine pesticides over 48 hr of personal ambient air monitoring during the third trimester of pregnancy among African-American and Dominican women from northern Manhattan and the South Bronx between 1998 and 2001.

	LOD	No. > LOD[a]/total no. (%)	Median	Mean ± SD[b]	Range
Organophosphates					
Chlorpyrifos	0.2	230/230 (100)	7.1	18.3 ± 36.8	0.7–345
Diazinon	0.2	228/228[c] (100)	22.2	129 ± 578	2.0–6010
Malathion	0.2	3/134[c] (2)	ND	NC	ND–11.0
Methyl parathion	0.2	3/110[c] (3)	ND	NC	ND–0.9
Carbamates					
Propoxur	0.2	230/230 (100)	28.0	66.1 ± 153	3.1–1420
Carbaryl	0.4	0/98[c] (0)	ND	NC	ND–0.4
Pyrethroids					
trans-Permethrin	0.7	53/204[c] (26)	ND	NC	ND–524
cis-Permethrin	0.4	47/226[c] (21)	ND	NC	ND–324
Fungicide					
o-Phenylphenol	0.6	140/140 (100)	29.4	48.8 ± 85.6	7.8–743

Abbreviations: LOD, limit of detection (ng/m^3); NC, not calculated; ND, not detected.
[a]Upper limit is given, actual detection limits varied depending of the concentration of the extract and the amount of air sampled. [b]Calculated if the pesticide was detected in > 45% of samples; levels in samples without detections were set at one-half of the detection limit. [c]Air concentration could not be calculated for remaining sample(s) because of interference peaks.

Table 6. Correlation between pesticide levels in maternal personal air samples during pregnancy and blood samples (maternal and cord) at delivery[a] for the total cohort and stratified by the elapsed time (in months) between the date of the personal air monitoring and delivery.

	Maternal personal air samples		
Blood samples	Chlorpyrifos	Diazinon	Propoxur[b]
Total cohort ($n = 230$)			
Maternal blood	$r = 0.17$, $p = 0.02$	$r = 0.15$, $p = 0.04$	$r = 0.19$, $p = 0.008$
Cord blood	$r = 0.18$, $p = 0.01$	$r = 0.04$, $p = 0.59$	$r = 0.10$, $p = 0.14$
Stratified by the elapsed time between monitoring and delivery[c]			
Personal monitoring > 1 month before delivery ($n = 158$)			
Maternal blood	$r = 0.09$, $p = 0.29$	$r = 0.10$, $p = 0.23$	$r = 0.20$, $p = 0.02$
Cord blood	$r = 0.13$, $p = 0.13$	$r = 0.01$, $p = 0.87$	$r = 0.05$, $p = 0.58$
Personal monitoring ≤ 1 month before delivery ($n = 63$)			
Maternal blood	$r = 0.45$, $p = 0.001$	$r = 0.20$, $p = 0.15$	$r = 0.19$, $p = 0.16$
Cord blood	$r = 0.30$, $p = 0.02$	$r = 0.13$, $p = 0.35$	$r = 0.20$, $p = 0.14$

[a]Correlations assessed by Spearman rank; analyses restricted to the pesticides detected in > 45% of personal air or plasma samples. [b]Metabolite measured in plasma corresponding parent to compound 2-isopropoxyphenol. [c]Missing data: date of air sampling ($n = 1$); date of delivery ($n = 8$).

Discussion

To our knowledge, this is the first study to measure levels of contemporary-use pesticides in blood samples collected at birth from mothers and their newborns. Eight of the pesticides were also measured in personal air samples collected from the mothers during pregnancy, allowing us to compare personal air and blood levels. The insecticides detected with the greatest frequency in both personal air and blood were the organophosphates diazinon and chlorpyrifos and the carbamate propoxur. All have been widely used for residential pest control. Before the recent regulatory action to phase out residential uses of chlorpyrifos and diazinon, the U.S. EPA estimated that approximately 75% of U.S. diazinon use and 50% of U.S. chlorpyrifos use were for residential pest control (U.S. EPA 2000a, 2001). Chlorpyrifos has been one of the pesticides most heavily applied in New York City (Thier et al. 1998), including by pest control operators for the New York City Housing Authority (Landrigan et al. 1999). Propoxur is registered for indoor uses to control cockroaches and other household pests and for use in pet sprays (U.S. EPA 1997b). The insecticide bendiocarb, which was detected frequently in blood samples but was not measured in air samples, is also registered

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Table 7. Multiple linear regression models of the associations between ethnicity and neighborhood of residence and pesticide levels[a] in personal air samples collected over 48-hr during the third trimester of pregnancy and blood samples (maternal and umbilical cord) collected at delivery.

	Ethnicity[b]			Neighborhood of residence: Harlem vs. Washington Heights[c]			Neighborhood of residence: Harlem vs. South Bronx[d]		
	B	SE	*p*-Value	B	SE	*p*-Value	B	SE	*p*-Value
Personal air									
Chlorpyrifos	0.1	0.2	0.6	–0.1	0.2	0.5	–0.2	0.2	0.4
Diazinon	0.2	0.2	0.5	–0.01	0.3	1.0	–0.04	0.3	0.9
Propoxur	0.7	0.2	< 0.001*	0.5	0.2	0.02*	0.2	0.2	0.3
Maternal blood									
Chlorpyrifos	0.6	0.2	0.008*	1.0	0.3	< 0.001*	0.5	0.3	0.08
Diazinon	0.2	0.1	0.2	0.3	0.2	0.03*	0.06	0.2	0.7
Bendiocarb	0.1	0.1	0.3	0.04	0.1	0.7	0.01	0.1	0.9
Tetrahydrophthalimide[e]	0.3	0.2	0.06	0.3	0.2	0.1	0.06	0.2	0.7
Dicloran	0.4	0.2	0.01*	0.3	0.2	0.16	0.5	0.2	0.008*
Phthalimide[e]	–0.13	0.1	0.2	0.2	0.1	0.2	–0.1	0.1	0.3
Cord blood									
Chlorpyrifos	0.5	0.2	0.03*	0.5	0.3	0.05	0.2	0.3	0.5
Diazinon	0.2	0.1	0.2	0.2	0.1	0.3	0.1	0.1	0.3
2-isopropoxyphenol[e]	0.03	0.1	0.8	0.06	0.1	0.6	0.2	0.1	0.2
Dicloran	0.3	0.2	0.03*	0.2	0.2	0.3	0.2	0.2	0.4
Phthalimide[e]	0.3	0.1	0.03*	0.02	0.1	0.9	0.07	0.1	0.6

B, unstandardized regression weights. Analyses of insecticides were controlled for the level of housing disrepair reported. [a]Analyses were restricted to the pesticides detected in > 45% of personal air or blood samples; pesticide levels were log-transformed prior to analyses. [b]Dominican = 0; African American = 1. [c]Harlem = 0; Washington Heights = 1. [d]Harlem = 0; South Bronx = 1. [e]Metabolites measured [corresponding parent compound(s)]: 2-isopropoxyphenol (propoxur), tetrahydrophthalimide (captan/captafol), phthalimide (folpet, phosmet, captan). *$p < 0.05$.

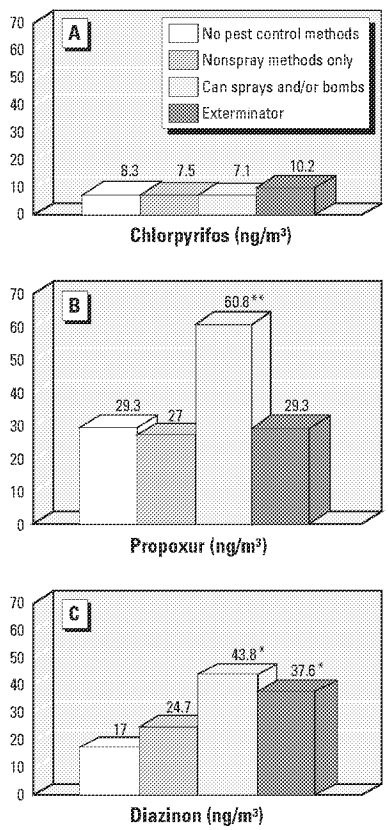

Figure 1. Geometric mean levels of (*A*) chlorpyrifos, (*B*) propoxur, and (*C*) diazinon in personal air samples (ng/m³) stratified by whether or not pest control methods were used during pregnancy. Pesticide levels were log-transformed prior to statistical analyses.
*$p < 0.05$ compared with levels among women not using pest control (ANOVA). **$p < 0.05$ compared with levels among women not using pest control or using nonspray methods only or using an exterminator (ANOVA).

for indoor uses (U.S. EPA 1999b) and has been used by the New York City Housing Authority for residential insect control (Landrigan et al. 1999).

Although chlorpyrifos, diazinon, and propoxur were detected frequently in both personal air and blood samples, air and blood levels were not always correlated. This may reflect the fact that the pesticides are rapidly excreted (half-life on the order of a few days) and blood levels provide a short-term dosimeter only (Barr 1999; Barr et al. 2002; Nolan et al. 1984). Our data support this hypothesis because the correlation between chlorpyrifos in personal air and blood was stronger among subjects for whom the personal air monitoring was conducted within 1 month of delivery compared with subjects who were monitored earlier in their pregnancy. In addition, pesticide levels in blood can reflect exposures from all routes, including dermal absorption and ingestion, as well as inhalation. It is likely that the women in the present cohort received some exposures to these insecticides through the diet. Both chlorpyrifos and diazinon are registered for use on multiple food crops (Smegal 1999; U.S. EPA 2000b). A recent study found chlorpyrifos residues in 38% of the food samples collected over 4 days from 75 individuals (MacIntosh et al. 2001b). Dietary intakes were estimated to account for approximately 13% of aggregate exposures (Pang et al. 2002) and 7% of chlorpyrifos metabolites in urine (MacIntosh et al. 2001a). Bendiocarb and propoxur are not registered for use on food crops but are registered for crack and crevice treatment in food processing and handling establishments (U.S. EPA 1997b, 1999b).

Diet is also a likely source of exposures to the fungicide dicloran and to phthalimide and tetrahydrophthalimide (metabolites of the fungicides captan, folpet, and captafol), which were detected frequently in both maternal and newborn blood samples. Dicloran is registered for use on multiple food crops for both pre- and postharvest treatment, including on apricots, peaches, nectarines, and sweet cherries; it is also registered for postharvest use on sweet potatoes and preharvest use on snap beans, celery, cucumbers, lettuce, grapes, potatoes, and tomatoes (Farm Chemicals Handbook 2001; R. Michell. Personal communication). Dicloran can also be used legally on imported carrots and peanuts as long as residues are below legal limits. Captan is also registered for use on multiple fruit and vegetable crops, and use appears widespread. According to U.S. EPA, more than a third of the apples, blueberries, peaches, prunes, raspberries, and strawberries grown in the United States are treated with captan (U.S. EPA 1999a). Captan is also applied as a postharvest dip for apples, cherries, and pears. In addition, captan is registered for use in paints, adhesives, and some plastic and rubber products, so nondietary exposures to this fungicide are also a possibility. Folpet is registered for use only on avocados in the United States, but fruits and vegetables treated with folpet in other countries can be legally imported into the United States as long as residues are below legal limits (U.S. EPA 1999c). This applies to imported apples, cranberries, cucumbers, grapes, lettuce, melons, strawberries, onions, and tomatoes (U.S. EPA 1999c). Folpet is also registered for use in paints, caulking compounds, coatings, and stains. In addition to being a metabolite of folpet and captan, phthalimide is also a metabolite of the organophosphate phosmet and is additionally used as a dye intermediate. These multiple exposure sources may account for the fact that levels of phthalimide in maternal and newborn blood samples were higher than levels of the other pesticides measured. *ortho*-Phenylphenol, which was detected in 100% of personal air samples but was not measured in blood, is a widely used fungicide and antibacterial agent for commercial and consumer purposes, including in the protection of stored fruit, and has been shown to be a rat bladder carcinogen (Appel 2000).

Our findings show that maternal and cord blood pesticide levels were similar and in most cases highly correlated. Consistent with experimental evidence (Richardson 1995), these findings indicate that the pesticides are readily transferred from the mother to fetus during pregnancy. Blood and personal air insecticide levels were generally low but highly variable. To our knowledge, no prior data are available on which to base risk assessments associated with plasma levels of these pesticides. How-

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Table 8. Insecticide levels in personal air by year of sampling and in blood by year of delivery[a] [geometric mean (95% confidence interval)].

	Personal air samples (ng/m^3)			Blood samples (pg/g)					
				Maternal			Umbilical cord		
	1999 (n = 114)	2000 (n = 88)	2001 (n = 27)	1999 (n = 71)	2000 (n = 88)	2001 (n = 34)	1999 (n = 87)	2000 (n = 83)	2001 (n = 33)
Chlorpyrifos	9.3 (7.5–11.4)	7.6 (6.0–9.7)	6.6 (3.8–11.4)	5.2 (4.1–6.6)	2.5 (1.9–3.2)[b]	0.5 (0.4–0.6)[b,c,d]	5.0 (4.1–6.2)	1.9 (1.4–2.4)[b]	0.5 (0.3–0.6)[b,c,d]
Diazinon	31.6 (24.0–41.6)	28.5 (21.3–38.1)	15.1 (9.5–23.9)[b,c,d]	1.0 (0.9–1.2)	0.8 (0.7–0.9)	0.8 (0.7–1.1)	1.0 (0.9–1.2)	0.7 (0.6–0.8)[b]	0.7 (0.6–0.9)[b,c]
Propoxur[e]	43.3 (35.0–53.5)	25.0 (20.3–31.0)[b]	12.9 (9.9–16.8)[b,c,d]	NC	NC	NC	3.6 (3.2–4.1)	2.0 (1.8–2.3)[b]	1.9 (1.5–2.5)[b,c]
Bendiocarb	NC	NC	NC	4.7 (4.3–5.2)	4.0 (3.6–4.6)	ND[b,c,d]	NC	NC	NC

NC, not calculated because not measured or because the pesticide was detected in ≤ 45% of samples.
[a]Analyses were restricted to insecticides detected in > 45% of personal air or blood samples; pesticide levels were log-transformed prior to statistical analyses; missing data: date of air sampling (n = 1); date of delivery (n = 8). [b]$p < 0.05$ compared with 1999 levels. [c]$p < 0.05$ test for linearity (ANOVA). [d]$p < 0.05$ compared with 2000 levels (ANOVA). [e]2-Isopropoxyphenol (metabolite of propoxur) was measured in blood samples.

ever, prior data are available on which to base risk assessments associated with insecticide levels in air. Estimated inhalation exposures to chlorpyrifos and propoxur even at the highest air concentration found in the present study are below health-based limits recommended by the U.S. EPA (Smegal 1999; U.S. EPA 1997b; Whitmore et al. 1994). However, inhalation exposures of some women to diazinon are likely to have exceeded health-based levels, and our results support recent regulatory action to phase out residential uses of this insecticide. Specifically, the U.S. EPA has set a reference dose (RfD) of 0.00009 mg/kg/day for inhalation exposures to diazinon (U.S. EPA 2000b). Based on the U.S. EPA's assumptions regarding absorption and using its default inhalation volumes (15.2 m^3/day) and body weight (70 kg) for adults, inhalation exposures of 9 of 230 (3.9%) subjects in our study would have exceeded the diazinon RfD. Exposures at the 95th percentile concentration would have been 81% of the RfD. Further, it is possible that the aggregate exposures associated with the air concentrations are greater than exposures from inhalation alone, because prior data indicate that exposure from residential pesticide use may also come from dermal absorption and ingestion. This is supported by studies that have shown a high correlation ($r \geq 0.7$) between pesticide levels in indoor and personal air with those in carpet dust, hand wipes (including from mothers and children), and surfaces in the home (Camann et al. 1995; Gordon et al. 1999; Whitmore et al. 1994). However, uncertainty remains over the extent of exposure from these sources (Lu and Fenske 1999), and inhalation appears to be the predominant route of exposure to pesticides used indoors in residential settings (Pang et al. 2002).

In the present study, we found that African Americans had significantly higher exposures than did Dominicans to several of the insecticides and that exposures also varied significantly among the neighborhoods of residence after controlling for ethnicity and level of housing disrepair. These variations may relate to differences in the quality of the built environment, because our prior research has shown housing disrepair to be a significant predictor of pest infestation levels, cockroach allergen levels, and pest control use among women in the present cohort (Rauh et al. 2002; Whyatt et al. 2002). However, we did not find the level of housing disrepair reported by the women to be a significant predictor of the insecticide levels in either personal air or blood samples. Therefore, it is likely that other factors are also contributing to the ethnic differences seen here. For example, as reported previously, African Americans were significantly more likely to use can sprays than were Dominicans (Whyatt et al. 2002).

Results from this study also indicate that insecticide exposures have been decreasing significantly between 1998 and 2001. This decrease may be attributed in part to the regulatory action taken by the U.S. EPA. In June 2000, the U.S. EPA entered into an agreement with the manufacturers to begin phasing out residential uses of chlorpyrifos and to terminate all retail sales for indoor use by December 2001 (U.S. EPA 2000a). In January 2001, the U.S. EPA entered into an agreement with the manufacturer to begin phasing out residential uses of diazinon and to terminate all retail sales for indoor use by December 2002 (U.S. EPA 2001). However, other factors may be operating as well, because levels of propoxur and bendiocarb have also been decreasing significantly over time and neither has been the subject of regulatory action. Therefore, there may be a general reduction in residential use of organophosphate and carbamate insecticides as a result of concerns over health effects of residential exposures and proactive efforts by manufacturers to reduce indoor uses (U.S. EPA 1997a).

Experimental evidence in laboratory rodents has linked organophosphate exposure during gestation or the early postnatal period to adverse neurodevelopmental sequelae in the offspring (Brimijoin and Koenigsberger 1999; Eskenazi et al. 1999). Our preliminary findings indicate that chlorpyrifos levels in blood samples of mothers and newborns in the present cohort are inversely associated with infant birth weight and length (Perera et al. 2003). The newborns in this cohort are being followed, and we are in the process of gathering measures of postnatal pesticide exposure. Associations between exposures and the infants' neurocognitive development will be assessed.

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