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Prenatal Exposure to *p,p′*-DDE and *p,p′*-DDT in Relation to Lower Respiratory Tract Infections in Boys From a Highly Exposed Area of Mexico

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Abstract

Background—Prenatal exposure to 1,1-dichloro-2,2-bis(p-chlorophenyl)ethylene (*p,p′*-DDE), the major breakdown product of DDT, has been associated with recurrent lower respiratory tract infections (LRTI) in infants. However, epidemiological investigations are limited.

Objective—To assess the association of prenatal exposure to *p,p′*-DDE and *p,p′*-DDT with the occurrence of LRTI in boys from Chiapas, a highly exposed area of Mexico.

Methods—We analyzed data from 747 singleton boys whose prenatal exposure to *p,p′*-DDE and *p,p′*-DDT was determined in maternal serum drawn at delivery (2002–2003). LRTI (i.e., pneumonia, bronchiolitis, and other illness of the bronchi) experienced by the children were reported by their mothers during in-person interviews. The median age of the children when they were last seen was 21.4 months (quartiles 19.1 and 25.3 months).

Results—Median exposure to *p,p′*-DDE in this population was higher (2.7 μg/g lipid) than recent U.S. levels (0.20 μg/g). There were 0.19 episodes of LRTI per child-year. After adjusting for potential confounders, children in the highest category of *p,p′*-DDE (>9.00 μg/g) exposure compared to those in the lowest (≤3.00 μg/g) had an adjusted incidence rate ratio (aIRR) of LRTI of 0.77 (95% confidence interval [CI], 0.41–1.46). The corresponding aIRR for *p,p′*-DDT (≥2.00 μg/g compared to ≤0.25 μg/g) was 0.65 (95% CI: 0.30–1.39).

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The study was approved by the Institutional Review Boards at the Instituto Nacional de Salud Pública in México and the National Institute of Environmental Health Sciences in the United States.

Conclusion—An association of prenatal exposure to *p,p′*-DDE and *p,p′*-DDT with LRTI during childhood was not supported in this population with relatively high levels of exposure.

Keywords

boys; lower respiratory tract infections; *p,p′*-DDE; *p,p′*-DDT; prenatal exposure

1. INTRODUCTION

Earlier studies have suggested a potential adverse effect of prenatal exposure to *p,p′*-DDE (1,1-dichloro-2,2-bis(p-chlorophenyl)ethylene) on respiratory outcomes in the first years of life (Gascon et al. 2012). Higher risk of lower respiratory tract infections (LRTI) were associated with prenatal exposure to *p,p′*-DDE among infants in three regions of Spain (Gascon et al. 2012; Sunyer et al. 2010); however, studies among other populations (i.e., Sweden and Inuit from Canada) have not confirmed such an association (Dallaire et al. 2004; Glynn et al. 2008). Understanding the potential role of prenatal exposure to *p,p′*-DDE on respiratory outcomes is critical as LRTI are the leading cause of mortality among children younger than five years, and most of the deaths among this group of age are caused by bronchiolitis and pneumonia (the major components of LRTI) (Nair et al. 2010; Rudan et al. 2004; Rudan et al. 2008). Bronchiolitis and pneumonia are LRTI that are common in young children; known risk factors associated with these infections include low birthweight (≤2,500 g), non-exclusive breastfeeding during the first four months of life, lack of measles immunization, indoor air pollution, living in crowding conditions, social disadvantage, and child's malnutrition (weight-for-age *z*-score <-2.0) (Koehoorn et al. 2008; Roth et al. 2008; Rudan et al. 2004). Both infections are associated with cough and difficulty breathing; bronchiolitis is an acute inflammation of the bronchioles (smaller conducting airways in the lungs) accompanied by wheeze and is mostly due to viral infections, while pneumonia is an infection of the lungs characterized by crepitations or crackles and is due to either bacteria or viruses (Roth et al. 2008; Rudan et al. 2004; Smyth and Openshaw 2006). Children who developed pneumonia during childhood may have impaired lung function as adults (Johnston et al. 1998).

Previous studies have documented suppression of the immune response with high levels of DDT exposure in animal and human populations (ATSDR 2002); thus, potential alterations of the immune system during early development is a plausible explanation for the association between *p,p′*-DDE exposure and a high risk of LRTI (Cooper et al. 2004; Nagayama et al. 2007).

p,p′-DDE is the main and most persistent breakdown product of the pesticide DDT (1,1,1-trichloro-2,2-bis(4-chlorophenyl)ethane), which was widely applied to crops in the past; ongoing use of DDT is now limited to only a few countries to control vector-borne diseases (Turusov et al. 2002; WHO 2010). Human populations with historical exposure to DDT tend to have higher concentrations of *p,p′*-DDE in their tissues because of DDT′s persistence. Adverse health effects related to high exposure to *p,p′*-DDE (e.g., cancer, pregnancy losses, and low birth weight) are not well defined; nonetheless, adverse health outcomes among children exposed to DDT *in utero* are still a concern given the potential alterations that may have occurred during development (Eskenazi et al. 2009). Hence, epidemiologic studies

among populations with high past exposure to DDT may provide insights to those making decisions about vector-borne disease control policy.

The purpose of the current research was to assess whether prenatal exposure to *p,p′*-DDE and *p,p′*-DDT is associated with a higher occurrence of recurrent lower respiratory tract infections during childhood among boys from Tapachula, Chiapas, an area of Mexico that experienced unusually high exposure to DDT for almost 40 years. In the study area, DDT was used for crops until 1991 and for malaria control until 1998 (Chanon et al. 2003; Instituto de Salud Ambiente y Trabajo 2000).

2. MATERIAL AND METHODS

The present analysis was based on a birth cohort of mothers and their singleton newborn sons from the State of Chiapas, Mexico; the cohort has been described in detail previously (Cupul-Uicab et al. 2008; Cupul-Uicab et al. 2010). Briefly, 870 healthy newborn males (born at term with normal birth weight) and their mothers were enrolled between 2002 and 2003 at the time of delivery. Maternal serum samples were collected at enrollment. The participation rate was 95% (Cupul-Uicab et al. 2010; Longnecker et al. 2007). Women and their sons were visited at their homes from January 2004 to June 2005 to ascertain the duration of lactation. At that time we also obtained information on growth and health status of the children; the follow-up rate was 91% (Cupul-Uicab et al. 2008). Because the initial study hypothesis was related to the potential androgen-blocking effects of DDT, only boys were enrolled. The study was approved by the Institutional Review Boards at the Instituto Nacional de Salud Pública in México and the National Institute of Environmental Health Sciences in the United States. All mothers gave written informed consent.

For this analysis, the following exclusion criteria were applied: no information on the outcome of interest (n=10, who answered an earlier version of the first follow-up questionnaire that did not inquire about child's health status) and those whose first follow-up visit occurred after 30 months of age (n=32), as visits after this age were scarce. After these exclusions, a total of 747 boys were included in our final analysis. The median age of these boys when the follow-up began was 12.3 months (quartiles 7.7 and 16.1 months). For logistic reasons they were visited between 1 and 6 times during the follow-up period (~17 months), with a median of 2 visits (quartiles 2 and 4); the median gap between each visit was 2.8 months (quartiles 1.8 and 4.1 months). The median age of the children when they were last seen was 21.4 months (quartiles 19.1 and 25.3 months).

2.1. DDE and DDT measurements

We used maternal serum samples collected within a day of delivery to measure *p,p′*-DDE and *p,p′*-DDT. Serum levels were quantified after solid phase extraction, using gas chromatography with mass spectrometry detection (Saady and Poklis 1990; Smith 1991). The limit of detection (LOD) was 0.2 μg/L and the recovery was 97% for both analytes. The between-assay coefficient of variation was 7% for *p,p′*-DDE (at 10 μg/L) and 6% for *p,p′*-DDT (at 2.5 μg/L). All samples had levels of *p,p′*-DDE that were above the LOD; for levels of *p,p′*-DDT that were below the LOD (n=18), we used the measured values reported by the laboratory in the analyses. Thus, no imputation of values below LOD was done. Total serum

lipid was calculated based on triglycerides, phospholipids, free and total cholesterol measured using standard enzymatic methods (Patterson et al. 1991). Concentrations of *p,p′*-DDE and *p,p′*-DDT were expressed as micrograms per gram of lipid (μg/g).

2.2. Lower respiratory tract infections

Lower respiratory tract infections experienced by the children were defined as doctor diagnosed pneumonia, bronchiolitis or other illness of the bronchi. This information was reported by the mothers during in-person interviews conducted by specially trained personnel during home visits. At the first follow-up visit women reported doctor's diagnosis of LRTI since the baby was born and at subsequent visits they reported doctor's diagnosis of LRTI since the previous visit. The mothers were asked these two questions: "Did the doctor diagnose [him] with pneumonia?" and "Did the doctor diagnose [him] with bronchiolitis or other illness of the bronchi?" Because there were few episodes of pneumonia alone, our main outcome (LRTI) included all episodes of pneumonia and/or bronchiolitis. We only asked for the number of episodes of LRTI that were diagnosed by a doctor and did not collect information about the exact date when each episode took place.

2.3. Covariates

Socio-demographic characteristics, reproductive history, and lifestyle of the women were ascertained at enrollment. Poverty status was measured using national standards according to the Mexican Secretariat of Social Development, which is based on monthly per capita income in Mexican pesos by residence area (Palacios-Escobar and Martinez-Romero 2004). For urban settings, women with an income under 672 Mexican pesos were in the poorest category (i.e., they struggled to buy adequate food) and women with less than 1367 were considered "less poor" (they lacked adequate income for other human needs). For rural settings, the cut points were 495 for the poorest and 946 for less poor categories (Cupul-Uicab et al. 2008; Palacios-Escobar and Martinez-Romero 2004). Maternal and paternal smoking during pregnancy was ascertained at enrollment and also during the follow-up period. Because very few women smoked, parental smoking was defined as smoking by at least one parent at any time during pregnancy or follow-up. Duration of breastfeeding was defined as the child's last age (months and days) he received any breast milk, irrespective of the introduction of liquids or solid foods. Exclusive breastfeeding was defined as the child's last age (months and days) he received only breastfeeding and no other liquids or solid food had yet been introduced. The duration of exclusive breastfeeding in this population was very short, therefore we used a variable on exclusive breastfeeding that was treated as dichotomous (no, yes). We defined child's underweight during follow-up as weight-for-age *z*-scores ≤ -2.00 based on the 2000 growth chart for boys from the Centers for Disease Control and Prevention (CDC) (Kuczmarski et al. 2000).

2.4. Statistical analysis

The association of prenatal exposure to *p,p′*-DDE and *p,p′*-DDT with recurrent LRTI (number of episodes) was assessed with Poisson regression with robust standard errors to adjust for the clustering of observations within children (for those with two or more visits, 90.5%). To account for the differences in length of time that each child was followed, all

models included an offset for person-time. The person-time (months) for each child was calculated as the date of birth to the first visit and as the time since the previous visit (when the child had two or more visits). For the main analysis the exposure variables (*p*,*p*′-DDE and *p*,*p*′-DDT) were categorized using the same cut points applied in previous analyses of these data; as described before these categories resulted in a large exposure difference between those in the high and low categories while maintaining adequate numbers for analysis (Cupul-Uicab et al. 2008; Longnecker et al. 2007). We also estimated the incidence rate ratio (IRR) of LRTI per interquartile (IQ) increase in exposure (μg/g).

The selection of potential confounders for inclusion in the model was based on directed acyclic graphs (DAGs) (Greenland et al. 1999; Textor et al. 2011). Maternal age, parity, poverty status, parental smoking, and residence area were selected as the minimal sufficient set for adjustment. Other variables not selected by the DAG (i.e., birth season, child's underweight, breastfeeding, exclusive breastfeeding, and maternal education) were assessed as potential confounders with the change in estimate method (i.e., change in IRR ≥10%), starting with all variables in the models and deletion of one by one in a stepwise manner (Greenland 1989). None of the tested variables cause a change ≥10% in the IRR.

We assessed potential interactions of the exposure with breastfeeding duration (≤6 vs. >6 months) by introducing cross-term products for these variables into the fully adjusted models (i.e., indicators for each category of exposure x breastfeeding [≤6 vs. >6 months]). Potential interactions were further assessed when at least one of the *p*-values for the cross-term products was ≤0.20. Only the cross term-product for the second category of *p*,*p*′-DDE (i.e., 3.01–6.00) was suggestive of a potential interaction with breastfeeding (*p*-interaction = 0.15); however, further stratification revealed no important variation in the IRR by breastfeeding status. There was no indication of a potential interaction between *p*,*p*′-DDT and breastfeeding (interaction p's were all >0.28).

Because low socioeconomic status and child's malnutrition are risk factors of LRTI (Roth et al. 2008) that might be related to or affected by the exposure, in sensitivity analyses we also assessed potential interactions of the exposure (*p*,*p*′-DDE and *p*,*p*′-DDT) with poverty status and child's underweight, but there was no evidence of such interactions (*p*-interactions were >0.20). Given the unequal number of follow-up visits that each child had in the present study, we additionally assessed whether number of visits was an important predictor of the outcome and then assessed potential interactions of this variable with the exposure. Number of follow-up visits was not a predictor of the outcome and there was no evidence of interaction between the exposures (*p*,*p*′-DDE and *p*,*p*′-DDT) and number of follow-up visits (*p*-interactions were >0.24). All analyses were conducted using Stata (release 10.1; StataCorp, College Station, TX, USA).

3. RESULTS

The mothers in the present study were young, and the majority had <10 years of education and were poor, from urban dwellings, and multiparous; the prevalence of parental smoking during pregnancy or follow-up was low (Table 1). The duration of breastfeeding was long (median, 11 months) and although the prevalence of exclusive breastfeeding was high, the

duration of exclusive breastfeeding was very short: median, 3 days (quartiles 1 and 30.5 days). The prevalence of children classified as underweight according to the CDC growth standards(2000) (Kuczmarski et al. 2000) was higher than reported recently for Mexican children nationwide (Table 1) (Gonzalez-de Cossio et al. 2009). As expected, the proportion of underweight children was higher among the poorest (20%) as compared with less poor and not poor (8%). Characteristics of the women and children not included (n=42) in the present analysis were similar to those included, except that non-included women had shorter duration of breastfeeding (median, 8.5; IQR, 9.0 months) and lower levels of *p,p′*-DDT (median 0.18; IQR, 0.59 μg/g). Overall, women from this study had higher median levels of *p,p′*-DDE (2.7 μg/g lipid) and *p,p′*-DDT (0.27 μg/g lipid) than those reported for the US adult population in 2003–2004 (medians: *p,p′*-DDE, 0.20 μg/g lipid; *p,p′*-DDT, <0.01 μg/g lipid) (CDC 2009).

The proportion of boys with at least one episode of LRTI during follow-up was 18.6% (n=139); of these, 67.6% (n=94) had only one episode and 32.4% (n=45) had two or more. Overall, there were 0.19 episodes of LRTI per child-year, and bronchiolitis accounted for most of the episodes (209/267). The incidence rate (IR) of LRTI tended to be higher among children with lower prenatal exposure to *p,p′*-DDE and *p,p′*-DDT (Table 2).

Higher levels of prenatal exposure to *p,p′*-DDE and *p,p′*-DDT were not associated with a higher IRR of LRTI before or after adjustment for potential confounders (Table 3). Compared to children with the lowest prenatal exposure to *p,p′*-DDE (≤3.00 μg/g), those with the highest exposure (>9.00 μg/g) had an adjusted IRR of LRTI of 0.77 (95% confidence interval [95% CI], 0.41–1.46); the corresponding adjusted IRR of LRTI for *p,p′*-DDT was also null (aIRR = 0.65; 95% CI: 0.30–1.39 for *p,p′*-DDT ≥2.00 compared to ≤0.25 μg/g). Adding duration of breastfeeding to the fully adjusted models showed results comparable to those in Table 3, overall the adjusted IRRs decreased by 4% or less for both *p,p′*-DDE and *p,p′*-DDT models (data not shown). Higher prenatal exposure to *p,p′*-DDE and *p,p′*-DDT remained unassociated with a higher risk of LRTI across strata defined by poverty status, residence area, and underweight. Our results were similar based on the aIRR of LRTI per IQ increase in *p,p′*-DDE and *p,p′*-DDT (Table 3).

4. DISCUSSION

In this population of boys, higher levels of prenatal exposure to *p,p′*-DDE and *p,p′*-DDT were not associated with a higher occurrence of LRTI. The adjusted IRR of LRTI was slightly lower among boys with higher exposure levels. The long median of lactation (11 months) in this population may have protected the boys against LRTI, as duration of lactation was associated with a lower IRR of LRTI (data not shown) (Kramer et al. 2001). Although LRTIs are associated with poverty and child's malnutrition (Roth et al. 2008), the proportion of children with LRTI in the present study was not statistically different across strata of poverty and among underweight and normal weight children. This might be explained by the little variation in socioeconomic status of the women included in the present study; most of them were either very poor or poor.

Our results did not support the previous finding of a moderately increased risk of recurrent LRTI with increasing levels of prenatal exposure to *p,p′*-DDE among children (ages 12 to 14 months) from three regions of Spain, which included a sample size (n=1,342) larger than ours (Gascon et al. 2012). A higher risk of LRTI was observed with increasing levels of prenatal exposure to *p,p′*-DDE among Inuit children (n=199) at 6 months of age, but not at 12 months of age (Dallaire et al. 2004). Our findings were similar to an earlier study that reported lower odds of respiratory infections with increasing levels of prenatal exposure to *p,p′*-DDE in infants (n=190) who were 3 months of age from Sweden (Glynn et al. 2008); as in the present study their results did not reach statistical significance. The strength of our study was the relatively large sample size and the high levels of exposure to *p,p′*-DDE observed. Medians of prenatal exposure to *p,p′*-DDE reported in these prior studies ranged from 0.088 to 0.294 μg/g, while median levels measured in the present was 2.7 μg/g (first percentile, 0.22 μg/g).

The exact mechanism by which exposure to DDE might be associated with a higher risk of LRTI remains unknown at this time. As noted above, previous studies have documented suppression of the immune response with high levels of DDT exposure in animal as well as in human populations (ATSDR 2002). In humans, DDE exposure has been related to alterations of immune markers such as immunoglobulins (IgG, IgA, AgE), blood cells (lymphocytes), and interleukins (IL-4 and IL-13 (ATSDR 2002; Brooks et al. 2007; Cooper et al. 2004; Eskenazi et al. 2009; Nagayama et al. 2007; Vine et al. 2001). DDE exposure has been also associated with decreased maternal T helper cell Type 1 cytokines during pregnancy (Noakes et al. 2006). Conceivably, developmental exposure to chemicals with immunotoxic effects such as DDT could lead to permanent alterations of the immune system, possibly affecting the body's ability to fight infections later in life.

Our population was limited to full term males with normal birthweight due to our initial hypothesis related to anti-androgenic effects of DDT; this could potentially account for our overall null findings. However, in the largest study, which included girls and preterm birth infants, the authors did not observe a differential association between LRTI and DDE among girls or boys, and their results remained unchanged when they excluded preterm births from their analysis (Gascon et al. 2012).

Differential report of LRTI with respect the exposure is unlikely in the present study, because interviewers and mothers were blinded about the levels of *p,p′*-DDE and *p,p′*-DDT. A limitation of the present study is that we did not obtain medical records to confirm the mother's report of the number of LRTI episodes that children experienced during the study period; thus, random errors in the classification of the outcome might have occurred. Our definition of an episode of LRTI was based on a report of a doctor's diagnosis-- mild episodes that did not warranted medical attention were therefore unaccounted in such definition-- likely leading to an underestimation of the incidence of LRTI. Nonetheless, the number of episodes of LRTI in the present study (0.19 per child-year) was within the range of LRTI episodes reported for developing countries (0.04 to 1.80 per child-year) among children younger than 4 years (Rudan et al. 2004).

Overall, our results did not support an association between increasing levels of *p,p′*-DDE and higher risk of LRTI, previously reported in a population with much lower levels of exposure than boys in the present study. The unexplored potential association of higher levels of prenatal exposure to *p,p′*-DDE with higher incidence of severe LRTI during childhood may require additional consideration.

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Abbreviations

***p,p′*-DDE**	1,1-dichloro-2,2-bis(p-chlorophenyl)ethylene
***p,p′*-DDT**	1,1,1-trichloro-2,2-bis(4-chlorophenyl)ethane
IQR	interquartile range
IRR	incidence rate ratio

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Highlights

- Median of *p*,*p*′-DDE in Mexico was ~13.5 times higher than recent U.S. levels.
- Higher levels of *p*,*p*′-DDE were not associated to higher risk of LRTI in childhood.
- Higher levels of *p*,*p*′-DDT were not associated to LRTI in childhood.
- First study assessing LRTI in relation to *p*,*p*′-DDE in a highly exposed population.

Table 1

Characteristics of the mothers and sons at recruitment. Tapachula, Chiapas, Mexico 2002–2003

Characteristics	% or median (IQR) n = 747
Mothers	
Age at delivery	23.7 (7.2)
Education (years)	
0 – 6	35.1
7 – 9	31.6
10 – 12	23.1
> 12	10.2
Parity	
1	41.1
2	34.9
3+	24.0
Poverty status[a]	
Poorest	71.1
Less poor	18.6
Not poor	10.3
Residence area	
Urban	59.6
Rural	40.4
Parental smoking[b]	
None	84.5
Dad only	14.3
Mom only	1.1
Both parents	0.1
p,*p*′-DDT (μg/g lipid)	0.27 (0.67)
p,*p*′-DDE (μg/g lipid)	2.70 (4.50)
Sons	
Birth season	
Winter	19.0
Spring	28.4
Summer	28.9
Fall	23.7
Underweight[c]	
No	83.3
Yes	16.7
Exclusive breastfeeding[d]	
No	16.1
Yes	83.9
Duration of breastfeeding (months)	11.0 (12.9)

IQR, interquartile range; SD, standard deviation

[a] Defined using Mexican national standards based on monthly per capita income: Urban (Poorest, ≤672 pesos; Less poor, >672 to ≤1367; Not poor, >1367) and Rural (Poorest, ≤495; Less poor, >495 to ≤946; Not poor, >946) (Cupul-Uicab et al. 2008)

[b] Smoking during pregnancy and/or anytime during follow-up

[c] Weight-for-age *z*-scores ≤−2.00 during follow-up based on the CDC 2000 growth charts for boys

[d] Median of exclusive breastfeeding, 3 days (quartiles 1 and 30.5 days)

Table 2

Incidence rate (IR) of LRTI by prenatal exposure to *p,p′*-DDE and *p,p′*-DDT among boys from Tapachula, Chiapas, Mexico 2002–2005

Organochlorines (μg/g lipids)	n	% with LRTI[a]	Episodes of LRTI	Child-year[b]	IR per child- year
Overall	747	18.6	267	1387	0.19
p,p′-DDE[c]					
≤ 3.00	400	19.3	164	732	0.22
3.01 – 6.00	166	16.9	46	309	0.15
6.01 – 9.00	68	20.6	23	129	0.18
> 9.00	113	17.7	34	218	0.16
p,p′-DDT[c]					
≤ 0.25	362	21.6	157	664	0.24
0.26 – 0.75	196	15.8	62	366	0.17
0.76 – 1.99	104	16.4	25	193	0.13
≥ 2.00	85	15.3	23	164	0.14

LRTI, lower respiratory tract infections

[a] Percentage of children with at least one episode of LRTI during FU

[b] The person-time for each child was calculated as the date of birth to the first visit and as the time since the previous visit (when the child had two or more visits)

[c] Categorized using the same cut points applied in previous analyses of these data (Cupul-Uicab et al., 2008; Longnecker et al., 2007)

Table 3

Unadjusted and adjusted incidence rate ratio (IRR) of LRTI in relation to prenatal exposure to *p,p′*-DDE and *p,p′*-DDT among boys from Tapachula, Chiapas, Mexico 2002–2005

Organochlorines (μg/g lipids)	n	Unadjusted IRR (95% CI)	Adjusted IRR[a] (95% CI)
p,p′-DDE			
≤ 3.00	400	1.00	1.00
3.01 – 6.00	166	0.67 (0.36, 1.25)	0.68 (0.36, 1.29)
6.01 – 9.00	68	0.80 (0.37, 1.70)	0.85 (0.41, 1.75)
> 9.00	113	0.70 (0.37, 1.33)	0.77 (0.41, 1.46)
P-trend*		*0.28*	*0.45*
Per IQ increase in *p,p′*-DDE[b]		0.90 (0.74, 1.08)	0.92 (0.78, 1.10)
p,p′-DDT (μg/g)			
≤ 0.25	362	1.00	1.00
0.26 – 0.75	196	0.72 (0.40, 1.29)	0.73 (0.41, 1.29)
0.76 – 1.99	104	0.55 (0.29, 1.03)	0.56 (0.30, 1.05)
≥ 2.00	85	0.59 (0.27, 1.30)	0.65 (0.30, 1.39)
P-trend*		*0.19*	*0.32*
Per IQ increase in *p,p′*-DDT[b]		0.93 (0.83, 1.04)	0.95 (0.86, 1.04)

IQ, interquartile; LRTI, lower respiratory tract infections

[a] Adjusted for mother's age, parity, poverty status, place of residence, and parental smoking

[b] IQR: *p,p′*-DDE, 4.5 μg/g; *p,p′*-DDT, 0.67 μg/g

* Trend test from models that included *p,p′*-DDE or *p,p′*-DDT as ordinal variables coded with median levels of each category