Published in final edited form as:

Environ Res. 2017 November ; 159: 606–612. doi:10.1016/j.envres.2017.08.050.

Prenatal DDT exposure and child adiposity at age 12: the CHAMACOS study

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Abstract

Objective: Using data from the Center for the Health Assessment of Mothers and Children of Salinas (CHAMACOS) birth cohort study, we assessed the association of *in utero* exposure to dichlorodiphenyltrichloroethane (DDT) and dichlorodiphenylethylene (DDE) with child adiposity at age 12.

Methods: We included 240 children with *o,p'*-DDT, *p,p'*-DDT, and *p,p'*-DDE concentrations measured in maternal serum collected during pregnancy (ng/g lipid) and complete 12-year follow-up data. Age- and sex-specific body mass index (BMI) *z*-scores were calculated from CDC growth charts. Children with BMI *z*-scores ≥85th percentile were classified as overweight or obese.

Results: At 12 years, BMI *z*-score averaged 1.09 (±1.03) and 55.4% of children were overweight or obese. Prenatal DDT and DDE exposure was associated with several adiposity measures in boys but not girls. Among boys, 10-fold increases in prenatal DDT and DDE concentrations were associated with increased BMI *z*-score (*o,p'*-DDT, adj-β=0.37, 95% CI: 0.08, 0.65; *p,p'*-DDT, adj-β=0.26, 95% CI: 0.03, 0.48; *p,p'*-DDE, adj-β=0.31, 95% CI: 0.02, 0.59). Results for girls were nonsignificant. The difference by sex persisted after considering pubertal status.

Conclusions: These results support the chemical obesogen hypothesis, that *in utero* exposure to DDT and DDE may increase risk of obesity in males later in life.

Keywords

body mass index; children; dichlorodiphenyltrichloroethane; obesity; prenatal exposure

INTRODUCTION

In utero exposure to endocrine disrupting chemicals has been hypothesized to increase risk of obesity in childhood and into adulthood (Heindel and vom Saal 2009; Tang-Peronard et al. 2011; Heindel and Schug 2013; Heindel et al. 2015). The organochlorine pesticide dichlorodiphenyltrichloroethane (DDT), and its primary breakdown product, dichlorodiphenyldichloroethylene (DDE), are persistent organic pollutants with known

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endocrine disruptor activity (Agency for Toxic Substances and Disease Registry 2002). DDT has been shown to have estrogenic effects, while DDE acts as an androgen antagonist (Kelce et al. 1995; Klotz et al. 1996; Kojima H 2004).

In experimental studies, both DDT and DDE exposure are associated with adipose dysfunction. *In vitro*, DDT and DDE increase adipocyte differentiation and expression patterns of CCAAT enhancer binding protein-α and peroxisome proliferator-activated receptor-γ, the main transcription factors regulating the adipogenic process (Moreno-Aliaga and Matsumura 2002; Kim et al. 2016). DDE has also been shown to increase basal free fatty acid uptake and adipokine (leptin, resistin, adiponectin) production in 3T3-L1 adipocytes (Howell and Mangum 2011).

Several longitudinal birth cohort studies have examined associations between prenatal exposure to DDT or DDE and child adiposity (Valvi et al. 2012; Cupul-Uicab et al. 2013; Warner et al. 2013; Delvaux et al. 2014; Hoyer et al. 2014; Tang-Peronard et al. 2014; Warner et al. 2014; Agay-Shay et al. 2015). With follow-up ages ranging from 5 to 9 years, significant positive associations between prenatal DDT and/or DDE exposure and body mass index (BMI) *z*-score or overweight status have been reported in some (Valvi et al. 2012; Warner et al. 2014; Agay-Shay et al. 2015), but not all studies (Cupul-Uicab et al. 2013; Hoyer et al. 2014; Tang-Peronard et al. 2014). Inconsistent sex-specific effects have been noted, with associations reported in males only (Valvi et al. 2012; Delvaux et al. 2014; Tang-Peronard et al. 2014; Warner et al. 2014), females only (Delvaux et al. 2014; Tang-Peronard et al. 2014), and both males and females (Agay-Shay et al. 2015).

Using data from the Center for the Health Assessment of Mothers and Children of Salinas (CHAMACOS) study, a longitudinal birth cohort in a California agricultural community, we previously reported sex-specific positive associations between prenatal DDT and DDE exposure and several adiposity measures at 9 years of age (Warner et al. 2014). Specifically, in boys, we reported that higher prenatal DDT concentrations were significantly associated with increased BMI *z*-scores. Also in boys, both prenatal DDT and DDE concentrations were associated with significantly increased waist circumference *z*-scores, and odds of increased waist circumference and overweight. In contrast, in girls, we found no evidence of associations between prenatal DDT and DDE concentrations and any measure of adiposity.

Here, we report results from follow-up of the CHAMACOS cohort at 12 years of age when almost all (93%) children had entered puberty based on assessment by the Tanner scale (Tanner 1986). We assessed the association of maternal serum concentrations of *o,p′*-DDT, *p,p′*-DDT, and *p,p′*-DDE during pregnancy with child adiposity at age 12 including BMI *z*-score, waist circumference, percent body fat, and overweight or obesity status. We also examined whether these relationships were modified by child sex.

METHODS

Study population

The CHAMACOS study is a longitudinal birth cohort study of environmental exposures and childhood growth and development. Details of the study population are presented elsewhere

(Eskenazi et al. 2003). Pregnant women were recruited from prenatal clinics serving the farmworker population in the Salinas Valley, California between 1999 and 2000. Eligible women were at least 18 years of age, less than 20 weeks gestation, English- or Spanish-speakers, qualified for government-sponsored health insurance, and planned to deliver at the county hospital. The study was approved by the Institutional Review Boards at participating institutions. Prior to participation, we obtained written informed consent from all mothers, oral assent from children beginning at age 7, and written assent from children at age 12.

Of 601 women who were initially enrolled, 527 were followed through delivery of a singleton liveborn child who survived the neonatal period, and 417 provided a serum sample during pregnancy for DDT and DDE analysis. Of these, complete follow-up interview, puberty assessment, and anthropometric measurements were available for 240 children at age 12. The children included in the analysis did not differ significantly from those who were excluded due to missing prenatal exposure measures or 12-year anthropometric data in terms of maternal sociodemographic characteristics (education, marital status, income), maternal pre-pregnancy BMI or child birthweight, maternal serum DDT and DDE levels, or child overweight status (data not shown).

Procedure

Details of the study methods are presented elsewhere (Eskenazi et al. 2003; Eskenazi et al. 2004). Briefly, women were interviewed in English or Spanish using structured questionnaires twice during pregnancy, after delivery, and when children were 6 months, 1, 2, 3½, 5, 7, 9, 10½, and 12 years old. During each interview, information collected included family sociodemographics, maternal characteristics, medical histories, child-based developmental milestones, and diet and behavioral information. Mothers were weighed and height was recorded. Beginning at the 9-year visit, clinical Tanner staging was conducted by trained research staff. Children were considered to have entered puberty if they were stage 2+ for breast development for girls or stage 2+ for pubic hair or genital development for boys.

At each visit, children were weighed and measured. At 12-years, barefoot standing height was measured to the nearest 0.1 cm using a stadiometer. Standing weight to the nearest 0.1 kg and percent body fat were measured using a bioimpedence scale (Tanita TBF-300A Body Composition Analyzer). For calculation of percent body fat, the scale was set to child mode and the manufacturer's algorithm, validated for children 7 years and older, was used. Waist circumference was measured to the nearest 0.1 cm by placing a measuring tape around the abdomen at the level of the iliac crest, parallel to the floor. Both height and waist circumference were measured in triplicate and averaged for analysis.

Serum DDT and DDE concentrations

Maternal serum samples were collected by venipuncture at about 26 weeks gestation (n=215) or delivery (n=25). Serum *o,p'*-DDT, *p,p'*-DDT, and *p,p'*-DDE concentrations were measured at the Centers for Disease Control and Prevention by isotope dilution gas chromatography-high resolution mass spectrometry methods (Barr et al. 2003) and reported on a whole-weight basis (pg/g). The limit of detection (LOD) was 1.3, 1.5, and 2.9 pg/g

serum for *o,p'*-DDT, *p,p'*-DDT, and *p,p'*-DDE, respectively. For values below the LOD, a serum level equal to one-half the detection limit was assigned (Hornung and Reed 1990). Lipid-adjusted values (ng/g) were calculated by dividing *o,p'*-DDT, *p,p'*-DDT, and *p,p'*-DDE on a whole-weight basis by total serum lipid content, estimated by a "summation" method (Phillips et al. 1989).

Statistical analysis

Lipid-adjusted concentrations of *o,p'*-DDT, *p,p'*-DDT, and *p,p'*-DDE were $\log_{10}$-transformed and analyzed as continuous variables. Age- and sex-specific BMI (kg/m^2) *z*-scores and percentiles for each child were calculated using 2000 Centers for Disease Control and Prevention growth charts (Kuczmarski et al. 2002). Children who were ≥85th percentile but <95th percentile for their age and sex were classified as overweight, and those who were ≥95th percentile were classified as obese. Age- and sex-specific waist circumference *z*-scores and percentiles for each child were calculated using NHANES III reference data for Mexican-American children (Cook et al. 2009). Children who were in the 90th percentile or higher were classified as having increased waist circumference (Zimmet et al. 2007).

For all outcomes, we used generalized additive models with a 3-degrees-of-freedom cubic spline to evaluate the shape of the exposure-response curves in the full sample, and in boys and girls separately. None of the digression from linearity tests was significant ($p \leq 0.15$), suggesting the relationships were linear. We examined the relationship of maternal serum DDT and DDE concentrations with continuous outcomes (BMI *z*-score, waist circumference *z*-score, percent body fat) using multivariable linear regression, and with binary outcomes (overweight (≥85th versus <85th percentile), obesity (≥95th versus <95th percentile), increased waist circumference (≥90th versus <90th percentile)) using multivariable Poisson regression with a robust variance estimator. Due to the high prevalence of binary outcomes, we used a Poisson link function to estimate the relative risk (RR) instead of the odds ratio.

Based on our review of the obesity literature and directed acyclic graphs, we considered the following variables as potential confounders. Maternal variables considered included country of birth, race, years in the United States at childbirth, education level, marital status, household socioeconomic status, pre-pregnancy BMI, weight gain during pregnancy, age at delivery, smoking during pregnancy, BMI at 12-year visit, and household food insecurity. Child variables considered included age, sex, birthweight, birth order, low birth weight (<2500 grams) and preterm (<37 weeks) status, breastfeeding duration, and pubertal status at 12-year visit. Based on the hypothesized causal relationships between these variables, the minimal set of confounders for adjustment were maternal pre-pregnancy BMI (continuous), years in the United States at childbirth (continuous), and puberty stage (ordinal). We considered effect modification by child sex in all analyses by including a cross-product term between exposure and sex. Interaction *p*-values <0.2 were considered significant.

We also examined the relationship between maternal serum DDT and DDE concentrations and 2- to 12-year BMI *z*-scores longitudinally, using generalized estimating equations (GEE) with robust standard errors and exchangeable correlation structure. We applied GEE to account for correlations among repeated outcome measures from the same child.

In sensitivity analyses, we reanalyzed the final models, first, excluding 17 children who were low birth weight and/or preterm; second, excluding the 17 pre-pubertal boys (stage 1); and third, excluding one outlier with standardized residuals with an absolute value >3. We reanalyzed the final models including prenatal concentrations of polybrominated diphenyl ether (PBDE) flame retardants, as we have previously reported associations with BMI (Erkin-Cakmak et al. 2015). We repeated final models including prenatal concentrations of other correlated organochlorine, hexachlorobenzene and β-hexachlorocyclohexane. In order to consider possible effect modification by breastfeeding, a proxy of postnatal exposure, we repeated the final models including a cross-product term between exposure and breastfeeding duration (<6 months versus ≥6 months). Finally, we reran the final models using inverse probability of treatment weights (IPTW) to account for potential bias due to loss to follow-up (Hernan et al. 2004). IPTW weights were calculated by first estimating the probability of each participant of the original cohort being included in the present analysis with the SuperLearner package in R (version 3.1.2), using baseline covariates and a binomial distribution. Stabilized weights were then calculated by dividing the proportion of participants seen at the 12-year follow-up (45.5%) by each participant's probability of inclusion. Standard errors for all models were estimated using the robust Huber-White sandwich estimator (Huber 1967; White 1980). All statistical analyses were performed using STATA, version 13.1 (Stata Corporation, College Station, TX).

RESULTS

Table 1 presents maternal and child characteristics of the study participants at 12 years of age. Most mothers were Latina (98.3%), Mexican-born (90.0%), had not completed high school (77.9%), were living at or below the federal poverty level (75.0%), and 29% reported being food insecure at the 12 year visit. At the time of their pregnancy, mothers were an average of 26.7 (± 5.0) years old. Almost all mothers (96.7%) initiated breastfeeding, and most (57.1%) breastfed for 6 months or more. Before pregnancy, 65.0% of mothers were classified as overweight or obese based on maternal report of pre-pregnancy weight (mean BMI = 27.6 (±5.4) kg/m^2).

As presented in Table 1, the 240 children were an average of 12.0 (±0.2) years old, 57.9% were female, 93% (100% of girls, 86% of boys) had entered puberty (stage 2+) and 24.6% were stage 5 (37.4% of girls, 6.9% of boys), indicating full pubertal maturity. The mean BMI *z*-score at 12 years was 1.09 (±1.03) with 15.4% classified as overweight and 40.0% classified as obese. Mean waist circumference *z*-score and percent body fat were 0.67 (±1.03) and 29.5% (±11.0), respectively. The three measures (BMI *z*-score, waist circumference *z*-score, percent body fat) were highly correlated (r > 0.85). A total of 82 (34.8%) children had increased waist circumference (≥ 90th percentile), and of these, 78 (95%) were also classified as obese. Children who were classified as obese were more likely to have a mother who was obese pre-pregnancy compared to children who were not obese (40.6% versus 14.6%, p<0.001). There was no significant difference in obesity status of children by maternal sociodemographic indicators, including country of birth, years lived in the U.S., education, poverty, or marital status. The association with covariates was similar when different adiposity measures were considered (data not shown).

Maternal serum concentrations of *o,p'*-DDT, *p,p'*-DDT, and *p,p'*-DDE collected during pregnancy and summarized in Table 2, were highly correlated (r=0.82–0.92). The median (interquartile ranges) *o,p'*-DDT, *p,p'*-DDT, and *p,p'*-DDE serum levels were 1.2 (0.7–3.3), 11.6 (7.4–47.4), and 1,129 (607–2,837) ng/g lipid, respectively. As reported previously (Bradman et al. 2007), maternal DDT and DDE concentrations were significantly higher in women who were Latina, born in Mexico, had less education, and had lived in the US for a shorter time. Maternal prenatal DDT and DDE concentrations did not vary by child characteristics including sex, birth order, birthweight, or puberty stage.

As presented in Table 3, maternal serum DDT and DDE concentrations were not associated with the child's BMI *z*-score, waist circumference *z*-score, or percent body fat at 12 years in the full sample. However, we observed statistically significant interaction by sex in models of BMI and waist circumference *z*-scores. A 10-fold increase in DDT and DDE was significantly positively associated with BMI *z*-score in boys (*o,p'*-DDT: adjusted β = 0.37, 95% confidence interval (CI): 0.08, 0.65; *p,p'*-DDT: adjusted β = 0.26, 95% CI: 0.03, 0.48; *p,p'*-DDE: adjusted β = 0.31, 95% CI: 0.02, 0.59), but not in girls (*o,p'*-DDT: adjusted β = −0.03, 95% CI: −0.30, 0.23, *p*-interaction = 0.04; *p,p'*-DDT: adjusted β = −0.02, 95% CI: −0.26, 0.22, *p*-interaction = 0.09; *p,p'*-DDE: adjusted β = −0.03, 95% CI: −0.39, 0.32, *p*-interaction = 0.14). DDT and DDE were also significantly positively associated with waist circumference *z*-score in boys only (*o,p'*-DDT: adjusted β = 0.31, 95% CI: 0.07, 0.56, *p*-interaction = 0.01; *p,p'*-DDT: adjusted β = 0.25, 95% CI: 0.05, 0.45, *p*-interaction = 0.03; *p,p'*-DDE: adjusted β = 0.27, 95% CI: 0.01, 0.53, *p*-interaction = 0.07). For percent body fat, there was no evidence of effect modification by sex (*o,p'*-DDT: *p*-interaction = 0.29; *p,p'*-DDT: *p*-interaction = 0.39; *p,p'*-DDE: *p*-interaction = 0.51) (Table 3).

As presented in Table 4, in the full sample maternal serum DDT and DDE concentrations were not associated with overweight, obesity or increased waist circumference, but we observed statistically significant interaction by sex. Among boys, a 10-fold increase in DDT was significantly associated with obesity (*o,p'*-DDT: adjusted RR = 1.46, 95% CI: 1.07, 1.97, *p*-interaction = 0.07; *p,p'*-DDT: adjusted RR = 1.28, 95% CI: 1.01, 1.64, *p*-interaction = 0.18); in girls, the risk of obesity was close to the null. DDT was also significantly positively associated with increased waist circumference in boys (*o,p'*-DDT: adjusted RR = 1.53, 95% CI: 1.12, 2.10, *p*-interaction=0.02; *p,p'*-DDT: adjusted RR = 1.36, 95% CI: 1.05, 1.76, *p*-interaction=0.05), but this was not the case in girls. The estimate for *p,p'*-DDE did not reach significance in boys, but there was still evidence of effect modification by sex (*p*-interaction=0.13). Results of GEE analyses of maternal serum DDT and DDE concentrations and BMI *z*-score at 2 to 12 years of age showed similar associations of increased BMI *z*-score across the study period for boys but not girls (see Supplementary Material, Table S1).

In sensitivity analyses, the results did not change when we repeated the final models excluding children who were low birthweight and/or preterm, excluding those who had not yet entered puberty or excluding one outlier (data not shown). Results were virtually unchanged when we additionally controlled for PBDEs, hexachlorobenzene, or β-hexachlorocyclohexane (data not shown). We found no evidence of effect modification by breastfeeding duration (data not shown). The results did not change materially after

adjusting for potential bias due to loss to follow-up (see Supplementary Material, Tables S4 and S5).

DISCUSSION

The CHAMACOS study provides evidence that *in utero* DDT and DDE exposure may alter risk for later obesity among males but not females. With three years additional follow-up that allowed us to control for puberty status, the results of this study confirm and strengthen our earlier reported findings (Warner et al. 2014). At 12 years of age, higher prenatal DDT concentrations were significantly associated with increased BMI *z*- and waist circumference *z*-score and risk of obesity and increased waist circumference in boys. Higher prenatal DDE concentrations were also significantly associated with increased BMI *z*- and waist circumference *z*-scores, and risk of overweight or obesity in boys. In contrast, prenatal DDT and DDE concentrations were not associated with any adiposity measure in girls.

Our findings of associations in boys only are consistent with two other studies that have assessed effect modification by sex (Valvi et al. 2012; Cupul-Uicab et al. 2013). Among 344 children in a population-based birth cohort study in Menorca, Spain, higher cord blood *p,p'*-DDT and *p,p'*-DDE levels were non-monotonically associated with increased BMI z-score and odds of overweight at 6.5 years, but associations with DDT were limited to males (Valvi et al. 2012). In the Collaborative Perinatal Project birth cohort study, which includes 1,809 births (1959 – 1965) before DDT was banned in the United States, Cupul-Uicab et al. (Cupul-Uicab et al. 2013) reported the association of maternal serum *p,p'*-DDT with BMI at age 7, although not significant, was more strongly positive in the boys (adj-β=0.08; 95% CI: −0.11, 0.26) than girls (adj-β=−0.02; 95% CI: −0.23,0.18) (*p*-interaction=0.20). In contrast, among 470 children in the IMMA cohort in Catalonia, Spain, maternal serum *p,p'*-DDE levels in pregnancy were associated with overweight at 7 years of age (tertile 3 vs 1: adj-RR = 2.21; 95% CI: 1.17, 4.15), but no evidence of effect modification by child sex was found (Agay-Shay et al. 2015). In the INUENDO birth cohort study of 1,109 mother-child pairs from Greenland (n=525, median, 300 ng/g lipid), Poland (n=92, median, 385 ng/g lipid), and Ukraine (n=492, median, 639 ng/g lipid), no associations were found between maternal *p,p'*-DDE levels in pregnancy and child BMI *z*-score at 5 to 9 years of age either overall or by sex (Hoyer et al. 2014). The authors noted due to considerable loss to follow-up, missing values for height, weight, and covariates were imputed for up to 27% of participants, which would be expected to bias the results towards the null.

With cohort follow-up at 12 years, we found positive associations between prenatal DDT and DDE exposure and markers of abdominal adiposity including waist circumference *z*-scores and increased waist circumference (≥90th percentile) in males. Two longitudinal birth cohort studies with shorter follow-up have reported associations of prenatal DDE exposure with abdominal adiposity (Delvaux et al. 2014; Tang-Peronard et al. 2014). Among 114 (10% of eligible) FLEHS cohort participants, higher cord blood *p,p'*-DDE levels were associated with increased waist circumference and waist-to-height ratio at 7 to 9 years, but associations were significant only in females (Delvaux et al. 2014). In the Faroe Islands study, maternal serum *p,p'*-DDE levels were associated with increased waist circumference at 7 years, but only in females with pre-pregnancy overweight mothers (Tang-Peronard et al.

2014). To our knowledge, our study is the first to investigate prenatal DDT exposure and abdominal adiposity. The International Diabetes Federation considers children with a waist circumference ≥90th percentile for their age and sex to be at-risk for metabolic syndrome (Zimmet et al. 2007). Thus our results suggest that prenatal DDT and DDE exposure may be associated with future risk for metabolic syndrome in boys. With future follow-up of the CHAMACOS cohort, we plan to examine this association.

Consistent with the other adiposity measures, we found a positive, albeit non-significant, association of DDT and DDE exposure with body composition as measured by percent body fat. To our knowledge, no other birth cohorts have assessed prenatal DDT and DDE exposure with body composition measurements. Although we did not find significant effect modification by sex, the observed associations were more strongly positive in males. Any effect of the smaller sample size with body fat measurements combined with the potentially lower accuracy of bioelectrical impedance for measuring fat mass in children would be expected to be non-differential, biasing associations towards the null. At present, there are no published reference values for percent body fat in Mexican-American children, which limits interpretation (Mueller et al. 2004; Laurson et al. 2011).

The biologic mechanisms underlying these findings are not clear. Human and *in vitro* data suggest androgens play an important role in the regulation of body fat distribution (Blouin et al. 2008). DDT and DDE have both been associated with adipose dysfunction in experimental studies (Moreno-Aliaga and Matsumura 2002; Howell and Mangum 2011; Kim et al. 2016). Since DDT, an estrogen agonist, is metabolized to DDE, an androgen antagonist, multiple mechanisms may be involved. The observed sex-specific associations seem plausible given that both estrogenic and anti-androgenic activity play key roles in adipogenesis during development (Cooke and Naaz 2004). *In utero* exposure to DDT and DDE could impact normal weight homeostasis directly through differentiation and proliferation of adipose cells or indirectly via disruption of the endocrine feedback loop (Cooke and Naaz 2004; Diamanti-Kandarakis et al. 2009). Given the high correlation in this study between maternal serum levels of DDT and DDE (r = 0.82 to 0.92), it is difficult to separate out the individual associations of each compound.

Strengths of this study include it is a longitudinal birth cohort with a long follow-up period for which considerable information was collected about potential confounders. We were able to measure *o,p'*-DDT, *p,p'*-DDT, and *p,p'*-DDE exposure in maternal serum collected during the pregnancy. The exposure levels were high relative to other Mexican-Americans (Centers for Disease Control and Prevention 2004), likely due to the mothers' recent immigration from Mexico (where DDT was used for mosquito control until 2000), but there was a wide range of exposure. We used standardized measures of adiposity based on BMI and waist circumference *z*-scores facilitating comparison across studies. Finally, we were able to consider pubertal status through use of Tanner staging, and to run longitudinal models to verify consistency in the observed relationships over time.

Limitations of the study include of the 417 mothers who had serum DDT and DDE measurements during pregnancy, only 240 children had complete anthropometric and puberty status data at 12 years. Prenatal DDT and DDE concentrations, however, were not

significantly different between those with and without 12-year anthropometric data. In addition, predictors of maternal DDT and DDE levels were similar to those reported previously in the larger group (Bradman et al. 2007). We were able to consider potential selection bias due to loss to follow-up using inverse probability weighting. An additional study limitation is that time constraints at the 12-year study visit prevented the collection of comprehensive dietary and physical activity data. Although we have not found these covariates to be confounders at previous visits, we plan to collect these data at future follow-up visits as they are well-known risk factors for the outcomes.

CONCLUSION

In summary, we examined the association of prenatal exposure to *o,p'*-DDT, *p,p'*-DDT, and *p,p'*-DDE with several measures of adiposity in the CHAMACOS cohort at 12 years of age. We found prenatal DDT and DDE concentrations to be significantly positively associated with BMI, waist circumference, and overweight or obesity status in boys. In contrast, prenatal DDT and DDE concentrations were not associated with any adiposity measure in girls. None of the observed findings changed when considering puberty status. With follow-up to age 12, our results support the chemical obesogen hypothesis, that *in utero* exposure to the endocrine disrupting chemicals, DDT and DDE, may increase risk of obesity in males later in life.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

ACKNOWLEDGEMENTS

We gratefully acknowledge the CHAMACOS field staff, community partners, the participants and their families; Robert Lustig, M.D. for pubertal assessment training and quality control; and Dana Barr, Ph.D. and colleagues at CDC for specimen analysis.

FUNDING

This research was supported by the National Institute of Environmental Health Sciences [grant numbers P01ES009605, R01ES017054] and the United States Environmental Protection Agency [grant numbers R82670901, RD83171001, RD83451301]. The funding sources had no involvement in the study design, the collection, analysis or interpretation of data, the writing of the manuscript, or the decision to submit the article for publication.

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Table 1.

Maternal and child characteristics, CHAMACOS Study, 2000–2012.

Characteristic	N	(%)
Total	240	(100.0)
Maternal Characteristics		
Country of birth		
United States	24	(10.0)
Mexico/Other	216	(90.0)
Race/ethnicity		
Latina	236	(98.3)
Non-Latina	4	(1.7)
Years of residence in USA		
≤ 1	57	(23.8)
2 – 5	71	(29.6)
6 – 10	55	(22.9)
≥ 11	57	(23.8)
Education		
≤ 6th grade	104	(43.3)
7th – 12th grade	83	(34.6)
≥ High school	53	(22.1)
Marital status		
Not married	34	(14.2)
Married/living as married	206	(85.8)
Household income status[a]		
At or below poverty	180	(75.0)
Above poverty	59	(24.6)
Household food insecurity[a]		
Food secure	168	(70.0)
Food insecure w/o hunger	52	(21.7)
Food insecure with hunger	17	(7.1)
Prepregnancy BMI, kg/m^2		
Underweight	2	(0.8)
Normal	82	(34.2)
Overweight	96	(40.0)
Obese	60	(25.0)
Smoking during pregnancy		
No	231	(96.3)
Yes	9	(3.8)
Age at delivery, years		
< 25	89	(37.1)
25 – 29	90	(37.5)

Characteristic	N	(%)
30 – 34	39	(16.3)
≥ 35	22	(9.2)
Breastfeeding, months		
0 – 2	56	(23.3)
2 – 6	60	(25.0)
6 – 12	57	(23.8)
> 12	67	(27.9)
Child Characteristics		
Child sex		
Male	101	(42.1)
Female	139	(57.9)
Birth order		
1	73	(30.4)
2	74	(30.8)
≥ 3	93	(38.8)
Birth weight (grams)		
< 2500	6	(2.5)
2500 – 3500	131	(54.6)
> 3500	103	(42.9)
Puberty stage at age 12		
1	17	(7.1)
2	54	(22.5)
3	65	(27.1)
4	45	(18.8)
5	59	(24.6)
BMI *z*-score at age 12		
<85th percentile	107	(44.6)
85–95th percentile	37	(15.4)
≥95th percentile	96	(40.0)
Waist circumference *z*-score at age 12		
<90th percentile	154	(65.3)
≥90th percentile	82	(34.7)
Weight (kg)		
mean (SD)	55.3	(15.9)
Height (cm)		
mean (SD)	152.7	(6.3)
BMI (kg/m^2)	23.5	(5.6)
mean (SD)		
Waist circumference (cm)	78.9	(13.5)
mean (SD)		
Percent body fat (%)	29.5	(11.0)

Characteristic	N	(%)
mean (SD)		

[a]Numbers do not add to 100% due to missing data for socioeconomic status (n=1), household food insecurity (n=3).

Table 2.

Summary of DDT and DDE concentrations measured in maternal serum collected during pregnancy (ng/g lipid), CHAMACOS, 2000–2012

Exposure	n	% Detect	GM(GSD)	Min	25%	Med	75%	Max
o,p'-DDT	239	96	1.76 (4.8)	0.1	0.7	1.2	3.3	1,257.3
p,p'-DDT	240	100	22.6 (5.9)	1.6	7.4	11.6	47.4	33,174.0
p,p'-DDE	240	100	1,511.1 (3.6)	48.8	606.9	1,129.2	2,837.4	159,303.3

Abbreviations: DDE, dichlorodiphenyldichloroethylene; DDT, dichlorodiphenyltrichloroethane; GM, geometric mean; GSD, geometric standard deviation; Min, minimum; Med, median; Max, maximum

Table 3.

Adjusted[a] linear regression models of the associations of maternal serum DDT and DDE concentrations in pregnancy with BMI[b] *z*-score, waist circumference *z*-score, and percent body fat at 12 years of age, overall and by child sex, CHAMACOS Study, 2000–2012.

Outcome	N[c]	Adjusted β[d]	95% CI	Child Sex				*p* - interaction
				Male		Female		
				Adjusted β[d]	95% CI	Adjusted β[d]	95% CI	
BMI *z*–score								
o,p'–DDT	239	0.14	−0.08, 0.35	0.37	0.08, 0.65	−0.03	−0.30, 0.23	0.04
p,p'–DDT	240	0.12	−0.07, 0.30	0.26	0.03, 0.48	−0.02	−0.26, 0.22	0.09
p,p'–DDE	240	0.16	−0.08, 0.39	0.31	0.02, 0.59	−0.03	−0.39, 0.32	0.14
Waist circumference *z*–score								
p,p'–DDT	235	0.06	−0.15, 0.28	0.31	0.07, 0.56	−0.14	−0.41, 0.14	0.01
p,p'–DDT	236	0.07	−0.11, 0.26	0.25	0.05, 0.45	−0.10	−0.35, 0.15	0.03
p,p'–DDE	236	0.09	−0.15, 0.32	0.27	0.01, 0.53	−0.15	−0.51, 0.22	0.07
Percent body fat								
o,p'–DDT	207	0.57	−1.86, 2.99	2.26	−0.67, 5.19	0.01	−3.20, 3.22	0.29
p,p'–DDT	208	0.28	−1.72, 2.27	1.65	−0.72, 4.03	0.12	−2.70, 2.94	0.39
p,p'–DDE	208	1.06	−1.55, 3.66	2.55	−0.42, 5.53	0.92	−3.03, 4.87	0.51

[a] Adjusted for maternal prepregnancy BMI, time in the US at birth, puberty stage

[b] Weight (kg)/height (m)^2

[c] BMI (101 male, 139 female); waist circumference (100 male, 136 female); percent body fat (92 male, 116 female)

[d] β is for a 10-fold increase in exposure

Table 4.

Adjusted[a] poisson regression models of the associations of maternal serum DDT and DDE concentrations in pregnancy with overweight, obesity, and increased waist circumference at 12 years of age, overall and by child sex, CHAMACOS Study, 2000–2012.

Outcome	Cases[b]	Total	Adjusted RR[c]	95% CI	Child Sex				*p* for interaction
					Male		Female		
					Adjusted RR[c]	95% CI	Adjusted RR[c]	95% CI	
Overweight or obesity									
o,p'–DDT	132	239	1.15	0.97, 1.35	1.35	1.06, 1.72	1.03	0.85, 1.26	0.08
p,p'–DDT	133	240	1.14	0.99, 1.31	1.27	1.04, 1.53	1.05	0.87, 1.25	0.14
p,p'–DDE	133	240	1.23	1.02, 1.48	1.38	1.08, 1.77	1.08	0.82, 1.42	0.18
Obesity									
o,p'–DDT	95	239	1.16	0.94, 1.44	1.46	1.07, 1.97	1.00	0.75, 1.34	0.07
p,p'–DDT	96	240	1.13	0.94, 1.35	1.28	1.01, 1.64	1.01	0.78, 1.31	0.18
p,p'–DDE	96	240	1.17	0.91, 1.50	1.35	0.98, 1.87	1.01	0.68, 1.49	0.26
Increased waist circumference									
o,p'–DDT	81	235	1.10	0.87, 1.40	1.53	1.12, 2.10	0.90	0.64, 1.27	0.02
p,p'–DDT	82	236	1.09	0.90, 1.34	1.36	1.05, 1.76	0.93	0.68, 1.26	0.05
p,p'–DDE	82	236	1.11	0.85, 1.46	1.39	0.97, 1.98	0.90	0.58, 1.39	0.13

[a] Adjusted for maternal pre-pregnancy BMI, time in the US at birth, puberty stage

[b] Cases of overweight (55 male, 78 female), obesity (40 male, 56 female), and increased waist circumference (32 male, 50 female)

[c] RR is for a 10-fold increase in exposure