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Perinatal exposure to chlordecone and infant growth

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ABSTRACT

Background: The intensive use of chlordecone (an organochlorine insecticide) in the French West Indies until 1993 resulted in a long-term soil and water contamination. Chlordecone has known hormonal properties and exposure through contaminated food during critical periods of development (gestation and early infancy) may affect growth.
Objectives: We aimed to assess the impact of prenatal and postnatal exposure to chlordecone on the growth of children from the TIMOUN mother–child cohort.
Methods: Chlordecone was determined in cord plasma at birth ($N=222$) and in breast milk samples (at 3 months). Dietary chlordecone intake was estimated at 7 and 18 months, with food-frequency questionnaires and food-specific contamination data. Anthropometric measurements were taken at the 3-, 7- and 18-month visits and measurements reported in the infants' health records were noted. Structured Jenss–Bayley growth models were fitted to individual height and weight growth trajectories. The impact of exposure on growth curve parameters was estimated directly with adjusted mixed non-linear models. Weight, height and body mass index (BMI), and instantaneous height and weight growth velocities at specific ages were also analyzed relative to exposure.
Results: Chlordecone in cord blood was associated with a higher BMI in boys at 3 months, due to greater weight and lower height, and in girls at 8 and 18 months, mostly due to lower height. Postnatal exposure was associated with lower height, weight and BMI at 3, 8 and 18 months, particularly in girls.
Conclusion: Chlordecone exposure may affect growth trajectories in children aged 0 to 18 months.

1. Introduction

Chlordecone (kepone) is a synthetic organochlorine compound that was intensively used as an insecticide in the French West Indies from 1973 to 1993, to control banana root borers. This intensive use led to persistent, widespread soil and water contamination, resulting in exposure of the population, through the ingestion of contaminated food (Seurin et al., 2012). Several studies have shown chlordecone to be present in the blood of adult men (Multigner et al., 2010), pregnant women, and newborns, and

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in maternal breast milk (Dallaire et al., 2012). Chlordecone is an endocrine-disrupting chemicals (EDC) with well-defined estrogenic properties (Hammond et al., 1979; Lemaire et al., 2006). Experimental studies in adult rodents have demonstrated that chlordecone exposure induced fat depletion as a consequence of altered energy balance of the animal (Klingensmith and Mehendale, 1982) . Moreover, neonatal exposure to chlordecone in rats is associated with significant sex-dependent changes in adult body weight, resulting in lighter males and heavier females (Mactutus and Tilson, 1985). It has been suggested that environmental exposure to EDCs, such as p,p′-DDE and PCBs during vulnerable periods of development may lead to permanent changes in weight control mechanisms, contributing to the current overweight and obesity epidemic (Tang-Péronard et al., 2011). Recent reviews of cohort studies exploring the effects of prenatal exposure to EDCs on growth have reported consistent associations between prenatal DDE exposure and a higher BMI in childhood, whereas associations between prenatal PCB exposure and growth appear to be less consistent (de Cock and van de Bor, 2014a, 2014b; Iszatt et al., 2015; Tang-Péronard et al., 2011).

The potential effect on the growth of human children of pre- or postnatal exposure to environmental levels of chlordecone remains completely unknown. We investigated the association between chlordecone exposure in early life and the growth of children up to the age of 18 months, within the TIMOUN mother–child cohort study conducted in Guadeloupe.

2. Materials and methods

2.1. Population

The TIMOUN study is a prospective mother–child cohort study currently underway in the Guadeloupe archipelago in the French West Indies. Between November 2004 and December 2007, 1068 pregnant women were enrolled in this study by obstetricians, during their second- or third-trimester prenatal visit at the Pointe à Pitre/Abymes or Basse-Terre public hospitals or at a local antenatal care dispensary. At inclusion, women were interviewed by trained midwives, to assess their medical history, socioeconomic conditions and dietary habits. At delivery, data about the delivery, maternal diseases during pregnancy, newborn health status and anthropometric characteristics were collected by the medical staff, and cord blood samples were obtained.

A subsample of children, excluding cases of multiple birth, preterm birth, intra-uterine growth restriction, neonatal disease or malformation, and serious maternal illness before or during pregnancy, was selected for follow-up ($N=589$). In total, 287 mothers could not be contacted or refused to participate. The final subsample followed consisted of 302 children.

Two hospital visits were organized for the children, at the ages of three and seven months. A third visit took place at the child's home, at the age of 18 months. All 302 families were invited to participate at each visit. Questionnaires about the child's health, lifestyle and dietary habits were completed by trained interviewers, during interviews with the mothers, and the children were measured. Only children with a known birth height and birth weight and at least one weight and height measurement at the 3-, 7- or 18-month visit were retained for the growth study and two children who have been hospitalized for severe disease during follow-up have been excluded ($N=299$). This group included 222 (74%) children for which cord blood chlordecone determinations were available (Supplementary Fig. S1).

2.2. Exposure assessment

Prenatal exposure to chlordecone was measured at birth and postnatal exposure was measured at three, seven and eighteen months. In addition, prenatal co-exposure to DDE and PCB 153 congener was quantified at birth to include them as covariates because of their potential effect on child growth.

A 10-ml cord blood sample was collected at delivery and a 5-ml breast milk sample was collected at three months, to document prenatal and breastfeeding exposure to chlordecone. Cord plasma and milk samples were stored at −30°C, until shipment, in dry ice, to the Center for Analytical Research and Technology (Liège, Belgium). The concentrations of chlordecone, DDE and the PCB 153 congener were determined by high-resolution gas chromatography with electron capture detection. Sample preparation and quantification methods were as previously described (Multigner et al., 2010). In cord plasma samples, the limit of detection (LOD) was 0.06 μg/L for chlordecone, and 0.05 μg/L for DDE and PCB 153. In milk samples, the LOD for chlordecone was 0.34 μg/L. Total cholesterol and triglyceride levels in cord plasma were determined by standard enzymatic procedures, and total lipid concentrations were calculated as described by Bernert et al. (2007). Breast milk lipid concentrations were quantified by gravimetry.

As cord plasma chlordecone concentrations followed a skewed distribution, they were subjected to $\log_{10}$ transformation. General additive models with restricted cubic splines for chlordecone concentration suggested a non-linear relationship to growth measurements. We therefore categorized cord plasma chlordecone concentration into three exposure groups: < LOD (0.06 μg/L; low), LOD–median of detected values (0.31 μg/L; medium), > median (high).

Breast milk chlordecone concentrations were available for 111 of the 153 infants still breast fed at three months. Missing breast milk chlordecone concentrations were imputed to the median value of chlordecone concentration measured in the breast milk of women with the same country of birth and zone of residence, as both variables were identified as predictors of breast milk contamination in the cohort ($p=0.07$ and $p<0.001$ respectively in a multivariate regression model). A variable combining breastfeeding status at 3 months (still breastfed/not breastfed) and breast milk contamination for breastfed children (3 categories : chlordecone not detected, chlordecone concentration below or above the median) was used to assess exposure through breast feeding (Supplementary Table S1).

At the ages of 7 and 18 months, exposure to chlordecone from contaminated food was estimated with a semi-quantitative food frequency questionnaire, describing the dietary habits of the children. This questionnaire was completed by trained interviewers. Levels of food and water contamination were obtained from a survey conducted in Guadeloupe from July 2006 to January 2007 by the public health authorities. The daily dietary intake of chlordecone was derived by combining the quantity of each food item ingested (g/day) and its level of contamination with chlordecone (μg/kg), expressed in μg/kg body weight/day (Seurin et al., 2012). Missing intake values for infants aged 7 months ($N=57$) or 18 months ($N=59$) were imputed with a linear regression model including children for whom at least one of these estimates was available ($N=36$), as intakes at 7 and 18 months were correlated ($r=0.40$, $p<0.0001$). The remaining missing values ($N=25$) were imputed to the median intake for children from the same residential area (contaminated or non-contaminated) at 7 and 18 months, as this variable was most predictive for dietary chlordecone intakes ($p<0.0001$, regression model). Postnatal intake via the ingestion of contaminated food at 7 and 18 months (μg/kg bw/day) was then categorized into quartiles defined among children with known intakes (Supplementary Table S1).