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Exposure to an organochlorine pesticide (chlordecone) and development of 18-month-old infants

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ABSTRACT

Chlordecone is a persistent organochlorine pesticide that was used in the French West Indies until the early 1990s for banana weevil borer control. Human exposure to this chemical in this area still occurs nowadays due to consumption of contaminated food. Although adverse effects on neurodevelopment, including tremors and memory deficits, have been documented in experimental studies conducted with rodents exposed during the gestational and neonatal periods, no study has been conducted yet to determine if chlordecone alters child development. This study examines the relation of gestational and postnatal exposure to chlordecone to infant development at 18 months of age in a birth-cohort of Guadeloupean children. In a prospective longitudinal study conducted in Guadeloupe (Timoun mother–child cohort study), exposure to chlordecone was measured at birth from an umbilical cord blood sample ($n = 141$) and from a breast milk sample collected at 3 months postpartum ($n = 75$). Toddlers were assessed using an adapted version of the Ages and Stages Questionnaire. Higher chlordecone concentrations in cord blood were associated with poorer fine motor scores. When analyses were conducted separately for boys and girls, this effect was only observed among boys. These results suggest that prenatal exposure to chlordecone is associated with specific impairments in fine motor function in boys, and add to the growing evidence that exposure to organochlorine pesticides early in life impairs child development.

1. Introduction

Chlordecone (also named Kepone) is an organochlorine (OC) pesticide intensively used between 1972 and 1993 in the French West Indies as an insecticide for banana weevil borer control. It is highly persistent in the environment, with no significant biotic or abiotic degradation, resulting in permanently polluted soils of current and older banana fields and waterways (Cabidoche et al., 2009; Coat et al., 2011). Nowadays, human exposure to chlordecone in the French West Indies mainly arises from consumption of contaminated food, especially seafood, root vegetables, and cucurbitaceous, as it has been shown in studies conducted in the general population (Dubuisson et al., 2007) and with pregnant women (Guldner et al., 2010).

The toxicity of chlordecone to humans has been discovered in 1975 following a poisoning episode among pesticide plant workers in the industrial city of Hopewell, VA, USA. Some workers had evidence of sustained toxicity involving the nervous system, liver and testes (Cannon et al., 1978; Cohn et al., 1978; Taylor, 1982). Major signs of neurological impairment included appendicular tremor, staggering speech, opsoclonus, and exaggerated startle response. Also evident were anxiety, irritability and short-term memory loss. Animal studies show effects similar to those reported

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in occupationally exposed humans including neurological effects, oligospermia, and hepatomegaly (Faroon et al., 1995; Guzelian, 1992).

Although the developing central nervous system is known to be especially vulnerable to neurotoxic agents (Rice and Barone, 2000), the developmental neurotoxicity of chlordecone has received little attention. Yet, chlordecone is known to cross the placental barrier in pregnant rodents (Kavlock et al., 1980) and is then transferred to the newborn through maternal breastfeeding, thus exposing the developing organism during the earliest stages of development. In utero exposure of rats and mice to doses producing overt toxicological effects in the dams results in severe fetotoxic effects, including stillbirths, reduced birth weight, and cerebral anomalies (Chernoff and Rogers, 1976). A series of experiments conducted with rodents showed that neonatal exposure to a single dose of chlordecone can result in reduced weight, increased tremors, and neurobehavioral impairments including memory deficits and altered response to stress among the developing pups (Mactutus et al., 1982, 1984; Mactutus and Tilson, 1984; Tilson et al., 1982). Some of these effects appeared to be sex-dependent, with males being generally more impaired (e.g., Mactutus and Tilson, 1985; Tilson et al., 1982), which may be related to chlordecone's estrogen-like activity (Hammond et al., 1979; Hudson et al., 1984).

While experimental studies with animals have documented deleterious effects of early chlordecone exposure on neurodevelopment, still no epidemiological study has been conducted yet to determine if similar effects can be found in humans. The Timoun mother–child cohort study was initiated to assess the effects of chlordecone exposure on child development in Guadeloupean children. Maternal exposure in this cohort has been attributed to the intake of contaminated food and water (Guldner et al., 2010). In a follow-up conducted when infants were 7 months of age, chlordecone-related adverse effects were reported on fine motor development, visual recognition memory, and speed of information processing (Dallaire et al., 2012). Because the developmental effects attributable to exposure to a neurotoxic chemical may be transient or permanent (Rice and Barone, 2000), and because a better characterization of these effects is possible as the child grows due to functional brain specialization and the emergence of new functions, further follow-up assessments conducted later during development are necessary to provide an optimal characterization of chlordecone's developmental neurotoxicity in humans. The present study examined the relation of pre- and postnatal exposure to chlordecone to child development in 18-month-old infants from the Timoun mother–child cohort.

2. Materials and methods

2.1. Population and data collection

A prospective epidemiological mother–child cohort (Timoun study) is currently being followed in Guadeloupe (French West Indies) in order to study the impact of prenatal chlordecone exposure on pregnancy outcome and infant development. Women in the second trimester of pregnancy who planned to give birth in the University Hospital of Pointe-à-Pitre and the General Hospital of Basse-Terre (accounting for 70% of all deliveries in Guadeloupe) from December 2004 to December 2007 were invited to participate in the study. Detailed recruiting procedures have been described elsewhere (Dallaire et al., 2012). Maternal diseases, adverse delivery incidents as well as newborn anthropometric parameters and health information were collected from child and maternal medical records. Exclusion criteria associated with maternal diseases were history of diabetes, gestational diabetes mellitus, hypertension, epilepsy, human immunodeficiency virus infection, and long term corticotherapy. Exclusion criteria for newborns were not singleton, gestational age < 37 week, birth weight < 2500 g, APGAR < 7 at 5 min, intrauterine growth restriction $<$10th percentile of birth weight for gestational age, severe respiratory distress, severe icterus (needing more than 3 intensive phototherapies), severe hypoglycemia, confirmed materno-fetal infection with antiobiotherapy $>$48–72 h.

Between September 2006 and October 2009, a research nurse visited the participating mothers and their child at home for a follow-up assessment 18 months after delivery. A total of 204 participants were administered a developmental assessment. Sixty-three were excluded because of incomplete data regarding chlordecone quantification in umbilical cord. A maternal interview was conducted to provide information on demographic background as well as quality of stimulation provided by the family. Written informed consent was obtained from parents of each participating child. The research procedures were approved by the Guadeloupean Ethics Committee for biomedical studies involving human subjects.

2.2. Infant assessment

Infant development was assessed with the Ages and Stages Questionnaire (ASQ), a parent-completed screening test aimed at identifying children at risk for developmental delay (Bricker and Squires, 1999). This 30-item questionnaire for children aged 2–60 months covers five developmental areas: personal–social, communication, problem-solving, fine motor, and gross motor. There are 19 versions of the ASQ, with questions adapted to the child's age. Each item corresponds to a developmental behavior or skill, which the parent must answer "yes" (10 points) if the child performs the given behavior, "sometimes" (5 points) if the behavior is performed occasionally or is emerging, and "not yet" (0 point) if the child does not yet perform the behavior. For each area, cut-off values, set at 2 SD below the mean using reference norms, are proposed for identifying children at risk for developmental delay. Specificity has been shown to be high ($>$80%) across age intervals. Sensitivity is somewhat lower, averaging 75%, and test-retest and inter-rater reliabilities are both of 94% (Squires et al., 1997). Administration procedures of the ASQ were adapted for the purpose of this study since a pilot phase of our study indicated that parents tended to respond positively to each item, which may be attributable to cultural factors. Each item from the communication, problem-solving, fine motor and gross motor areas of both the 18- and the 20-month questionnaires was administered directly to the child by a trained research personnel. As these items are found in the Bayley Scales of Infant Development-II (BSID-II), their administration was standardized according to the BSID-II procedures (Bayley, 1993) in order for each item to be administered in the same way for each participant. When a child was unable to adequately perform an item, the examiner asked the mother whether her child "can", "sometimes can" or "cannot yet" perform the behavior or the skill as specified in the ASQ. Thereafter, 10 points were allocated following a success to the administered item or to an item answered "can" by the mother, 5 points when the mother responded "sometimes can" and 0 point for a "cannot yet" answer. Points were then summed to yield a total score for the communication, problem-solving, gross motor and fine motor areas. For the personal–social area, the items from the 18- and the 20-month questionnaires were administered according to the ASQ's original procedure. A total score was calculated for each area by adding the points obtained by the child. All scores were then converted to IQ-like scores, with a mean of 100 and a SD of 15. A similar adapted, examiner-administrated version of the ASQ has previously been proven sensitive to developmental delays in infants exposed to organophosphate pesticides (Handal et al., 2007).