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LATENT EFFECTS OF GESTATIONAL EXPOSURE TO HEPTACHLOR

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Introduction:

The objective is to determine whether gestational exposure to the insecticide, heptachlor, permanently alters neurological, reproductive, or immune function. The study is based on a well characterized episode in which the commercial milk supply on the Hawaiian island of Oahu was contaminated with heptachlor epoxide (HE) during a 15 month period (1981-82), resulting in gestational exposure to offspring of women who drank cows' milk at that period.

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Methods:

The study has two phases. First, we conducted an island-wide survey of 20,408 high school students to identify 1,891 young adults who were born during 1981-82 and lived on Oahu for at least 15 years. Using this sampling frame, we selected 332 Oahu-born and 113 not Oahu-born participants to assess neurobehavioral function and academic achievement using standard test instruments and school records. For the study of reproductive and immune function, we are using the same sampling frame to recruit 400 Oahu-born young adults and 200 comparison participants who were not born on Oahu, matched by age and ethnicity. Indicators of reproductive function include: serum testosterone in males, estradiol and progesterone in females; and luteinizing hormone and follicle-stimulating hormone in both sexes; semen samples; and daily first morning urine specimens in females for one menstrual cycle to measure luteinizing hormone, estrone-3-glucuronide, and pregnanediol 3-alpha-glucuronide. Indicators of immune function include skin tests for standard recall antigens; antibody titer response to immunization with tetanus and pneumococcal vaccine; Th1 and Th2 type CD4+ cell subsets in peripheral blood; and susceptibility of peripheral blood T cells to activation-induced cell death using *in vitro* analysis of Fas (CD95) and its ligand (CD95L) expression. The analysis compares outcomes between the Oahu-born and comparison groups, controlling for relevant confounders. Secondary comparisons among the Oahu-born population are to be made based on individual estimates of gestational heptachlor epoxide exposure.

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Results:

For the neurobehavioral study, multivariate analyses controlling for confounding factors indicated that gestational HE was associated with lower neurobehavioral performance, especially abstract concept formation, visual perception, and motor planning, and with more reported behavioral problems. There were no strong associations for school-based performance measures, such as GPA. Data are now being analyzed for the first half of participants in the reproductive and immune function study.

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Discussion:

The findings indicate that gestational exposure to HE may be associated with subtle latent effects on neurobehavioral performance. It is relevant to evaluate whether gestational HE exposure is also associated with latent effects on reproductive and immune function.