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IN UTERO DIOXIN EXPOSURE AND BIRTH OUTCOMES IN THE SEVESO SECOND GENERATION

B. Eskenazi[1], J. Ames[1], P. Mocarelli[2], P. Brambilla[2], S. Signorini[2], M. Warner[1]

[1]*Center for Environmental Research & Children's Health (CERCH), School of Public Health, University of California, Berkeley, California*

[2]*Department of Laboratory Medicine, University of Milano-Bicocca, School of Medicine, Hospital of Desio, Desio-Milano, Italy*

Introduction
In animal studies, maternal exposure to 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) is associated with adverse pregnancy outcomes including fetal loss and reduced birth weight (1-7). Epidemiologic studies that have examined effects of in utero exposure to dioxin-like compounds on birth outcomes are less consistent (8-16).

The Seveso Women's Health Study (SWHS) of women exposed to TCDD in 1976 during or before their child-bearing years is unique in that we measured TCDD blood levels near the time of the explosion (17-19). In 2014, we initiated the Seveso Second Generation Health Study. Previously with follow-up through 2008, we found no association between maternal TCDD and birth weight, though associations were slightly stronger for pregnancies within a half-life of exposure (20). We also found no relationship of TCDD with spontaneous abortion or birth defects. The highest-exposed Seveso women were under-represented in this earlier analysis due to their younger age and fewer pregnancies. We aim to confirm these associations now that reproduction in the cohort is complete.

Materials and Methods
We interviewed all SWHS women who were not menopausal at last interview about additional pregnancies. All children 2 years and older were invited to undergo blood draw and anthropometric measurements. Children 18+ years had a personal interview; for children <18 years, we interviewed mothers about the children. We examined in utero TCDD exposure as 1) the initial maternal level and 2) estimated TCDD at pregnancy. We examined exposure in relation to birthweight and adverse pregnancy outcomes (spontaneous abortion, low birth weight, preterm delivery, and birth defects).

Results and Discussion
We have located 100% of eligible SWHS mothers and 98% of the 895 known children. Data collection began in May 2014 and will be finished by end of May. To date, 640 women had 1,267 post-explosion pregnancies including 943 (74.4%) livebirths, 174 (13.7%) spontaneous abortions, 128 (10.1%) voluntary abortions, 5 (0.4%) stillbirths, 15 (1.2%) ectopic and 2 (0.1%) molar pregnancies.

Among the 943, average birthweight was 3,279 (±503) grams with 5.5% low birth weight (<2,500 grams). Mean gestational age was 39.4 (±1.7) weeks with 5.6% born preterm (<37 weeks gestation). In utero TCDD exposure based on initial maternal TCDD level is high (median=69.7 ppt) with a wide range of exposure (4.5–9,140). Preliminary analysis suggests results are consistent with our earlier study (20).

We have successfully followed-up the second generation of children born to women exposed to TCDD in Seveso Italy in 1976. We find little evidence that TCDD is related to adverse pregnancy outcomes.

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