

TCDD and birth weight of Vietnamese infants

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Received: 9 June 2016 / Accepted: 16 June 2016 / Published online: 25 June 2016
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To the editor:

We read with interest the paper by Tung et al. (2016) on the birth weight of Vietnamese infants. The authors concluded that birth weight was inversely correlated with maternal milk concentrations of 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (TCDD) and 2,3,4,7,8-pentachlorodibenzo-*p*-dioxin based on a comparison of the so-called hot spots, where persistent exposures from Agent Orange were present, with control areas. We suggest that the results might have been influenced by recall bias and confounding and that the authors' data are inconsistent with exposure to Agent Orange or its TCDD contaminant.

A non-Agent Orange source of the dioxins and furans reported by Tung et al. is demonstrated by the low proportion of the total toxic equivalents (TEQ) attributable to TCDD. The authors' Table 1 shows that TCDD accounted for 12.3 % of the total TEQ of polychlorinated dioxins and furans in the "hotspot region" and 13.1 % in the control region. Inasmuch as TCDD was virtually the only

dioxin found in Agent Orange (Schecter et al. 2006; Hatfield Consultants 2007, 2011), the dioxin/furan profile reported by Tung et al. is not compatible with an important role of Agent Orange as a source of exposure and points towards a source of these compounds other than Agent Orange, possibly industrial or incineration activities. The lack of evidence of persistent Agent Orange components in human milk has been demonstrated repeatedly in contemporary samples from Vietnam (reviewed by Scialli et al. 2015).

Tung et al. do not indicate with precision the source of information they used to assess birth weight, but it is plausible that they used the questionnaire administered to mothers. If so, it is possible that information on birth weight was subject to recall bias with hotspot mothers over-reporting low birth weight of their children compared to control mothers, because of concern about possible effects of their exposure to dioxins. It is noteworthy that no differences were observed for measurements of children made by the authors, which were less likely to be subject to systematic differences between the two groups. The correlations between different dioxins and furans in milk and birth weight were calculated using the combined sample of 58 mother/child pairs from the hotspots and 62 pairs from the control area, and even a small degree of recall bias could have generated the correlation with dioxin in milk reported in the table. We wonder if there was a correlation between dioxins in milk and low birth weight within the group of hotspot mothers, who were likely to have been equally affected by recall bias.

The correlations reported by Tung et al. were not adjusted for potential confounders, that is, determinants of low birth weight that might differ according to dioxin exposure. These potential confounders include gestational age, maternal age, multiple births, use during pregnancy of tobacco, ethanol, or other recreational drugs, and low socioeconomic status,

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possibly acting through poor nutrition during pregnancy and poor prenatal care. The authors write that the two regions they studied were “rural and have not been affected by industrial pollution.” However, there still might have been differences in known risk factors for low birth weight between hotspot and control mothers and even within each group of mothers in relation to dioxin concentration in milk. Moreover, Phù Cát, the “hotspot” region studied by Tung et al., remains the site of a civilian and military airport, perhaps accounting for the evidence of industrial and incineration byproducts in human milk reported in the paper. This potential confounding could be addressed by multivariable analysis based on individual-level data on known and suspected risk factors for birth weight; if such adjustment is not possible, the authors should at least repeat the analysis after restriction to the group of mothers and children from the hotspot area.

Compliance with ethical standards

Conflict of interest The authors have been consultants for former manufacturers of Agent Orange. No stakeholders were involved in the writing or review of this letter. No external funds were used to support the preparation of this letter.

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