PBDE Flame Retardants and Thyroid Hormones during Pregnancy

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Chevrier et al. (2010) assessed the association between 10 polybrominated diphenylethers (PBDEs) and free and total thyroxine (T4) and thyroid-stimulating hormone (TSH) in 270 women around the 27th week of gestation. They concluded that PBDEs are associated with lower TSH levels during pregnancy, but several factors that likely influenced the results were not considered in their analysis.

Normal pregnancy can lead to low TSH levels without affecting T4 levels, as can several other factors (e.g., starvation; stress; psychiatric disorders; depression; acute or chronic nonthyroidal disorders; alterations in thyrotropin-releasing hormone, cortisol, opioidergic, dopaminergic, or somatostatinergic activity; and alterations in leptin and cytokine production) (Braverman and Utiger 2000; Krasas et al. 2010). None of these were included in the analyses of Chevrier et al. (2010), yet any of them could have contributed to lower TSH levels.

Chevrier et al. (2010) classified women in their second and third trimesters as having subclinical hyperthyroidism if their serum TSH levels were < 0.5 mIU/L and < 0.8 mIU/L, respectively. Krasas et al. (2010) recently reported TSH reference ranges: 5th percentile = 0.03–0.39 and 0.13 mIU/L, respectively, suggesting that the cutoffs used by Chevrier et al. (2010) led to an incorrect classification of at least some women.

Chevrier et al. (2010) reported that blood was drawn at 27.3 ± 3.1 (mean ± SD) weeks gestation; however, it is unclear which women were in the second trimester and which were in the third trimester. Although Chevrier et al. (2010) adjusted for gestational age, the use of different cutoffs for a binary variable (subclinical hyperthyroidism) for women in the same analyses likely biased results, particularly considering that differences between women near the end of the second and beginning of the third trimester are not great.

With the exception of a few outliers, the range of each PBDE among study subjects was quite small (all with the ratio of the 75th to the 25th percentile < 3.4). Because blood was drawn only once and all associations noted were quite weak, even a small difference between the measured PBDE level and the actual level in an individual could have biased the results.

All of the PBDE congeners were moderately to strongly intercorrelated (r = 0.6–0.9; p < 0.001), yet analyses were conducted only by individual congener, leaving the inappropriate impression that several of the PBDE congeners may have been causally associated with lower TSH levels.

The limitations discussed above preclude one from drawing conclusions regarding associations between serum PBDEs and TSH. It is notable, however, that even if associations are shown to be causal, the decrements in TSH reported are very small and mostly within the reference range for pregnant women. Thus, they are unlikely to result in adverse health effects in either pregnant women or their fetuses.

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PBDE Flame Retardants and Thyroid Hormones: Chevrier et al. Respond
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Goodman et al. raise concerns regarding our study (Chevrier et al. 2010) in which we reported associations between serum levels of polybrominated diphenyl ethers (PBDEs) and lower thyroid-stimulating hormone (TSH) in pregnant women participating in the Center for the Health Assessment of Mothers and Children of Salinas (CHAMACOS) cohort study. The points they raise are unlikely to have affected the validity of our conclusion.

Goodman et al. correctly point out that, as for most health outcomes, thyroid hormone levels may be affected by a number of factors. However, these factors must be related to PBDE serum levels to confound the associations that we reported. Although it would be of interest to evaluate associations between exposure to PBDEs and the adverse health effects cited by Goodman et al. (e.g., psychiatric disorders, depression, neurotransmitter and hormonal alterations), we are aware of no study that investigated these relationships. Furthermore, should PBDEs cause these health effects, they would be on the causal pathway between exposure and disease, and as such, should not be adjusted for. Consequently, it is unlikely that the factors identified by Goodman et al. substantially confounded our results. On the other hand, we considered a large number of demographic and environmental factors that may be related to both PBDE serum levels and thyroid function, and we observed little confounding (Chevrier et al. 2010). Goodman et al. also suggest that our results may be due to exposure and outcome misclassification based on a) the reference range that we used to determine subclinical hyperthyroidism; b) our use of different cutoffs for women in the second and third trimesters of pregnancy; and c) the fact that we measured PBDEs at one time point during pregnancy. As explained below, we believe that substantial misclassification is unlikely; even if misclassification did occur, it would most likely be nondifferential with regard to

References
