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A Strong Dose-Response Relation Between Serum Concentrations of Persistent Organic Pollutants and Diabetes: Results From the National Health and Nutrition Examination Survey 1999–2002

Response to Lee et al.

Lee et al. (1) and *Diabetes Care* deserve praise for publishing what may be the first study worldwide to analyze, in a sample of a general population, serum concentrations of persistent organic pollutants (POPs) and plasma fasting glucose. The main implication of the study is that POPs stored in the adipose tissue may be a key player in the etiopathogenesis of type 2 diabetes. It is even rational to speculate that POPs might be, if not "the single factor" (2), then one factor linking some core components of the metabolic syndrome.

In the study by Lee et al. and other studies (3,4), it seems likely that a relationship exists between diabetes and POPs. Hence, patients, clinicians, and other health professionals may need to cope with the possible fact that on average, diabetic subjects have higher concentrations of POPs and may thus be more likely to suffer the adverse effects of POPs. The mechanistic, clinical, and public health implications of the study by Lee et al. are potentially high (1,3–5). However, several questions remain unanswered regarding the nature of the relationship between prevalence of diabetes and population distribution of POPs (6,7). Therefore, I would appreciate it if Lee et al. could address the following issues.

1) What is the direction of the relationships with the poverty income ratio? For example, in Table 1, did wealthier individuals have lower concentrations of DDE and higher concentrations of PCB153 after adjusting for confounders?

2) Many of the estimates (e.g., in Table 2) were adjusted for age, sex, race, income, lipids, BMI, and waist circumference. This is coherent with several aims (e.g., to "isolate" the effect of POPs from that due to obesity, age, race, or income). However, adjusting by BMI and waist circumference may also be an overadjustment, since fat intake is the most common source of exposure to POPs (1,5) and since the body burden of some of these lipophilic chemicals, but not all and not always, increases with increasing BMI (8,9). Thus, crude or less adjusted odds ratios (ORs) would also be relevant for determining the prevalence of diabetes in people with specific concentrations of POPs. Could the authors provide some crude ORs?

3) The finding that there was no association between obesity and diabetes among subjects with nondetectable levels of POPs is highly surprising and calls for additional results to be presented. A figure may be warranted.

4) Also crucial is what we may call "the changes in BMI-POPs relationship." Could the authors please comment on the possible influence upon BMI measurements of the cross-sectional design of the study? Could they suggest possible consequences upon findings of weight gain and weight loss in diabetic and nondiabetic participants?

5) High-prevalence ORs were found for the summary or composite of the six POPs with the highest concentrations. Are the results similar if the joint effects of multiple POPs are assessed through alternative methods?

6) Finally, the authors state that "reverse causality is unlikely." Indeed, evidence supporting the hypothesis that diabetes increases accumulation of POPs seems scarce (4). Do the authors know of studies on the toxicokinetics of POPs in diabetic subjects demonstrating that they accumulate POPs more than nondiabetic subjects?

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