# Invited Perspective: Can Eating a Healthy Diet during Pregnancy Attenuate the Obesogenic Effects of Persistent Organic Pollutants?

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# Invited Perspective: Can Eating a Healthy Diet during Pregnancy Attenuate the Obesogenic Effects of Persistent Organic Pollutants?

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The problem of childhood obesity is substantial. For most of the 20th century, childhood obesity was rare, even in high-income countries.[1] However, today obesity affects an estimated 50 million girls and 75 million boys 5–19 years of age around the world.[1] The etiology of obesity is complex; it is not always as simple as eating more calories than you expend. Early life exposures to obesogenic synthetic chemicals, particularly persistent organic pollutants (POPs),[2] can influence how our bodies metabolize food, acting through epigenetic mechanisms.[3] Pregnant women are, therefore, an important population to target to reduce the obesogenic effects of POPs on future generations.[4]

The persistence of these chemicals means that even after regulations are enacted to restrict or prohibit their use, they can still be detected in the general population. For example, the insecticide dichlorodiphenyltrichloroethane (DDT) was banned in the United States in 1972,[5] yet studies have shown that DDT's primary metabolite, dichlorodiphenyldichloroethene (DDE), continues to be detected in nearly 100% of the biomonitoring subsample of the National Health and Nutrition Examination Survey.[6] The pervasiveness of these chemicals also makes it remarkably challenging to reduce exposures through behavior change interventions.[7,8]

So how can we protect pregnant women and their offspring from potentially obesogenic synthetic chemicals? Nutrition interventions have been proposed as one potential solution, and there is precedent for such interventions in other fields. For example, the COVID-19 pandemic highlighted the role that healthy diets play in reducing susceptibility to viral infection.[9] Analogously, healthy diets may reduce susceptibility to the adverse effects of obesogens.[10] In addition, some research has shown that certain components of healthy diets, such as fiber,[11,12] can bind to POPs and prevent their absorption. On the other hand, high-fat diets may enhance the absorption of POPs.[13]

In this issue of *Environmental Health Perspectives*, Cano-Sancho et al. aimed to determine if certain nutrients interact with POPs early in pregnancy and affect risk of obesity in children at 7 years of age.[14] To do so, they presented a "comprehensive exploratory framework within a hypothesis-driven context" to screen for two-way interactions between 10 POPs and 17 nutrients. To my knowledge, this is the first study to assess the joint effects of POPs and nutrients on obesity.

After identifying two potential two-way interaction pairs—hexachlorobenzene (HCB) and vitamin $B_{12}$, and perfluorooctane sulfonate (PFOS) and β-cryptoxanthin (an antioxidant)—the authors characterized each pair's interactive relationships using multivariable regression. They found that the increased risk of childhood obesity associated with HCB exposure was greatest in women with the highest blood levels of vitamin $B_{12}$; in other words, a synergistic effect. In contrast, the increased risk of childhood obesity associated with PFOS exposure was attenuated in women with the highest blood levels of β-cryptoxanthin, although the effect was smaller and less consistent.

The lack of studies on nutrient–pollutant interactions is surprising given that it was posited in *Environmental Health Perspectives* >50 y ago that nutritional status plays an important role in susceptibility to toxicity.[15] How can we make more substantive progress? To start, we need more training and research to be conducted by multidisciplinary teams that combine epidemiologists, toxicologists, nutritionists, data scientists, and clinicians, among others. Given that pregnant women's chemical mixture exposures and their underlying nutritional status will vary widely across populations, it is important that these multidisciplinary teams conduct studies in a diversity of settings around the world.

One of the key limitations of the study by Cano-Sancho et al.[14] is the small sample size, which, as they pointed out, increased their false negative discovery rate. Efforts to collate data across birth cohorts and conduct pooled analyses (i.e., a mega-analysis) could help address issues of small sample size. In Europe alone, a recent systematic review identified 111 birth cohorts.[16] The Environmental Health Risks in European Birth Cohorts project, which launched in 2009, reviewed environmental exposure and health data available in 37 European birth cohorts.[17] At the time of that review, 20 of the 37 cohorts were assessed for metals, 18 for pesticides, 19 for POPs, and 18 for other chemicals.[17] More recently, the Environment and Child Health International Birth Cohort Group demonstrated the feasibility of harmonizing blood lead levels across five cohorts.[18,19] Two studies published in 2016 combined results of four birth cohorts in the United States that evaluated biomarkers of organophosphorus pesticide exposure.[20,21]

Can eating a healthy diet during pregnancy attenuate the obesogenic effects of POPs? It is too soon to say conclusively one way or the other. In their study, Cano-Sancho et al.[14] suggest "maybe antioxidants can." However, much more research is needed, and we should proceed with caution in making clinical recommendations. This is particularly true as relates to supplements, given the observed increased risk of childhood obesity related to HCB exposure in women with the highest intakes of vitamin $B_{12}$, which was related to supplement intake.[14] Nonetheless, existing recommendations for pregnant and lactating women, such as the *Dietary Guidelines for Americans, 2020–2025*,[22] already advise a diet rich in fresh fruits and vegetables (an important source of antioxidants), whole grains, low-fat or fat-free dairy products, and high-protein foods, including lean meats, chicken, eggs, seafood, beans, lentils, nuts, seeds, and tofu. Therefore, continuing to recommend they follow these guidelines may have co-benefits by reducing the consequences of obesogen exposure.

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