was present in 59% of the patients; recurrent infections during childhood were common; 20% required amigdalectomy. One patient suffered rheumatic fever; one patient had not been effectively immunized after repeated hepatitis vaccines; and another had defective CD4 and suffered recurrent pneumococcal infections.

It would be surprising if these illnesses did not share a common root in the immune system. Schmidt (2011) underlined rising prevalence rates of autoimmunity and discussed causes. I believe that this trend is relevant in general to immune disorders because of different reactions within the same scope of lymphocyte dysfunction in response to our new aggressive environment.

The author declares that he has no actual or potential competing financial interests.

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Dietary Intervention and DEHP Reduction

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Rudel et al. (2011) reported a surprising reduction in metabolites of bis(2-ethylhexyl) phthalate (DEHP) in their dietary intervention study, considering that—to the best of the industry's knowledge—the plasticizer is no longer used in the food packaging products that the authors removed from the subjects' dietary routine. Although we question the public health significance of a potential reduction of a few micrograms per liter of DEHP metabolites, we initially saw the study as having the potential to improve our understanding of how low-level exposure to DEHP, suggested by the presence of the metabolites, may be occurring. Unfortunately, in reviewing the Rudel et al. analysis more thoroughly, we were disappointed.

The 56% reduction in mean levels suggested by Rudel et al. (2011) is based on the concentration of DEHP metabolites—before correcting for creatinine levels. With little more than a sentence, Rudel et al. dismissed the accepted practice of correcting for creatinine levels to account for the substantial variability in an individual's urine output. They suggested that such adjustment may "bias associations between urine metabolite concentrations and age or sex" (Rudel et al. 2011) without explaining that the correction is widely used in urinary biomonitoring (by the Centers for Disease Control and most others) to improve the comparability of measurements across individuals.

To their credit, Rudel et al. (2011) did conduct a comparison of the creatinine-adjusted levels of DEHP metabolites and found no statistically significant difference in the mean levels of two of the three metabolites before and after dietary intervention. The authors did not report the change in the adjusted levels of the third metabolite in the article.

The authors also did not address the variability in preintervention levels among the study participants. The presence of two individuals with very high metabolite levels clearly skewed the mean value upward and, consequently, exaggerated the significance of the intervention. Although Table 2 of Rudel et al. (2011) provides the minimum, mean, and maximum values, the variability is best seen in their Supplemental Material, Figure 3 (doi:10.1289/ehp.1003170), and on Silent Spring Institute's web site (Silent Spring Institute 2011). It is unfortunate that Rudel et al. (2011) chose not to address the variability in their article—and a bit surprising—because the postintervention increase in DEHP metabolites was significantly lower than the reported decrease (16% versus 56%).

The author is employed by the American Chemistry Council to represent the manufacturers of phthalates, including DEHP.

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Dietary Intervention and DEHP Reduction: Rudel et al. Respond

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Steven Risotto, representing phthalate manufacturers for the American Chemistry Council (ACC), commented on our study that found a 3-day diet with limited food packaging reduced participants' average bis(2-ethylhexyl) phthalate (DEHP) exposure by > 50% (Rudel et al. 2011).

Risotto's statement that creatinine adjustment by normalization is accepted practice is misleading. Creatinine normalization is appropriate in a longitudinal study if the daily creatinine excretion of the participants remains approximately constant. That assumption is not reasonable in a dietary intervention because short-term changes in diet can strongly influence creatinine levels (Kesteloot and Joossens 1993). In our article (Rudel et al. 2011), we addressed urinary dilution by including creatinine as a variable in the mixed-effects model that estimates exposure reduction from the intervention, as currently recommended by researchers at the Centers for Disease Control and Prevention (Barr et al. 2005). Our analysis showed significant decreases of 53–56% in the three DEHP metabolites. Because creatinine normalization is common, we also included normalized results. Creatinine levels dropped significantly during the intervention, indicating that creatinine normalization artificially reduced the observed change. Nonetheless, results showed a 42–45% decrease in all three DEHP metabolites; the decrease was statistically significant for the most abundant metabolite, MEHHP (mono-(2-ethyl-5-hydroxyhexyl) phthalate).

Risotto also questions whether DEHP reductions are attributable to two individuals with high initial exposures. However, we reported the decreases in geometric means, which are not strongly influenced by a few high values. After removing these two participants, we still observed decreases of 37–42% in the geometric means of DEHP metabolites, and reductions in the two most abundant metabolites remain statistically significant. Removing participants with high preintervention exposures is appropriate if an unknown exposure may have covaried with the intervention, but because the two highest exposures were in different families, such confounding seems unlikely.

As to why DEHP metabolite levels dropped during the intervention but did not increase significantly after the intervention—as discussed in detail in our article (Rudel et al. 2011)—the discrepancy may be attributable to the different-length "washout periods" (~ 48 hr between the beginning of the intervention and the first intervention urine sample, and ~ 36 hr between when participants resumed their regular diet and the first postintervention urine sample).

Risotto questions the public health significance of our observed reduction in DEHP exposure. However, DEHP exposure levels in our study (Rudel et al. 2011)—and in the U.S. population—are similar to or higher than those recently reported to exceed health guidelines. Koch et al. (2011) found that 5 of 108 children studied had daily DEHP intakes in excess of the current U.S. Environmental Protection Agency reference dose, and 25% exceeded the tolerable daily