A Section 508–conformant HTML version of this article is available at https://doi.org/10.1289/EHP6637.

Bisphenol Exposure and Type 2 Diabetes: New Evidence for a Potential Risk Factor

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https://doi.org/10.1289/EHP6637

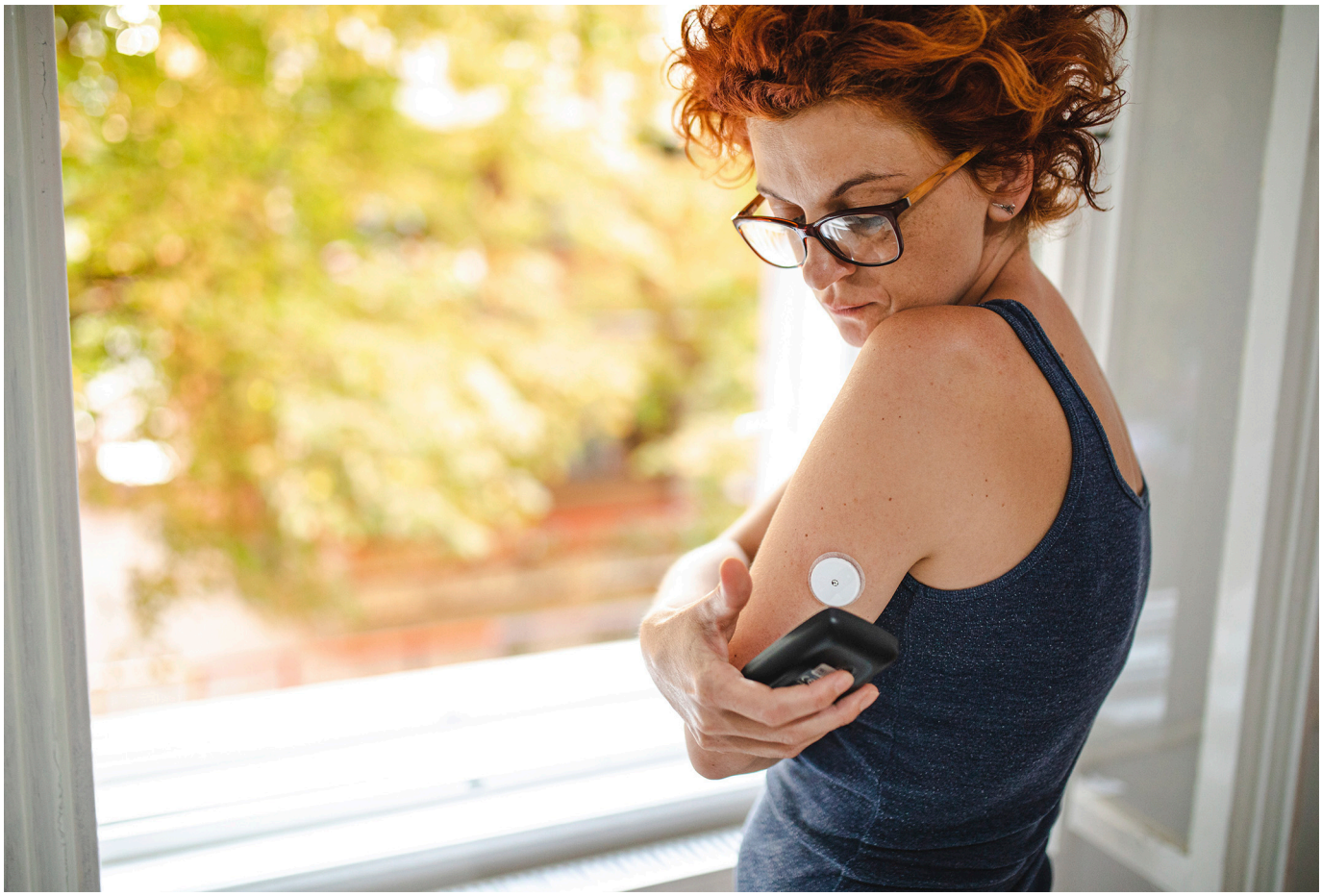
The plasticizer bisphenol A (BPA), used in can linings, thermal paper, and polycarbonate plastics,[1,2] has been associated with a wide range of health outcomes, including type 2 diabetes.[3] Numerous experimental[4] and population-based[5,6] studies over the last decade have explored the BPA–diabetes relationship. Now a longitudinal study published in *Environmental Health Perspectives*, examining not just BPA but also its widely used substitute bisphenol S (BPS), adds to the evidence.[7] The study found positive associations between incidence of diabetes and exposure to both BPA and BPS, independent of traditional risk factors.

The research included 755 individuals followed over 9 years as part of the French cohort Data from an Epidemiological Study on the Insulin Resistance Syndrome (D.E.S.I.R.).[8] The participants, who were diabetes-free when recruited, provided urine samples at enrollment (between 1994 and 1996) and again 3 years later. The authors estimated participants' exposure to BPA and BPS based on urine metabolites of these bisphenols.

A total of 201 D.E.S.I.R. participants received diabetes diagnoses during the 9-year follow-up period, but the risk was not equally distributed. The authors estimated that participants in the second and third quartiles of estimated BPA exposure were more than twice as likely to develop diabetes as those in the lowest quartile. Participants with the highest estimated exposures were at increased risk as well, but less so than more moderately exposed individuals. The analysis also suggested that participants with any urine BPS metabolites were nearly three times as likely to develop diabetes compared with participants with no detectable exposure.

"I think this paper is particularly good because it's longitudinal and there are very few [such papers on bisphenols]," says Angel Nadal, a professor at Spain's Miguel Hernandez University. Nadal, who was not involved in the current study, has researched the physiological link between BPA exposure and diabetes since 2006.[9] In 2018 he co-led an experimental study in which low doses of BPA triggered an insulin response (a predictor of type 2 diabetes) in a small group of men and women.[10]

Human and animal studies have shown that BPA is metabolized in the body within a day, or potentially sooner.[11,12] This means that urine levels may fluctuate dramatically depending on recent food consumption and other activities, making single measurements of



It is well established that eating a healthful diet and staying active can protect against type 2 diabetes, given that obesity and a sedentary lifestyle are by far the greatest predictors of this disease.[8] But even in individuals without these known risk factors, exposure to endocrine disruptors such as BPA and BPS may set the stage for diabetes. Image: © iStockphoto/Kosamtu.

urinary BPA an unreliable predictor of past exposures. "Having a couple of samples that have been measured makes a stronger connection between BPA exposure and type 2 diabetes," Nadal says.

The mechanisms through which BPA and BPS exposure may affect diabetes risk are complex and not fully understood, but certainly plausible, according to Fanny Rancière, the study's first author and an associate professor at Paris Descartes University in France. "Several biological pathways through which BPA could affect the development of diabetes have been identified,[13] such as insulin resistance and pancreatic beta-cell dysfunction," she says.

Rancière points out that there is a smaller body of literature for BPS. "However," she adds, "a recent systematic review[14] of experimental studies concluded that BPS has endocrine-disrupting effects similar to those of BPA, which is not surprising given the similarity between their chemical structures."

Other endocrine-disrupting chemicals besides BPA and BPS have been associated with diabetes incidence in other studies,[13,15] says senior author Dianna Magliano. "Make no mistake, the best way to get diabetes is to put on weight and become obese," she says. "But [certain endocrine disruptors] do have some association by themselves, independent of obesity and diet and whether you smoke or not and whether you exercise."

The pattern of associations with BPA suggests a nonmonotonic dose response, with the highest estimated diabetes risk among those who were moderately exposed. However, the authors note that the trend might also be a chance finding. Nonmonotonic dose responses may be a hallmark of hormone-mimicking chemicals, such that effects of very low levels are consistent with effects of endogenous hormones. On the other hand, high exposures could cause overwhelmed cell receptors to down-regulate or desensitize.[16]

University of Illinois at Chicago associate professor Robert Sargis, coauthor of a review of the link between endocrine-disrupting chemicals and type 2 diabetes,[17] says the team's findings illustrate the need for safer products. "With BPA finally getting attention and companies starting to recognize that people are attuned to its adverse effects, the move has been to replace it with other bisphenols. And what this paper underscores is that the replacement compounds aren't always better," says Sargis, who was not involved in the current study. "Companies take pride in putting 'BPA-free' on their label, which is admirable in part, but it may be misrepresenting a risk that is highly relevant."

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