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Looking beyond Cancer: Glyphosate and Liver, Metabolic Diseases in Youth

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The role that glyphosate, a herbicide used in the product Roundup, may play in increasing the prevalence of liver and metabolic diseases in children[1] is the focus of new research published in *Environmental Health Perspectives*.[2] The study is centered on residents of the Salinas Valley, one of California's most productive agricultural regions.

In the past few years, study coauthor and family physician Charles Limbach has seen a high rate of metabolic and liver disease in youth in the Salinas Valley. After reading a small case–control study[3] that noted a relationship between liver disease and glyphosate residues in urine, Limbach wondered if glyphosate, which is widely used in the surrounding agricultural fields,[2] could be involved in the diseases in his young patients. The danger glyphosate poses to human health is debated. In 2015, the International Agency for Research on Cancer (IARC) classified glyphosate as probably carcinogenic to humans based largely on experimental data,[4] but the U.S. Environmental Protection Agency (EPA) has concluded there is no risk to human health when products are used according to directions.[5] Regarding noncancer disease outcomes, the epidemiological research related to glyphosate exposure has found inconsistent evidence of risks; however, this body of work is limited and of mixed quality.[6–8]

Limbach contacted Brenda Eskenazi, director of the Center for Environmental Research and Community Health (CERCH) in the School of Public Health at the University of California, Berkeley. He knew of her work as founder of the Center for the Health Assessment of Mothers and Children of Salinas (CHAMACOS), which is a prospective study of exposures to pesticides and other environmental agents—and potentially related outcomes—among children in a farmworker community.

Limbach's concern for his patients prompted Eskenazi to collaborate with him on a new study analyzing urine samples in the CHAMACOS biorepository, collected previously from children who were now 18 years old. "We were able to go back into the data, pull the biosamples, and send them to a lab to be analyzed," says Eskenazi, the paper's lead author. "That made the cost of the resulting study much lower because we didn't have to go into the field to collect additional samples, which would have cost millions of dollars." Although the samples were from children living in an agricultural area, the authors note that diet is also a potentially important source of exposure.[9–13]

Food is a common source of glyphosate exposure, so experts recommend reducing pesticide residues by washing. Using water mixed with baking soda is more effective than rinsing with water alone,[17] and peeling also reduces residual pesticides. Another alternative is to buy organic, if possible.[18] Image © iStockphoto/andresr.

The research team sought to determine whether lifetime exposure to glyphosate and its degradation product, aminomethylphosphonic acid (AMPA), could contribute to elevated liver transaminases (associated with nonalcoholic fatty liver disease[14]) and metabolic syndrome—conditions that increase risk for heart disease, diabetes, and stroke.[15] They modeled this lifetime exposure using glyphosate and AMPA concentrations in urine samples collected when the children were 5, 14, and 18 years of age. A second exposure estimate was based on agricultural use data from the California Department of Pesticide Regulation. (Eskenazi notes that the data do not include other pesticide uses, such as on golf courses, rights-of-way, and lawns.)

The researchers found a 2-fold increase in urinary AMPA during childhood was associated with a 14% increased risk of elevated liver transaminases and a 55% increased risk of metabolic syndrome in early adulthood. "The focus of concerns about glyphosate has primarily been on its potential for carcinogenicity," says Eskenazi. "This paper suggests we need to look at other outcomes. We need to better study the potential endocrine mechanisms as well as other mechanisms from exposures at lower doses."

Samples collected in 2000, when the mothers were pregnant, had nondetectable levels of glyphosate and AMPA, which the researchers noted is consistent with the relatively low use of glyphosate at that time. By 14 years of age, however, many of the study participants had measurable levels of glyphosate and AMPA in their urine, consistent with rising global glyphosate application levels.[16]

"Glyphosate is the most widely used herbicide worldwide—which means that many of us are exposed to this chemical, not only farmworkers and their families—and many of its health effects are not well understood," says Ana Maria Mora, an assistant researcher at CERCH and a study coauthor. "Cardiometabolic and liver outcomes are on the rise among children and young adults in the United States,[1] and more research on the environmental exposures associated with these outcomes is warranted."

Eskenazi says the glyphosate levels their study recorded are on par with the general U.S. child population. She recommends that families rinse their fruits and vegetables before consuming them to reduce exposure to pesticides; using water mixed with baking soda is more effective than rinsing with water alone,[17] and peeling also reduces residual pesticides. Another alternative is to buy organic if possible.[18]

Cynthia Curl, an associate professor in the School of Public and Population Health at Boise State University, who was not involved in the study, says that the strengths of the work include measurement of glyphosate and AMPA concentrations *in utero* and at three different ages. "The consistency with which higher biomarker concentrations were associated with elevated transaminases and increased risk of metabolic syndrome is striking," adds Curl.

A limitation noted by the study authors is the potential exposure misclassification that can occur when concentrations of compounds with short half-lives are measured in single urine samples. The half-life of glyphosate and AMPA in urine is between 3.5 and 14.5 hours.[19] However, Curl points out that the body's rapid metabolism of glyphosate suggests that exposure effects could be even greater than indicated. "A single urine sample is limited in its ability to represent long-term exposure," she explains, meaning it may underestimate true exposure. "Therefore, if we see significant effects using these imperfect markers of exposure, the true effects could be larger."

Dana Boyd Barr, a professor of environmental health in the Rollins School of Public Health at Emory University, who was not involved in the study, confirms that little research has been conducted around nonoccupational exposures, and even fewer studies have measured biomarkers of glyphosate exposure.

"This study is particularly intriguing as it looks at exposure prenatally through early adulthood, and it offers some of the first concrete evidence linking nonoccupational exposures with disease outcomes in young adults," she says. "It's particularly interesting given the disparate findings between the U.S. EPA and the IARC on cancer probability," she adds. "This study demonstrates there may be other relevant outcomes at exposures lower than the U.S. EPA reference doses, which would indicate that perhaps those risk assessments are not health-protective enough."

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