A RESEARCH STRATEGY FOR TRACKING HERBICIDE IMPACTS ON CHILDREN'S HEALTH Philip J. Landrigan, MD, MSc, FAAP



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Children are Exquisitely Vulnerable to Pesticides, Including Herbicides



- Children are especially vulnerable during the 9 months of pregnancy, and this vulnerability extends into the first years after birth
- Children have greater exposures pound-for-pound than adults. Exploratory behaviors lead to increased exposure
- Reduced capacity to detoxify and excrete
- More years of future life

Children Are Not Little Adults

Children Today are Surrounded by Chemicals



Increasing Use of Herbicides - Glyphosate

Glyphosate is "A Probable Human Carcinogen" – IARC, 2015

Glyphosate Applied to Major Crops on National Acres



Increasing use of Chemical Herbicides - Dicamba

Dicamba Applied to Major Crops on National Acres



GMO Crops – The Main Driver of Rising Herbicide Use

- Application of broad-spectrum herbicides on food crops is made possible by the incorporation of herbicide-tolerance genes into seeds,
 - e.g., Tolerance to glyphosate-based herbicides (Roundup), or dicamba, or 2,4-D
- Farmers planting GMO seeds can spray herbicides "over-the-top" of growing crops, killing weeds but leaving crops unharmed
- Over 90% of corn, soybeans and cotton grown in the USA are GMO

The same companies that produce GMO seeds also make the herbicides sprayed on them These companies could have introduced other genes, e.g., vitamin fortification or drought resistance, but chose not to



The Herbicide Treadmill



GMO crop systems usually work well for the first few years, but then resistant weeds emerge and farmers are drawn onto an herbicideuse treadmill.

Glyphosate-resistant weeds have now spread to more than 150 million acres!

The Key Public Health Questions



- Is rising herbicide use, especially in the Midwest, impairing children's development?
- Is rising herbicide use triggering more frequent and/or more serious adverse birth outcomes?
- Will simultaneous application of multiple herbicides (ExTendiMax Technology) magnify risks to early development?

We hope not, but it is essential to know for sure.

Strengths of Prospective, Multi-Year Birth Cohort Studies: Key to Detecting Health Effects Of Early-life Herbicide Exposures

- Exposures are measured in real time during pregnancy as they are occurring
 - increasing accuracy and avoiding recall bias
- Ability to identify linkages between individual exposures and later outcomes
- Long-term, secure storage of early-life biosamples can enable recognition of the life-long consequences of early exposures
- Opportunities to advance epidemiology via new technologies: genomic sequencing, exposomics, and epigenetics
- Generate robust scientific information that can build political will to confront and eliminate hazards



The Heartland Study



- Sponsored by nonprofit Heartland Health Research Alliance (hh-ra.org)
- Tracking developmental consequences of prenatal herbicide exposure in a cohort of 2,000 Mother-Infant Pairs (MIPs) born in the US Midwest
- Phase 1: Mothers enrolled during pregnancy, infants assessed at birth, and in Phase 2, children followed prospectively through age 16 (we hope)
- Prenatal herbicide levels measured in urine including glyphosate, glufosinate, dicamba, and 2,4-D
- Accurate diagnosis of adverse health and developmental outcomes through regular, standardized medical follow-up of children in Phase 2
- Long-term follow-up to track neurobehavioral development and adult-onset disease

The Heartland Study

First study in the world quantifying dicamba levels in human urine --

- Required development of a new, 13-analyte analytical method in partnership with Centre de Toxicologie du Québec (CTQ) in Canada
- This birth cohort study is designed to gain insights into mechanisms underlying observed adverse birth outcomes
- Markers of epigenetic change identified by the Ramazzini Institute via the Global Glyphosate Study will be used to assess heritable epigenetic impacts of early-life herbicide exposures







Current Herbicide Exposures in the Midwest: Preliminary Estimates from The Heartland Study

In 2021-2022 HHRA worked with CTQ to quantify levels of glyphosate and glufosinate and their metabolites (AMPA and 3-MPPA) in –

~600 stored urine samples from the nuMoM2b birth-cohort study collected in 2010-2014, before commercial launch of dicamba-tolerant soybeans
~90 samples collected at Heartland Study clinical sites in 2020-2022, *after* widespread planting of dicamba-tolerant seeds



And 61 nuMoM2b and 91 Heartland Study samples for - 13 pesticide analytes including 2,4-D, dicamba

Percent of Urine Samples from Pregnant Women in the Midwest with Detectable Herbicide Residues



Key Finding: Over a 50% increase in the frequency of detectable levels of dicamba in women's urine

Average Herbicide Levels in Urine



Key Finding: More than three-fold increase in the average level of dicamba in urine, and a 45% increase in 2,4-D levels

Future Scientific Challenges

- Need for accurate and affordable analytical methods to detect multiple pesticides in biological samples
- Better methods to sort out cumulative toxicity and mixture effects, needed because pregnant women (and most everyone else) are exposed to a dozen or more pesticides on most days
- Better understanding of how confounders may alter developmental outcomes
- New recognition of the cellular, genetic and epigenetic mechanisms of herbicide toxicity





Thank You!

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For more on The Heartland Study: See hh-ra.org or contact info@hh-ra.org