Emerging Science and Birth Center Challenges
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Background

- 300 million pounds of glyphosate (GLY) (Roundup®) are applied each year in the US
- Though glyphosate has been in use since 1974, no previous measures of GLY exposure in US pregnancies have been published
- Rodent models of pesticide exposure in pregnancy correlate with adult and transgenerational disease through epigenetic mechanisms
- Measured GLY in pregnant women to estimate fetal exposure and potential adverse effects on pregnancy outcomes
Environmentally Induced Epigenetic Transgenerational Disease

How does it work?

• Chemicals (or stressors) in environment
• Induce DNA methylation of genome (in child, adolescent or fetus)
• Which alters adult disease risk (shifts in gene expression)
• And can be transmitted to future generations
Pregnant Rat

Vinclozolin Exposure (PC days 8-14)

Offspring

Vinclozolin Methoxychlor

F0

F1

F2

F3
Failed Experiment!
The Baby Rats Were Normal

Adult Rats had Diseases
Fetal Exposure: Adult disease

- Low sperm count
- Infertility
- Cancer
- Kidney
- Prostate
- Pregnancy abnormalities
- Immune dysfunction
- High cholesterol
- Accelerated aging
- Non “Sexy” scent
- Anxiety prone
Transgenerational Effects of Fetal Pesticide Exposure

The graph illustrates the percent disease prevalence across different organ systems for each generation: F1, F2, F3, and F4. The organs are categorized as Tumors, Prostate, Kidney, Testis, and Immune. The prevalence is indicated by colored bars, with F1 in red, F2 in yellow, F3 in green, and F4 in blue.
Declining Age of Menarche (Japan)

BMC Women’s Health 2012 Jul 16;12(1):19
Hosokawa, Imazeki, Mizunuma, Kubota, Hayashi
Males Developing 2 years Earlier Too!

*Age to 3ml Testicular Volume*
(US white male) Pediatrics 2012
New Study: Objectives

Prospective cross-sectional birth cohort study to measure:
• How many Midwest pregnant women are exposed to glyphosate (GLY)?
• Is drinking water an important source of exposure?
• What risk factors and adverse pregnancy outcomes correlate with exposure?
Design/Methods

- Pregnant women ages 18-40 years, newborn infants enrolled prospectively at a private obstetrical practice
- Same day urine and household water samples were collected during a subsequent clinical visit
- Urine and water samples were measured for GLY in ng/mL with liquid chromatography-tandem mass spectrometry (LLOQ 0.5 ng/mL)
Design/Methods, continued

- Electronic medical records reviewed and pregnancy outcome data were collected
- Food and water consumption questionnaires administered during pregnancy
- Statistical linear models used to assess relationships between GLY level and clinical outcomes of gestation age and adjusted birth weight, as well as pregnancy-related risk factors
Study Population

• A total of 69 pregnant women with live-born infants were studied
• 69 drinking water samples were tested
• Mean maternal age was 29 years (range 18-39 years)
• Maternal race was 94.2% Caucasian, 7.8% Asian
Results

- 65 of 69 pregnant women (91%) tested positive for GLY (>LLOD)
- Mean GLY concentration was $3.6 \pm 0.12$ ng/mL
- None of the drinking water samples had detectable GLY, suggesting that diet and beverages likely source of exposure
Fetal Exposure: Chemicals
Tracey J. Woodruff, Ami R. Zota, Jackie M. Schwartz, EHP, 2011;
Paul Winchester, Shahid Parvez, Cathy Proctor, Jun Ying, Roy Gerona; PAS SFO 2017

Chemicals in Pregnant Women

% LOD

Chemical

Benzene, 1,4-D, Cadmium, Cotinine, OPs, MTBE, Tridosan, Mercury, Glyphosate, Lead, Toluene, BPA, PFC, PFOS, PBDE, PCB, DDE, HCB, BenzP-3, Phthalates, PAH, Perchlorate
Maternal Weight vs. Glyphosate Levels

GLYPHOSATE VS. MATERNAL BMI (PREPREGNANCY)

MATERNAL BMI

healthy weight  overweight  obese

Glyphosate (ng/mL)

GLYPHOSATE VS. MATERNAL BMI

R = .286
p = .017

p = .069
Pre-pregnancy Obesity ($\geq 30$ BMI) vs. GLY

![Graph showing Glyphosate vs Pre-pregnancy Obesity]

- Pre-pregnancy BMI: 18.9-29.3
- Pre-pregnancy BMI: 30-39.5

Glyphosate vs Pre-pregnancy Obesity

GLY ng/mL

- 0.5
- 1
- 1.5
- 2
- 2.5
- 3
- 3.5
- 4

Pre-pregnancy BMI

p = 0.0268
Do you currently consume beverages containing caffeine (coffee, caffeinated soda, tea, energy drinks)?
Pregnancy Length vs. Glyphosate

* Only includes singleton ≥37week gestation infants.
Gestation-Corrected Birth Weight (Bwt %tile) vs. Glyphosate

*B Only includes singleton ≥37 weeks gestation infants
Summary

• The most heavily used pesticide in the US is found in over 90% of pregnancies in a Midwestern state

• Higher GLY levels were associated with shorter gestations and with lower gestation-adjusted birth weights

• Since water samples were largely negative, the source of exposure is probably food

• Maternal pre-pregnancy weight and caffeine intake were associated with higher GLY
Study Implications

• The majority of fetuses must be assumed to have exposure to glyphosate during critical periods of fetal development

• Policy makers need to ensure that significant increases in herbicide use and fetal exposures in the Midwest do not result in altered DNA methylation and potential multigenerational disease
Limitations

• Small sample size and regional and demographic differences are not addressed – but study is ongoing, with many more samples by the end of 2017

• No $$ to exam GLY variability by trimester and comparisons in blood

• GLY residues in food not addressed
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