PFAS AND PLACENTAL TOXICITY

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UNC-Chapel Hill

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PFAS: Integrating Science and Solutions in NC
Human studies suggest PFAS exposure may...

- increase risk of thyroid disease
- increase blood cholesterol levels
- decrease the body’s response to vaccines
- decrease fertility in women
- increase risk of high blood pressure & preeclampsia
- lower infant birth weight

Information sourced from Agency for Toxic Substances and Disease Registry
Human studies suggest PFAS exposure may:

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Do PFAS in drinking water pose a risk to pregnant women and could they affect the health and function of her placenta?

Information sourced from Agency for Toxic Substances and Disease Registry
Do PFAS in drinking water pose a risk to pregnant women and could they affect the health and function of her placenta?

What are the levels of PFAS in the placenta??

What is the effect of PFAS on placental health and function?
What are the levels of PFAS in the placenta?

<table>
<thead>
<tr>
<th></th>
<th>PFPeS</th>
<th>PFHxS</th>
<th>PFHpS</th>
<th>PFOS</th>
<th>PFHxA</th>
<th>PFOA</th>
<th>PFNA</th>
<th>PFDA</th>
<th>PFUnA</th>
<th>PFTriA</th>
<th>PFTA</th>
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<td>11</td>
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<td>14</td>
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<tr>
<td>% &gt; LOD</td>
<td>31.1</td>
<td>74.6</td>
<td>54.9</td>
<td>99.2</td>
<td>1.6</td>
<td>27.0</td>
<td>21.3</td>
<td>39.3</td>
<td>49.2</td>
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<td>Maximum</td>
<td>0.035</td>
<td>0.446</td>
<td>0.063</td>
<td>4.87</td>
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<td>1.23</td>
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<td>0.24</td>
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<td>Minimum</td>
<td>&lt;0.005</td>
<td>&lt;0.033</td>
<td>&lt;0.008</td>
<td>&lt;0.001</td>
<td>&lt;1.32</td>
<td>&lt;0.290</td>
<td>&lt;0.148</td>
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<tr>
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<td>0.009</td>
<td>0.48</td>
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<td>&lt;0.031</td>
<td>&lt;0.031</td>
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- 122 placentas from high-risk pregnancies at UNC Hospitals
- Pre-Term Birth cohort
- Monitored for a total of 26 PFAS
- Including GenX, Nafion BP2 previously seen in Wilmington serum
- 11 legacy PFAS found above limit of detection (LOD)

PFAS results are presented as ng/g wet weight
What are the levels of PFAS in the placenta?

PFAS results are presented as ng/g wet weight

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PFAS results from 122 placentas from high-risk pregnancies at UNC Hospitals.

Monitored for a total of 26 PFAS, including GenX, Nafion BP2 previously seen in Wilmington serum.

11 legacy PFAS found above limit of detection (LOD): n = 34, n = 78, n = 32, n = 122.
Risk factors associated with elevated PFAS in PTB placenta

PFOS, PFHxS, PFHps, and PFUnA were investigated for associations with risk factors including:

- Maternal age
- Maternal smoking status
- Maternal race/ethnicity
  - Child’s gender
- Maternal pre-pregnancy BMI
- Maternal medical insurance
  - Maternal education
  - Marital status
Risk factors associated with elevated PFAS in PTB placenta

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Risk factors associated with elevated PFAS in PTB placenta:

\[ p = 0.0283 \]

\[ p = 0.0002 \]
PFAS in relation to pregnancy outcomes and birth outcomes

PFOS, PFHxS, PFHps, and PFUnA in relation to adverse outcomes:

• Preeclampsia

• Birthweight

• Gestational age at delivery
PFAS and adverse outcomes

No significant associations were observed for any adverse outcome (Table 1).
PFAS and adverse outcomes

No significant associations were observed between PFAS and any investigated adverse outcome for this study.
Examining the effects of PFAS in cell culture

- Late in the first trimester, cells of the placenta known as trophoblast cells migrate to invade and remodel the arteries of the uterine wall.
- Remodeling allows for increased blood flow to the placenta and growing fetus.
- When this migration and invasion of trophoblast is compromised, pregnancy complications develop like Preeclampsia.
PFAS reduce migration in SVneo/HTR8

- Time post seeding (h)
- Migration Slope (Normalized to CTR)

N = mean of 3 experiments
* p < .05 compared to control
Immune regulation of trophoblast migration

- Trophoblast-immune crosstalk
  - Prevents maternal immune cells from attacking fetal tissue
  - Protects fetus against pathogens
  - Controls trophoblast invasion/migration
- PFAS modulate immune signaling in other tissues

https://www.rndsystems.com/resources/articles/chemokines-pregnancy
Chemokine expression

- Involved in preeclampsia

- CCL2
- CCL7
- IL6
- CXCL8
- CXCL2
- CXCL6

PFAS (ng/mL)

N = mean of 4 experiments
*p < .05 compared to control
Environmental exposure to PFAS in the placenta at UNC

Potential Toxicological Changes

PFAS induced changes in migration

Potential Disease Outcomes

Maternal Health

Fetal Growth and Development

Pregnancy Disorders

Later-in-Life Health Effects
OUR TEAM: UNC at Chapel Hill

Dr. Rebecca Fry
Dr. Tracy Manuck
Dr. Jackie Bangma
Dr. Martha Scott Tomlinson
Dr. John Szilagyi
Lauren Eaves
Kirsi Oldenburg
Discussion Questions

• Who needs to know about this research?
• How can these results inform clinical practice?
• Can we use these data to drive in vivo work?
EXTRA SLIDES