PHTHALATES:
LATEST RESEARCH FROM
THE UNIVERSITY OF ROCHESTER

Emily S. Barrett, PhD
Department of Obstetrics and Gynecology
December 12, 2013
Disclosures

No conflicts or financial interests.
Outline

• **Background**
  - What are phthalates and where are they found?
  - Why are we concerned about them?
  - The “phthalate syndrome”

• **Recent research at University of Rochester**
  - The Infant Development and the Environment Study (TIDES)
  - Dietary intervention pilot study
  - Future directions
Industrialization
Annual World Plastics Production

Source: PlasticsEurope Market Research Group
Where are phthalates found?
Why do we care that we are all exposed to these chemicals?
Endocrine-Disrupting Compounds (EDC)
The Phthalate Syndrome

DEHP

Reduced AGD

Malformations of
Epididymis
Vas deferens
Seminal Vesicles
Prostate

Hypospadias
Undescended Testicles

Gray and Foster 2003, Foster 2005
What about in humans?
What about in humans?

Can phthalates alter AGD in humans?

Can they cause the “phthalate syndrome”? 
Human studies...

- Mid-pregnancy urine sample for phthalate metabolites
- Measure penile width
- Measure testicular descent
- Measure AGD
- Measure scrotal size
<table>
<thead>
<tr>
<th>Monoester Metabolite</th>
<th>25th</th>
<th>50th</th>
<th>75th</th>
</tr>
</thead>
<tbody>
<tr>
<td>MEHHP</td>
<td>6.0</td>
<td>11.4</td>
<td>20.1</td>
</tr>
</tbody>
</table>

Likelihood of short AGD

- 4.6x
- 13x
Higher phthalate exposure was also associated with other genital endpoints:

- Decreased testicular descent
- Reduced penile width
- Reduced AGD
- Reduced scrotal size

Swan et al, 2005, 2008
TIDES Population

1st trimester pregnant women from four study centers (n=875)

Seattle, WA
San Francisco, CA
Rochester, NY
Minneapolis, MN
The Infant Development and the Environment Study (TIDES)

- **PHASE I:**
  - Urine in each trimester
  - Blood at 12-14 weeks
  - Questionnaires in each trimester

- **PHASE II:** Birth exam of male and female newborns including AGD measurements (n=718)

- **PHASE III:** 12-month follow-up exam of male infants (underway)
TIDES Study Aims

We are currently examining:

1) Prenatal phthalate exposure and anogenital distance (AGD)

*We hypothesize that phthalate exposure is associated with shorter AGD in boys, but not girls.*

2) Critical periods of exposure

*We hypothesize that the first trimester is the critical period during which phthalates can affect reproductive development.*
Is phthalate exposure dropping?

Median phthalate metabolite concentrations (ng/mL)

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>MEHP</td>
<td>3.0</td>
<td>3.3</td>
<td>1.3</td>
<td>2.6</td>
</tr>
<tr>
<td>MEHHP</td>
<td>10.9</td>
<td>11.4</td>
<td>11.6</td>
<td>7.5</td>
</tr>
<tr>
<td>MEOHP</td>
<td>9.5</td>
<td>11.1</td>
<td>7.4</td>
<td>5.5</td>
</tr>
<tr>
<td>MBzP</td>
<td>10.8</td>
<td>8.3</td>
<td>6.4</td>
<td>3.9</td>
</tr>
<tr>
<td>MiBP</td>
<td>2.8</td>
<td>2.5</td>
<td>7.5</td>
<td>5.0</td>
</tr>
<tr>
<td>MEP</td>
<td>129</td>
<td>128</td>
<td>60</td>
<td>30.2</td>
</tr>
</tbody>
</table>

* Pregnant women

And if so, why?
Geographical differences: How does Rochester compare?

<table>
<thead>
<tr>
<th></th>
<th>San Francisco</th>
<th>Minneapolis</th>
<th>Rochester</th>
<th>Seattle</th>
</tr>
</thead>
<tbody>
<tr>
<td>mHINCH</td>
<td>0.88</td>
<td>0.45</td>
<td>0.4</td>
<td>0.43</td>
</tr>
<tr>
<td>MBP</td>
<td>11.92</td>
<td>11.04</td>
<td>17.95</td>
<td>9.52</td>
</tr>
<tr>
<td>MBzP</td>
<td>5</td>
<td>7.76</td>
<td>12.34</td>
<td>6.42</td>
</tr>
<tr>
<td>MCNP</td>
<td>3.41</td>
<td>4.26</td>
<td>5.14</td>
<td>4.75</td>
</tr>
<tr>
<td>MCOP</td>
<td>17.89</td>
<td>51.14</td>
<td>75.24</td>
<td>39.12</td>
</tr>
<tr>
<td>MECPP</td>
<td>2.84</td>
<td>8.58</td>
<td>15.49</td>
<td>4.21</td>
</tr>
<tr>
<td>MECPP</td>
<td>11.27</td>
<td>14.51</td>
<td>19.64</td>
<td>25.17</td>
</tr>
<tr>
<td>MEHHP</td>
<td>10.86</td>
<td>11.5</td>
<td>17.78</td>
<td>25.83</td>
</tr>
<tr>
<td>MEHP</td>
<td>3.37</td>
<td>3.89</td>
<td>6.09</td>
<td>6.91</td>
</tr>
<tr>
<td>MEOHP</td>
<td>7.25</td>
<td>7.86</td>
<td>11.89</td>
<td>17.19</td>
</tr>
<tr>
<td>MEP</td>
<td>79.49</td>
<td>119.19</td>
<td>210.88</td>
<td>84.07</td>
</tr>
<tr>
<td>MIBP</td>
<td>6.03</td>
<td>7.16</td>
<td>10</td>
<td>5.45</td>
</tr>
<tr>
<td>Sum DEHP</td>
<td>11.04</td>
<td>12.71</td>
<td>18.67</td>
<td>25.31</td>
</tr>
</tbody>
</table>
The bigger picture
Why are these subtle changes in reproductive development important?
Why are these subtle changes in reproductive development important?

- AGD may be an indicator of reproductive health

- Rochester Young Men’s Study (RYMS):
  
  short AGD  ➔  low semen quality!

- 20% met the criteria for low sperm count (<20 million/mL) even higher in African-American men) (Mendiola et al. 2011)
Trends in Sperm Count

Swan et al. 2000 (reanalysis of Carlsen et al 1992)

Swan et al. 2000 (reanalysis of Carlsen et al 1992)
Male Reproductive Development: Global Trends

Hypospadias

Year of Birth

Rate per 10,000 Births

Testicular cancer

Paulozzi et al., 1997
Male Reproductive Development: Global Trends

Hypospadias

Testicular cancer

How can we reduce our exposure to phthalates?
How can we reduce our exposure to phthalates?

- Diet is the greatest source of DEHP
- Main dietary sources are somewhat unclear, but highest DEHP concentrations seem to be in fatty foods
  - Dairy
  - Cooking oils
  - Meat products
As a rule…

The more manufacturing, processing, and packaging involved in food preparation, the more opportunity for phthalates to be introduced.

There may be migration from:

- Food processing films
- PVC tubing and gloves
- Inks used on packages
- Recycled paper used for packaging
Can we lower our exposure to phthalates by changing our diet?
“Temple Stay” Study

Day 1:
14:00 - Arrival & Registration (Uniforms distributed & rooms assigned)
15:00 – Opening Ceremony & Orientation
16:00 – Temple Tour and Rest
18:00 – Dinner
19:00 – Evening Buddhist Ceremonial Service
19:30 – Tea Ceremony & Conversation with Monks
20:30 –Preparing for Bed
21:00 – Bedtime

Day 2:
3:30 – Pre-dawn Buddhist Ceremonial Service
4:00 – Seon Meditation & Rest (Sitting and Walking Meditation)
6:00 – Breakfast
7:00 – Community Work
8:00 – Temple Tour
11:00 – Packing & Closing Ceremony
12:00 – Lunch
13:00 – Departure
Can we do this within industrialized society?
Can we do this within industrialized society?

Maybe...
Can we do this within industrialized society?

Maybe...

but it’s not as simple as you’d hope.
A tale of two dietary interventions

Rudel et al (2011)

In 20 families who were high canned good consumers, 3 days on an organic, minimally processed diet lowered DEHP levels by over 50%

SUCCESS!
A tale of two dietary interventions

Rudel et al (2011)

In 20 families who were high canned good consumers, 3 days on an organic, minimally processed diet lowered DEHP levels by over 50%

SUCCESS!

Sathyanarayana et al (2013)

Recruited 10 families with high canned, processed food consumption. Fed half a minimally processed diet, gave the other half pamphlets on how to eat better.

FAILURE!
Dietary intervention in low-income, pregnant Rochester women

AIMS:
Can we lower phthalate exposure in this high risk group through a brief dietary intervention?

Can we work with women to develop doable guidelines for healthy eating during pregnancy?

Can women lower their phthalate exposure by following those guidelines on their own?
10 Participants

Non-City Resident

Income: Less than 25K per year

Average age: 26.4

6 African American
1 African American/Hispanic
2 Hispanic
1 Caucasian

Not selected based on any typical dietary habits
Organic or BPA/Phthalate free products were used whenever possible.

No seasonings were added

Foods were stored in ziploc plastic containers and delivered to homes

Participants were asked to heat foods by microwaving on ceramic dishes or by stovetop on pans without non-stick coatings.

2 women were given glass plates because they did not have access to ceramic dishes.
What did the subjects think?

Their priorities:
- Food needs to taste good
- Food needs to be easily and cheaply obtained
- Food needs to be easily prepared

They wanted:
- More variety
- More seasonings and condiments
- Snack foods
Our take-away messages:

- Among women with a “typical” diet (not high canned good and processed food eaters), attempts to lower phthalates through diet may not be effective.
- Very difficult to know which foods/brands are highest in phthalates—“smartest” or “safest” choices are not obvious.
- Women don’t want to sacrifice flavor/taste.

If we want to reduce phthalate exposure through diet, it is not going to happen on an individual level—needs larger scale change!
Future directions

- **TIDES II:**
  - Prenatal phthalate exposure and neurodevelopment
  - How do stress and phthalates interact to affect child development?

- **ECHO:** Environmental chemical, hormones, and the ovary

- **Hunter-gatherer study:** Are there any populations that are not exposed to these chemicals today?
Phthalates are just the tip of the iceberg

Over 80,000 chemicals are in production in the U.S. alone.

Most of them have not been tested for potential adverse health effects.

Over 800 are known endocrine disruptors.

As we phase out known hazards like phthalates, they are often replaced with other chemicals about which we may know even less!
Thanks to...

• Collaborators:
  • Shanna Swan, PhD
  • Shaw-Ree Chen, PhD
  • Sheela Sathyanarayana, MD, MPH
    (University of Washington)
  • J. Bruce Redmon, MD
    (University of Minnesota)
  • Ruby Nguyen, PhD
    (University of Minnesota)
  • Sarah Janssen, MD, PhD
    (UCSF)

• Funders:
  • NIEHS
  • URMC EHSC and IHSFC
  • BIRCWH program

And especially all of the study subjects and staff who made these studies possible!