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Topics included: Air Quality, Pesticides, Natural Disasters, BPA, Mold, Lead, Mercury

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Acknowledgements

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Understanding the Role of Environmental Chemicals in Fertility and Reproduction: From Research to Prevention

Carmen Messerlian, PhD
Harvard T.H. Chan School of Public Health
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• Dr. Paige Williams
• Dr. Blair Wylie
• Dr. Antonia Calafat
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• Dr. Minguez-Alarcon

Study and Clinical Staff
• Jennifer Ford
• Myra Keller
• Ramace Dadd
• Massachusetts General Hospital Clinical Staff

EARTH Study Participants

Funding
• National Institute of Environmental Health Sciences (NIEHS)
• Canadian Institutes of Health Research (CIHR)
1. Define endocrine disrupting chemicals (EDCs) and describe sources, routes, and timing of exposure.

2. Understand the toxicological and human literature on phthalates, a large chemical classes with widespread population exposure.

3. Describe how phthalates and phenols may impact reproductive, perinatal, or pediatric health.

4. Understand primary prevention strategies and methods to reduce exposure.
Part I

Why Study Environmental Chemicals and Fertility, Pregnancy, and Child Health Outcomes?
Our chemical world

• We live in an increasingly more complex chemical world

• Global chemical production facts:

  > 3 trillion USD sales

  >83,000 chemicals in production

  >2,700 high production volume chemicals (>1 million kg/year)

Source: http://www.cefic.org/
Projected growth of worldwide production

The vast majority of chemicals in production today have not been tested for safety.

The environment and children’s health

Approximately 16,000 premature births per year in the U.S. are attributable to air pollution.

60% of acute respiratory infections in children worldwide are related to environmental conditions.

Children in 4 million U.S. households may be exposed to high levels of lead.

Genetics were once thought to contribute 90% to autism, but are now thought to only contribute 41-56% in boys and 13-16% in girls.

The role of environmental factors in autism is greater than previously thought.

Air pollution contributes to 600,000 deaths worldwide in children under 5 years old.

Source: NIEHS/EPA Children's Environmental Health and Disease Prevention Research Centers Impact Report, 2017
Socio-economic burden

Source: NIEHS/EPA Children's Environmental Health and Disease Prevention Research Centers Impact Report, 2017
Environmental chemicals of concern

“Endocrine disrupting chemicals (EDCs) are exogenous chemicals, or mixtures of chemicals, that interfere with any aspect of hormone action.”

Zoeller et al., 2012, A Statement of Principles from the Endocrine Society

- Chemicals that can be found in our environment, food, or consumer products that can interfere with hormonal synthesis, metabolism, or action resulting in dysregulation and disruption of hormonal homeostasis
- >800 chemicals identified as known or suspected EDCs
- A small fraction has been tested for safety
Persistent and short-lived EDCs

**Persistent**
- Dioxins
- Polybrominated flame retardants (PBDEs)
- Polychlorinated biphenyls (PCBs)
- Perfluoroalkyl substances (PFASs)
- Organochlorine pesticides (OCPs)

**Short-lived**
- Phthalates
- Organophosphate flame retardants (OPFRs)
- Phenols
  - Bisphenol A (BPA)
- Parabens
- Triclosan
EDC exposure routes

- **Dermal Exposure**
  - Cosmetics, body creams
  - Deodorants
  - Shampoos
  - Perfumes

- **Inhalation Exposure**
  - PAHs
  - PBDEs
  - Plasticisers
  - Heavy metals

- **Accumulation of Lipophylic chemicals**
  - (DDT, DDE, PCBs, PBDEs)

- **Oral Exposure**
  - Food contaminants
  - Plasticisers
  - PAHs
  - Organochlorines
  - Pesticides or fungicides
  - Heavy metals

- **Transfer** of lipophylic chemicals to offspring by breast feeding

- **Transfer** from mother to fetus or to amniotic fluid, or both

EDC activity

- EDCs can have diverse effects in the body
- They have been shown to interfere with production, release, transport, metabolism, binding, and/or elimination of endogenous hormones.
Why should we care about EDCs and reproductive and child health?

Adapted from Casarett & Doull’s Essentials of Toxicology, 2015

EDCs

Growth, Development, Puberty

Gamete Production & Release

Fertilization

Zygote Transport

Implantation

Embryogenesis

Fetal Development

Parturition

Postnatal Dev’nt
Why is timing so important?

Timing of exposure is a critical determinant of disease susceptibility

Fig. 1.2. Important developmental time periods during which perturbations, such as from exposure to environmental contaminants, can result in changes that can increase risk of subsequent immediate or long-term adverse health outcomes. (Modified from Louis et al. [32].)

Part II

Phthalates, Phenols and Reproductive Health
Phthalates

- Large class of chemicals
- Diverse industrial and consumer applications
- Used since 1920
- Global production: 3 billion kg/year
- 20 + different phthalate compounds on the market (e.g., plasticizers and solvents)
- Short half-life: urine biomarker

\[
\begin{align*}
\text{OR} & \quad \text{OR'} \\
\text{O} & \quad \text{O}
\end{align*}
\]
Di (2-ethylhexyl) Phthalate (DEHP)

- Used to impart durability and flexibility to plastics - PVC
- Diet is a major source of exposure
- Most of the general population is exposed
What are the reproductive effects in animals?

Reproductive toxicant: male and female animals

- Disrupts ovarian function and inhibits growth of follicles (Hannon et al. 2014)
- “Phthalate Syndrome” - reduced anogenital distance, malformations (Gray and Foster, 2005)

Embryofetotoxic and teratogenic

- Dose, timing and route of exposure

Dams dosed with DEHP in gestation

- Fewer litters
- Fewer live pups per litter
- Lower proportion of pups born alive
- Reduced pup weight (Gray et al. 2006)
What are the reproductive effects in humans?

Prenatal exposure

- Preterm birth: 30-70% increased odds (Ferguson et al. 2014)
- Birth weight: reduced BW in IVF infants (Messerlian et al. 2017)
- Preeclampsia: unclear

Cycle-specific exposure

- IVF outcomes (Hauser et al. 2016)
  - Lower oocyte yield, fewer mature oocytes
  - Reduced clinical pregnancy and live birth rates
Phenols

- A large group of high production volume chemicals
  - Bisphenol A and substitutes: plastics and epoxy resins (bottles, cans)
  - Triclosan: antibacterial properties (personal care and cleaning products)
  - Parabens: preservatives (cosmetics, creams, pharmaceuticals)
  - Benzophenone 3: UV filter (sunscreen, face creams)
- Short half-life: urine biomarker
Part III

Endocrine Disrupting Chemicals and Adverse Fertility, Pregnancy, and Child Health Outcomes
The Environment and Reproductive Health (EARTH) Study

Prospective **preconception** cohort study of couples recruited from the Massachusetts General Hospital Fertility Center

- Women 18 to 45 years
- Men 18 to 55 years
- Eligible to enroll independently or as couple
- Followed: time of entry, through fertility care, pregnancy, and delivery

2004 – present
800 women
500 men
>565 live births
The Environment and Reproductive Health (EARTH) Study: a prospective preconception cohort

Urinary phthalate metabolites and ovarian reserve among women seeking infertility care

Carmen Messerlian\textsuperscript{1,\textdagger,*}, Irene Souter\textsuperscript{2,\textdagger}, Audrey J. Gaskins\textsuperscript{3}, Paige L. Williams\textsuperscript{4,5}, Jennifer B. Ford\textsuperscript{1}, Yu-Han Chiu\textsuperscript{3}, Antonia M. Calafat\textsuperscript{6}, and Russ Hauser\textsuperscript{1,2,5} for the Earth Study Team
Rationale: Phthalates and ovarian reserve

- Ovary: suspected target of DEHP
  - Inhibits antral follicle growth and interferes with estrogen synthesis, metabolism

- Size of the growing antral follicle pool:
  - Indicator of ovulatory potential in both assisted reproduction and natural fertility

- No study on phthalates and the growing antral follicle pool in humans
Objective: To determine whether urinary phthalate metabolite concentrations were associated with antral follicle growth among women seeking fertility care.
Maternal Preconception Window: average of all urines prior to AFC Scan

Outcome
- Antral Follicle Count (AFC): left + right follicles
- Ultrasound AFC scans on day 3 of unstimulated cycle

Analysis
- Poisson regression: to estimate mean AFC by phthalate quartiles
- Analyses were also stratified by age: <37 and ≥37 years
- Covariates: age, body mass index (BMI), and smoking status
## Results

### Study Sample
- 215 women
- Excluded
  - PCOS
  - Oophorectomy
  - Difficult to visualize scans

### Characteristics
- Average age: 36 years
- Average BMI: 25 kg/m²
- Mostly white, educated, non-smokers
- Causes of Infertility:
  - 42% had a female factor
  - 23% had a male factor
  - 35% had unexplained infertility
CHANGE IN AFC BY QUARTILE OF MEHP

Women <37 years

Mean AFC

-21% (-29, -12) *

-31% (-38, -23)

-19% (-26, -11)

Quartiles of urinary MEHP levels (µg/L)
Conclusions

- DEHP metabolites: impact the growing antral follicle pool among women in this cohort
- Strongest findings among women <37 years
- First human study to show reduced ovulatory potential associated with urinary DEHP metabolites
- More studies needed to determine if DEHP diminishes the primordial follicle population or influences follicle recruitment
Urinary Concentrations of Phthalate Metabolites and Pregnancy Loss Among Women Conceiving with Medically Assisted Reproduction

Messerlian, Carmen; Wylie, Blair J.; Mínguez-Alarcón, Lidia; Williams, Paige L.; Ford, Jennifer B.; Souter, Irene C.; Calafat, Antonia M.; Hauser, Russ for the Earth Study Team

Epidemiology: November 2016 - Volume 27 - Issue 6 - p 879–888
doi: 10.1097/EDE.00000000000000525
Perinatal Epidemiology
Rationale: Phthalates and pregnancy loss

Experimental studies on DEHP

- Embryofetotoxic/teratogenic
- Early and late fetal death
- Fewer litters and decrease in number of pups born alive

Pregnancy loss: most frequent unintended outcome

- Affects ~31% of all conceptions

Predictors not well established

- Environmental causes may play a role
Objective: To examine the prospective association of urinary phthalate metabolite concentrations with pregnancy loss among women conceiving with medically assisted reproduction.
CDC: 11 Phthalate Metabolites and ΣDEHP

Maternal Periconception Window:
average of 2 urines in cycle of index conception

Outcomes
- **Biochemical Loss**: demise of a pregnancy confirmed by β-hCG, but not visualized
- **Total Pregnancy Loss**: all loss of <20 weeks gestation

Analysis
- Estimated Risk Ratios (RR) by phthalate quartiles
- Covariates: age, BMI, smoking, infertility diagnosis
- Test for trend: assess dose-response across quartiles
## Results

<table>
<thead>
<tr>
<th>Study Sample</th>
<th>Characteristics</th>
</tr>
</thead>
<tbody>
<tr>
<td>- 256 women</td>
<td>- Mean age: 34.9 years</td>
</tr>
<tr>
<td>- 303 pregnancies</td>
<td>- Caucasian: 86%</td>
</tr>
<tr>
<td>- 556 urine samples</td>
<td>- College/graduate: 92%</td>
</tr>
<tr>
<td>- measured during conception cycle of index pregnancy</td>
<td>- Nulliparous: 86%</td>
</tr>
<tr>
<td></td>
<td>- Female Factor: 34%</td>
</tr>
<tr>
<td></td>
<td>- IVF (73%); IUI (27%)</td>
</tr>
<tr>
<td></td>
<td>- Biochemical loss: 31/303 (10%)</td>
</tr>
<tr>
<td></td>
<td>- All losses: 82/303 (27%)</td>
</tr>
</tbody>
</table>
Biochemical Pregnancy Loss by Quartiles of ΣDEHP

Biochemical Loss

<table>
<thead>
<tr>
<th>Quartile</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Q1</td>
<td>4%</td>
</tr>
<tr>
<td>Q2</td>
<td>10%</td>
</tr>
<tr>
<td>Q3</td>
<td>9%</td>
</tr>
<tr>
<td>Q4</td>
<td>17%</td>
</tr>
</tbody>
</table>

RR (95%CI): Q2 = 2.3 (0.6 - 8.5) | Q3 = 2.0 (0.6 - 7.2) | Q4 = 3.4 (1.0 - 11.7)  p-trend=0.04
Total Pregnancy Loss (<20 weeks) by Quartiles of ΣDEHP

RR (95%CI): 1.1 (0.6 - 2.0) | 1.0 (0.6 - 1.8) | 1.6 (1.0 - 2.7)  
p-trend: 0.06
Conclusions

Periconception DEHP exposure

- **Biochemical Loss:** 2-3 fold higher risk
- **Total Pregnancy Loss:** 60% higher risk

Other non-DEHP phthalates

- Not associated with either outcome

Preliminary evidence

- DEHP may adversely impact early pregnancy outcomes
What about preconception exposure?

An important and unexplored window of vulnerability
**Rationale: Preconception window**

<table>
<thead>
<tr>
<th>Prenatal</th>
<th>Preconception</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Most epidemiologic studies on EDCs focus on <em>in utero</em> exposure</td>
<td>• Paternal and maternal exposures prior to pregnancy</td>
</tr>
<tr>
<td>➢ highly relevant critical window of vulnerability</td>
<td>may impact pregnancy, perinatal, and child health</td>
</tr>
<tr>
<td>➢ large and growing body of evidence</td>
<td>outcomes</td>
</tr>
<tr>
<td></td>
<td>• Few studies able to examine the critical preconception</td>
</tr>
<tr>
<td></td>
<td>window of vulnerability</td>
</tr>
<tr>
<td></td>
<td>• Isolating the periconception period may also be</td>
</tr>
<tr>
<td></td>
<td>important to adverse outcomes</td>
</tr>
</tbody>
</table>
Male-mediated developmental toxicity (Olshan and Faustman, 1993)

Fathers’ exposure before conception may impact offspring health via epigenetic alterations transmitted through sperm

- Sperm carry more than the 23 chromosomes
- Epigenetic cargo: methylated DNA, non-coding RNAs, protamines, histones critical to fertilization and early embryo programming

Paternal epigenetics and off-spring phenotypes

Epigenetic inheritance of acquired traits through sperm RNAs and sperm RNA modifications

Qi Chen, Wei Yan & Enkui Duan

Published online: 03 October 2016

Daddy Issues: Paternal Effects on Phenotype

Oliver J. Rando

The once popular and then heretical idea that ancestral environment can affect the phenotype of future generations is coming back into vogue due to advances in the field of epigenetic inheritance. How paternal environmental conditions influence the phenotype of progeny is now a tractable question, and researchers are exploring potential mechanisms underlying such effects.

Progress in Biophysics and Molecular Biology 138 (2015) 79–85

Review
Epigenetic inheritance and evolution: A paternal perspective on dietary influences
Adelheid Soubry

Abstract
The earliest indications for paternally induced transgenerational effects from the environment to future generations were based on a small number of long-term epidemiological studies and some empirical observations. Only recently have experimental animal models and a few analyses on human data...
Paternal and maternal urinary phthalate metabolite concentrations and birth weight of singletons conceived by subfertile couples

Carmen Messerlian\textsuperscript{a,\textdagger}, Joseph M. Braun\textsuperscript{b}, Lidia Mínguez-Alarcón\textsuperscript{a}, Paige L. Williams\textsuperscript{c,d}, Jennifer B. Ford\textsuperscript{a}, Vicente Mustieles\textsuperscript{e}, Antonia M. Calafat\textsuperscript{f}, Irene Souter\textsuperscript{g}, Thomas Toth\textsuperscript{g}, Russ Hauser\textsuperscript{a,d,h}, for the Environment and Reproductive Health (EARTH) Study Team
Rationale: EDCs and birth weight

Birth weight

- Predictor of neonatal morbidity and mortality
- ~ 8% of babies are born low birth weight (<2500 g)
- Determinants:
  - gestational age, maternal/paternal anthropometry, maternal nutrition/weight status, and environmental exposures (e.g. tobacco, DES)

Accumulating evidence

- non-persistent chemicals → reduced fetal and infant birth weight

Messerlian et al. 2018
**Objective:** To examine the association of paternal and maternal preconception and prenatal urinary phthalate metabolite and phenol concentrations with birth weight among singletons conceived by subfertile couples.
Maternal Preconception Window:
average of all urines before index conception

Maternal Prenatal Window:
average of all pregnancy urines

6 w  21 w  34 w

11 Phthalate Metabolites, ΣDEHP, Σanti-androgenic, phenols

Paternal Preconception Window:
average of all urines before index conception

S1  S1  S1

Study Entry  Tx Cycle i  Tx Cycle C  Pregnancy  Birth

S1  S1 S2  S1 S2

Study Entry  Tx Cycle i  Tx Cycle C  Pregnancy  Birth
Methods

Exposures Assessment

- Urinary quantification by the Centers for Disease Control
  - Phthalates:
    - 11 individual metabolites and the sum of DEHP (ΣDEHP)
    - The sum of anti-androgenic phthalates
  - Phenols:
    - Triclosan, Parabens, Benzophenone-3
    - BPA/BPS (under review)

Outcome Assessment

- Birth weight (grams) and head circumference (cm) abstracted from delivery records by study nurses
Methods

Analysis

- **Multivariable Linear Regression**
  - Estimated difference in birth weight for every log-unit increase in phthalate or phenol concentration

- **A priori covariates**
  - Maternal and paternal age, BMI and smoking status, maternal education, infertility diagnosis

- **Additional adjustment for partner’s or prenatal exposure**

- **Stratified by mode of conception (IVF vs. Non IVF) in phthalate analysis**
## Results: Parents

<table>
<thead>
<tr>
<th>Parent Characteristics</th>
<th>Mothers N=364</th>
<th>Fathers N=195</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age at study entry (years)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>35.2 ± 3.9</td>
<td>36.0 ± 4.6</td>
</tr>
<tr>
<td>Range</td>
<td>27 – 44</td>
<td>26 – 48</td>
</tr>
<tr>
<td><strong>BMI (kg/m²)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>23.8 ± 3.8</td>
<td>26.9 ± 3.8</td>
</tr>
<tr>
<td>Range</td>
<td>16 – 39</td>
<td>20 – 39</td>
</tr>
<tr>
<td><strong>Education (graduate degree), n (%)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Never Smoked, n (%)</td>
<td>268 (74%)</td>
<td>137 (70%)</td>
</tr>
<tr>
<td>Infertility Diagnosis, n (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female factor</td>
<td>118 (32%)</td>
<td>42 (40%)</td>
</tr>
<tr>
<td>Male factor</td>
<td>91 (25%)</td>
<td>28 (27%)</td>
</tr>
<tr>
<td>Unexplained</td>
<td>155 (43%)</td>
<td>36 (33%)</td>
</tr>
</tbody>
</table>
## Results: Singleton infants

<table>
<thead>
<tr>
<th>Infant Characteristics</th>
<th>All Infants N=364</th>
<th>Boys n=192</th>
<th>Girls n=172</th>
</tr>
</thead>
<tbody>
<tr>
<td>Birth Weight</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean grams (min-max)</td>
<td>3406 (1310-4790)</td>
<td>3432 (1310-4790)</td>
<td>3376 (2185-4451)</td>
</tr>
<tr>
<td>Low Birth Weight</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;2500 g, n (%)</td>
<td>14 (4%)</td>
<td>6 (3%)</td>
<td>8 (5%)</td>
</tr>
<tr>
<td>Gestational age at birth</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean weeks (min-max)</td>
<td>39.3 (29-42)</td>
<td>39.4 (32-42)</td>
<td>39.3 (29-42)</td>
</tr>
<tr>
<td>Preterm birth</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;37 weeks, n (%)</td>
<td>28 (8%)</td>
<td>14 (7%)</td>
<td>14 (8%)</td>
</tr>
</tbody>
</table>
### Paternal Preconception Window

<table>
<thead>
<tr>
<th>MODELS</th>
<th>β (95% CI)</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>ΣDEHP</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Covariates + Gestational Age</td>
<td>-90 (-165, -15)</td>
<td>0.02</td>
</tr>
<tr>
<td>Benzophenone-3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Covariates</td>
<td>137 (60, 214)</td>
<td>0.0005</td>
</tr>
</tbody>
</table>

- Paternal ΣDEHP: associated with decreased birth weight in IVF singletons (no sex-specific differences: boys ~ girls)

- Paternal Benzophenone-3: associated with increased birth weight in all infants (boys>girls); however, more apparent among men with high vs normal BMI

Messerlian et al. 2017; Messerlian et al. 2018
## Maternal Preconception Window

### Difference in birth weight (g) for every log-unit increase in EDC

<table>
<thead>
<tr>
<th>MODELS</th>
<th>β (95% CI)</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>ΣDEHP</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Covariates</td>
<td>-22 (-102, 58)</td>
<td>0.59</td>
</tr>
<tr>
<td>BPA</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Covariates</td>
<td>-119 (-212, -27)</td>
<td>0.01</td>
</tr>
<tr>
<td>Covariates + Gestational Age</td>
<td>-79 (-153, -5)</td>
<td>0.04</td>
</tr>
<tr>
<td>Covariates + Prenatal BPA</td>
<td>-89 (-186, 8)</td>
<td>0.07</td>
</tr>
</tbody>
</table>

- Maternal Preconception ΣDEHP: not associated with birth weight
- **No** association with the 11 individual phthalate metabolites, benzophenone-3, parabens, or triclosan
- BPA associated with an 80 g decrease in birth weight: boys~girls

Messerlian et al. 2017; Mustieles et al., under review
Maternal Prenatal Window

Difference in birth weight (g) for every log-unit increase in EDC

<table>
<thead>
<tr>
<th>MODELS</th>
<th>β (95% CI)</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>ΣDEHP</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Covariates</td>
<td>-122 (-199, -45)</td>
<td>0.002</td>
</tr>
<tr>
<td>Covariates + Paternal DEHP</td>
<td>-18 (-137, 100)</td>
<td>0.76</td>
</tr>
<tr>
<td>Triclosan</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Covariates</td>
<td>-38 (-76, 0)</td>
<td>0.05</td>
</tr>
<tr>
<td>Propylparaben</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Covariates, boys</td>
<td>-67 (-133, -2)</td>
<td>0.05</td>
</tr>
</tbody>
</table>

- Maternal DEHP association no longer present after adjusting for paternal DEHP
- Triclosan associated with decreased birth weight: boys~girls
- Propylparaben associated with decreased birth weight in boys; not in girls

Messerlian et al. 2017; Messerlian et al. 2018
Conclusions

**Paternal Preconception**
- ΣDEHP: decreased birth weight in IVF conceived singletons
- Benzophenone-3: increased birth weight – probably BMI related
- Paternal exposures may impact offspring health

**Maternal Preconception**
- No notable associations with most EDCs examined
  - BPA decreased birth weight even after adjusting for GA

**Maternal Prenatal**
- ΣDEHP: not associated w/ adjustment for paternal ΣDEHP
- Triclosan and propylparaben: decreased birth weight
  - Propylparaben: possibly sexually dimorphic
Part IV

Primary Prevention of EDCs in Reproductive and Pediatric Health
Why does EDC exposure matter?

- Population level exposure → Risk → Population Burden

- Risk may be small, but population level exposure may lead to large burden of disease
Population exposure burden

See: Geoffrey Rose, The Strategy of Preventive Medicine, 1992
Primary prevention strategies

- Reduce exposure across the continuum of exposure, regardless of risk.
- All couples and children present should be encouraged to decrease exposure.
- We don’t know which couple, pregnancy or child will be at risk of adverse outcomes so shifting the distribution of exposure down will benefit those at higher risk as well as those in the middle.
Reducing exposure in areas of choice

**Products**
- Use non-toxic personal care products
- Use less plastic
- Avoid pesticides and herbicides (e.g., Raid)
- Select flame retardant-free foam products
- Don’t dry clean clothing

**Food and Diet**
- Avoid canned foods/beverages
- Avoid toxics in your food and water
- Keep mercury out of your diet
- Limit foods high in animal fat
- Avoid storing food/beverages in plastics

Source: https://prhe.ucsf.edu/
Things you can do differently at home

- Clean with non-toxic household cleaners
- Dust and mop often
- Avoid scented products
- Remove your shoes
- Choose safer home improvement products

➢ Contain harmful chemicals
➢ Lead, pesticides, flame retardants in dust
➢ Source of phthalates
➢ Outdoors can bring in toxic substances into home
➢ Paints, glues, flooring – VOC

Source: https://prhe.ucsf.edu/
How can we decrease exposure to phthalates?

**Food & Beverage**
- Common source of exposure to phthalates from processing and packaging materials.
- We can make food and drink choices to reduce exposure.
  - Reduce use of plastic food wrap/bags
  - Replace plastic bottles and food containers with glass or stainless steel
  - Avoid reheating food in plastic containers

**Perfumes & Personal Care Products**
- Phthalates can be found in some lotions, soaps, make-up, nail-polish.
- Products with “fragrance” listed can contain phthalates.
  - Use “phthalate-free” lotions and soaps
  - Reduce use of products with “fragrance” opting for “fragrance-free” choices
  - Use nail-polish brands that advertise “No Di-Butyl Phthalate” or “No DBP”

**Household Goods**
- Flooring, blinds, shower curtains, electronics, and other PVC products can be a source of DEHP.
- Scented cleaning products, laundry detergent, synthetic air fresheners can contain phthalates.
  - Use PVC-free products: replace with cotton, bamboo or polyethylene vinyl acetate (PEVA)
  - Use “fragrance-free” cleaning and laundry products


Slide #19:
- Img.2 Source: https://pixabay.com/en/yellow-toys-toddler-play-childhood-2139903/
- Img.3 Source: https://www.google.com/search?q=rubber&oq=rubber&gs_l=psy-ab..0.12.792.0...39.qdDWKD_mpFI#imgrc=gq6JW0jPC4lJsM


Slide #36 Img.1 Source: https://pixabay.com/en/animal-mouse-experiment-laboratory-1554745/

Slide #21:
- Img.2 Source: Free Google Photos: https://www.google.com/search?q=plastic+food+packaging&oq=plastic&gs_l=psy-ab..0.12.792.0...39.ROX8plS-wXw#imgrc=qUXuxBm6W404WUM:
- Img.3 Source: https://pixabay.com/en/meat-box-packaging-red-beef-2370601/
- Img.4 Source: Free Google Photos: https://www.google.com/search?q=food+processing&oq=food+processing&gs_l=psy-ab..0.12.792.0...39.ROX8plS-wXw#imgrc=SN8HvAlZn7rwM:

Slide #2, #23, #36, #42, #44, #48, #59: Shutterstock
THANK YOU!

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