

# Environmental Exposures and Reproductive Outcomes: *A Call to Action!*

*A Global Problem Needing a Global Solution*

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Tuesday October 6, 2015



# How is the Global Health Report Card?



- Marked increase in non-communicable diseases (NCDs)
  - obesity and diabetes
  - neurodevelopmental disorders
  - reproductive compromise
  - respiratory and thyroid dysfunction
  - cancers
- Marked increase in unregulated global chemical production, use, disposal
- Increasing evidence that environmental chemicals (e.g., endocrine disrupting chemicals) and air pollution contribute to NCDs and DOHaD

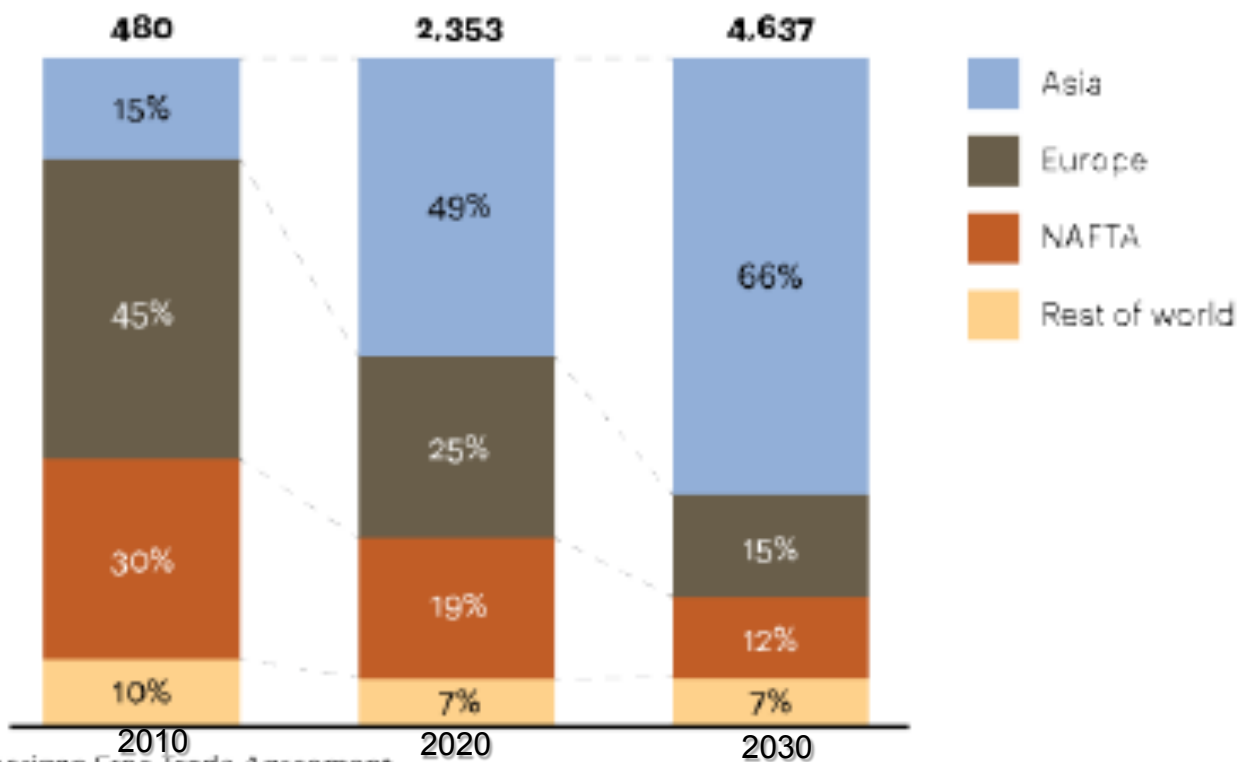
# What Might Contribute to the Documented Increase in NCDs?

- Diagnostic criteria
- Diagnostic acumen/technology
  - Globalization
- Nutrition/ultra-processed foods
- Air quality (indoor/outdoor)
- Personal behaviors/habits
- **Chemical exposures**

# The Global Chemical Production Will Shift Geography by 2030

The core of the chemical industry is shifting to Asia and the Middle East

In euro billions - 2030 is calculated at 2010 prices and exchange rates



Note: NAFTA is North American Free Trade Agreement.

<sup>1</sup>1985 assumed exchange rate is: \$1.39/€.

<sup>2</sup>Assumes the following growth rates 2010-30: Asia 5%, Europe 1%, NAFTA 1.2%, Rest of world 3%

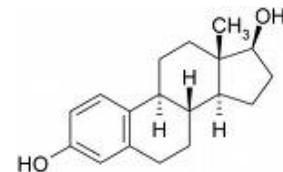
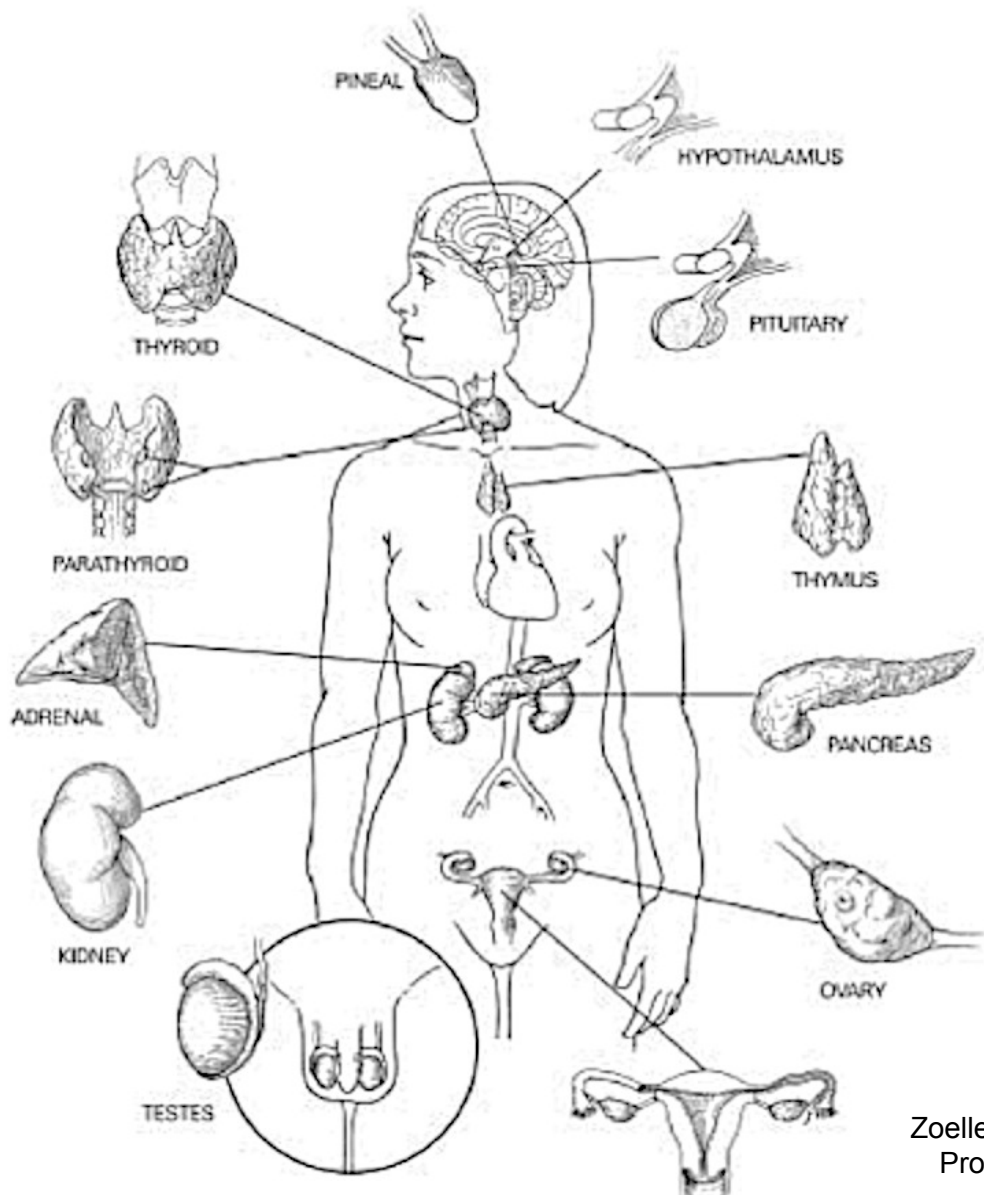
# Environmental chemicals cross borders through trade, food, wind, and water



Inequities and injustices prevail on toxic chemicals moving about the world.



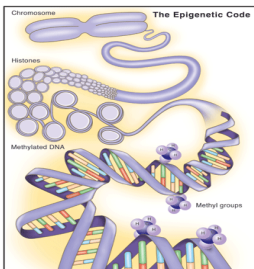
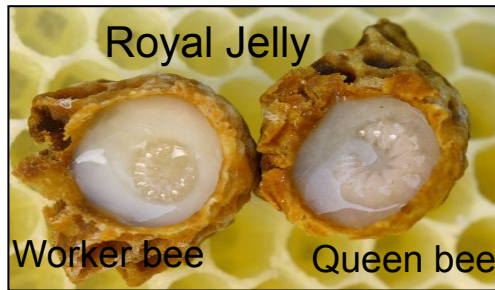
# Endocrine Disrupting Chemicals (EDCs)



EDCs = chemicals or mixtures of chemicals that interfere with any aspect of hormone action at any time of development and/or during the life course.

# What Are Some of the Underlying Mechanisms?

- Hormone receptor binding, blocking, mimicking
- Signaling pathway activation, repression
- Hormone clearance, binding
- Epigenetic changes - honey beest? YES!!!



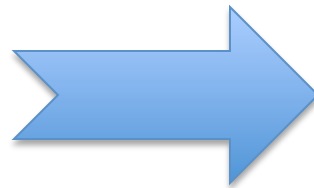
Changes in DNA and gene expression not due to changes in gene sequence but to modifications of the DNA (e.g., methylation, histone acetylation, other).

Dutch hunger famine  
chemical exposures

# There is a Connection Between Adult Diseases and Pre-conceptual and Pre-natal Exposures to EDCs



- Environmental contaminants (e.g., PCBs, TCDD, TBT)
- Plasticizers (e.g., BPA, phthalates)
- Pesticides (e.g., methoxychlor, DDT)
- Preservatives (e.g., parabens/cosmetics)
- Sanitizers (e.g., triclosan)
- Air pollution



- Obesogens
- Diabetogens
- Reproductive disrupters
- Thyroid disrupters
- Neurodevelopmental disrupters

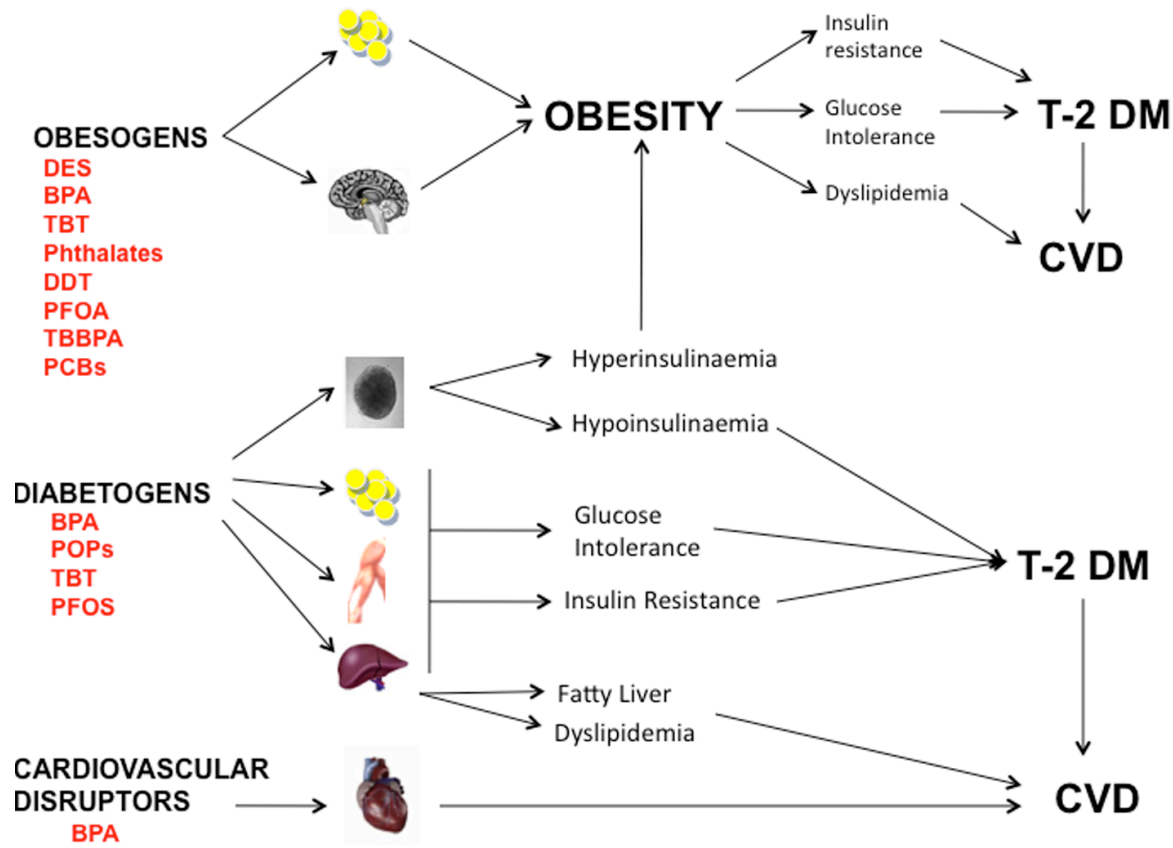


# Endocrine Disruptors, obesogens and Diabetogens

Pre/peri-natal exposures to EDCs disrupt homeostatic control of adipogenesis, energy balance and cause obesity in animals.

Epidemiologic studies associate EDCs (BPA, phthalates) with obesity in humans

Animal models: EDCs alter insulin production, secretion, function and T2 DM

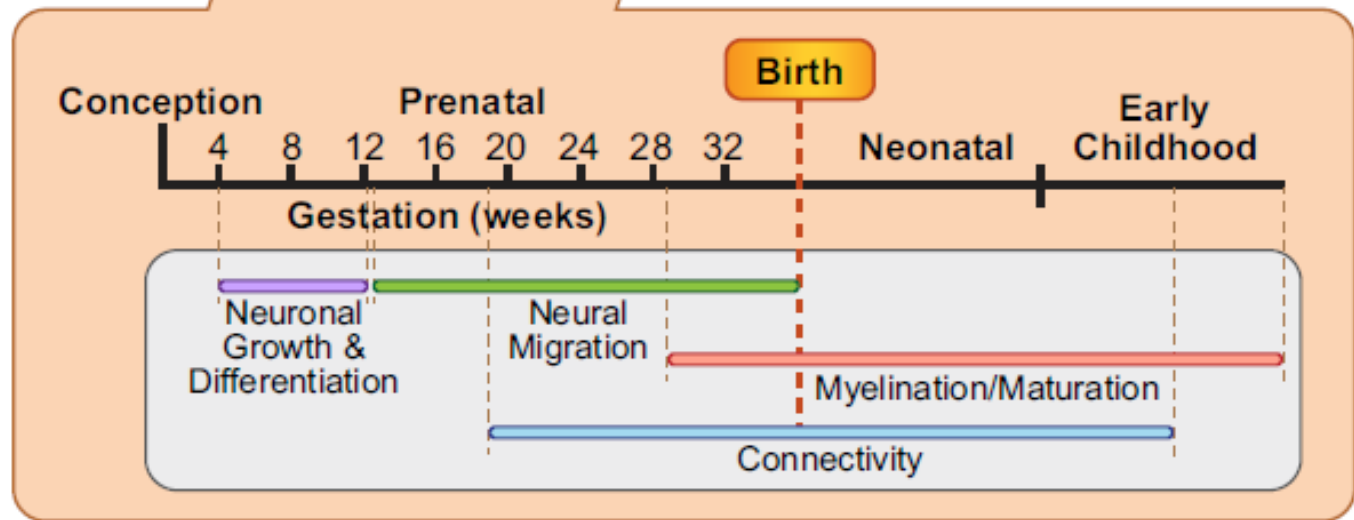
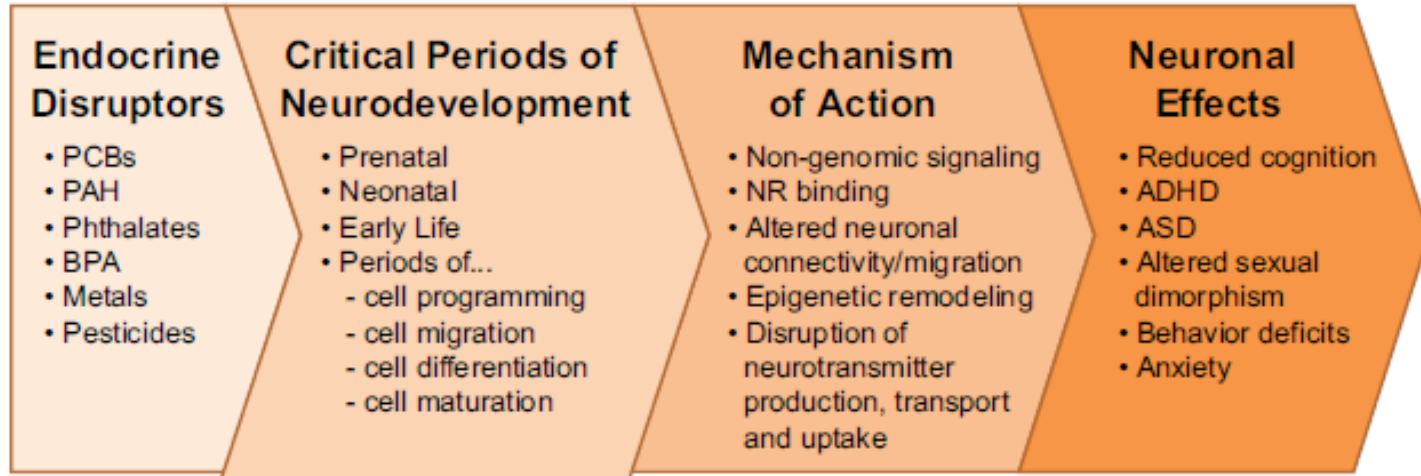


# BPA Exposure Disrupts Metabolic Health Across Multiple Generations in the Mouse

Stable inheritance of DNA methylation changes at the *Igf2* locus



# Endocrine Disruptors Affect Neurodevelopment, Behavior, and IQ



**12% of U.S. children have a neurodevelopmental/behavioral disorder.**

# Relation of Prenatal Methylmercury Exposure from Environmental Sources to Childhood IQ

Hg – naturally occurring metal; increase, e.g., in coal-burning power plant pollution → ground → bacteria → methylmercury → food chain → fish → people

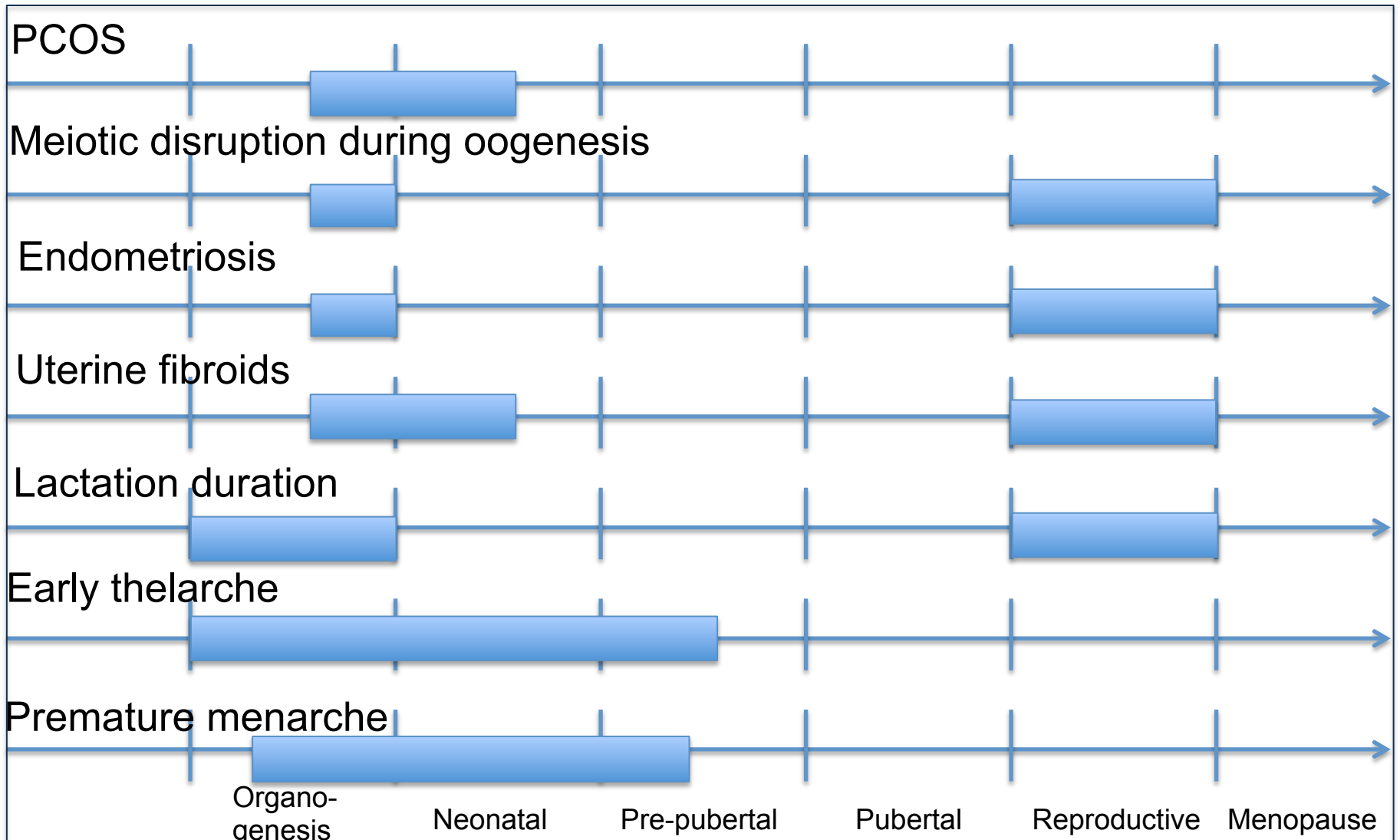
IQ was estimated in 282 school age Inuit children in arctic Quebec whose cord blood had been obtained and analyzed for mercury and other environmental exposures.

## Results:

- Prenatal Hg exposure correlated with poorer IQ after adjustment for confounders.
- Children whose cord blood > 7.5 mg/l were 4x more likely to have IQ < 80 (clinical cutoff for intellectual disability).

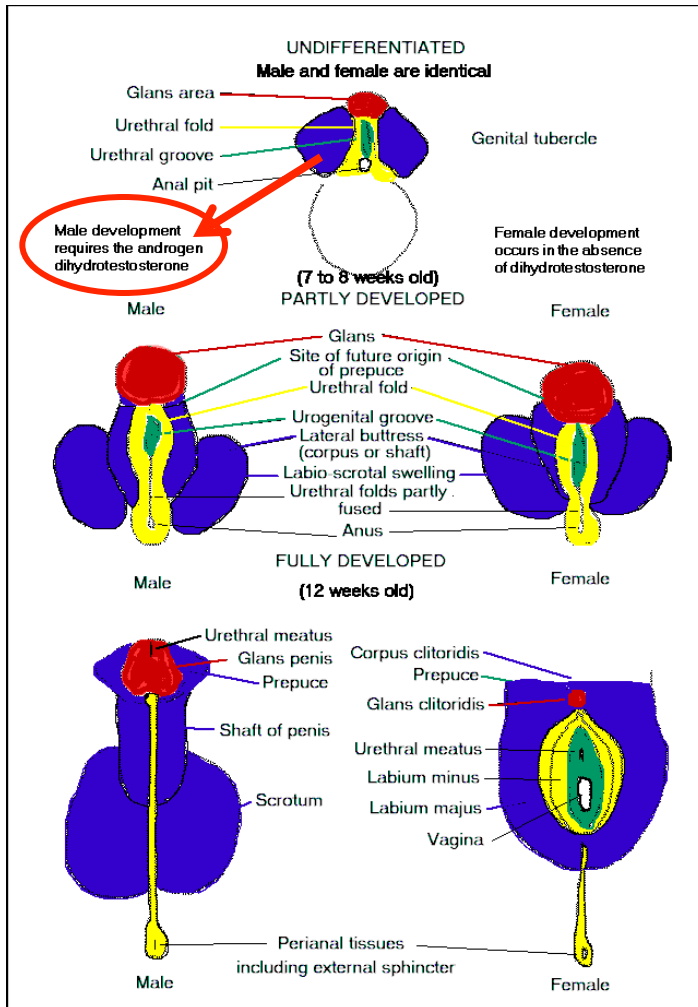
# Sensitive Developmental Periods When EDC Exposures Greatly Increase Risk of Female Reproductive Disorders

*mice, rats, lamb, sheep, humans*





# EDCs Affect the Male Reproductive System



- INSL3, androgens, AMH, E<sub>2</sub> drive testicular descent
- ANDROGENS drive external genitalia masculinization

- **ANTI-ANDROGENS, ESTROGENS and DIOXINS** are main players in male reproductive disruption.

# Maternal Phthalate Exposure Is Associated with Increased Odds of Preterm Birth



- Review of 35 studies
- **PTB** and **anogenital distance** most commonly reported outcomes from moderate level of exposure to phthalates
- Main metabolites detected: DEHP and DmBP
- Urine most suitable matrix to assess the association between in utero exposure to phthalates and pregnancy outcomes (easy sampling, non-invasive, multiple samples).

# Biomass Fuels (Wood Fuel) Are Associated with Preterm Birth in Central East India



**Table 3 Pregnancy outcomes comparing women cooking with wood versus gas, unadjusted and adjusted analyses<sup>a</sup>**

	Birth Weight		Stillbirth <sup>b</sup>		Preterm delivery (<37 weeks)
	Mean birth weight (grams)	Low birth weight (<2500 grams)	Small for gestational age (birth weight < 10%)		
Gas	2736 ± 409	48/253 (19.0%)	20/244 (8.2%)	0/253 (0%)	33/245 (13.5%)
Wood	2623 ± 429	286/1199 (23.9%)	71/1190 (6.0%)	50/1255 (40%)	390/1194 (32.7%)
Effect size (wood vs gas), unadjusted (95% CI)	-112 (-170, -55)	1.33 (0.95, 1.88)	0.71 (0.42, 1.019)	2.71 (0.99, ∞)	3.11 (2.12, 4.59)
Adjusted effect size (95% CI)	-14 (-93, 66) <sup>c</sup>	0.95 (0.58, 1.57) <sup>d</sup>	0.53 (0.23, 1.19) <sup>e</sup>	2.06 (0.08, ∞) <sup>f</sup>	2.29 (1.24, 4.21) <sup>g</sup>

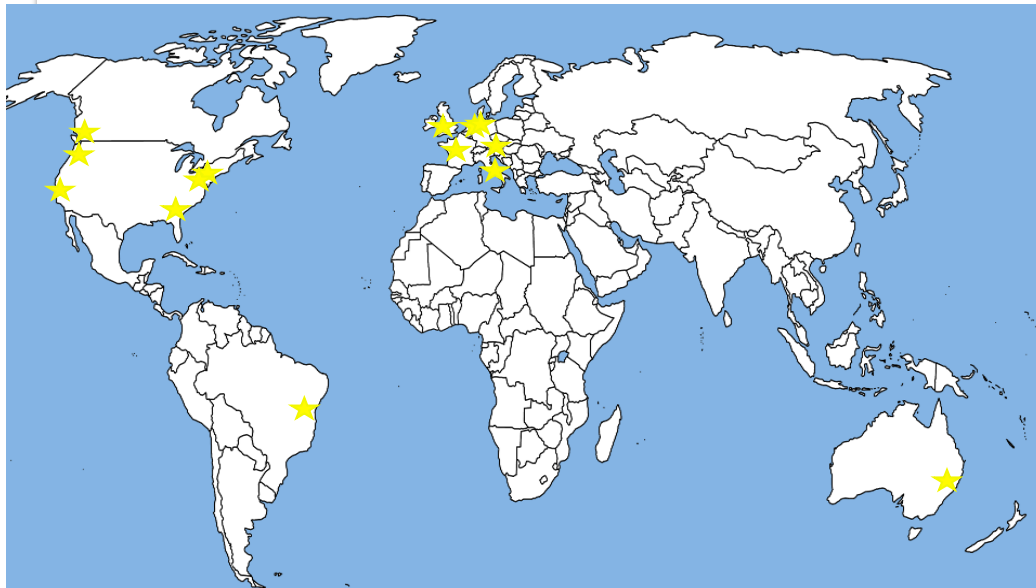
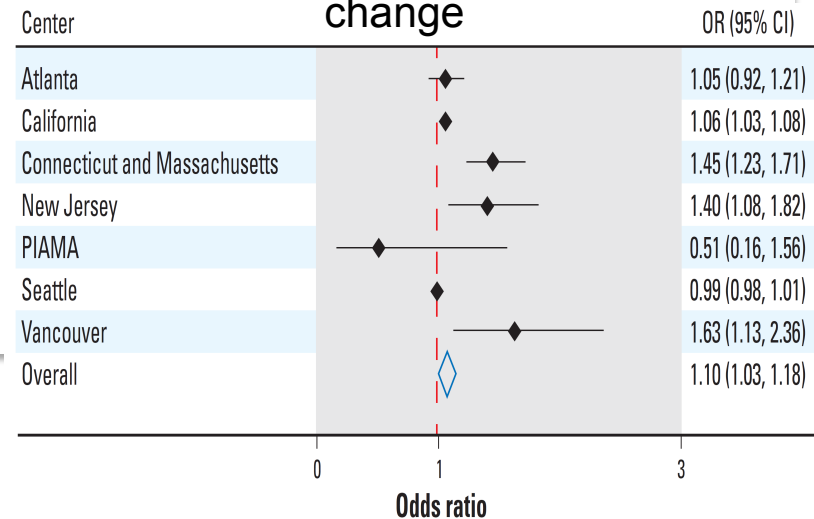
<sup>a</sup>For birth weight outcomes, analyses limited to singleton live births with recorded birth weights. For stillbirths, all singleton births included. For preterm delivery, analyses limited to singleton live births with recorded Ballard examinations. Values represent n(%) or mean ± STD.

# Maternal Exposure to Particulate Air Pollution and Term Birth Weight: A Multi-Country Evaluation of Effect and Heterogeneity

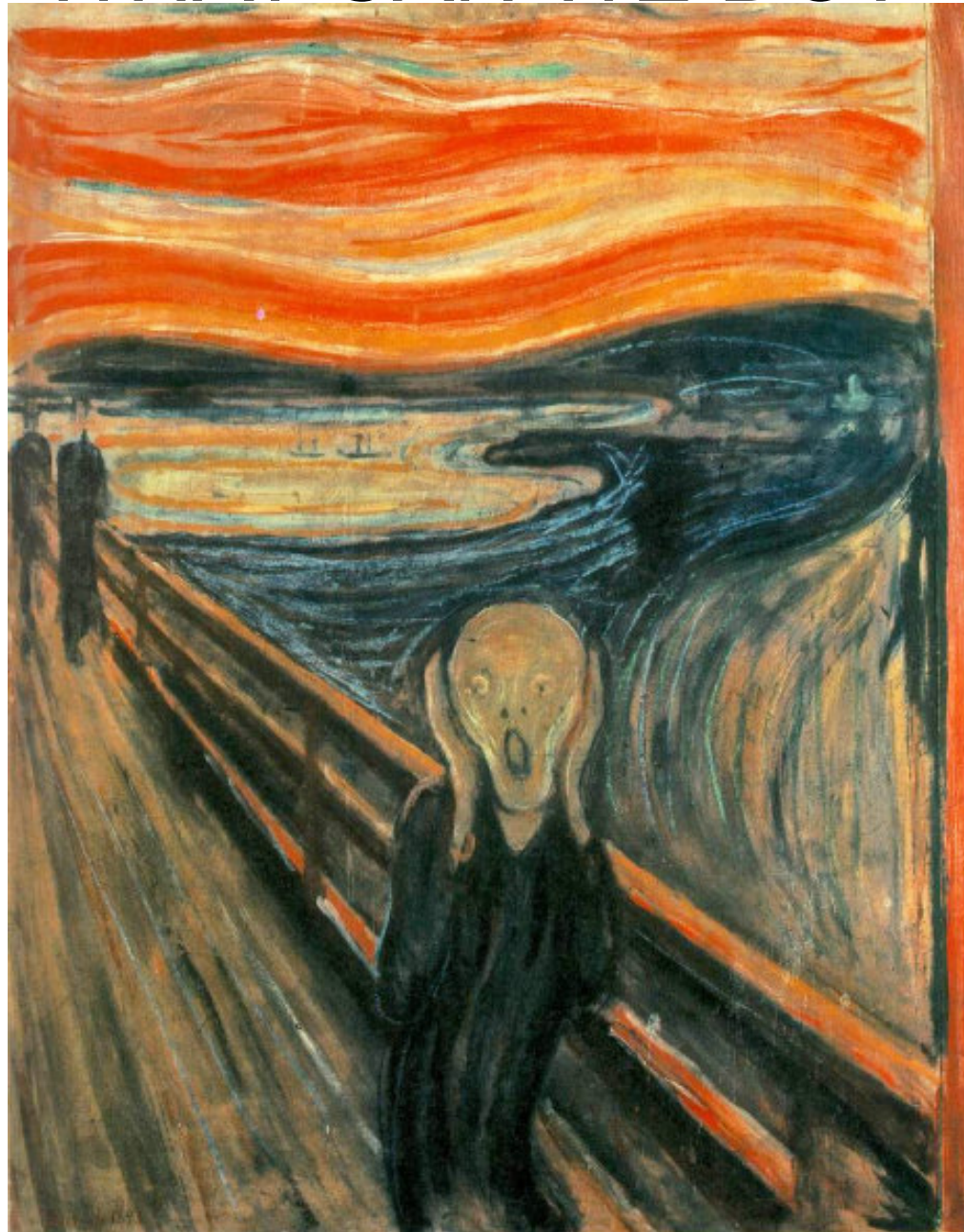
*Payam Dadvand,<sup>1,2,3</sup> Jennifer Parker,<sup>4</sup> Michelle L. Bell,<sup>5</sup> Matteo Bonzini,<sup>6</sup> Michael Brauer,<sup>7</sup> Lyndsey A. Darrow,<sup>8</sup> Ulrike Gehring,<sup>9</sup> Svetlana V. Glinianaia,<sup>10</sup> Nelson Gouveia,<sup>11</sup> Eun-hee Ha,<sup>12</sup> Jong Han Leem,<sup>13</sup> Edith H. van den Hooven,<sup>14,15</sup> Bin Jalaludin,<sup>16,17,18</sup> Bill M. Jesdale,<sup>19</sup> Johanna Lepeule,<sup>20,21,22</sup> Rachel Morello-Frosch,<sup>19,23</sup> Geoffrey G. Morgan,<sup>24,25</sup> Angela Cecilia Pesatori,<sup>26</sup> Frank H. Pierik,<sup>15</sup> Tanja Pless-Mulloli,<sup>10</sup> David Q. Rich,<sup>27</sup> Sheela Sathyanarayana,<sup>28</sup> Juhee Seo,<sup>12</sup> Rémy Slama,<sup>21,22</sup> Matthew Strickland,<sup>8</sup> Lillian Tamburic,<sup>29</sup> Daniel Wartenberg,<sup>30</sup> Mark J. Nieuwenhuijsen,<sup>1,2,3</sup> and Tracey J. Woodruff<sup>31</sup>*

> 3 million births in this meta-analysis.

PM<sub>2.5</sub> and OR LBW for 10 µg/m<sup>3</sup> change



# WHAT CAN WE DO?








INTERNATIONAL FEDERATION OF GYNECOLOGY & OBSTETRICS

# Recommendations for Preventing Exposure to Toxic Chemicals


Published October 1, 2015

**Recommendation 1:** Advocate for policies to prevent exposure to toxic environmental chemicals


**Recommendation 2:** Work to ensure a healthy food system for all



Advocate for policies to prevent exposure to toxic environmental chemicals



Work to ensure a healthy food system for all



Make environmental health part of health care



Champion environmental justice

**Recommendation 3:** Make environmental health part of health care

**Recommendation 4:** Champion environmental justice

# FIGO Summit “Shaping Our Planetary Legacy: Setting an Agenda for Environmental Reproductive Health”

October 4, 2015

Pre-Congress Workshop to help set the agenda for the new FIGO Reproductive and Developmental Environmental Health Working Group



22 countries/territories were represented at the FIGO Summit on Shaping Our Planetary Legacy

**It is time to take action!**



**Thank You**