Children's Health: Environmental Chemicals & Endocrine Disruptors

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Gastroschisis

Increasing Prevalence of Gastroschisis: Population-based Study in California


Prevalence of chronic conditions among children and youth increased from 1988 to 2006

JAMA
Dynamics of Obesity and Chronic Health Conditions Among Children and Youth

Prevalence of chronic conditions

- Any condition: 27.8%
- Obesity: 51.5%
- Other physical condition
- ADHD

1988 to 1994
1994 to 2000
2000 to 2006
During the past three decades, increases in the incidence of some childhood cancers, such as leukemia and brain tumors, may implicate prenatal exposure to environmental carcinogens.

What's Changing?

U.S. Chemical Production

Chemical production has increased 23.5-fold between 1947 and 2007.
By 2006 ...

Vast majority of chemicals in commerce have entered the marketplace without comprehensive and standardized information on their reproductive or other chronic toxicities.

Decision-Context Differences

In general, Pharmaceuticals must show efficacy and safety prior to exposing humans.

Manufactured chemicals need to show evidence of harm prior to removing human exposure.

Woodruff, Sutton et al. Health Affairs 2011
Toxic Environmental Chemicals Are Found Everywhere, Everyday ... In Virtually Everybody

- Chlorinated hydrocarbons, pesticides, industrial solvents, dioxins
- Persistent Halogenated Organic Pollutants (PCBs, DDEs)
- BPA, phthalates, Bisphenol A, PBTs
- PBDEs, phthalates, formaldehyde, parabens, toluene, 1,4-dioxane
- Pesticides

Children Take in More Air, Water and Food Per Pound Than Adults

- 2 times resting air intake
- 3 times skin absorption
- 3 times water intake
- 3 - 4 times food intake

PBDE levels in California children aged 2-5 years are similar to levels in occupationally exposed adults

Adapted from Rose et al., Environmental Science & Technology, 2010
Health Impacts of “Everyday” Toxic Environmental Exposures

Studies show the levels of chemicals an average person is exposed to can perturb biological processes:

Endocrine Disrupting Chemicals: Chemicals which can alter or interfere with natural hormone levels in the body

Interfere with the hormonal regulation critical to healthy reproduction

Endocrine Disrupting Chemicals

- Puberty
- Menstruation
- Endometriosis
- Time-to-pregnancy
- Pregnancy loss
- Reproductive Cancers

Toft et al., 2004

Timing Matters
**Child Development and Windows of Susceptibility**

- **Blastocyst**
- **Embryo**
- **Fetus**
- **Infant**
- **Child**
- **Adolescent**

**Environmental Chemical Exposure**

**Immediate & Long Term Consequences**

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**Childhood brain development**

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**DDT, Breast Cancer and Age at Exposure**

No risk for girls exposed after 14 years old

- Breast cancer in women <50 years old
- Exposures occurred at peak DDT use in US

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*From Cohn et al. 2007*
Percent of Pregnant Women with Chemicals in their Body

% of Pregnant Women with Chemicals in their Body

<table>
<thead>
<tr>
<th>Contaminant</th>
<th>Percent of US population with measurable levels</th>
<th>Some evidence can disrupt endocrine system?</th>
<th>Sources</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phthalates (4 kinds)</td>
<td>80 – 100%</td>
<td>Yes</td>
<td>Flooring, wall covering, medical devices, food, personal care products, lacquers</td>
</tr>
<tr>
<td>Bisphenol A</td>
<td>92%</td>
<td>Yes</td>
<td>Polycarbonate plastic, food, long-term water</td>
</tr>
<tr>
<td>Polyfluoralkyl Chemicals (PFOS) (4 kinds)</td>
<td>91-99%</td>
<td>Yes</td>
<td>Non-stick cookware, stain resistant fabrics, food packaging, dental products</td>
</tr>
<tr>
<td>Parabens (4 kinds)</td>
<td>36-99%</td>
<td>Yes</td>
<td>Personal care products, food</td>
</tr>
<tr>
<td>Benzophenone-3</td>
<td>100%</td>
<td>Yes</td>
<td>Personal care products, food, sunscreen</td>
</tr>
<tr>
<td>PCBs (many)</td>
<td>100% (with at least one congener)</td>
<td>Yes</td>
<td>Banned in 1977 – persistent through food</td>
</tr>
</tbody>
</table>

*Representative US sample from NHANES/CDC generally from 2003/2004
Mixtures

Impact of mixtures can be dramatically greater than effects of chemicals one by one.

Together these 11 contaminants double the effect of estrogen

Phthalates found in

- Medical devices
- Toys
- Food Wrap
- Personal care products (perfumes, lotions, cosmetics, hair spray)
- Air Fresheners
- Flooring, wall coverings, lacquers, varnishes, and wood finishes and coatings

- Dibutyl phthalate
- Dethylhexyl phthalate
- Dimethyl phthalate
- Butyl benzyl phthalate

Prenatal exposure to phthalates

- Decreased testosterone
- Reduced anogenital distance
- Cryptorchidism
- Hermaphroditism
- Infertility

Prenatal phthalate exposure in animals

* Howdeshell et al. 2007 Toxicology
And People?

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Decrease in Anogenital Distance among Male Infants with Prenatal Phthalate Exposure

Phthalates in pregnant women associated with decrease in anogenital distance – a marker for feminization
OR for MPB 10.2 (2.5 – 42.2)

Effects of PBDEs on early development

- In vitro, PBDEs disturb development of fetal human brain cells (Schreiber et al., 2010)
- In animal studies, neonatal and postnatal PBDE exposures affect learning, memory, and attention (Driscoll et al., 2008; Viberg 2006)
- Thyroid hormone disruption has been identified as possible mechanistic link

PBDE effects on the developing human brain

Children with higher prenatal exposures to PBDEs 47, 99, or 100 scored lower on tests of mental and physical development (including IQ tests).

Strength of the Evidence

Evidence for adverse reproductive outcomes (infertility, cancers, malformations) from exposure to endocrine-disrupting chemicals is strong, and there is mounting evidence for effects on thyroid, neuroendocrine, obesity and metabolism, and insulin and glucose homeostasis.

“...In addition to fetal ‘over-nutrition’ or ‘under-nutrition,’ it is possible that developmental exposure to endocrine disrupting chemicals (EDCs) or other chemicals plays a role in the development of diabetes and childhood obesity” (pg. 17)
Interventions Matter

- 20 people/five families
- Changed from canned/packaged food to none
- Change in BPA and MEHP levels

**FASTEP** - Reproductive Environmental Health Toolkit

- Clinical guidance based on AAP-Endorsed PSR Pediatric Environmental Toolkit© and other authoritative sources
- Co-branded by FASTEP Alliance partners
- Disseminating with PSR Pediatric Environmental Toolkit©, Centers for Excellence in Women’s Health, Magee Women’s Hospital, and other partners
- Concrete advice on how women can avoid harmful chemicals

www.prhe.ucsf/prhe
Three things I do!

- Shop smart organic
- Don’t eat plastic
- Wash my hands

We Can’t Shop Our Way out the Problem

5 Areas of Focus

- Prevent Exposure At Home
  - Example – don’t smoke, eat organic when possible
- Prevent Exposure At Work
  - Example – know what is in your workplace and talk with your healthcare provider
- Prevent Exposure In Your Community
  - Example – drive less, do not burn trash
- Become A Smart Consumer
  - Example – consumer guides can help you buy less toxic products
- Make The Government Work For You
  - Example – the government should know you care
MEET MOLLY GRAY.
Eats organic. Avoids BPA. Buys natural cleaners.
Loaded with toxic chemicals.

Nine pregnant women tested from Washington, Oregon, and California, during the second trimester had detectable
- Bisphenol A, mercury, at least four phthalates, at least two and up to 4 perfluorinated chemicals

Actions can reduce exposures

We expect to know about drugs before they go to market, why not chemicals?

- Pharmaceuticals must have data to show efficacy and safety prior to use
- Do manufactured chemicals have to have data on safety before use?

NO
Program on Reproductive Health and the Environment

Jackie Schwartz  Patrice Sutton
Jason Harless  Joanne Perron
Amy Zota  Linda Giudice
Carrie Dickenson (chair and founder)

Mission: To create a healthier environment for human reproduction and development by advancing scientific inquiry, clinical care, and health policies that prevent exposures to harmful chemicals in our environment

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Percent of U.S. population with detectable pesticides in their bodies

A meta-analysis of 15 human studies found positive associations between childhood leukemia and residential pesticide exposures during pregnancy and childhood. (30% to 200% increased risk)

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Where do we get our information?

Wildlife  Laboratory  Humans

In general, there is concordance of developmental effects between animals and humans and that humans are as sensitive or more sensitive than the most aggressive animal species. NAS 2000 Scientific Frontiers in Dev. Tox and Risk Ass.
Streams of Evidence for Toxicity Assessment

- Critical
  - New pharmaceutical developed
  - In vitro & in vivo toxicity testing
  - Human experimental studies (Randomized Control Trials)
  - Post exposure observational studies

- Environmental
  - Chemicals introduced prior to 1970 (n= 52,000)
  - Science/evaluation
  - Ad hoc post exposure observational studies
  - Ad hoc in vitro & in vivo toxicity testing

Evaluating the evidence base

- Decisions and evidence
  - Pharmaceuticals must show efficacy and safety prior to use
    - Requires extensive animal and human data
  - Manufactured chemicals need to show evidence of harm before removing/regulating
    - No specific toxicity testing required
    - Except for pesticides
    - Human studies are mostly byproduct of already exposed populations
    - Ethical issues with intentional dosing studies
  - Decisions must be made in a timely manner to prevent ongoing harmful exposures

Limitations of Human Evidence

- Human
  - Measurement of exposure often limited
  - Increase “risk” from environmental contaminant exposure often small
    - Many risks in range of 2 fold increase
      - Exposure reclassification can hide true associations
    - But exposure ubiquitous – so still a public health problem
      - Example – particulate matter air pollution
      - Increases risk of respiratory and cardiovascular morbidity and mortality
    - RR mortality ~ 1.06 for estimating benefits in the United States
      - > 184,000 lives “saved” per year
TH AND BRAIN DEVELOPMENT

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PBDE levels in CA pregnant women are elevated

Woodruff et al., EHP 2011; Zota et al., submitted

California Technical Bulletin 117 (TB 117)

- 1975 standard
- Performance-based standard
- Foam in furniture must withstand open flame for 12 seconds
- Unique standard; no other state has a parallel standard
PBDEs and thyroid hormone disruption during pregnancy

Higher levels of PBDEs and OH-PBDEs correlated with higher levels of TSH in second trimester California pregnant women

Zota et al., submitted

$R^2 = 0.15$
P-value = 0.03

Mixtures Are the Rule

Yet all regulatory standards to protect people are based on considering one chemical at a time.

By themselves, these contaminants appear to have no effect.