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Children's Health and the Environment: Opportunities for Prevention

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Why are children are uniquely vulnerable?

- Pound for pound, drink more water, eat more food and breathe in more air
- Less well able to detoxify or eliminate chemicals from their bodies
- Developing organ systems are more susceptible
- Greater years of life in which chronic conditions can occur as a result of early life exposures

National Academy of Sciences 1993

Evidence confirming child vulnerability

- Epidemic increases in chronic disease in US and other industrialized nations (asthma, childhood cancers, certain birth defects, learning/developmental disabilities)
  - Contemporaneous with widespread increase in use of chemicals

Trasande et al Dec 2011 Health Affairs

Evidence confirming child vulnerability

- Population studies quantify strong and consistent associations with chemical exposures
  - US National Academy of Sciences: 28% of developmental disabilities at least in part due to environment
  - Benzene and 1,3-butadiene associated with childhood cancer
  - Outdoor air pollutants are well documented to worsen and may increase risk of development of asthma

Trasande et al Dec 2011 Health Affairs

Why have we been slow to protect children?

- Regulation does not require premarket testing of chemicals
  - Fewer than ½ of most produced chemicals in US have any toxicity testing data; fewer than 1/5 have data with respect to impacts on development
- Epidemiologic studies post hoc take years
- Outcomes have many potential confounders
- Criteria of reproducibility, consistency
- Uncertainty about dose-response relationships (also linear pedagogy), thresholds
- Subclinical effects are not as powerful as the Minamata or Bhopal disasters

Failing to protect children is costly

EXHIBIT 1

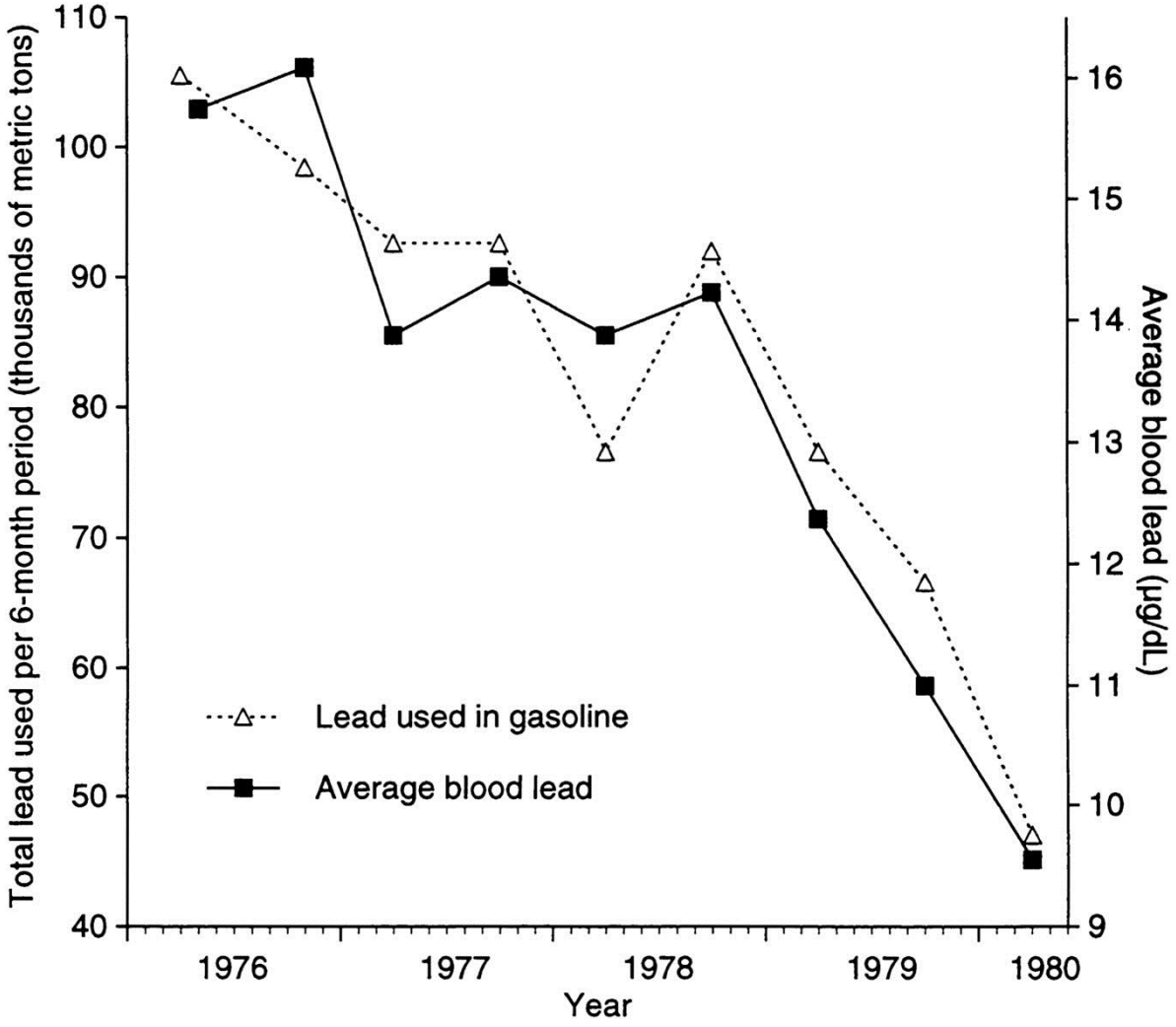
Aggregate Costs Of Environmentally Mediated Diseases In US Children, 2008

Environmentally attributable costs by condition	Base-case estimate	Low-end estimate	High-end estimate
Lead poisoning	$50.9 billion	$44.8 billion	$60.6 billion
Methylmercury toxicity	$5.1 billion	$3.2 billion	$8.4 billion
Asthma	$2.2 billion	$730.0 million	$2.5 billion
Intellectual disability	$5.4 billion	$2.7 billion	$10.9 billion
Autism	$7.9 billion	$4.0 billion	$15.8 billion
Attention deficit hyperactivity disorder	$5.0 billion	$4.4 billion	$7.4 billion
Childhood cancer	$95.0 million	$38.0 million	$191.0 million
Total	**$76.6 billion**	**$59.8 billion**	**$105.8 billion**

SOURCE Authors' analysis.

Trasande and Liu May 2011 Health Affairs

Prevention works and saves money



- Global Benefits of Phasing Out Lead From Gasoline
  - Range from $1-$6 trillion/year, with a best estimate of $2.45 trillion/year. These benefits may also be expressed as 4% of global GDP.

Solutions

- Clinical
- Research
- Policy

Clinical Solutions

- What is a Pediatric Environmental Health Specialty Unit (PEHSU)?
  - A resource for pediatricians, public health officials, school personnel, parents and others to get questions answered about children's health and the environment
- Goals of a PEHSU
  - Education of health professionals and others about children's health and the environment
  - Serve as a consultant to physicians, nurses, public health professionals, parents and others with questions about children's health and the environment

PEHSU
Pediatric Environmental Health Specialty Units

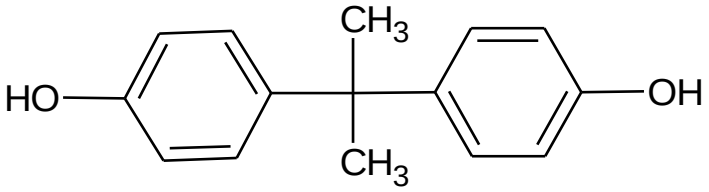
Research Solutions

- Endocrine disruptors (EDs) are chemicals that have the capacity to interfere with hormonal signaling systems
  - May mimic, block, or modulate the synthesis, release, transport, metabolism, binding, or elimination of natural hormones
  - May temporarily or permanently alter feedback loops in the brain, pituitary, gonads, thyroid, and other components of the endocrine system

Endocrine disrupting chemicals

- Highly heterogeneous group of molecules
  - industrial solvents/lubricants and their byproducts [polychlorinated biphenyls (PCBs), polybrominated biphenyls (PBBs), dioxins], plastics [bisphenol A (BPA)],
  - plasticizers (phthalates),
  - pesticides [methoxychlor, chlorpyrifos, dichlorodiphenyltrichloroethane (DDT)],
  - fungicides (vinclozolin), and
  - pharmaceutical agents [diethylstilbestrol (DES)].”

Bisphenol A (BPA)



- Used to manufacture polycarbonate resin
- Recently banned from baby bottles and sippy cups by US Food and Drug Administration
- Breakdown product of coatings intended to prevent metal corrosion in food and beverage containers
- In children, dietary sources constitute 99% of BPA exposure

Schecter et al. *Environ Sci Technol.* 2010;44(24):9425-9430
Wilson et al.*Environ Res.* Jan 2007;103(1):9-20.
Tavernise S. *New York Times, 17 July 2012 edition.*

BPA and obesity

- Laboratory studies suggest that BPA
  - Increases fat cell size
  - Disrupt adiponectin function
  - Low-grade synthetic estrogen
    - Estrogen-testosterone balance may have sex-specific differences in influence on body mass

Masuno et al. *J Lipid Res.* 2002;43(5):676-684; Sakurai K et al. *Br J Pharmacol.* 2004;141(2):209-214;

Association of urinary BPA with childhood obesity

- Nationally representative sample of 2838 US children
  - Urinary BPA measured by the Centers for Disease Control and Prevention
  - Divided population into four groups, lowest to highest
  - Children with lowest levels of BPA: 10.3% obese
  - Children with higher levels of BPA: 20.1-22.1% obese
  - Linear association of BPA with standardized measure of Body Mass Index accounting for age and gender
  - Levels of other phenols found in sunscreens and soaps not associated

Trasande et al JAMA 2012; 308(11):1113-21

Other chemicals with data suggesting role in obesity, diabetes and cardiovascular disease

- Phthalates
  - Found in shampoos, soaps, lotions, flooring, food wraps

Janesick et al 2011, Trasande et al 2013

- Perfluoroalkyl chemicals
  - Used in nonstick cooking, carpets and upholstery, microwave popcorn bags

Halldorsson et al 2012

- Polycyclic aromatic hydrocarbons
  - Breakdown product of fuel burning, also food contaminant

Rundle et al Am J Epidem 2012

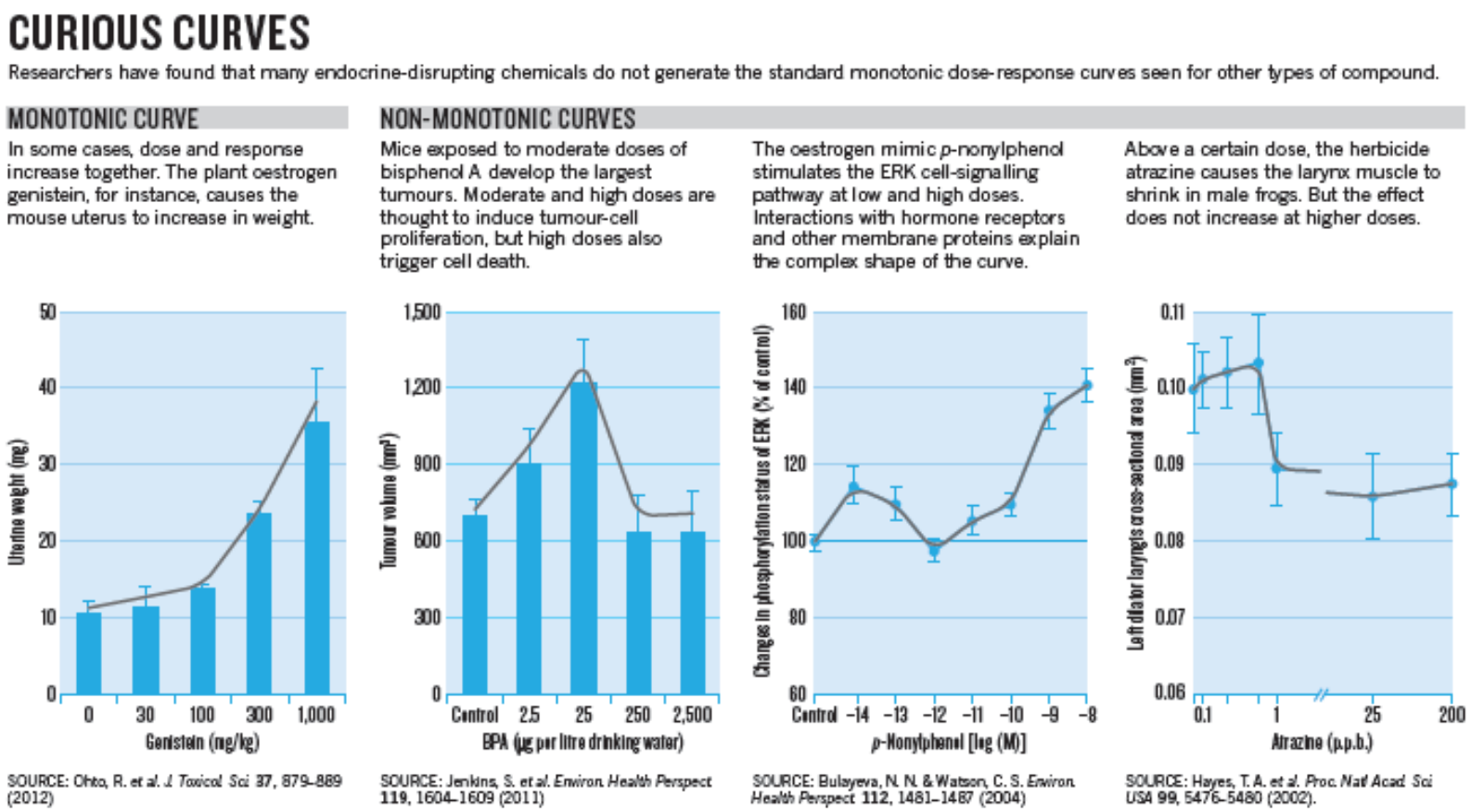
  - Proximity to oil refinery in Jeddah associated with increased BP

Trasande et al Env Research 2015

- Polybrominated diphenyl ethers
  - Flame retardants found in furniture, electronics

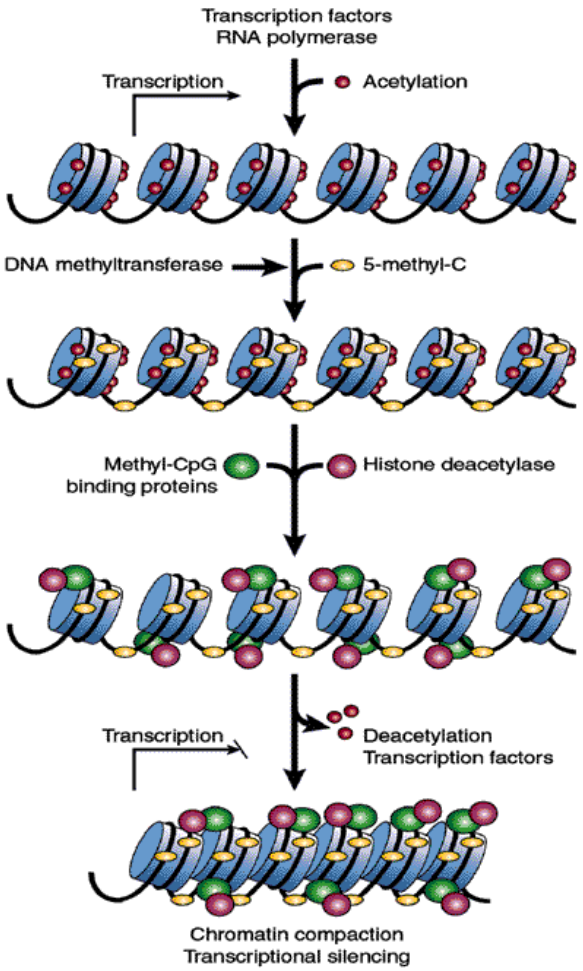
Lim et al Diabetes Care 2008

Non-linearity and non-monotonicity

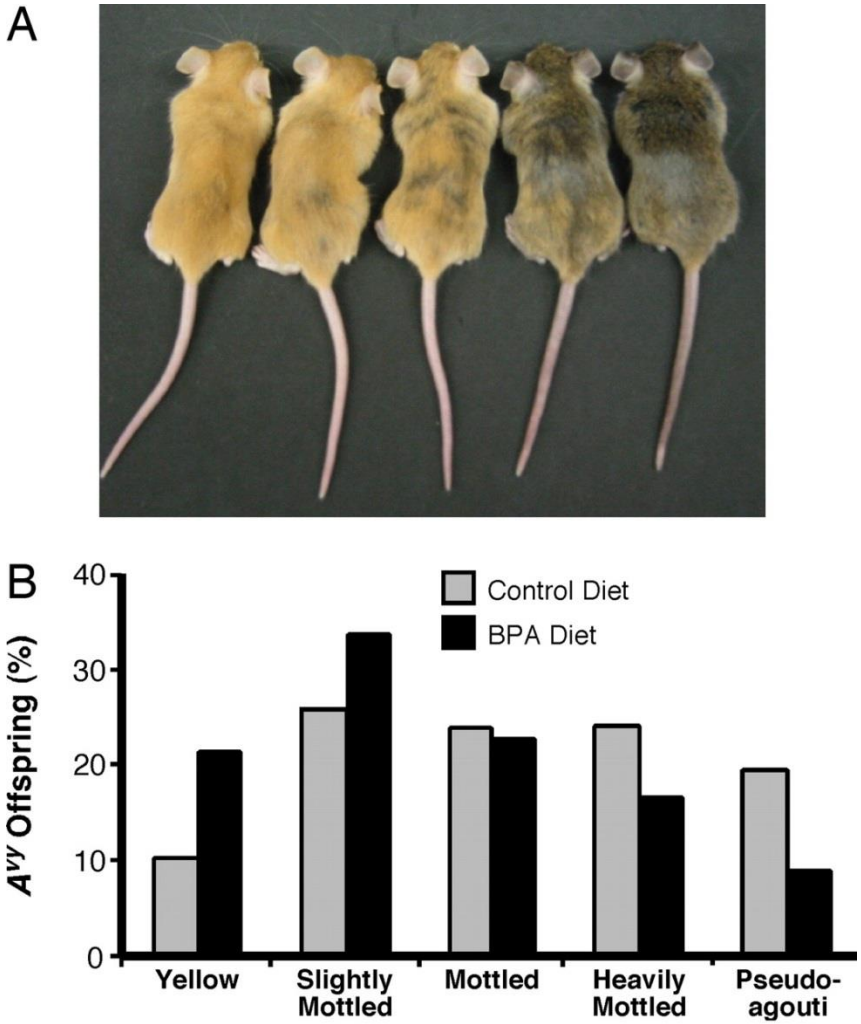


Fagin Nature 2012

Chemical exposures and epigenetics



Maternal BPA exposure shifts offspring coat color distribution toward yellow.



Dolinoy D C et al. PNAS 2007;104:13056-13061

Policy action on BPA

- BPA banned in baby bottles and sippy cups
  - But not in other food uses

Costs of BPA exposure

- 12,404 cases of childhood obesity
- 33,863 cases of newly incident coronary heart disease
- Estimated social costs of $2.98 billion in 2008

Trasande Health Affairs 2014

Benefits and costs of replacing BPA

- Potential cost of one BPA alternative, oleoresin = $0.022 per can
  - 100 billion aluminum cans are produced annually
  - 100 billion x $0.022 = **$2.2 billion**

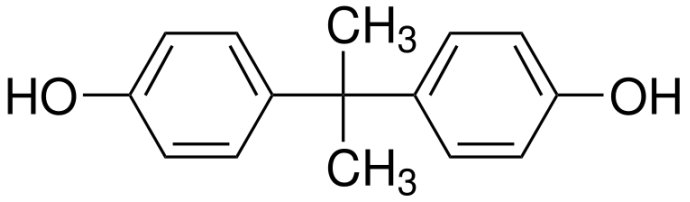
- Potential benefit of replacing BPA with lining free of health effects = **$1.74 billion**
  - Does not include other effects (cognitive, asthma, breast cancer)

- Sensitivity analyses suggest as high as $13.8 billion

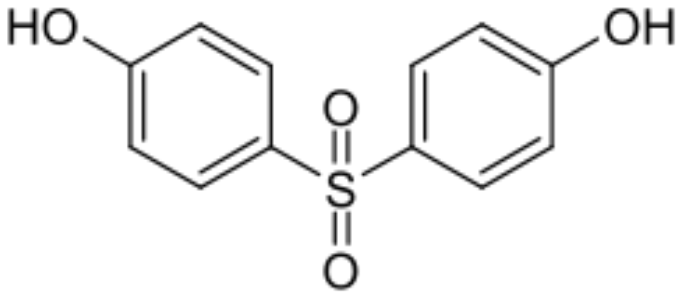
Trasande Health Affairs 2014

BPS replacing BPA?

- Emerging evidence suggests replacement of BPA and BPS
- Similar, weak estrogen like BPA
- Disrupts signaling of estrogen in animal studies
- Does not degrade as easily in seawater



Bisphenol A



Bisphenol S

Liao et al Environ Sci Technol. 2012 Jun 19;46(12):6860-6.
Liao et al Environ Sci Technol. 2012 Jun 19;46(12):6515-22.
Grignard et al Toxicol In Vitro. 2012 Aug;26(5):727-31.
Vinas and Watson EHP doi:10.1289/ehp.1205826
Danzl et al Int J Environ Res Public Health. 2009 Apr;6(4):1472-84

The increasingly global chemical picture

- OECD estimates in 2020: industrializing nations will account for 33% of global chemical demand and 31% of production
  - compared with 23 percent and 21 percent, respectively, in 1995
  - industrializing nations are expected to lead in the manufacture of high production volume chemicals
  - occurs against a backdrop of insufficient infrastructure to protect public health and the environment

Summary

- Clinical resources can be very useful to guide prevention and management of environmental exposures in children
- Substantial research is ongoing to better understand the complex relationships of environmental chemicals to disease, especially endocrine disruptors
- Regulation is needed to proactively prevent chronic childhood diseases that are increasing both in industrializing and industrialized countries
  - Benefits of improved health may be greater than costs of safer alternatives

Thanks!

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