

# Putting it into Practice: Pediatric Environmental Health Training Resource

## Endocrine Disrupting Chemicals and Children's Health: Phthalates and Bisphenol A

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User Guide



Children's  
Environmental  
Health  
Network

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# Endocrine Disrupting Chemicals and Children's Health: Phthalates and Bisphenol A

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## User Guide

### I. What are Endocrine Disrupting Chemicals (EDCs)?

Endocrine disruptors (ED's) are chemicals that interfere with endocrine system function. They can mimic, block, alter synthesis, metabolism or excretion of hormones thus setting off similar chemical reactions in the body, as well as prevent the action of normal hormones, or alter the concentrations of natural hormones. Lead, pesticides and flame retardants are some examples of the wide array of environmental exposures that have endocrine disrupting properties. For the purposes of this discussion, we will focus on phthalates and bisphenol A.

### II. Examples of EDCs: Phthalates and bisphenol A (BPA)

Phthalates and bisphenol A (BPA) are 2 classes of chemicals added to plastics and other products to impart flexibility and durability. These chemicals have recently been discussed in the media because of concerns that they may adversely impact children's health. Phthalates and BPA are high production volume (HPV) chemicals meaning that they are either produced or imported to the United States in quantities of 1 million pounds or more per year (McGinn, 2000). Bisphenol A production volume in the United States is approximately 2.3 billion pounds per year (SRI, 2004).

#### a) Characteristics/Sources

Phthalates are found in common consumer products such as children's toys, food packaging and processing, vinyl flooring, wall coverings and building supplies; medical devices such as intravenous tubing; medications including enterically-coated tablets such as the antacid omeprazole which is sometimes taken in pregnancy; and personal care products including fragrances, cosmetics and nail polish. The food supply is generally considered a major source of phthalate exposure e.g., through the processing of foods.

Bisphenol A is found in linings of canned foods including ready-to-eat infant formulas, and in hard plastics made of polycarbonate (found in sports water bottles, water dispensers and baby bottles). Another source of exposure is carbonless receipts which can contain high concentrations of BPA that can leach from the paper onto hands. Bottled water (single serve) is typically made from plastics that do not contain BPA. The primary sources of exposures vary by age, gender, developmental stage and individual behavior. The primary route of exposure for both phthalates (DEHP) and BPA is probably ingestion. For other phthalates, (eg. DEP) it is dermal absorption of personal care products.



Since these substances are not chemically bound to the plastics to which they are added, they can leach out of products causing exposure through ingestion of foods found in plastic packaging and processing, mouthing of products, breathing in dust generated from these products, or through direct contact with skin. Exposure of phthalate- and BPA-containing products to high temperatures – as occurs with heating or sterilizing baby bottles in the microwave – promotes leaching of the chemicals. Young children may be uniquely vulnerable to these exposures as they frequently place toys and other plastic products in their mouths, an age appropriate behavior.

The Centers for Disease Control and Prevention (CDC) tracks exposures to many environmental chemicals in a nationally representative sample of people ages 6-85 years old (CDC, 2008). Measurements of phthalate and BPA metabolites in urine are included in the CDC report. Nearly all Americans have measurable concentrations of phthalates and BPA in their bodies. Children and adolescents have disproportionately high levels of DEHP metabolites compared to adults. Possible explanations include varying routes and sources of exposure, differences in metabolism, or a combination of these factors. Babies in the neonatal intensive care unit (NICU) are one “special population” known to be highly exposed to phthalates because they receive medical therapies via intravenous tubing, though some NICUs are now using phthalate-free medical devices (Weuve et al., 2006).

The half life for both phthalates and BPA is very short, indicating that these chemicals are rapidly cleared from the body. Urine tests to assess exposure to phthalates and BPA are currently conducted for research purposes only. Some studies suggest that a one-time measurement of urinary levels is likely to be a good measure of long-term exposure given the relative constancy of exposures in children’s daily lives (Teitelbaum, 2008).

#### **b) Diagnostic Tests and Treatment**

Urine tests for phthalates and BPA are only conducted for research purposes at this time. There is as yet no clinical reference level to indicate what level of exposure is associated with human health effects. For this reason, it is not recommended that patients seek out tests for phthalates or BPA. Treatment is aimed at reducing exposures where feasible.

#### **c) Potential Health Effects**

Due to the widespread use of these chemicals as well as evidence of universal exposure in the US population, concerns have been raised that young children may be vulnerable to developing long-term health effects. Health information about phthalates initially came from studies in animals, most typically exposed to high doses *in utero*. These studies demonstrate that phthalates can affect birth outcomes and reproductive systems (Shea, 2003); the male reproductive tract is the most sensitive to phthalate exposure (Foster, PMD, 2006). In animals, there are associations between phthalate exposures and hypospadias, undescended testes, male infertility, germ cell tumors and decreased anogenital distance (Foster, PMD, 2006). Studies in humans now show associations between phthalate exposures *in utero* and decreased anogenital distances in male infants,



and cross sectional associations with atopic diseases, and obesity in adults (Marsee et al., 2006; Bornehag et al., 2004; Jaakkola and Knight 2008; Hatch et al., 2008).

Many studies in animals have shown an association of exposure to prenatal BPA and adverse health effects including neurobehavioral disorders such as hyperactive behavior, (Ishido, 2004; Braun ) learning disorders (Carr, 2003), wheezing in children (Spanier), and endocrinologic disorders such as obesity (Masuno, 2005), altered insulin sensitivity (Roper, 2008), and cancers of the breast (Markey, 2001; Vandenberg, 2007), prostate (Maffini, 2006; Prins; 2008) and uterus (Maffini, 2006; Newbold, 2007). Human studies for BPA, however, are limited, though humans are exposed to concentrations similar to or higher than doses used in several animal studies that document adverse health effects. A recent study of adults reported a relationship between high BPA exposures and heart disease, Type 2 diabetes, and abnormal liver function tests (Lang, 2008; Trasande, 2012). BPA has not yet been classified as a human carcinogen (IARC, 1989, 1999).

#### **d) What Parents Ask**

- How do I know if toys contain phthalates?
- Are bottles made with bisphenol A harmful?
- What are the current regulations?
- What health effects should I look for?
- What alternatives can my child use?

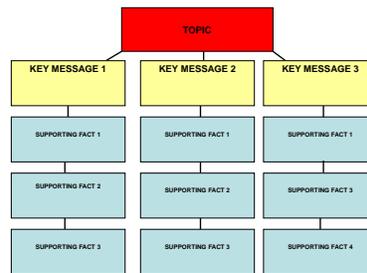
#### **e) How to Best Communicate About Environmental Exposures**

It is sometimes challenging to discuss the health impacts of environmental hazards such as the ones above, especially in the absence of scientific certainty. Because we are trusted advisors to the families and communities that we serve, pediatricians often are in a good position to communicate health information. Whether speaking with individual parents or community groups, it is helpful to understand basic areas about explaining the risks of environmental hazards. Pediatricians can improve how we communicate environmental health information. Important steps include:

- Prepare messages in advance.
- Craft messages that are clear and appropriate for your patients
- Frame messages positively whenever possible – avoid negatives.
- Use easy to understand comparisons to explain exposures. When typical background levels are not available, look to historical background levels.
- Facilitate trust of public health officials by working along with them to communicate risks to families.
- Consider using the “rule of 3’s.”
  - Develop 3 key messages around these three questions: What is the exposure? What are the health effects? What can parents do?



- Develop 3 supporting facts for each of the three messages.



By providing families with simple measures they can take to reduce any further risks, you can reduce the perception of risk, helping families make the safest and most appropriate decisions. In times of high concern, overcome parents' mental noise by crafting clear and concise messages. These basic principles of pediatric environmental health and risk communication will enhance your effectiveness in addressing parents' concerns in office and community settings.

The slide set includes a general message map for phthalates and BPA. The messages encompass simple steps families can take to reduce exposures. This is by and large how we respond to common clinical questions on whether a product contains a chemical of concern. There are readily available websites that help consumers navigate these decisions as well <http://www.ewg.org/skindeep/>

**f) What can parents do to minimize a child's exposure to phthalates and BPA?**

It is important to present families with evidence-based information so that they may make informed decisions about whether and how to reduce exposures. Because studies in humans are very limited, we recommend that families take a precautionary approach. There are a few simple steps families can take to reduce exposures in to phthalates and BPA:

- Select fresh foods rather than canned food products.
- Look for children's products that are marked free of phthalates and/or BPA.
- Avoid placing plastics in the dishwasher and microwave since high temperatures may promote leaching of the plasticizers.
- Look to recycling labels in the absence of mandatory labeling.
  - #3 plastics may contain lead and phthalates.
  - #7 plastics may contain BPA.
  - Instead, choose plastics that are labeled #1, 2, 4, and 5.
- Choose stainless steel water bottles rather than plastic. Most stainless steel bottles have no plastic lining. Consult bottle manufacturers' web sites to obtain descriptions of the bottles, including whether or not they contain BPA.
- If using formula, choose powdered rather than prepared canned infant formula. (If tap water is used to reconstitute formula, it should be run for 2 minutes, or until cold, to lessen the risk of exposure to any lead present in water. Tap water should



- not be over-boiled because this may concentrate lead. One minute of a rolling boil is sufficient to kill microorganisms.)
- Although breakage is an important issue, consider using glass baby bottles and glass containers for food storage.
  - Dust and mop frequently using wet techniques such as a mop or damp rag to minimize exposure to phthalates in dust.

### **g) Legislation**

The European Union (EU) has had a permanent ban on phthalates in children's products since 2005; prior to that, a temporary ban was in place as a precautionary measure. Alternative plastics that offer durability while not exposing children to phthalates, have been used in the EU for children's toys and products. A voluntary ban on phthalates in children's toys and products has been in place in the US since 2002. In the absence of mandated labeling, however, the challenge to consumers is to ensure that children's toys and products are phthalate-free. And ultimately, the burden should not be on the consumer to determine which products are in fact safer. Transparency with respect to labeling, premarket safety testing, third party certification and information on alternatives used, are needed to shift the burden away from the consumer and ensure products on the market are safe.

California was the first US state to ban 6 phthalates from toys and products marketed to children less than 3 years of age. This legislation will take effect in 2009. The subsequent passage of the Consumer Product Safety Improvement Act of 2008 (CPSIA): ensures that this legislation is applicable nationwide; broadens its scope by making the legislation applicable to children's toys and products for children under 12; includes a permanent ban on 3 phthalates and a temporary ban on 3 higher molecular weight phthalates until more is known about their safety; and requires pre-market testing of products to ensure that products are in compliance with new regulations.

In 2008, Canada banned BPA in baby bottles and formula and infant food packaging as a precautionary measure. The first legislation of this kind in the US was passed unanimously by the Suffolk County Legislature on Long Island, NY in March 2009. Due to widespread concerns about BPA, several baby bottle manufacturers and major retailers have already voluntarily withdrawn BPA from use as well as from store shelves, with signage in stores reflecting such measures. In 2012, France passed legislation banning BPA in all baby foods by 2013 and in all food containers by 2015.



### III. Discussion Question

There has been controversy over BPA and potential health effects in humans. Outline the current controversies regarding low dose exposures.

How do you counsel families that ask about exposures that occurred in the past? For example, when my first child was a baby we used baby bottles that had BPA, what should I do? Should I be worried?

### KEY RESOURCES FOR FURTHER READING

The American Academy of Pediatrics' *Pediatric Environmental Health* handbook enables health care providers to become familiar with a broad scope of environmental health issues. Handbooks may be ordered from the AAP at [www.aap.org/bookstore](http://www.aap.org/bookstore) or 1-800-433-9016.

- American Academy of Pediatrics. *Pediatric Environmental Health*. 3rd Edition. Etzel RA, Balk SJ, Eds. Elk Grove Village IL: 2012.

Centers for Disease Control and Prevention. Fourth Report on Human Exposure to Environmental Chemicals, Updated Tables. Available at: <http://www.cdc.gov/exposurereport/>. Updated March 2013.

The Agency for Toxic Substances and Disease Registry (ATSDR) exposure-specific fact sheets entitled "ToxFAQS" address frequently asked questions for environmental exposures including what is known about the exposure, sources and routes of exposures, and potential health effects. [www.atsdr.cdc.gov/toxfaq.html](http://www.atsdr.cdc.gov/toxfaq.html).

To speak with an expert in Pediatric Environmental Health, contact the Pediatric Environmental Health Specialty Unit (PEHSU) in each EPA Region by visiting the Association for Occupational and Environmental Clinics website at <http://www.aoec.org/pehsu/index.html>. PEHSU physicians can assist with crafting risk communication messages in response to or in anticipation of parental or community questions. PEHSU fact sheets are also available on phthalates and BPA and other topics.

Locate other fact sheets from city, state and federal agencies by using the ".gov" search engine.

To identify safer products look to Environmental Working Group's website at: <http://www.ewg.org/skindeep/>



## Select Additional Resources

### Health Effects: Animal studies

Foster, PMD. Disruption of reproductive development in male rat offspring following in utero exposure to phthalate esters. *Int J Androl.* 2006;29(1):140-147.

Gray LE, Jr., Wilson VS, Stoker T, Lambright C, Furr J, Noriega N, Howdeshell K, Ankley GT, Guillette L. Adverse effects of environmental antiandrogens and androgens on reproductive development in mammals. *Int J Androl.* 2006 Feb;29(1):96-104; discussion 5-8.

Markey CM, Luque EH, Munoz De Toro M, Sonnenschein C, Soto AM. In utero exposure to bisphenol A alters the development and tissue organization of the mouse mammary gland. *Biol Reprod.* 2001;65(4):1215-1223.

Newbold RR, Jefferson WN, Padilla-Banks E. Long-term adverse effects of neonatal exposure to bisphenol A on the murine female reproductive tract. *Reprod Toxicol.* 2007;24(2):253-258.

Richter CA, Birnbaum LS, Farabollini F, Newbold RR, Rubin BS, Talsness CE, Vandenberg JG, Walser-Kuntz DR, von Saal FS. In vivo effects of bisphenol A in laboratory rodent studies. *Reproductive Toxicology.* [Review]. 2007;24(2):199-224.

Vandenberg LN, Maffini MV, Wadia PR, Sonnenschein C, Rubin BS, Soto AM. Exposure to environmentally relevant doses of the xenoestrogen bisphenol-A alters development of the fetal mouse mammary gland. *Endocrinology.* 2007;148(1):116-127.

### Health Effects: Human Studies

Calafat AM, Ye X, Wong LY, Reidy JA, Needham LL. Exposure of the U.S. population to bisphenol A and 4-tertiary-octylphenol: 2003-2004. *Environ Health Perspect.* 2008 Jan;116(1):39-44.

NIEHS. Since You Asked - Bisphenol A. NTP Brief; 2008.

Bornehag CG, Sundell J, Weschler CJ, Sigsgaard T, Lundgren B, Hasselgren M, Hägerhed-Engman L. The association between asthma and allergic symptoms in children and phthalates in house dust: a nested case-control study. *Environ Health Perspect.* 2004;112:1393-7.

Braun J, Yolton K, Dietrich KN, Hornung RW, Ye X, Calafat A, Lanphear RW. Prenatal Bisphenol A Exposure and Early Childhood Behavior. *Environ Health Perspect.* 2009.  
doi:10.1289/ehp.0900979.

Engel SM, Miodovnik A, Canfield RL, Zhu C, Silva MJ, Calafat AM, Wolff MS. Prenatal phthalate exposure is associated with childhood behavior and executive functioning. *Environ Health Perspect.* 2010 Apr;118(4):565-71.



Engel SM, Zhu C, Berkowitz GS, Calafat AM, Silva MJ, Miodovnik A, Wolff MS. Prenatal phthalate exposure and performance on the Neonatal Behavioral Assessment Scale in a multiethnic birth cohort. *Neurotoxicology*. 2009 Jul;30(4):522-8.

Hatch EE, Nelson JW, Qureshi MM, Weinberg J, Moore LL, Singer M, Webster TF. Association of urinary phthalate metabolite concentrations with body mass index and waist circumference: a cross-sectional study of NHANES data, 1999-2002. *Environ Health*. 2008;7:27.

Hauser R, Meeker JD, Duty S, Silva MJ, Calafat AM. Altered semen quality in relation to urinary concentrations of phthalate monoester and oxidative metabolites. *Epidemiology*. 2006 Nov;17(6):682-91.

Institute of Medicine. Prins GS, Tang WY, Belmonte J, Ho SM. Perinatal exposure to oestradiol and bisphenol A alters the prostate epigenome and increases susceptibility to carcinogenesis. *Basic Clin Pharmacol Toxicol*. 2008;102(2):134-138.

Jaakkola JJ, Knight TL. The role of exposure to phthalates from polyvinyl chloride products in the development of asthma and allergies: a systematic review and meta-analysis. *Environ Health Perspect*. 2008; 116(7):845-53.

Lang IA, Galloway TS, Scarlett A, et al. Association of urinary bisphenol A concentration with medical disorders and laboratory abnormalities in adults. *JAMA*. 2008;300(11):1303-1310.

Main KM, Mortensen GK, Kaleva MM, Boisen KA, Damgaard IN, Chellakooty M, Schmidt IM, Suomi AM, Virtanen HE, Petersen DV, Andersson AM, Toppari J, Skakkebaek NE. Human breast milk contamination with phthalates and alterations of endogenous reproductive hormones in infants three months of age. *Environ Health Perspect*. 2006 Feb;114(2):270-6.

Maffini MV, Rubin BS, Sonnenschein C, Soto AM. Endocrine disruptors and reproductive health: The case of bisphenol-A. *Mol Cell Endocrinol*. 2006;254-255:179-186.

Marsee K, Woodruff TJ, Axelrad DA, Calafat AM, Swan SH. Estimated daily phthalate exposures in a population of mothers of male infants exhibiting reduced anogenital distance. *Environ Health Perspect*. 2006 Jun;114(6):805-9.

Miodovnik A, Engel SM, Zhu C, Ye X, Soorya LV, Silva MJ, Calafat AM, Wolff MS. Endocrine disruptors and childhood social impairment. *Neurotoxicology*. 2011 Mar;32(2):261-7.

Sathyanarayana S, Karr CJ, Lozano P, Brown E, Calafat AM, Liu F, Swan SH. Baby care products: possible sources of infant phthalate exposure. *Pediatrics*. 2008 Feb;121(2):e260-8. doi: 10.1542/peds.2006-3766.

Sathyanarayana S. Phthalates and children's health. *Curr Probl Pediatr Adolesc Health Care*. 2008 Feb;38(2):34-49. doi: 10.1016/j.cppeds.2007.11.001.



Shea, K. M. and the American Academy of Pediatrics Committee on Environmental Health. Pediatric Exposure and Potential Toxicity of Phthalate Plasticizers. *Pediatrics*. 2003; 111(6, pt. 1), 1467–1474.

Swan SH, Main KM, Liu F, Stewart SL, Kruse RL, Calafat AM, Mao CS, Redmon JB, Ternand CL, Sullivan S, Teague JL. Decrease in anogenital distance among male infants with prenatal phthalate exposure. *Environ Health Perspect*. 2005 Aug;113(8):1056-61.

Teitelbaum, S. L., Britton, J. A., Calafat, A. M., Ye, X., Silva, M. J., Reidy, J. A., et al. 2008. Temporal variability in urinary concentrations of phthalate metabolites, phytoestrogens and phenols among minority children in the United States. *Environmental Research*. 106(2), 257-269.

Teitelbaum SL, Mervish N, Moshier EL, Vangeepuram N, Galvez MP, Calafat AM, Silva MJ, Brenner BL, Wolff MS Associations between phthalate metabolite urinary concentrations and body size measures in New York City children. *Environ Res*. 2012 Jan;112:186-93.

United States Department of Health and Human Services National Toxicology Program. Center for the Evaluation of Risks to Human Reproduction. NTO-CERHR Monograph on the Potential Human Reproductive and Developmental Effects of BPA. 2008. <http://cerhr.niehs.nih.gov/chemicals/bisphenol/bisphenol.pdf>

Weuve J, Sánchez BN, Calafat AM, Schettler T, Green RA, Hu H and R Hauser: Exposure to Phthalates in Neonatal Intensive Care Unit Infants: Urinary Concentrations of Monoesters and Oxidative Metabolites. *Environ Health Perspect*. 2006 September; 114(9): 1424–1431.

Wolff MS, Teitelbaum SL, Pinney SM, Windham G, Liao L, Biro F, Kushi LH, Erdmann C, Hiatt RA, Rybak ME, Calafat AM; Breast Cancer and Environment Research Centers. Investigation of relationships between urinary biomarkers of phytoestrogens, phthalates, and phenols and pubertal stages in girls. *Environ Health Perspect*. 2010 Jul;118(7):1039-46.

Wolff MS, Engel SM, Berkowitz GS, Ye X, Silva MJ, Zhu C, Wetmur J, Calafat AM. Prenatal phenol and phthalate exposures and birth outcomes. *Environ Health Perspect*. 2008 Aug;116(8):1092-7.

**Federal Legislation:**

United States Consumer Products Safety Commission. Consumer Product Safety Improvement Act of 2008. <http://www.cpsc.gov/cpsia.pdf>.



***Note: This User Guide is intended to accompany the PowerPoint module of the same name. It elaborates on some studies which may require more in-depth information than what is provided on the slides. However, the contents of all slides in the module are equally important to present.***

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