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# 17

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ALFÂNDEGA DO PORTO

PEDIATRIA  
2000-2030  
DOS DESAFIOS DO MILÉNIO  
À SUSTENTABILIDADE

100 ANOS do Ensino  
da Pediatria  
em Portugal



PROGRAMA



## Plásticos na alimentação da criança

**Conceição Calhau**

Nutrition & Metabolism

Nova Medical School - FCMUNL

[ccalhau@nms.unl.pt](mailto:ccalhau@nms.unl.pt)

NOVA

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# Plásticos na alimentação da criança



# The Perils of Plastic

By Bryan Walsh | Thursday, Apr. 01, 2010



1 of 13



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On the first Earth Day, celebrated 40 years ago this month, the U.S. was a poisoned nation. Dense air pollution blanketed cities like Los Angeles, where smog alerts were a fact of life. Dangerous pesticides like DDT were still in use, and water pollution was rampant — symbolized by raging fires on Cleveland's Cuyahoga River, captured in a famous 1969 story for *TIME*. But the green movement that was energized by Earth Day — and the landmark federal actions that followed it — changed much of that. Today air pollution is down significantly in most urban areas, the water is cleaner, and even the Cuyahoga is home to fish again. Though climate change looms as a long-term threat, the 40th anniversary of Earth Day will see a much cleaner country.

But if the land is healing, Americans may be sickening. Since World War II, production of industrial chemicals has risen rapidly, and the U.S. generates or imports some 42 billion lb. (19 billion kg) of them per day, leaving Americans awash in a sea of synthetics. These aren't the sorts of chemicals that come to mind when we picture pollution — huge plants spilling contaminated wastewater into rivers. Rather, they're the molecules that make good on the old "better living through chemistry" promise, appearing in items like unbreakable baby bottles and big-screen TVs. Those chemicals have a habit of finding their way out of everyday products and into the environment — and ultimately into living organisms. A recent biomonitoring survey



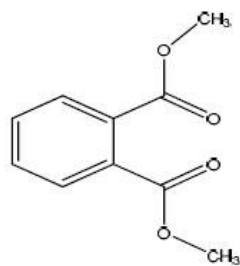
Photograph by James Day for *TIME*

Young children are subjected to plastics in their every day life such as eating utensils, plates, bowls that might contain dangerous toxins.

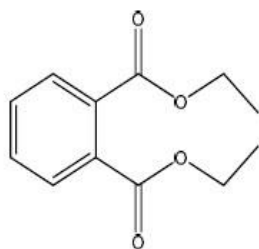


# The Smoking Water Bottle?

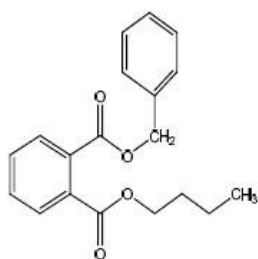
Environmental Health



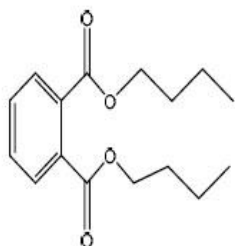
Dimethyl phthalate (DMP)



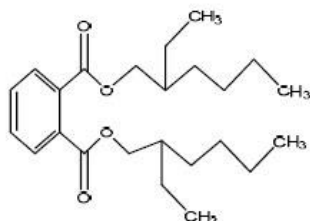
Diethyl phthalate (DEP)



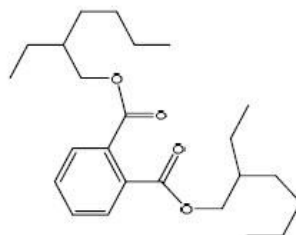
Butyl benzyl phthalate (BBP)



Dibutyl phthalate



Di-(2-ethylhexyl) phthalate (DEHP)



Dioctyl phthalate

Figure 2  
Chemical structures of phthalates

## INOVAÇÕES DO PLÁSTICO NO SETOR DA

# Alimentação



### Menor risco de contaminação

O material plástico protege e preserva alimentos perecíveis por mais tempo, sem afetar o sabor e a qualidade do produto, diminuindo o desperdício.

### Mais segurança e tempo de prateleira

O plástico permite maior tempo de prateleira e confere impermeabilidade, mais segurança alimentar, além de evitar a contaminação.



### Melhor acondicionamento

As embalagens plásticas proporcionam melhor acondicionamento, podem ser levadas à mesa, e os alimentos são mantidos na própria embalagem. Leves, resistentes e portáteis, são perfeitos para o consumo on-the-go, ou seja, em situações em que os alimentos precisam ser transportados (viagens, reuniões de trabalho etc.).

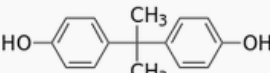


Além das embalagens, os materiais plásticos estão presentes em aparelhos indispensáveis na nossa cozinha, como os eletrodomésticos: mais design, leveza e durabilidade.

### Maior praticidade

Maior praticidade para o transporte, maior segurança, com diferentes funcionalidades, tamanhos e formas, a garrafa PET faz parte do dia a dia das pessoas.



| Structural formula                                                              | Name        | CAS     | Reactants |         | Systematic name                 |
|---------------------------------------------------------------------------------|-------------|---------|-----------|---------|---------------------------------|
|  | Bisphenol A | 80-05-7 | Phenol    | Acetone | 2,2-Bis(4-hydroxyphenyl)propane |

3,8 milhões de toneladas em 2006;

65% polímero policarbonato;

30% polímero resinas epóxido

... aplicações adicionais

**Table 3**  
 Overview of various BPA applications.

| Polymer       | Application class              | Application                                                                                        |
|---------------|--------------------------------|----------------------------------------------------------------------------------------------------|
| Polycarbonate | Bottles and packaging          | Baby bottles, food and beverage containers, containers for microwave heating                       |
|               | Construction                   | Roofing, glazing, roof lights, cabins of ski lift, road signs, protective paneling                 |
|               | Medical and healthcare         | Eye lenses, tube connections, blood oxygenators, dialysers, inhaler housing, newborn incubators    |
|               | Appliances and consumer goods  | Fridges, food mixers, hair dryers, electric kettles, electrical razors                             |
|               | Electrical and electronics     | Cell phones, computers, fax machines, distributor boxes, plugs, plugs connector                    |
|               | Optical media                  | CDs, DVDs                                                                                          |
|               | Leisure and safety             | Helmets, sun glasses, safety goggles, mouth pieces for musical instruments                         |
|               | Automotive                     | Rear windows, fixed side windows, bumpers, dashboard                                               |
| Polysulfone   | Membranes                      | Hemodialysis, drinking and ultra-pure waters, gas separation, food & beverage concentration, dairy |
|               | Medical and healthcare         | Surgical trays, nebulizers, humidifiers                                                            |
|               | Food service                   | Microwave cookware, beverage and food dispensers, milking machine parts                            |
|               | Plumbing                       | Hot water fittings, manifolds, mixer tap cartridges                                                |
| Epoxy resin   | Marine and protective coatings | Sea containers, underwater ship hulls, drinking water distribution pipes                           |
|               | Powder coatings                | Automotive parts, construction panels, steel furniture                                             |
|               | Electrical and electronics     | Encapsulation electronic parts, printed circuit boards                                             |
|               | Can coatings                   | Food and drink cans, general line cans                                                             |
|               | Coil coatings                  | Construction panels, office furniture, household appliances                                        |
|               | Adhesives                      |                                                                                                    |
|               | Photocure                      |                                                                                                    |
|               | Composites                     |                                                                                                    |



A review on the safety of bisphenol A, found in baby bottles, is under scrutiny for conflicts of interest.

**NATURE|Vol 446|26 April 2007**

# Regulators pull contract for chemical review

When US government regulators hired the firm Sciences International to help review a potentially dangerous chemical, they almost certainly didn't intend to ignite a political firestorm.

But the company's links to the chemical industry have enraged environmentalists and forced the National Institute of Environmental Health Sciences (NIEHS) to pull the contract. Last week, in the face of growing pressure from both Congress and the public, the agency announced that it would re-review the 20 chemicals that the company had been involved in studying.

**"The panel should be shut down."**

commonly found in plastics, including baby bottles and microwave containers. The chemical disrupts the endocrine system in mice, and some researchers think that it might cause similar effects in humans. Both Japanese and European regulators say that more research is needed to determine whether the chemical is harmful.

In July 2005, the NIEHS hired Sciences International of Alexandria, Virginia, as part of a panel to summarize hundreds of studies on bisphenol A. The firm had done the same sort of work many times before for the agency. But this time, the Envi-



# Potential Sources of Bisphenol A in the Neonatal Intensive Care Unit

PEDIATRICS Volume 131, Number 3, March 2013

**AUTHORS:** Susan M. Duty, ANP-BC, MSN, ScD,<sup>a</sup> Kaitlin Mendonca, ANP-BC, MSN,<sup>a</sup> Russ Hauser, MPH, MD, ScD,<sup>b</sup> Antonia M. Calafat, PhD,<sup>c</sup> Xiaoyun Ye, MS,<sup>c</sup> John D. Meeker, MS, ScD,<sup>d</sup> Robin Ackerman, JD, SM, MSN,<sup>e</sup> Judi Cullinane, MSN,<sup>a</sup> Josephine Faller, MSN,<sup>a</sup> and Steven Ringer, MD, PhD<sup>f</sup>

<sup>a</sup>Department of Nursing, School of Nursing and Health Sciences, Simmons College, Boston, Massachusetts; <sup>b</sup>Department of Environmental Health, Harvard School of Public Health, Boston, Massachusetts; <sup>c</sup>National Center for Environmental Health, Centers for Disease Control and Prevention, Atlanta, Georgia; <sup>d</sup>Environmental Health Sciences, School of Public Health, University of Michigan, Ann Arbor, Michigan; <sup>e</sup>Occupational Safety and Health Administration, Washington, District of Columbia; and <sup>f</sup>Department of Newborn Medicine, Brigham and Women's Hospital, Boston, Massachusetts

## KEY WORDS

bisphenol A, exposure, medical devices, nutrition, premature



**WHAT'S KNOWN ON THIS SUBJECT:** Bisphenol A (BPA) is an environmental endocrine disruptor that can leach from polycarbonate plastics and epoxy resins, leading to widespread exposure. Fetal and early postnatal periods are particularly vulnerable to exposure to BPA.



**WHAT THIS STUDY ADDS:** This study identified medical devices as a potential source of exposure to BPA among premature infants in the NICU, even when efforts to reduce polycarbonate plastics were taken.

abstract

NIH

## Phthalate Levels and Low Birth Weight: A Nested Case-Control Study of Chinese Newborns

Yunhui Zhang, PhD, Ling Lin, MD, Yang Cao, PhD, Bingheng Chen, MD, Lixing Zheng, MSC, and Ren-Shan Ge, MD

**Objective** To assess maternal–fetal exposure to phthalates and investigate whether in utero phthalate exposure is associated with low birth weight (LBW).

**Study design** A total of 201 newborn–mother pairs (88 LBW cases and 113 controls) residing in Shanghai were enrolled in this nested case-control study during 2005–2006. Maternal blood, cord blood, and meconium specimens were collected and analyzed for phthalates by high-performance liquid chromatography–mass spectrometry. Nonparametric tests were used to compare demographic characteristics in cases and controls. Conditional logistic regression and Spearman correlation were used to analyze the association between phthalate exposure and LBW.

**Results** No significant differences in gestational age, prepregnancy body mass index, prenatal care, vitamin supplementation, or socioeconomic levels were found between the LBW and control infants. More than 70% of the bio-samples had quantifiable levels of phthalates, with higher levels in the LBW infants compared with the controls. Prenatal di-n-butyl phthalate (DBP) exposure was associated with LBW, and di-2-ethylhexyl phthalate (DEHP) was negatively associated with birth length. After adjusting for the potential confounders, DBP concentrations in the highest quartile were associated with an increased risk of LBW.

**Conclusions** Newborns in China are ubiquitously exposed to phthalates; significantly higher phthalate levels were detected in LBW cases compared with controls. In utero DBP and DEHP exposures were associated with LBW in a dose-dependent manner. Prenatal phthalate exposure may be a risk factor for LBW. (*J Pediatr* 2009;155:500–4).

## Exposure to Bisphenol A and Other Phenols in Neonatal Intensive Care Unit Premature Infants

Antonia M. Calafat,<sup>1</sup> Jennifer Weuve,<sup>2,3</sup> Xiaoyun Ye,<sup>1</sup> Lily T. Jia,<sup>1</sup> Howard Hu,<sup>4</sup> Steven Ringer,<sup>5</sup> Ken Huttner,<sup>6</sup> and Russ Hauser<sup>3,7</sup>

<sup>1</sup>Centers for Disease Control and Prevention, Atlanta, Georgia, USA; <sup>2</sup>Rush Institute for Healthy Aging, Rush University Medical Center, Chicago, Illinois, USA; <sup>3</sup>Department of Environmental Health, Harvard School of Public Health, Boston, Massachusetts, USA; <sup>4</sup>Schools of Public Health and Medicine, University of Michigan, Ann Arbor, Michigan, USA; <sup>5</sup>Brigham and Women's Hospital, Harvard Medical School, Boston, Massachusetts, USA; <sup>6</sup>Neonatology Unit, and <sup>7</sup>Vincent Memorial Obstetrics and Gynecology Service, Massachusetts General Hospital, Harvard Medical School, Boston, Massachusetts, USA

**OBJECTIVE:** We previously demonstrated that exposure to polyvinyl chloride plastic medical devices containing di(2-ethylhexyl) phthalate (DEHP) was associated with higher urinary concentrations of several DEHP metabolites in 54 premature infants in two neonatal intensive care units than in the general population. For 42 of these infants, we evaluated urinary concentrations of several phenols, including bisphenol A (BPA), in association with the use of the same medical devices.

**MEASUREMENTS:** We measured the urinary concentrations of free and total (free plus conjugated) species of BPA, triclosan, benzophenone-3, methyl paraben, and propyl paraben.

**RESULTS:** The percentage of BPA present as its conjugated species was > 90% in more than three-quarters of the premature infants. Intensity of use of products containing DEHP was strongly associated with BPA total concentrations but not with any other phenol. Adjusting for institution and sex, BPA total concentrations among infants in the group of high use of DEHP-containing products were 8.75 times as high as among infants in the low use group ( $p < 0.0001$ ). Similarly, after adjusting for sex and DEHP-containing product use category, BPA total concentrations among infants in Institution A were 16.6 times as high as those among infants in Institution B ( $p < 0.0001$ ).

**CONCLUSION:** BPA geometric mean urinary concentration (30.3  $\mu\text{g/L}$ ) among premature infants undergoing intensive therapeutic medical interventions was one order of magnitude higher than that among the general population. Conjugated species were the primary urinary metabolites of BPA, suggesting that premature infants have some capacity to metabolize BPA. The differences in exposure to BPA by intensity of use of DEHP-containing medical products highlight the need for further studies to determine the specific source(s) of exposure to BPA.

**KEY WORDS:** benzophenone, biomonitoring, BPA, glucuronidation, neonate, NICU, paraben, triclosan. *Environ Health Perspect* 117:639–644 (2009). doi:10.1289/ehp.0800265 available via <http://dx.doi.org/> [Online 10 December 2008]

a variety of these medical products (Food and Drug Administration 2001). Four additional phenols, namely benzophenone-3 (BP-3), methyl paraben (MePB), propyl paraben (PrPB), and triclosan (TCS), may also have potential applications in health- and in personal care scenarios. TCS is a broad-spectrum antimicrobicide used extensively in medical settings (Jones et al. 2000; Weber and Rutala 2006). BP-3 is used as a sunscreen agent in numerous cosmetics and everyday products (Gonzalez et al. 2006). MePB and PrPB are antimicrobial preservatives used in personal care products and pharmaceuticals (Cashman and Warshaw 2005). TCS, BP-3, MePB and PrPB may be endocrine disruptors (Darbre and Harvey 2008; Schlumpf et al. 2001; U.S. Environmental Protection Agency 2008), and human exposure to these compounds is widespread in the United States (Calafat et al. 2008a, 2008b; Ye et al. 2006a). However, the potential health effects of these compounds in humans are largely unknown.



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## Nonylphenol and octylphenol in human breast milk

N. Ademollo<sup>a</sup>, F. Ferrara<sup>a,\*</sup>, M. Delise<sup>b</sup>, F. Fabietti<sup>b</sup>, E. Funari<sup>a</sup>

<sup>a</sup> *Dipartimento di Ambiente e Connessa Prevenzione Primaria, Istituto Superiore di Sanità, Viale Regina Elena, 299–00161 Rome, Italy*

<sup>b</sup> *Centro Nazionale per la Qualità degli Alimenti e dei Rischi Alimentari, Istituto Superiore di Sanità, Viale Regina Elena, 299–00161 Rome, Italy*

## Review

Laura N. Vandenberg\*, Patricia A. Hunt, John Peterson Myers and Frederick S. vom Saal

# Human exposures to bisphenol A: mismatches between data and assumptions

**Human studies suggest plausible links between BPA exposures and disease**

**Human biomonitoring studies reveal widespread human exposure to BPA**

## Review

Laura N. Vandenberg\*, Patricia A. Hunt, John Peterson Myers and Frederick S. vom Saal

# Human exposures to bisphenol A: mismatches between data and assumptions

**Table 1** Summary of known and suspected human exposure sources.

| Product                                           | Route of exposure         | Concentration in product or amount leaching           |
|---------------------------------------------------|---------------------------|-------------------------------------------------------|
| Canned foods                                      | Dietary (gut/oral mucosa) | Up to 1140 ng/g food                                  |
| Fresh foods                                       | Dietary (gut/oral mucosa) | Up to 0.35 ng/g food                                  |
| Baby bottles                                      | Dietary (gut/oral mucosa) | Up to 10 ng/mL food simulant                          |
| Water bottles                                     | Dietary (gut/oral mucosa) | Up to 200 ng/L water                                  |
| Other polycarbonate plastics in contact with food | Dietary (gut/oral mucosa) | Unknown                                               |
| Food contact papers                               | Dietary (gut/oral mucosa) | Up to 26 µg/g paper                                   |
| PVC plastic wraps (food contact)                  | Dietary (gut/oral mucosa) | Up to 483 µg/g wrap                                   |
| Drinking water                                    | Dietary (gut/oral mucosa) | Up to 10 ng/L water                                   |
| Bathing water                                     | Dermal, inhalation        | Up to 10 ng/L water                                   |
| Thermal papers                                    | Dermal, oral              | Up to 46 µg transferred to skin                       |
| Cigarette filters                                 | Oral, inhalation          | Unknown                                               |
| Indoor and outdoor air                            | Inhalation                | Up to 5 ng/m <sup>3</sup>                             |
| Dust                                              | Oral, gut, inhalation     | Up to 9730 ng/g dust                                  |
| Eyeglasses (lenses and frames)                    | Dermal                    | Unknown                                               |
| Plastic dishware, utensils                        | Oral, gut                 | Unknown                                               |
| Sports equipment                                  | Dermal                    | Unknown                                               |
| Children's toys                                   | Oral, dermal              | Unknown                                               |
| Household detergents                              | Dermal                    | Unknown                                               |
| Cosmetics, personal care products                 | Dermal                    | <100 µg/g product                                     |
| Medical equipment                                 | Subcutaneous              | Unknown                                               |
| Dental sealants                                   | Oral, gut                 | Up to 30,000 ng/mL saliva (shortly after application) |
| Paint                                             | Dermal, oral, inhalation  | Unknown                                               |
| Other resins, epoxies                             | Oral, gut, dermal         | Unknown                                               |

**Table 2** Levels of concern identified by the CERHR-NTP for other environmental chemicals.

| Compound                      | End point                                                                                                                                 | NTP evaluation (score out of 5) | References |
|-------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------|------------|
| Soy infant formula            | Developmental effects                                                                                                                     | Minimal concern (2/5)           | (227)      |
| Hydroxyurea <sup>a</sup>      | Sperm production in males postpuberty                                                                                                     | Serious concern (5/5)           | (228)      |
| Hydroxyurea <sup>a</sup>      | Birth defects, abnormalities of fetal growth, or abnormal postnatal development in offspring following maternal exposure during pregnancy | Concern (4/5)                   | (228)      |
| Hydroxyurea <sup>a</sup>      | Growth (exposures from ages 5–15 years)                                                                                                   | Minimal concern (2/5)           | (228)      |
| Styrene <sup>b</sup>          | Developmental and reproductive effects                                                                                                    | Negligible concern (1/5)        | (229)      |
| Methylphenidate <sup>c</sup>  | Induced tics and movement disorders                                                                                                       | Negligible concern (1/5)        | (230)      |
| Methylphenidate <sup>c</sup>  | Growth restriction                                                                                                                        | Minimal concern (2/5)           | (230)      |
| DEHP <sup>d</sup>             | Development of the male reproductive tract following intensive medical treatments                                                         | Serious concern (5/5)           | (231)      |
| DEHP <sup>d</sup>             | Development of the male reproductive tract in fetuses or offspring <1 year via high medical exposures of mother                           | Concern (4/5)                   | (231)      |
| DEHP <sup>d</sup>             | Development of the male reproductive tract in boys >1 year of age                                                                         | Some concern (3/5)              | (231)      |
| Amphetamine <sup>e</sup>      | Developmental effects including neurobehavioral alterations following prenatal (therapeutic and non-therapeutic) exposures                | Some concern (3/5)              | (232)      |
| Methamphetamine <sup>f</sup>  | Adverse developmental effects including altered growth and neurobehaviors                                                                 | Concern (4/5)                   | (232)      |
| Ethylene glycol <sup>g</sup>  | Reproductive effects                                                                                                                      | Negligible concern (1/5)        | (233)      |
| Ethylene glycol <sup>g</sup>  | Developmental effects                                                                                                                     | Negligible concern (1/5)        | (233)      |
| BBP <sup>h</sup>              | Reproductive effects in men                                                                                                               | Negligible concern (1/5)        | (234)      |
| BBP <sup>h</sup>              | Developmental effects                                                                                                                     | Minimal concern (2/5)           | (234)      |
| DBP <sup>i</sup>              | Reproductive toxicity                                                                                                                     | Negligible concern (1/5)        | (235)      |
| DBP <sup>i</sup>              | Developmental effects                                                                                                                     | Minimal concern (2/5)           | (235)      |
| DBP <sup>i</sup>              | Development of the male reproductive tract                                                                                                | Some concern (3/5)              | (235)      |
| Propylene glycol <sup>j</sup> | Developmental and reproductive effects                                                                                                    | Negligible concern (1/5)        | (236)      |
| Fluoxetine <sup>k</sup>       | Developmental effects including gestational length and neonatal adaptation                                                                | Some concern (3/5)              | (237)      |
| Fluoxetine <sup>k</sup>       | Reproductive effects                                                                                                                      | Minimal concern (2/5)           | (237)      |
| DnOP <sup>l</sup>             | Reproductive effects                                                                                                                      | Negligible concern (1/5)        | (238)      |
| DIDP <sup>m</sup>             | Developmental effects                                                                                                                     | Minimal concern (2/5)           | (239)      |
| DIDP <sup>m</sup>             | Reproductive effects                                                                                                                      | Negligible concern (1/5)        | (239)      |
| DINP <sup>n</sup>             | Developmental and reproductive effects                                                                                                    | Minimal concern (2/5)           | (240)      |

## Pilot Study of Urinary Biomarkers of Phytoestrogens, Phthalates, and Phenols in Girls

Mary S. Wolff,<sup>1</sup> Susan L. Teitelbaum,<sup>1</sup> Gayle Windham,<sup>2</sup> Susan M. Pinney,<sup>3</sup> Julie A. Britton,<sup>1</sup> Carol Chelimo,<sup>1</sup> James Godbold,<sup>1</sup> Frank Biro,<sup>4</sup> Lawrence H. Kushi,<sup>5</sup> Christine M. Pfeiffer,<sup>6</sup> and Antonia M. Calafat<sup>6</sup>

<sup>1</sup>Mount Sinai School of Medicine, Division of Environmental Health Sciences, Department of Community and Preventive Medicine, New York, New York, USA; <sup>2</sup>Division of Environmental and Occupational Disease Control, California Department of Health Services, Oakland, California, USA; <sup>3</sup>Department of Environmental Health, University of Cincinnati College of Medicine, Cincinnati, Ohio, USA; <sup>4</sup>Division of Adolescent Medicine, Cincinnati Children's Hospital Medical Center, Ohio, USA; <sup>5</sup>Division of Research, Kaiser Permanente, Oakland, California, USA; <sup>6</sup>Division of Laboratory Sciences, National Center for Environmental Health, Centers for Disease Control and Prevention, Atlanta, Georgia, USA

**BACKGROUND:** Hormonally active environmental agents have been measured among U.S. children using exposure biomarkers in urine. However, little is known about their variation by race, age, sex, and geography, and no data exist for newly developed biomarkers.

**OBJECTIVE:** Our goal was to characterize relevant, prevalent exposures for a study of female pubertal development.

**METHODS:** In a pilot study among 90 girls from New York City, New York, Cincinnati, Ohio, and northern California, we measured 25 urinary analytes representing 22 separate agents from three chemical families: phytoestrogens, phthalates, and phenols. Exposures occur chiefly from the diet and from household or personal care products.

**RESULTS:** Participants represented four racial/ethnic groups (Asian, black, Hispanic, white), with mean age of 7.77 years. Most analytes were detectable in > 94% of samples. The highest median concentrations for individual analytes in each family were for enterolactone (298 µg/L), monoethylphthalate (MEP; 83.2 µg/L), and benzophenone-3 (BP3; 14.7 µg/L). Few or no data have been reported previously for four metabolites: mono(2-ethyl-5-carboxypentyl) phthalate, triclosan, bisphenol A (BPA), and BP3; these were detected in 67–100% of samples with medians of 1.8–53.2 µg/L. After multivariate adjustment, two analytes, enterolactone and BPA, were higher among girls with body mass index < 85th reference percentile than those at or above the 85th percentile. Three phthalate metabolites differed by race/ethnicity [MEP, mono(2-ethylhexyl) phthalate, and mono-3-carboxypropylphthalate].

**CONCLUSIONS:** A wide spectrum of hormonally active exposure biomarkers were detectable and variable among young girls, with high maximal concentrations (> 1,000 µg/L) found for several analytes. They varied by characteristics that may be relevant to development.

**KEY WORDS:** biomarkers, children, exposure, phenols, phthalates, phytoestrogen, urine. *Environ Health Perspect* 115:116–121 (2007). doi:10.1289/ehp.9488 available via <http://dx.doi.org/> [Online 19 October 2006]

including bisphenol A (BPA), a chemical with hormonal activity relevant to pubertal development (vom Saal and Hughes 2005). In addition, prevalence and variability of these exposure biomarkers have not been described among young girls, and it is not known how these exposures may vary by race, geographic location, or age. In this report we

Address correspondence to M.S. Wolff, Department of Community and Preventive Medicine, Division of Environmental Health Sciences, Mount Sinai School of Medicine, One Gustave L. Levy Place, Box 1057, New York, NY 10029 USA. Telephone: (212) 241-6183. Fax: (212) 996-0407. E-mail: mary.wolff@mssm.edu

Supplemental Material is available online at <http://www.ehponline.org/docs/2006/9488/suppl.pdf>

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**Table 1.** Biomarkers, their parent compounds, and examples of their environmental sources.

| Chemical class and examples                              | Abbreviation          | Main parent compound (if applicable)                 | Exposure sources                                                                                               |
|----------------------------------------------------------|-----------------------|------------------------------------------------------|----------------------------------------------------------------------------------------------------------------|
| Phytoestrogens                                           |                       |                                                      | Dietary intake                                                                                                 |
| Isoflavones (genistein, daidzein)                        |                       |                                                      | Soy products, including processed meats, meat substitutes, breads, and protein food bars                       |
| Lignans (enterolactone)                                  |                       |                                                      | Flax, seeds, grains                                                                                            |
| Phthalate metabolites                                    |                       |                                                      | Industrial and personal product additives                                                                      |
| Mono(2-ethylhexyl) phthalate                             | MEHP                  | Di(2-ethylhexyl) phthalate (DEHP)                    | Soft plastic including tubing, especially polyvinyl chloride (PVC; e.g., sometimes present in clear food wrap) |
| Mono(3-carboxypropyl) phthalate                          | MCPP                  | Di- <i>n</i> -octyl phthalate                        | Soft plastic                                                                                                   |
| Monobenzyl phthalate                                     | MBzP                  | Butylbenzyl phthalate                                | Vinyl flooring, adhesives                                                                                      |
| Monoethyl phthalate                                      | MEP                   | Diethyl phthalate (DEP)                              | Shampoo, scents, soap, lotion, cosmetics                                                                       |
| Monomethyl phthalate                                     | MMP                   | Dimethyl phthalate (DMP)                             | Insect repellent, plastic                                                                                      |
| Mono- <i>n</i> -butyl phthalate, mono-isobutyl phthalate | MBP, MiBP             | Dibutyl phthalate (DBP), diisobutyl phthalate (DiBP) | Adhesives, caulk, cosmetics                                                                                    |
| Phenols                                                  |                       |                                                      | Commercial and personal products and additives                                                                 |
| Bisphenol A                                              | BPA                   |                                                      | Polycarbonate containers and coatings (cans, cups), dental sealant                                             |
| Benzophenone-3(2-hydroxy-4-methoxy-benzophenone)         | BP3                   |                                                      | Sunscreen                                                                                                      |
| Triclosan [5-chloro-2-(2,4-dichlorophenoxy)phenol]       | TRCS                  |                                                      | Microbicide in cleaning fluids                                                                                 |
| 2,4-Dichlorophenol and trichlorophenols                  | 24DCP, 245TCP, 246TCP | Phenoxy- and other derivatives                       | Herbicides                                                                                                     |
| 2,5-Dichlorophenol                                       | 25DCP                 | 4-dichlorobenzene                                    | Mothballs                                                                                                      |
| <i>ortho</i> -Phenylphenol                               | <i>o</i> -PP          |                                                      | Fungicide                                                                                                      |
| 4- <i>tert</i> -Octylphenol                              | 4- <i>t</i> -OP       |                                                      | Detergent surfactant                                                                                           |

## **Urinary, Circulating, and Tissue Biomonitoring Studies Indicate Widespread Exposure to Bisphenol A**

Estudos de biomonitoração do sistema urinário, circulatório  
e tecidos indicam grande exposição ao Bisfenol A

Laura N. Vandenberg <sup>1</sup>

Ibrahim Chahoud <sup>2</sup>

Jerrold J. Heindel <sup>3</sup>

Vasanth Padmanabhan <sup>4</sup>

Francisco J.R. Paumgarten <sup>5</sup>

Gilbert Schoenfelder <sup>6</sup>

**Table 5.** BPA levels in human tissues and fluids during pregnancy and lactation.

| Reference               | Detection method           | LOD (ng/mL) | Sample size | End point(s)                                                | Study population                                    | BPA level[ng/mL (ppb), mean $\pm$ SE]           |
|-------------------------|----------------------------|-------------|-------------|-------------------------------------------------------------|-----------------------------------------------------|-------------------------------------------------|
| Ikezuki et al. 2002     | ELISA                      | 0.3         | 32          | Early amniotic fluid (15–18 weeks)                          | Pregnant Japanese women                             | 8.3 $\pm$ 1.573                                 |
|                         |                            |             | 38          | Late amniotic fluid (at full term, before delivery)         | Pregnant Japanese women undergoing cesarian section | 1.1 $\pm$ 0.162                                 |
|                         |                            |             | 36          | Follicular fluid                                            | Japanese women undergoing IVF procedures            | 2.4 $\pm$ 0.133                                 |
| Schönfelder et al. 2002 | Derivatization-GC/MS       | 0.01        | 37          | Placenta                                                    | German women at delivery                            | 11.2 $\pm$ 1.512 ng/g                           |
| Todaka and Mori 2002    | GC-MS                      | NR          | NR          | Umbilical cord tissue at birth                              | Samples collected in Japan                          | Mean, 4.4 $\pm$ 1.5 ng/g; range, 0.11–15.2 ng/g |
| Yamada et al. 2002      | ELISA                      | 0.5         | 200         | Normal fetal amniotic fluid (14–18 weeks)                   | Pregnant Japanese women                             | Median, 0.26; range, ND–5.62                    |
|                         |                            |             | 48          | Abnormal fetal karyotype fetal amniotic fluid (14–18 weeks) | Pregnant Japanese women                             | Median, 0                                       |
| Otaka et al. 2003       | SPE-GC-MS                  | 0.09        | 3           | Breast milk                                                 | Japanese women                                      | Range, ND–0.70 ng/g                             |
| Sun et al. 2004         | DIB-Cl derivatization-HPLC | 0.11        | 23          | Breast milk                                                 | Japanese women                                      | 0.61 $\pm$ 0.042                                |



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Int. J. Hyg. Environ. Health

journal homepage: [www.elsevier.de/ijheh](http://www.elsevier.de/ijheh)

## Short Communication

## GerES IV: Phthalate metabolites and bisphenol A in urine of German children

Kerstin Becker<sup>a,\*</sup>, Thomas Göen<sup>b</sup>, Margarete Seiwert<sup>a</sup>, Andre Conrad<sup>a</sup>, Helga Pick-Fuß<sup>a</sup>, Johannes Müller<sup>b</sup>, Matthias Wittassek<sup>b</sup>, Christine Schulz<sup>a</sup>, Marike Kolossa-Gehring<sup>a</sup>

<sup>a</sup> Federal Environment Agency (UBA), Dessau-Roßlau/Berlin, Germany

**Table 2**

Levels of phthalate metabolites in urine (µg/l) of German children aged 3 to 14 years.

| Phthalate   | Metabolite | N > LOQ | P50  | P90  | P95  | Max  | GM   | CI GM       |
|-------------|------------|---------|------|------|------|------|------|-------------|
| <b>DnBP</b> | MnBP       | 599     | 93.4 | 236  | 310  | 1090 | 95.6 | 90.4 – 101  |
| <b>DiBP</b> | MiBP       | 599     | 88.1 | 223  | 308  | 2050 | 94.3 | 89.2 – 99.7 |
| <b>BBzP</b> | MBzP       | 599     | 18.1 | 53.4 | 76.2 | 468  | 17.5 | 16.2 – 18.8 |
| <b>DEHP</b> | MEHP       | 598     | 6.7  | 16.2 | 25.1 | 319  | 6.4  | 6.0 – 6.8   |
|             | 5OH-MEHP   | 599     | 46.0 | 110  | 164  | 3640 | 47.9 | 45.1 – 50.8 |
|             | 5oxo-MEHP  | 599     | 36.3 | 87.5 | 123  | 2490 | 37.0 | 34.9 – 39.1 |
|             | 5cx-MEPP   | 599     | 61.4 | 151  | 209  | 4490 | 62.5 | 58.9 – 66.2 |
|             | 2cx-MMHP   | 599     | 20.4 | 51.7 | 76.7 | 1080 | 20.8 | 19.6 – 22.2 |
| <b>DINP</b> | 7OH-MMeOP  | 599     | 11.0 | 37.6 | 50.6 | 198  | 11.2 | 10.5 – 12.1 |
|             | 7oxo-MMeOP | 588     | 5.4  | 19.1 | 28.9 | 86.7 | 5.4  | 5.0 – 5.9   |
|             | 7cx-MMeHP  | 598     | 12.7 | 42.5 | 58.9 | 195  | 13.8 | 12.9 – 14.8 |

Notes: N (sample size) = 599; LOQ = limit of quantification, P50, P90, P95 = percentiles; Max = maximum value; GM = geometric mean; CI GM = 95% confidence interval of GM.

The mean concentration of BPA in urine was 2.7 µg/l. A rough calculation of the daily intakes on the basis of the measured concentrations in urine resulted in daily intakes two orders of magnitude lower than the current EFSA reference dose of 50 µg/kg bw/d.



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## International Journal of Hygiene and Environmental Health

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## Mini-Review

## Are potential sources for human exposure to bisphenol-A overlooked?

Tinne Geens<sup>a,\*</sup>, Leo Goeyens<sup>b</sup>, Adrian Covaci<sup>a</sup><sup>a</sup> Toxicological Centre, Department of Pharmaceutical Sciences, University of Antwerp, Universiteitsplein 1, 2610 Antwerp, Belgium<sup>b</sup> Analytical and Environmental Chemistry, University of Brussels, Pleinlaan 2, 1050 Brussels, Belgium

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## ABSTRACT

This review summarizes the numerous applications of bisphenol-A (BPA) and the potential sources for human exposure. The exposure to humans is believed to occur mainly through food contamination from polycarbonate bottles, as well as through food and beverage cans coated with epoxy resins. However, there seems to be a discrepancy between exposure assessments based on biomonitoring data and those based on food/drink concentrations. Several recent studies indicated also the importance of non-food sources. Although the main use of BPA is polymerization to polycarbonate and epoxy resins, it can also be used as an additive, from which it may be easily released. Several studies have already provided scientific evidence for the contribution of sources for dermal BPA absorption, such as thermal paper where BPA is used as an additive. Polymeric applications of BPA require further investigation regarding the amounts of BPA present, as well as the factors affecting its release and potential dermal or non-dermal exposure from these sources. It is clear that not all sources of BPA have been identified. This overview emphasizes the necessity to study also the exposure to these unexpected sources of BPA.

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## Mini-Review

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Tinne Geens<sup>a,\*</sup>, Leo Goeyens<sup>b</sup>, Adrian Covaci<sup>a</sup>

<sup>a</sup> Toxicological Centre, Department of Pharmaceutical Sciences, University of Antwerp, Universiteitsplein 1, 2610 Antwerp, Belgium

<sup>b</sup> Analytical and Environmental Chemistry, University of Brussels, Pleinlaan 2, 1050 Brussels, Belgium

## ARTICLE INFO

## ABSTRACT

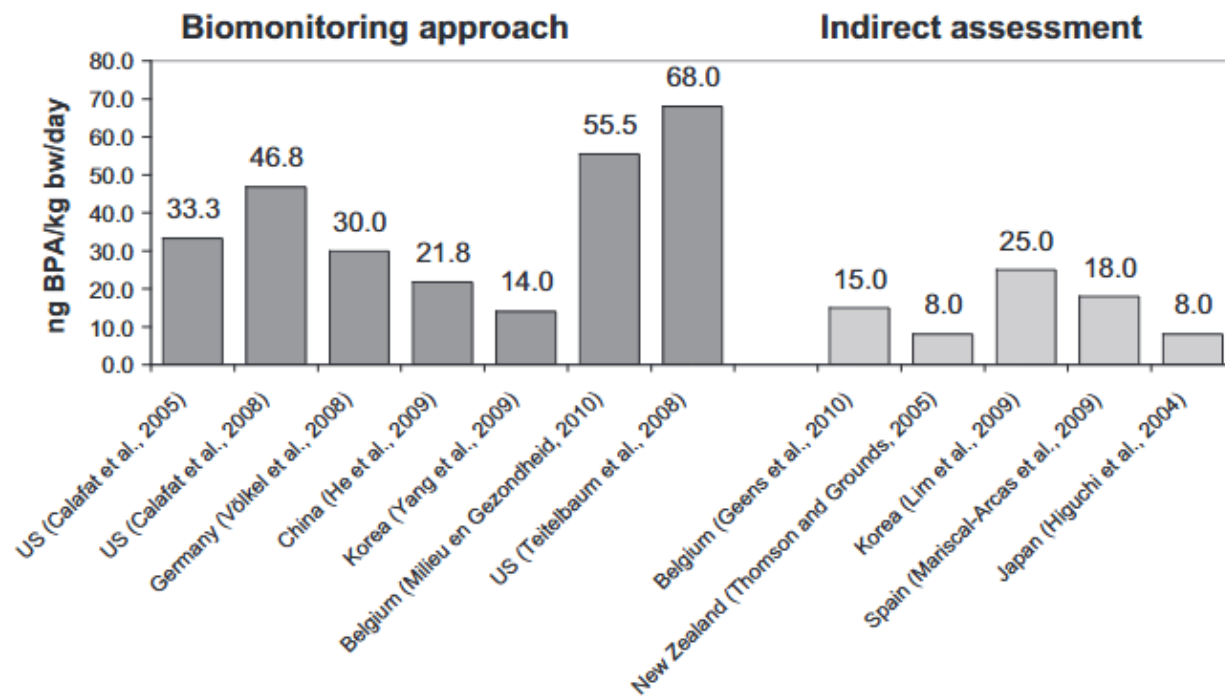
**Table 2**  
Intake assessment based on analysis of canned food combined with consumption survey.

| Country            | Type of food                         | Average intake<br>(ng/kg bw/day) | High intake<br>(ng/kg bw/day) | Reference                    |
|--------------------|--------------------------------------|----------------------------------|-------------------------------|------------------------------|
| Belgium            | Canned food and beverages            | 15                               | 86 (p. 95)                    | Geens et al. (2010)          |
| New Zealand        | Canned food and beverages            | 8                                | 290 (max)                     | Thomson and Grounds (2005)   |
| Korea              | Canned food                          | 25                               |                               | Lim et al. (2009)            |
| Spain <sup>a</sup> | Canned food and microwave containers | 18                               | 78 (max)                      | Mariscal-Arcas et al. (2009) |
| Japan              | Prepared hospital meals              | 8                                |                               | Higuchi et al. (2004)        |

<sup>a</sup> Not based on levels in food, but on migration studies.

the necessity to study also the exposure to these unexpected sources of BPA.

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**Fig. 1.** Comparison between studies using urinary biomonitoring concentrations (dark grey) with studies using the indirect assessment approach based on BPA levels in food products.



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## **Migration of 4-nonylphenol from polyvinyl chloride food packaging films into food simulants and foods**

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A migração pode atingir os 410 ng/g se no micro-ondas 1 min, até 76,5 ng/g se à temperatura ambiente durante 30 min.



Contents lists available at [ScienceDirect](#)

## Environment International

journal homepage: [www.elsevier.com/locate/envint](http://www.elsevier.com/locate/envint)



# Simultaneous determination and assessment of 4-nonylphenol, bisphenol A and triclosan in tap water, bottled water and baby bottles

Xu Li, Guang-Guo Ying<sup>\*</sup>, Hao-Chang Su, Xiao-Bing Yang, Li Wang

*State Key Laboratory of Organic Geochemistry, Guangzhou Institute of Geochemistry, Chinese Academy of Sciences, Guangzhou 510640, China*

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### ABSTRACT

This study investigated the levels of 4-nonylphenol (4-NP), bisphenol A (BPA) and triclosan (TCS) in bottled water and tap water in Guangzhou and release of these chemicals from baby bottles using gas chromatography–mass spectrometry with negative chemical ionization. Results show that 4-NP was present in all the bottled water while 17 out of 21 contained BPA and 18 out of 21 contained TCS. Their concentrations in bottled water ranged from 108 to 298 ng/L, 17.6 to 324 ng/L and 0.6 to 9.7 ng/L, respectively. Five of the tap water samples from six drinking water plants were found to contain 4-NP and BPA both in June and December, while TCS was detected in the same five plants only in June. The highest concentrations in tap water for 4-NP, BPA and TCS were 1987, 317 and 14.5 ng/L, respectively. Daily intakes of 4-NP, BPA and TCS of adults by drinking 2 L of tap water were estimated to be 1410, 148 and 10 ng/day, respectively. BPA was found to be released within 24 h from four brands of baby bottles at room temperature (24 °C), 40 °C and 100 °C. Increased temperature led to higher release of BPA from the baby bottles. Estimated daily intakes of 4-NP, BPA and TCS for infants were 705, 1340 and 5 ng/day, respectively, by drinking 1 L of tap water from a baby bottle at 40 °C. This study showed that the exposure to the three compounds from drinking water is unlikely to pose a health risk.



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## Environment International

journal homepage: [www.elsevier.com/locate/envint](http://www.elsevier.com/locate/envint)



Simultaneous determination and assessment of 4-nonylphenol, bisphenol A and triclosan in tap water, bottled water and baby bottles

Daily intakes of 4-NP, BPA and TCS through drinking water.

| Compounds <sup>a</sup> | Adults (ng/day) <sup>b</sup> |           | Infants (ng/day) <sup>b</sup>    |
|------------------------|------------------------------|-----------|----------------------------------|
|                        | Bottled water                | Tap water | Tap water (baby bottle at 40 °C) |
| 4-NP                   | 340                          | 1410      | 705                              |
| BPA                    | 165                          | 148       | 1340                             |
| TCS                    | 7                            | 10        | 5                                |

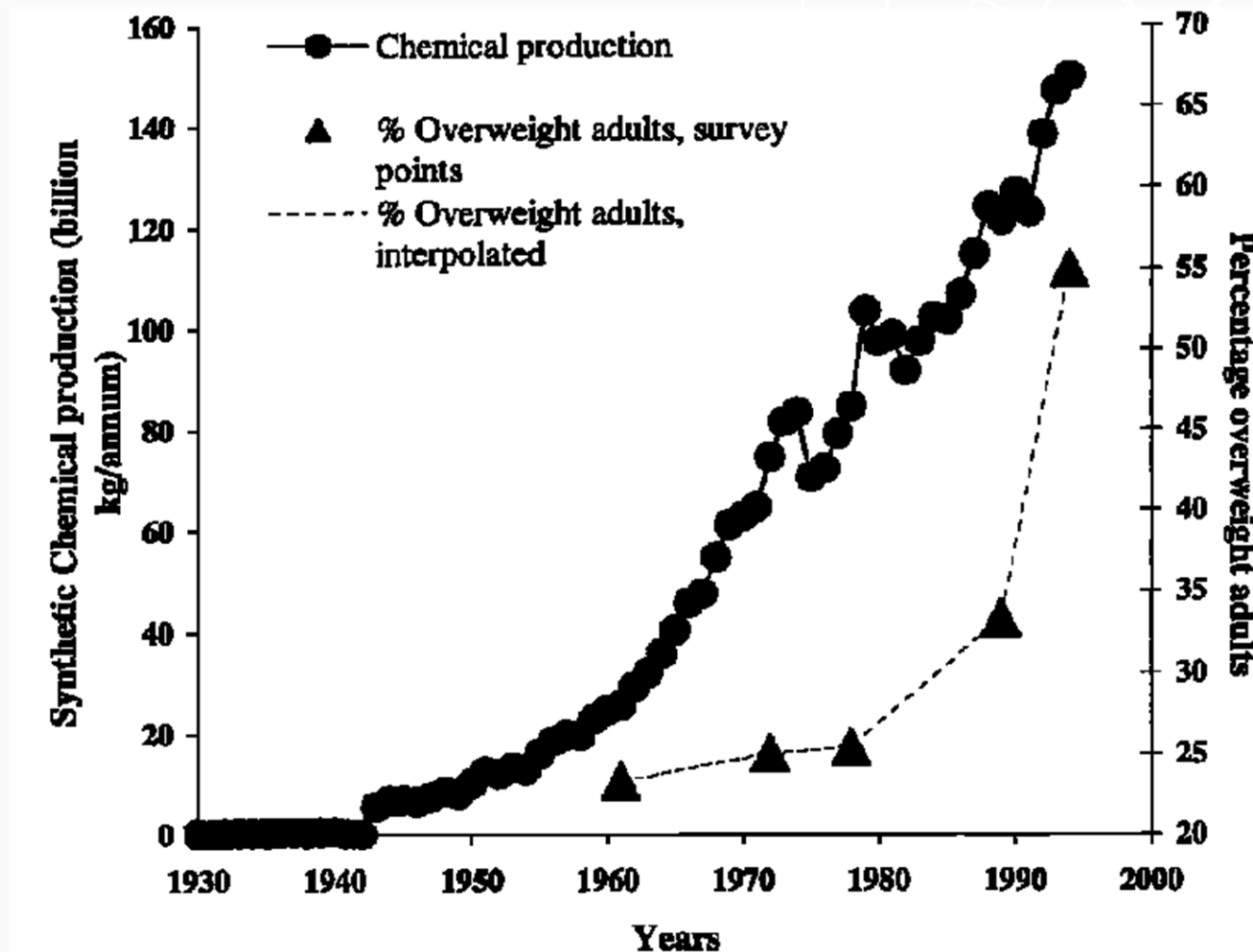
<sup>a</sup> 4-NP: 4-nonylphenol; BPA: bisphenol-A; TCS: triclosan.

<sup>b</sup> Calculated based on the average concentrations in the water samples and baby bottles.

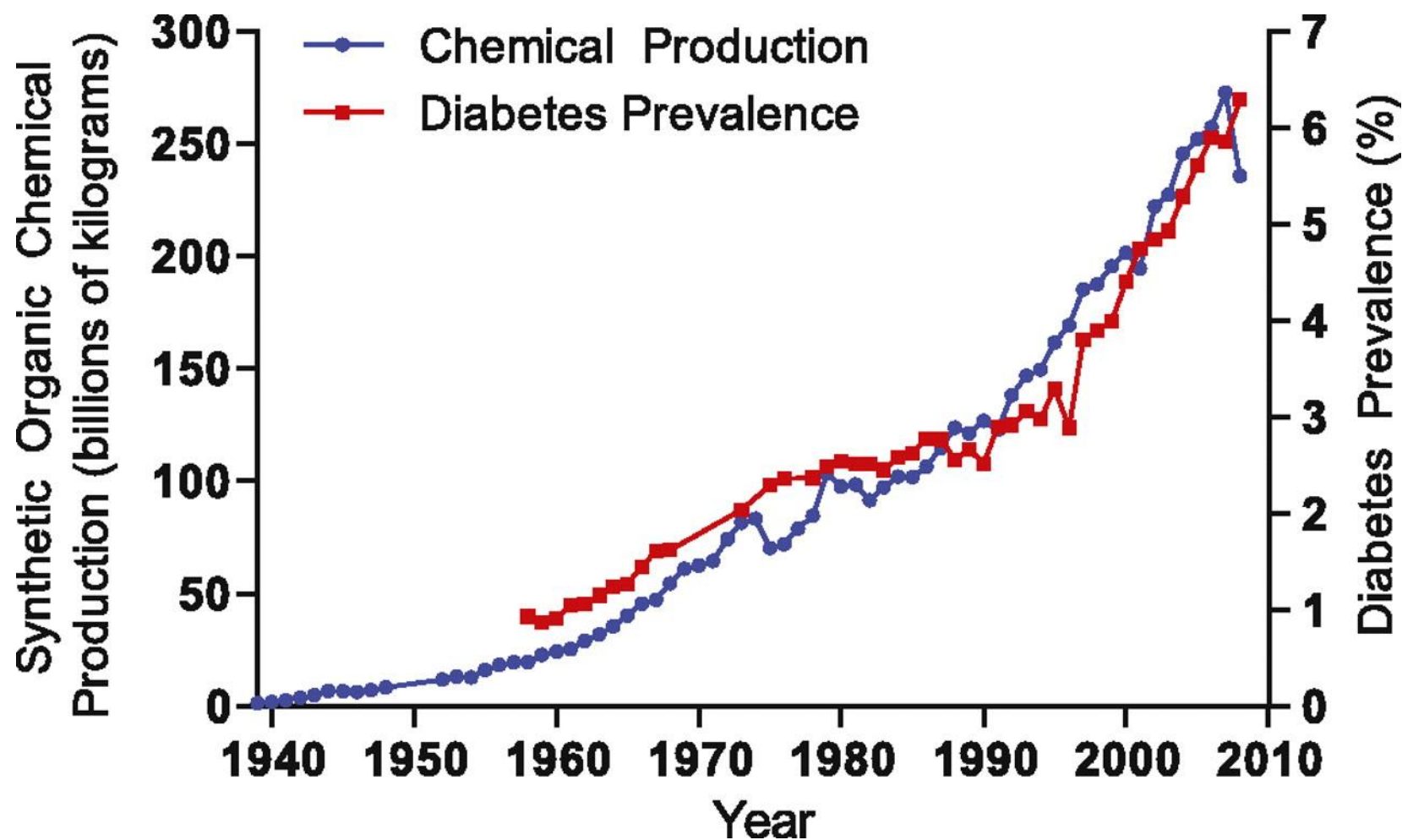


- your genes don't change;
- the way your genes are expressed can be influenced;
- this influence may even pass from parents to children;
- your diet influences your genes!

# THE OBESOGEN HYPOTHESIS



## U.S. synthetic chemical production and diabetes prevalence.

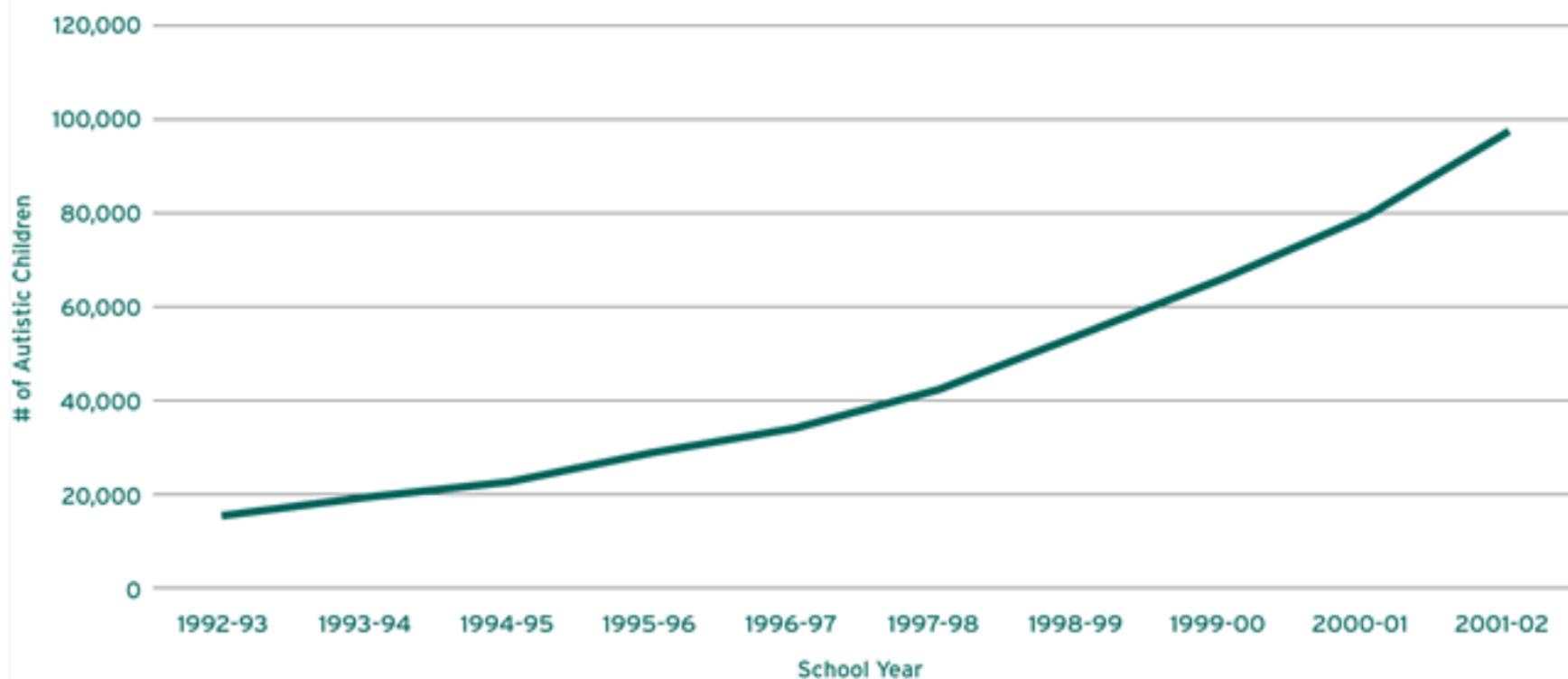


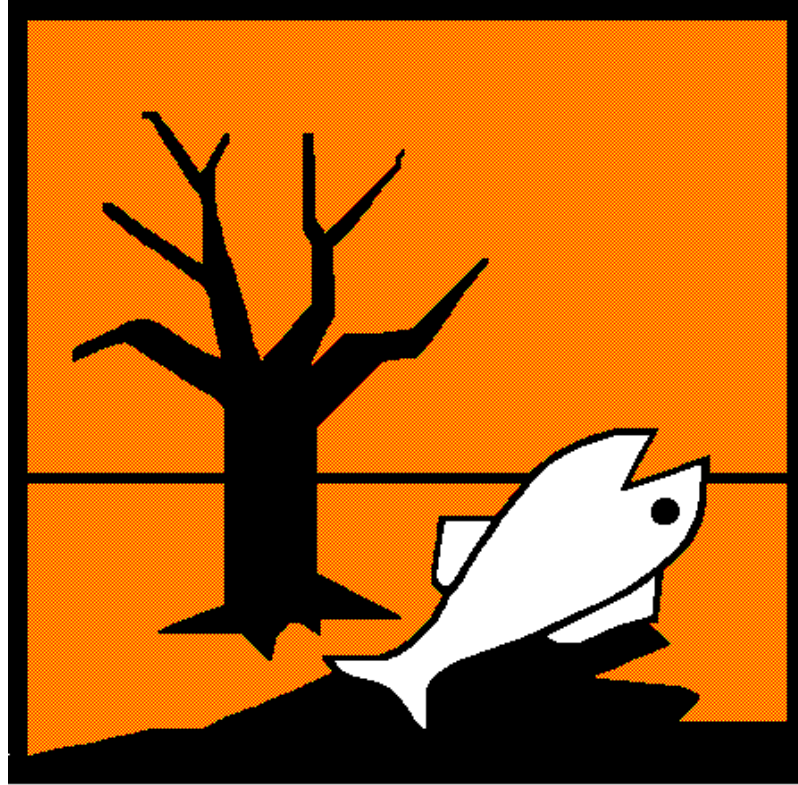
Neel B A , Sargis R M Diabetes 2011;60:1838-1848

## Autism on the Rise (Figure 1)

*Over the last decade, the number of students diagnosed with autism in America's schools has increased more than fivefold.*

Growth in the Number of Autistic Students Served under the Individuals with Disabilities Education Act





## **ENVIRONMENTAL HAZARD**

Accumulating data suggest an important role for toxicology in the etiology of obesity!

To find a diet free from DDT and related chemicals, it seems one must go to a remote and primitive land, still lacking in the amenities of civilization. Such a land appears to exist, at least marginally, on the far Arctic shores of Alaska— although even there one may see the approaching shadow.

(Rachel Carson, 1962)







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## Environment International

journal homepage: [www.elsevier.com/locate/envint](http://www.elsevier.com/locate/envint)



# Flame retardants and legacy contaminants in polar bears from Alaska, Canada, East Greenland and Svalbard, 2005–2008

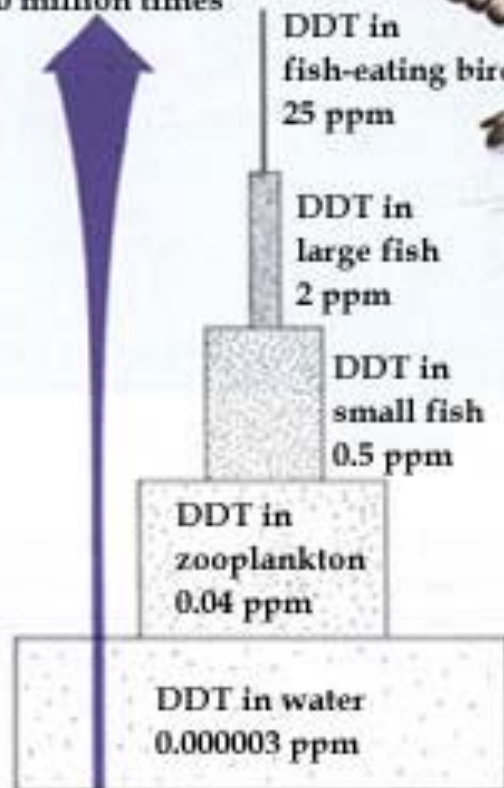
Melissa A. McKinney<sup>a,b,\*</sup>, Robert J. Letcher<sup>a,b,\*</sup>, Jon Aars<sup>c</sup>, Erik W. Born<sup>d</sup>, Marsha Branigan<sup>e</sup>, Rune Dietz<sup>f</sup>, Thomas J. Evans<sup>g</sup>, Geir W. Gabrielsen<sup>c</sup>, Elizabeth Peacock<sup>h,1</sup>, Christian Sonne<sup>f</sup>

<sup>a</sup> Ecotoxicology and Wildlife Health Division, Science and Technology Branch, Environment Canada, Ottawa, Ontario K1A 0H3, Canada

The Environmental Protection Agency (**EPA**) defines an **endocrine disrupting chemical** (EDC) as

“an exogenous agent that interferes with the production, release, transport, metabolism, binding, action, or elimination of natural hormones in the body responsible for the maintenance of homeostasis, reproduction, development, and/or behavior”

DDT concentration:  
increase of  
10 million times



DDT in  
fish-eating birds  
25 ppm

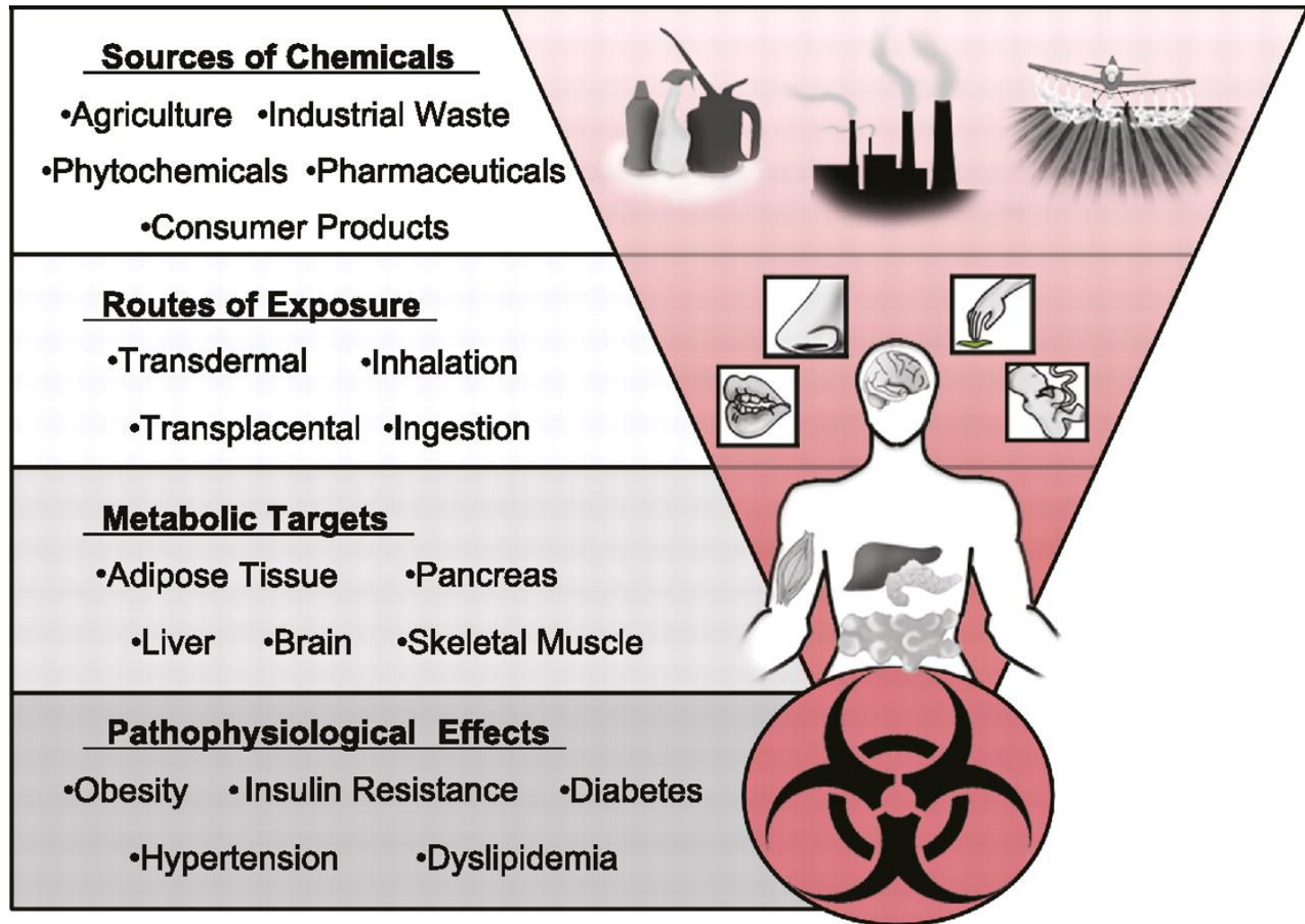
DDT in  
large fish  
2 ppm

DDT in  
small fish  
0.5 ppm

DDT in  
zooplankton  
0.04 ppm

DDT in water  
0.000003 ppm

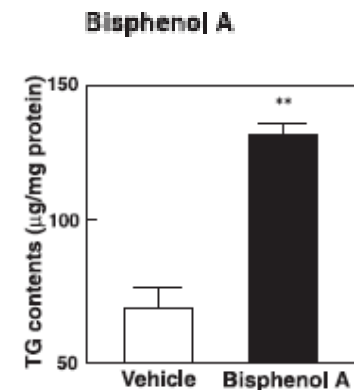
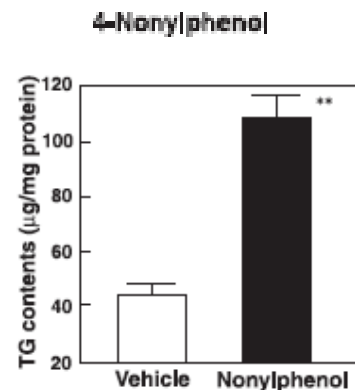
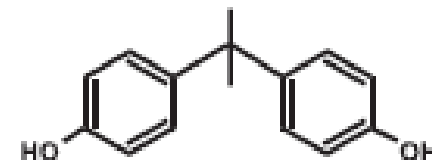
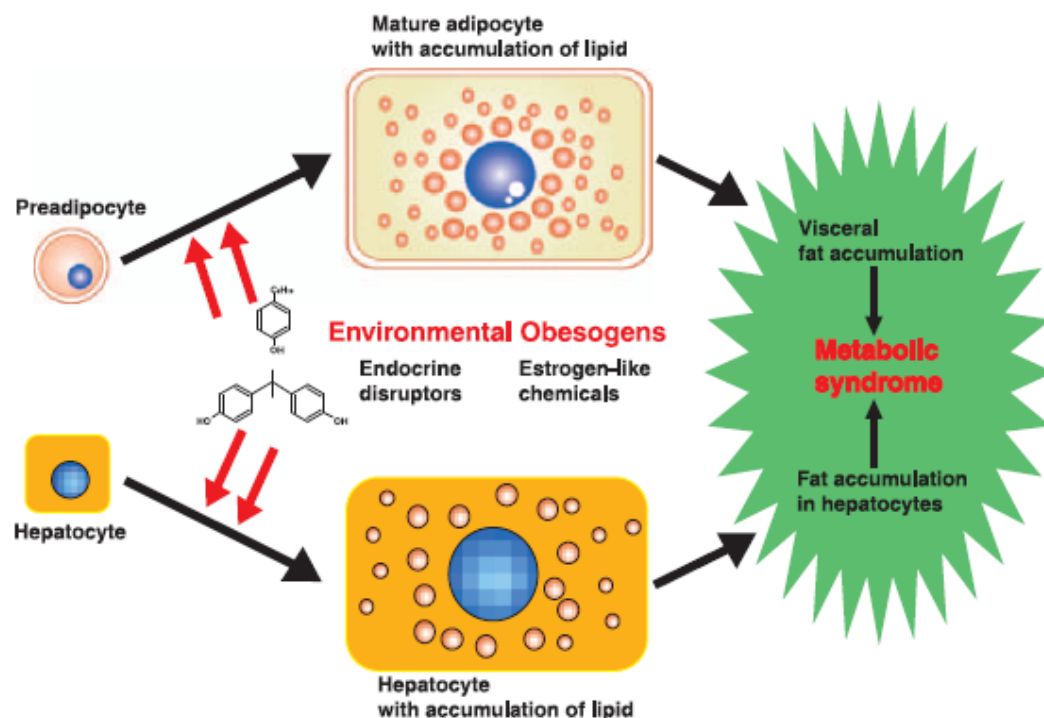
## Sources and targets of metabolic disruptors.



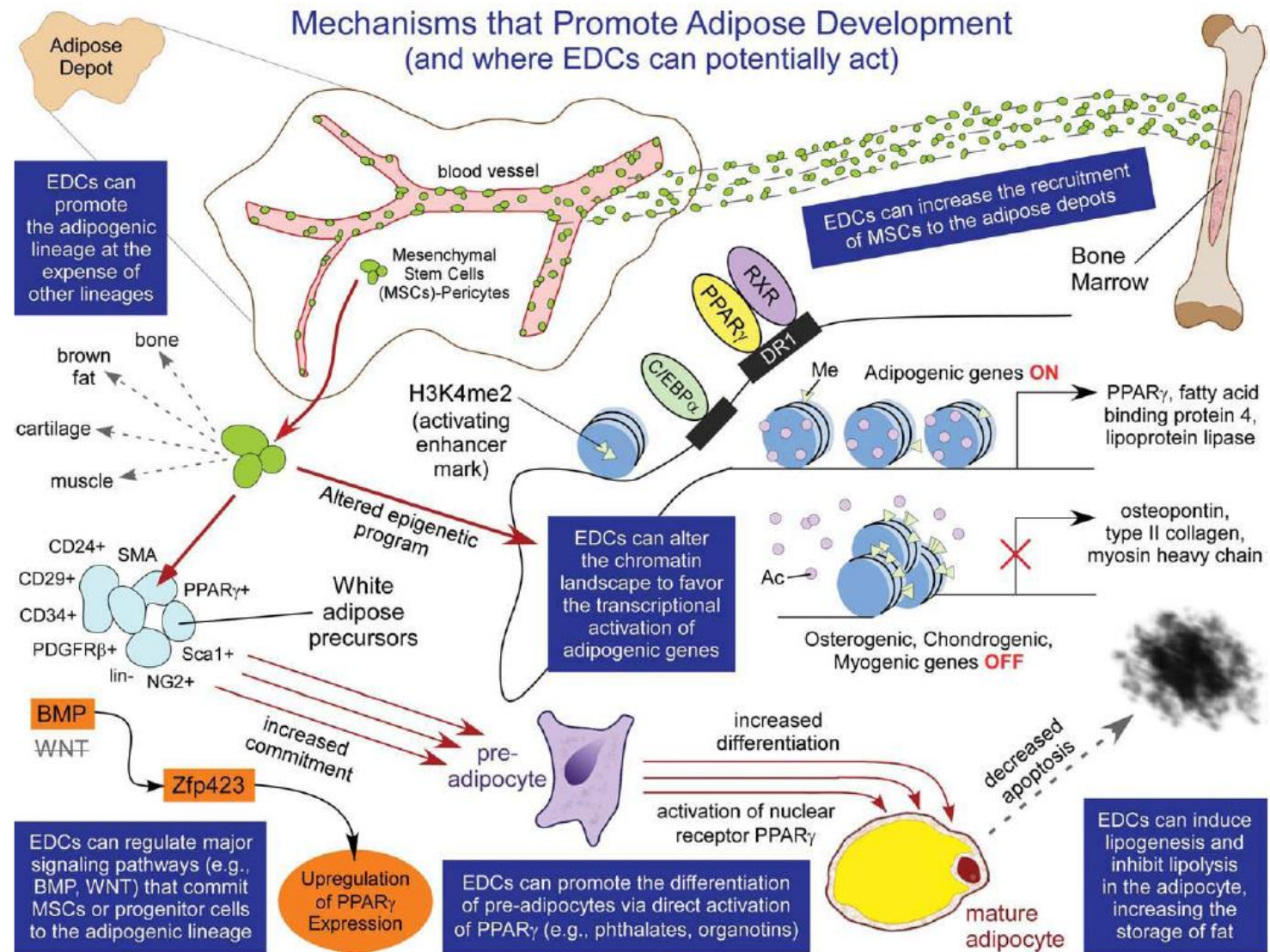
Neel B A , Sargis R M Diabetes 2011;60:1838-1848

## Life Style-Related Diseases of the Digestive System: Endocrine Disruptors Stimulate Lipid Accumulation in Target Cells Related to Metabolic Syndrome

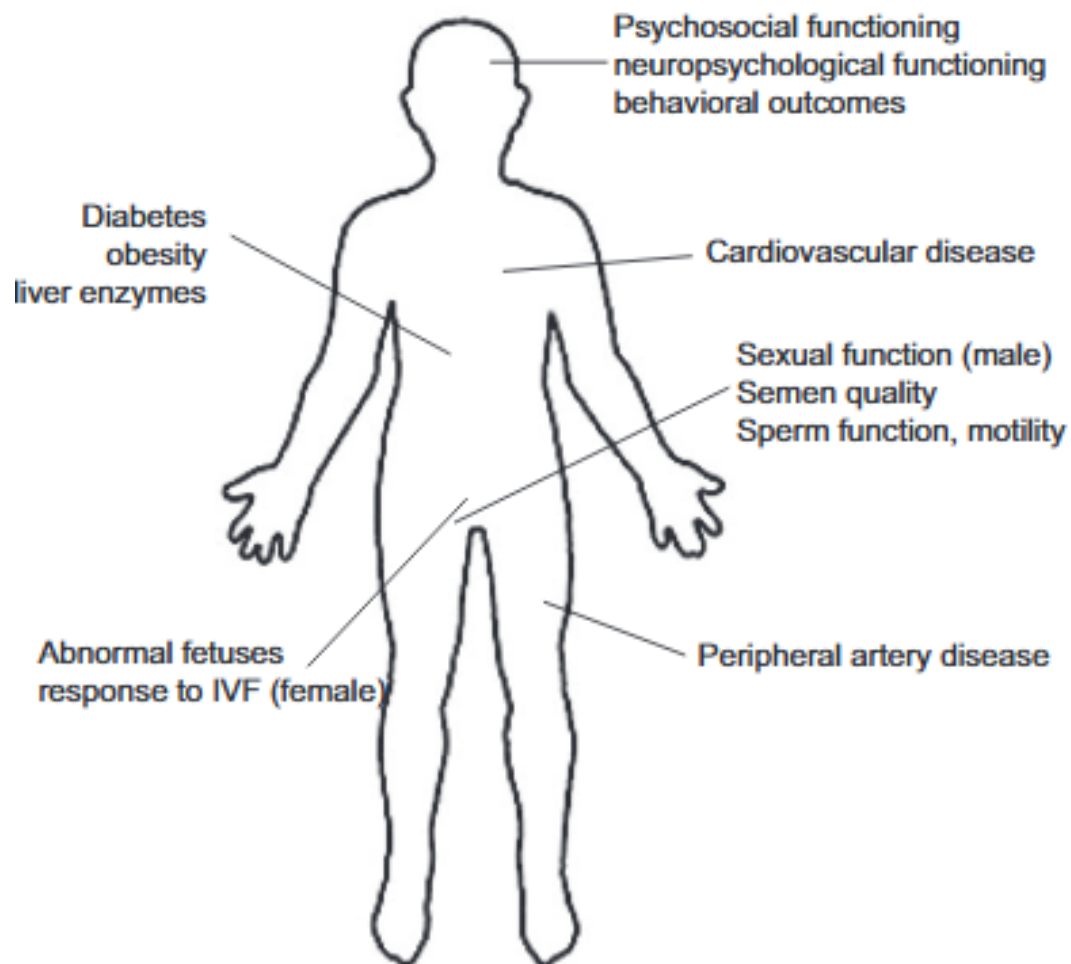
Koichiro Wada<sup>1,\*</sup>, Hirotada Sakamoto<sup>2</sup>, Kenji Nishikawa<sup>2</sup>, Satoru Sakuma<sup>2</sup>, Atsushi Nakajima<sup>3</sup>,  
Yohko Fujimoto<sup>2</sup>, and Yoshinori Kamisaki<sup>1</sup>



. Schematic illustration of possible involvement of EDs in lipid accumulation in adipocytes and hepatocytes.



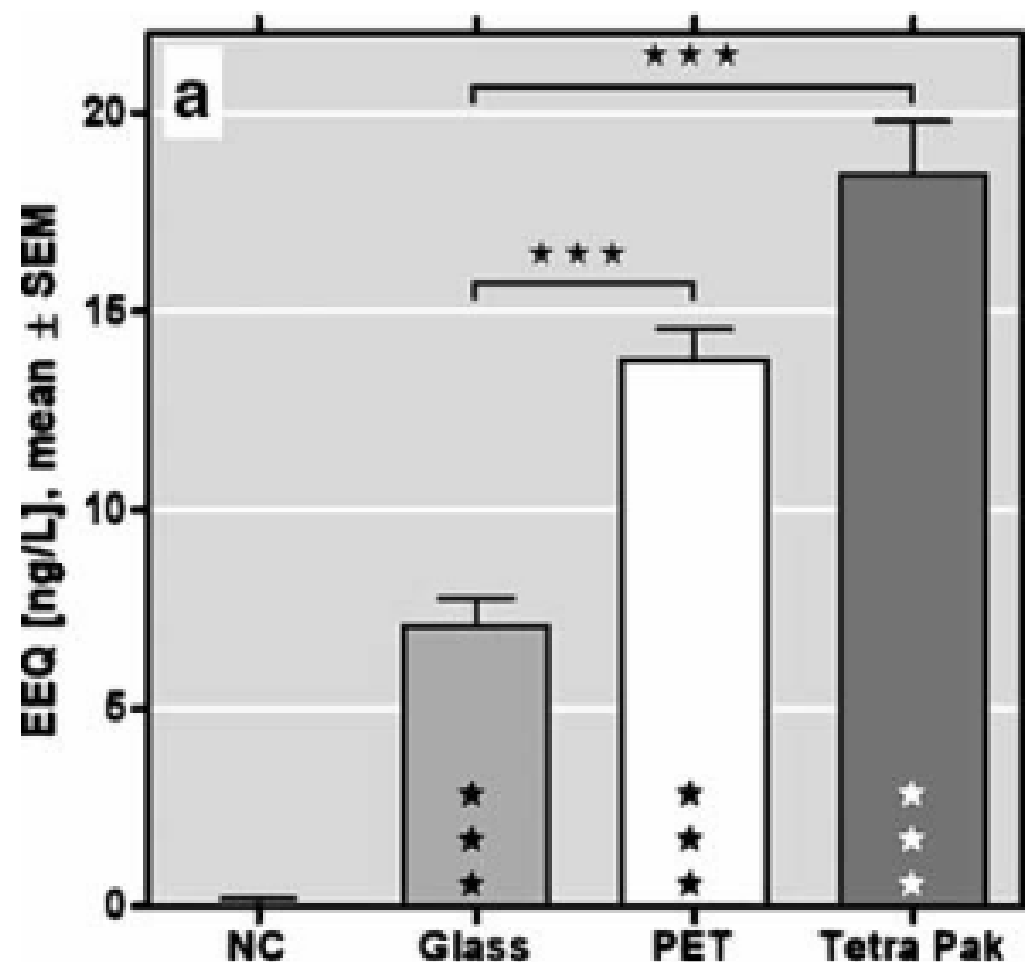
**Figure 2.** Diagram of the potential interactions of endocrine disrupting chemicals during various stages of adipose tissue development.



**Figure 1** A summary of end points examined in human studies of BPA. A number of epidemiology studies have identified relationships between exposure levels and human diseases. Many similar end points are affected by controlled BPA exposures in laboratory animal experiments.

# **Endocrine disruptors in bottled mineral water: total estrogenic burden and migration from plastic bottles**

**Martin Wagner • Jörg Oehlmann**



**Fig. 3** Estrogenic potencies of mineral water in vitro (**a**) and reproduction of *Potamopyrgus antipodarum* (**b**). Data were pooled according to packaging material. **a** Estrogenic potencies (*EEQ*) measured with the yeast estrogen screen. Negative control (*NC*),  $n=226$ ; glass,  $n=610$ ; PET,  $n=620$ ; Tetra Pak,  $n=133$ . **b** Number of



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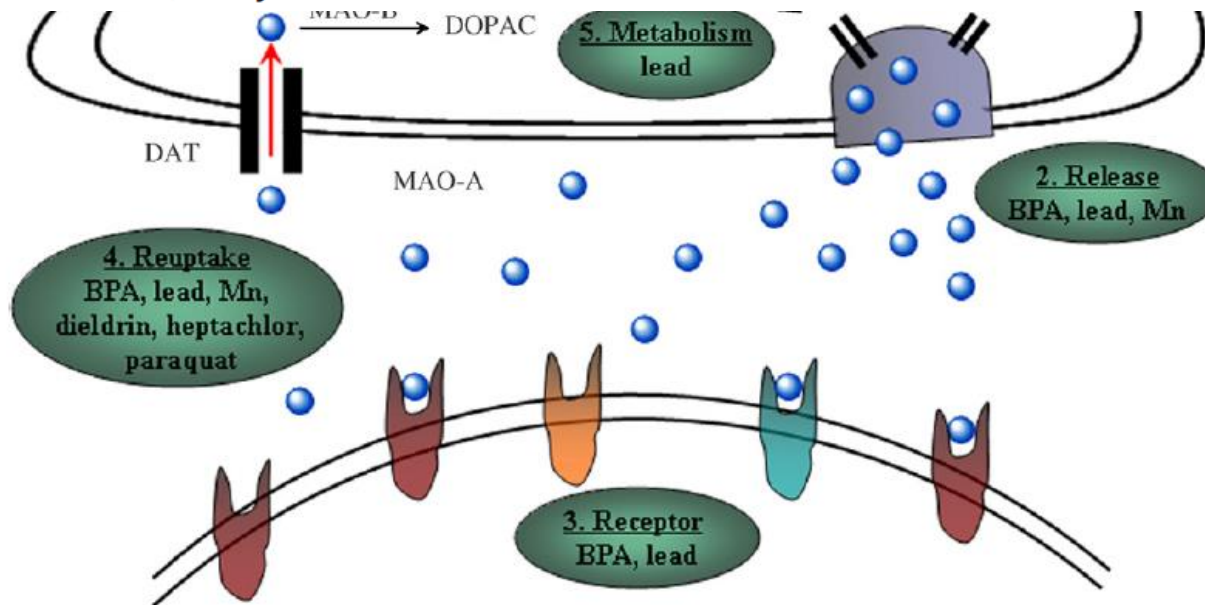


journal homepage: [www.elsevier.com/locate/biochempharm](http://www.elsevier.com/locate/biochempharm)



## Commentary

# The effects of environmental neurotoxins on the dopaminergic system: A possible role in drug addiction

Douglas C. Jones<sup>a,\*</sup>, Gary W. Miller<sup>b</sup>

## Research

## The Estrogenic Effect of Bisphenol A Disrupts Pancreatic $\beta$ -Cell Function *In Vivo* and Induces Insulin Resistance

Paloma Alonso-Magdalena,<sup>1</sup> Sumiko Morimoto,<sup>1,2</sup> Cristina Ripoll,<sup>1</sup> Esther Fuentes,<sup>1</sup> and Angel Nadal<sup>1</sup>

<sup>1</sup>Instituto de Bioingeniería, Universidad Miguel Hernández de Elche, Alicante, Spain; <sup>2</sup>Departamento de Biología de la Reproducción, Instituto Nacional de Ciencias Médicas y Nutrición "Salvador Zubirán," México City, México

The function of the pancreatic  $\beta$ -cell is the storage and release of insulin, the main hormone involved in blood glucose homeostasis. The results in this article show that the widespread environmental contaminant bisphenol-A (BPA) imitates 17 $\beta$ -estradiol (E<sub>2</sub>) effects *in vivo* on blood glucose homeostasis through genomic and nongenomic pathways. The exposure of adult mice to a single low dose (10  $\mu$ g/kg) of either E<sub>2</sub> or BPA induces a rapid decrease in glycemia that correlates with a rise of plasma insulin. Longer exposures to E<sub>2</sub> and BPA induce an increase in pancreatic  $\beta$ -cell insulin content in an estrogen-receptor-dependent manner. This effect is visible after 2 days of treatment and starting at doses as low as 10  $\mu$ g/kg/day. After 4 days of treatment with either E<sub>2</sub> or BPA, these mice developed chronic hyperinsulinemia, and their glucose and insulin tolerance tests were altered. These experiments unveil the link between environmental estrogens and insulin resistance. Therefore, either abnormal levels of endogenous estrogens or environmental estrogen exposure enhances the risk of developing type 2 diabetes mellitus, hypertension, and dyslipidemia. **Key words:** bisphenol A, diabetes, endocrine disruptors, estradiol, estrogen receptor, insulin, islet of Langerhans, nongenomic, xenoestrogens. *Environ Health Perspect* 114:106–112 (2006). doi:10.1289/ehp.8451 available via <http://dx.doi.org/> [Online 20 September 2005]

et al. 2002). Recently, a similar receptor has been found in *Drosophila* (Srivastava et al. 2005). E<sub>2</sub> rapidly potentiates  $\beta$ -cell signaling systems and insulin release via this ncmER, an effect that is mimicked by EDCs, including bisphenol A (BPA) (Nadal et al. 2004). BPA is one of the most common chemicals that behaves as an endocrine disruptor. It was the first synthetic estrogen without a steroid structure (Dodds and Lawson 1936), but because of its properties as a cross-linking chemical, BPA was widely chosen by the chemical industry to produce plastic polymers, mainly polycarbonates. Nowadays, it is used in the manufacture of barrier coatings for the inner surfaces of food and beverage cans. High concentrations of BPA have been detected in food and water extracted from autoclaved cans (Birnbaum et al. 1995; BPA<sup>+</sup> = 100–1,000 ng/g).



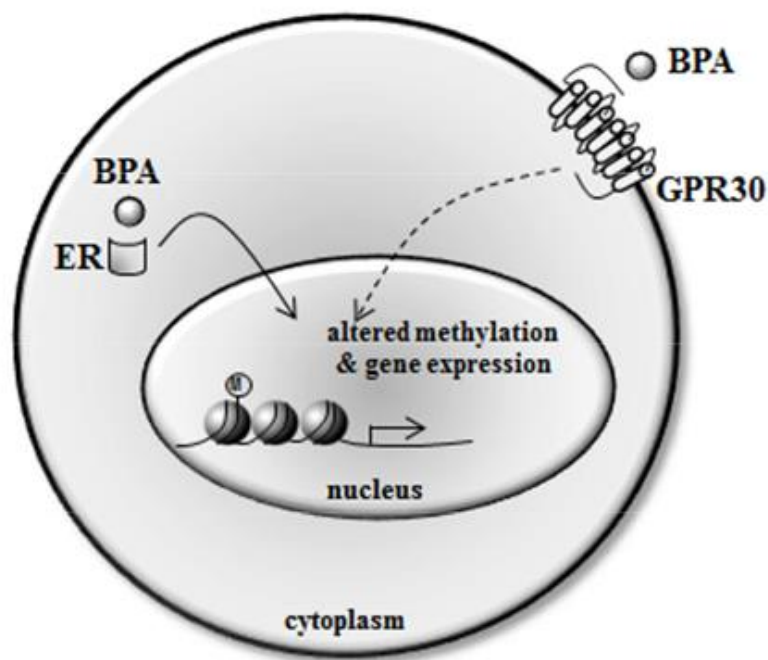
## A Review of the Carcinogenic Potential of Bisphenol A

### Abstract

The estrogenic properties of bisphenol A (BPA), a ubiquitous synthetic monomer that can leach into the food and water supply, have prompted considerable research into exposure-associated health risks in humans. Endocrine-disrupting properties of BPA suggest it may impact developmental plasticity during early life, predisposing individuals to disease at doses below the oral reference dose (RfD) established by the Environmental Protection Agency in 1982. Herein, we review the current *in vivo* literature evaluating the carcinogenic properties of BPA. We conclude that there is substantial evidence from rodent studies indicating that early-life BPA exposures below the RfD lead to increased susceptibility to mammary and prostate cancer. Based on the definitions of “carcinogen” put forth by the International Agency for Research on Cancer and the National Toxicology Program, we propose that BPA may be reasonably anticipated to be a human carcinogen in the breast and prostate due to its tumor promoting properties.

## Figure Captions

**Figure 1.** While the mechanism of action of BPA in humans is largely unknown, *in vitro* BPA effects are primarily mediated through its binding to classical nuclear ERs or through membrane-initiated non-genomic signaling by GPR30. *In vivo*, early life exposure to BPA rewrites the epigenetic code to stably alter gene expression in the breast, uterus and prostate. M=methylation.





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Perspectives/Opinion

## Les relations entre le bisphénol A et les troubles du spectre autistique se précisent : la sérotonine est-elle le lien manquant ?

*Autism spectrum disorders and bisphenol A: Is serotonin the lacking link in the chain?*

D. Sarrouilhe<sup>a,\*</sup>, C. Dejean<sup>b</sup>

<sup>a</sup> Physiologie humaine, faculté de médecine et pharmacie, université de Poitiers, BP 199, 6, rue de la Milétrie, bâtiment D1, TSA 51115, 86073 Poitiers cedex 9, France

<sup>b</sup> Service de pharmacie, pavillon Janet, centre hospitalier Henri-Laborit, 370, avenue Jacques-Cœur, 86021 Poitiers cedex, France



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## Bisphenol A Exposure in Children with Autism Spectrum Disorders

T. Peter Stein<sup>1</sup>, Margaret D. Schluter<sup>1</sup>, Robert A. Steer<sup>2</sup>, Lining Guo<sup>3</sup>, and Xue Ming<sup>4</sup>

<sup>1</sup>Department of Surgery, Rowan University-SOM, 2 Medical Center Drive, Stratford, NJ 08084

<sup>2</sup>Department of Psychiatry, Rowan University-SOM, 2 Medical Center Drive, Stratford, NJ 08084

<sup>3</sup>Metabolon Inc., 617 Davis Drive, Suite 400, Durham, NC 27713

<sup>4</sup>Departments of Neurosciences and Neurology, Rutgers University–New Jersey Medical School, 90 Bergen Street, Newark, NJ 07103

<sup>5</sup>Sleep Medicine Center, JFK Hospital, Seton Hall University, Edison, NJ 08820

### Abstract

**INTRODUCTION**—The etiology of autism spectrum disorders (ASD) is believed to involve genetic and environmental components. The present study focused on the plasticizer, Bisphenol-A (BPA). The major pathway for BPA metabolism and excretion is via glucuronidation.

**OBJECTIVES**—To determine whether there was a relationship between BPA exposure and ASD.

**METHODS**—Urine specimens were collected from 46 children with ASD and 52 controls. Free and total BPA concentrations were determined by mass spectrometry. The fraction glucuronidated was calculated from the difference. A metabolomics study was done to investigate metabolite distribution in the urine.

**RESULTS**—(i) Most of the BPA excreted in the urine was as the glucuronide. (ii) About 20% of the ASD children had BPA levels beyond the 90<sup>th</sup> percentile (> 50 ng/ml) of the frequency distribution for the total sample of 98 children. (iii) Mann-Whitney U tests and multiple regression analyses found significant differences ( $p < .05$ ) between the groups in total and % bound BPA.