Food Additives and Child Health:


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Introduction to American Academy of Pediatrics (AAP)

The AAP is an organization of 67,000 pediatricians committed to the optimal physical, mental, and social health and well-being for all infants, children, adolescents, and young adults.

The Council on Environmental Health (COEH) is the home for Academy members interested in and concerned about children’s environmental health and toxic exposures.
Our key activities include:

• Advising the AAP Board of Directors on issues pertaining to environmental health and toxic exposure. Council-authored policy statements address issues such as air pollution, lead screening, pesticides, radiation disasters, and secondhand smoke.

• Supporting legislative initiatives designed to protect the health of the fetus, infant, and child from debilitating or hazardous environmental agents.

• Developing educational initiatives related to children's environmental health.

• Publishing the Academy landmark Pediatric Environmental Health manual, currently in its third edition.
Introduction to AAP Statements

Food Additives and Child Health

Leonardo Trasande, MD, MPP, FAAP, Rachel M. Shaffer, MPH, Sheela Sathyasurya, MD, MPH
COUNCIL ON ENVIRONMENTAL HEALTH

POLICY STATEMENT Organizational Principles to Guide and Define the Child Health Care System and/or Improve the Health of all Children

American Academy of Pediatrics
DEDICATED TO THE HEALTH OF ALL CHILDREN

Food Additives and Child Health

Leonardo Trasande, MD, MPP, FAAP, Rachel M. Shaffer, MPH, Sheela Sathyasurya, MD, MPH
COUNCIL ON ENVIRONMENTAL HEALTH
Goal: Review evidence of harm to child health from food additives

- Epidemiological & toxicological data
- Exposure data & trends

Categories of food additives:
- **Indirect**: food contact materials, used in packaging or processing
  - Adhesives, coatings, plastics, paperboard
- **Direct**: deliberately added to food
  - Colorings, flavorings
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: An Endocrine Society Scientific Statement

Evanthia Diamanti-Kandarakis, Jean-Pierre Bourguignon, Linda C. Giudice, Russ Hauser, Gail S. Prins, Ana M. Soto, R. Thomas Zoeller, and Andrea C. Gore

Endocrine Section of First Department of Medicine (E.D.-K.), Laiko Hospital, Medical School University of Athens, 11527 Athens, Greece; Department of Pediatrics (J.-P.B.), Centre Hospitalier Universitaire de Liege, 4000 Liege, Belgium; Department of Obstetrics, Gynecology, and Reproductive Sciences (L.C.G.), University of California San Francisco, San Francisco, California 94118; Department of Environmental Health (R.H.), Harvard School of Public Health, Boston, Massachusetts 02115; Department of Urology (G.S.P.), University of Illinois at Chicago, Chicago, Illinois 60612; Department of Anatomy and Cell Biology (A.M.S.), Tufts University School of Medicine, Boston, Massachusetts 02111; Biology Department (R.T.Z.), University of Massachusetts, Amherst, Massachusetts 01003; and Division of Pharmacology and Toxicology (A.C.G.), The University of Texas at Austin, Austin, Texas 78712

There is growing interest in the possible health threat posed by endocrine-disrupting chemicals (EDCs), which are substances in our environment, food, and consumer products that interfere with hormone biosynthesis, metabolism, or action resulting in a deviation from normal homeostatic control or reproduction. In this first Scientific Statement of The Endocrine Society, we present the evidence that endocrine disruptors have effects on male and female reproduction, breast development and cancer, prostate cancer, neuroendocrinology, thyroid, metabolism and obesity, and cardiovascular endocrinology. Results from animal models, human clinical observations, and epidemiological studies converge to implicate EDCs as a significant concern to public health. The mechanisms of EDCs involve divergent pathways including (but not limited to) estrogenic, antiandrogenic, thyroid, peroxisome proliferator-activated receptor γ, retinoid, and actions through other nuclear receptors; steroidogenic enzymes; neurotransmitter receptors and systems; and many other pathways that are highly conserved in wildlife and humans, and which can be modeled in laboratory in vitro and in vivo models. Furthermore, EDCs represent a broad class of molecules such as organochlorinated pesticides and industrial chemicals, plastics and plasticizers, fuels, and many other chemicals that are present in the environment or are in widespread use. We make a number of recommendations to increase understanding of effects of EDCs, including enhancing increased basic and clinical research, invoking the precautionary principle, and advocating involvement of individual and scientific society stakeholders in communicating and implementing changes in public policy and awareness. (Endocrine Reviews 30: 293–342, 2009)
State of the Science of Endocrine Disrupting Chemicals - 2012

Edited by Åke Bergman, Jerrold J. Heindel, Susan Jobling, Karen A. Kidd and R. Thomas Zoeller
Response to WHO/UNEP Report


- Footnote identifies only chemical and pesticide industries as having concerns about state of science
- Concerns voiced in response by Lamb et al rebutted by WHO/UNEP report authors in Reg Tox Pharm Bergman et al 2015
# Indirect Food Additives

<table>
<thead>
<tr>
<th>Chemical</th>
<th>Food-Related Use</th>
<th>Health Concerns</th>
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</thead>
</table>
| Bisphenols (Bisphenol-A & related compounds) | • Polycarbonate plastic containers  
• Polymeric epoxy resins for food & beverage cans | • Endocrine disruption  
• Obesogenic activity  
• Neurodevelopmental disruption |
| Phthalates                        | • Clear plastic food wrap  
• Plastic tubing & storage containers for food production  
• Food manufacturing equipment | • Endocrine disruption  
• Obesogenic activity  
• Oxidative stress  
• Cardiotoxicity |
| Perfluoroalkyl chemicals (PFCs)   | • Grease-proof paper and paperboard                                              | • Immunosuppression  
• Endocrine disruption  
• Obesogenic activity |
| Perchlorate                       | • Antistatic agent in food packaging  
• Contamination from food manufacturing cleaning products | • Thyroid hormone disruption |
# Direct Food Additives

<table>
<thead>
<tr>
<th>Chemical</th>
<th>Food-Related Use</th>
<th>Health Concerns</th>
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<tbody>
<tr>
<td>Nitrates/nitrites</td>
<td>• Preservative</td>
<td>• Carcinogenicity</td>
</tr>
<tr>
<td></td>
<td>• Color enhancer</td>
<td>• Thyroid hormone disruption</td>
</tr>
<tr>
<td>Artificial food coloring</td>
<td>• Coloring</td>
<td>• Potential effects on neurobehavioral outcomes; (ex: exacerbation of attention-deficit/hyperactivity disorders)</td>
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Policy Statement

Goals:

• Review regulatory system for food additives
• Provide guidance for pediatricians to incorporate into clinical visits
• Propose reforms to current regulatory process
Regulatory Framework for Food Additives

Federal Food, Drug, and Cosmetic Act (FFDCA) (1938)
- Gave authority to US Food and Drug Administration (FDA) to oversee safety of food, drugs, medical devices, & cosmetics

FFDCA Food Additive Amendment (1958)
- Established food additives regulatory program
- Definition of “food additives”
- Exemption for substances Generally Recognized as Safe (GRAS)

- Created approval process for food contact substances (FCS)
What is a “Food Additive?”

Food additive: substances “the intended use of which results or may reasonably be expected to result, directly or indirectly, in becoming a component or otherwise affecting the characteristics of any food” (21 USC 321(s) and 21 CFR 170.3)

- **Direct:** intentionally added to food
  - ex: colorings, flavorings
- **Indirect:** not intentionally added to foods but reasonably expected to be part of food
  - ex: materials in food packaging & processing equipment
Does the current regulatory system ensure food safety?

Most food additives have not been tested

- Neltner et al. 2013 study on 3941 direct food additives
  - 63.9% had no oral toxicology data
  - 93.3% had no reproductive toxicology data

Reasons for shortcomings

1. Extensive use of “GRAS” designation
2. Limitations to FDA authority & procedures


Key Loophole: “GRAS”

**Generally Recognized as Safe (GRAS):** substances “generally recognized, among experts qualified by scientific training and experience to evaluate the safety as having been adequately shown…to be safe under conditions of their intended use” (21 USC 321(s))

No opportunity or legal obligation for FDA or public review

Intended for limited use, but now widespread (~1000 chemicals)

Extensive conflict of interest in GRAS designations
  - Manufacturers or consultants can self-designate products as “GRAS”

Limitations to FDA authority & procedures

No authority to obtain data or re-assess safety of chemicals already on the market
No consideration of cumulative or synergistic effects
Outdated toxicological testing recommendations may not be sufficiently protective for children
  • Testing guidelines based on estimated daily exposure, without consideration of body weight
  • Limited/no evaluation of neurobehavioral or endocrine endpoints
Recommendations for Pediatricians & Patients

• Prioritize consumption of fresh or frozen fruits & vegetables
• Avoid processed meats, especially during pregnancy
• Avoid microwaving food or beverages in plastics
• Avoid putting plastics in dishwasher
• Avoid plastics with recycling codes 3 (phthalates), 6 (styrene), and 7 (bisphenols)
• Encourage hand-washing before handling foods
• Wash all fruits & vegetables that cannot be peeled

Bisphenol and phthalate exposures are preventable

Limiting canned food consumption and avoiding processed foods
  • Intervention reduced mean concentrations of BPA by 66% and DEHP metabolites by 53–56%.
Recommendations for Government & Policy

FDA should:
- Revise the “GRAS” process
- Coordinate with other agencies to address existing data gaps
- Establish requirements for prioritization and re-testing of approved chemicals
- Update safety assessment guidelines
  - Ex: endocrine disruption testing, safety factors for children, synergistic & cumulative effects
- Establish requirements for labeling of food additives with little or no toxicity data, and those not reviewed for safety by FDA

Congress should:
- Provide FDA with authority to collect information about food additives (ex: use & toxicity data)
- Provide FDA with dedicated resources to support strengthened agency activities
- Support provisions to ensure transparency and minimize conflict of interest
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

Vinas and Watson EHP doi:10.1289/ehp.1205826
HEALTH EFFECTS FROM ENDOCRINE DISRUPTING CHEMICALS COST THE EU 157 BILLION EUROS EACH YEAR. This is the tip of the iceberg: Costs may be as high as €270B.

€157B Cost by Health Effect

NOTE: The economic estimates do not include all costs associated with these conditions.

- Male Reproductive Disorders: 4
- Premature Death: 6
- Oesophy & Diabetes: 15
- Neurological Impacts (including ADHD): 132

€157B Cost by EDC Type

- Pesticides: 120
- Plastic: Phthalates & BPA: 26
- Flame Retardants: 9
- Other: 2

SOME EDC-RELATED HEALTH OUTCOMES NOT INCLUDED:

- Breast Cancer
- Prostate Cancer
- Immune Disorders
- Female Reproductive Disorders
- Liver Cancer
- Parkinson’s Disease
- Osteoporosis
- Endometriosis
- Thyroid Disorders

SOME EDCs NOT INCLUDED:

- Atrazine
- 2,4-D
- Styrene
- Triclosan
- Nonylphenol
- Polycyclic Aromatic Hydrocarbons
- Bisphenol S
- Cadmium
- Arsenic
- Ethylene glycol

Endocrine Disrupting Chemicals (EDCs) interfere with hormone action to cause adverse health effects in people.

“THE TIP OF THE ICEBERG”
The data shown to the left are based on fewer than 5% of likely EDCs. Many EDC health conditions were not included in this study because key data are lacking. Other health outcomes will be the focus of future research.

Health Effects From Endocrine Disrupting Chemicals Cost The U.S. $340 Billion Annually

Endocrine Disrupting Chemicals (EDCs) interfere with hormone action to cause adverse health effects in people.

$340 Billion by Health Effect

- Neurological Conditions (including ADHD): $282 Billion
- Endometriosis & Fibroids: $43 Billion
- Premature Death: $8 Billion
- Obesity & Diabetes: $5 Billion
- Male Reproductive Problems: $2 Billion

$340 Billion by EDC Type

- Flame Retardants: $240 Billion
- Plastic, Cans: $56 Billion
- Pesticides: $42 Billion
- Other Mixes of Chemicals (including Teflon-like materials): $2 Billion
Thank you

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