# The Pediatrician's Role in Protecting Children from Environmental Hazards

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**KEYWORDS**

• Lead • Pesticides • Flame retardants • Endocrine disruption • Phthalates
• Bisphenols

**KEY POINTS**

- Children are uniquely vulnerable to a broad suite of environmental contaminants.
- Although metals and air pollutants are the focus of environmental health training in medical school and residency, endocrine disrupting chemicals have emerged as major drivers of disease and disability.
- Regulatory measures have and will continue to prove crucial in preventing diseases of environmental origin in youth.
- Anticipatory guidance in primary care settings should routinely emphasize steps families can take to limit exposures.

## THE INCREASINGLY CHEMICAL WORLD EXPERIENCED BY CHILDREN

The 1993 National Academy of Sciences (NAS) report on Pesticides in the Diets of Infants and Children documented the biological basis of children's unique vulnerability to environmental hazards. Children have greater dietary intake and inhalation rates per unit body weight that magnify exposure.[2] Dermal barriers are physiologically thinner.[3] They also have more years of life in which consequences of exposure can manifest. The work of the late Sir David Barker emphasized the exquisite sensitivity of developmental programming, producing consequences for organ systems that can be permanent and lifelong.[4,5]

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**Box 1**
**Selected steps that families can take to limit EDC exposures**

- Avoiding microwaving food or beverages in plastic
- Eating organic
- Not cleaning plastics in the dishwasher
- Using alternatives, such as glass or stainless steel, when possible
- Avoiding plastics with recycling codes 3 (phthalates), 6 (styrene), and 7 (bisphenols) via the recycling code on the bottom of products
- Using cast iron and/or stainless steel pans instead of nonstick cooking materials
- Selecting personal care products using tools such as Environmental Working Groups' SkinDeep app
- Avoiding cleaning materials without fragrances or undisclosed ingredients
- Recirculating indoor air with outdoor air
- Using a wet mop to remove dust from electronics and furniture

Lead,[6–8] mercury,[9–11] tobacco smoke,[12] alcohol,[13] and polychlorinated biphenyls (PCBs)[14] were among the earliest known hazards identified in children, with consequences for cognitive impairments and other developmental disabilities.[15] Air pollutants were identified to exacerbate and induce asthma in children.[16–19] Understandably, residency programs focused training in environmental health on heavy metals and airborne contaminants.[20] The positive benefits of educational initiatives are manifest in the high self-efficacy pediatricians describe in managing lead exposures and communicating advice for prevention to families (Trasande L, Ziebold C, Schiff JS, et al. The environment in pediatric practice in Minnesota: attitudes, beliefs, and practices towards children's environmental health. Minnesota Medicine, submitted. 2008).[21–23]

However, in the 30 years since the NAS report,[1] technologic advances have further transformed the landscape of environmental exposures and identified that an even broader array of chemicals can interfere with hormone action. Endocrine-disrupting chemicals (EDCs) are ubiquitous in the human environment, and include: pharmaceuticals (eg, ethinylestradiol, rosiglitazone); ingredients in cosmetics and personal care products (eg, phthalates, parabens); pesticides, herbicides and fungicides (eg, chlorpyrifos, glyphosate); industrial chemicals (eg, bisphenols, polybrominated diphenyl ethers, PBDEs); metals (eg, arsenic, cadmium); and synthetic and naturally occurring hormones (eg, progesterone, testosterone).[24] More than 1000 chemicals have been

**Box 2**
**Selected advocacy organizations leading on behalf of children's environmental health**

Children's Environmental Health Network (cehn.org)

Defend Our Health (defendourhealth.org)

Endocrine Society (endocrine.org)

Environmental Working Group (ewg.org)

Food Packaging Forum (foodpackagingforum.org)

Health Care Without Harm (noharm.org)

International POPs Elimination Network (ipen.org)

identified as endocrine disruptors, including many common-use chemicals, with the vast majority of chemicals in commerce still not evaluated for EDC properties.

Health care facilities also use many products that increase the risk of EDC exposures.[25] Phthalates, for example, are abundant in polyvinylchloride-based medical devices such as blood bags, nutrition pockets, tubing, umbilical venous catheters or disposable gloves, where they can account for up to 40% of the final product by mass.[26] They are also used to make coatings for oral medications and in flooring.[27] Exposures are likely the greatest per pound body weight in neonatal intensive care units, where noninvasive respiratory support and feeding tubes have been identified as the most significant drivers of phthalate exposure.[28] In addition, bisphenols are used in polycarbonate-based medical tubing, hemodialysis equipment, newborn incubators, syringes and nebulizers.[29] Parabens are used in medications and intravenous catheters for their antimicrobial properties.[30]

The endocrine system is crucial to the functioning of nearly all human biological functions, with EDCs inducing a broad array of consequences.[31] The implications of EDCs for children's health have been codified by the World Health Organization and the United Nations Environment Program,[32] Endocrine Society,[33,34] American Academy of Pediatrics (AAP),[35] and International Federation of Obstetricians and Gynecologists (FIGO).[36] The Developmental Origins of Health and Disease hypothesis has also been expanded beyond the effects of nutritional deprivation described by Barker and colleagues[16–19] to recognize the broader range of subtler insults, including environmental exposures, which can also disrupt developmental programming.[37] The science of epigenetics has further unraveled the multigenerational consequences of environmental hazards,[38–42] and reinforced the reality that EDCs need not be structurally similar to hormones to have effects on their function.[34]

### *Known Effects of Environmental Hazards on Children's Health*

Beginning in 1997, the NIEHS-EPA Children's Environmental Health and Disease Prevention Research Centers (Children's Centers) produced much of the direct evidence of harm induced by environmental exposures, and particularly EDCs. Multiple birth cohorts independently documented how organophosphate (OP) pesticide, and polybrominated diphenylether (PBDE) exposures resulted in consistent decrements in cognitive function in relation to prenatal exposure, controlling for multiple other potential predictors (eg, socioeconomic status and other environmental exposures); these effects are consistent with those previously observed with lead.[43–49] Specifically, prenatal exposure to OPs has been associated with magnetic resonance imaging findings in children including frontal and parietal cortical thinning that are consistent with the neurobehavioral deficits identified in psychological testing.[46]

The Children's Centers identified contributions of polycyclic aromatic hydrocarbons, traffic-related air pollution (TRAP), bisphenols and phthalates to obesity and insulin resistance in youth, independent of diet and physical activity.[50–54] These findings changed the paradigm of childhood obesity from a simple imbalance in energy consumption versus expenditure to embrace the built environment and chemicals as also being obesogenic.[50–55] Center investigators also revealed second-hand tobacco smoke, PBDEs, PAHs, and PCBs as risks for childhood leukemia,[56–58] and disruption of pubertal timing by phthalates and PBDEs.[59,60] PCBs and PBDEs were found to induce immune disruption,[61] whereas air pollution and OP exposures *in utero* were associated with increased risk for autism spectrum disorder.[62,63]

Findings from these and other studies worldwide support substantial contribution of EDCs to disease and disability in children.[24] In children born in 2010 alone, PBDE exposures in the United States accounted for 11 million IQ points lost and 43,000 cases

of intellectual disability, costing $266 billion in health care and other associated costs. OP pesticide exposures accounted for another 1.8 million IQ points lost and 7500 cases of intellectual disability, costing $42 billion. Of 4-year-old children with obesity, 6.7% were attributed to prenatal bisphenol exposure, with associated costs of $2.4 billion.[64] These are an annual cost insofar as exposures continue at current levels. Importantly, these costs only accounted for the relative health impacts of a few select EDCs with substantial epidemiologic and mechanistic evidence; studies evaluating human health impacts from hundreds of other identified EDCs with known human exposures are not established enough to provide this level of evidence to calculate health costs.

### *The Importance of Environmental Regulation in Shaping the Health of Children*

The importance of public policy in reducing children's exposure to lead is a crucial and positive example of the benefits that can be produced by protecting children from environmental hazards. Between 1976 and 1980, as the ban on lead from gasoline in the United States was being instituted, the average child blood lead level was 17.1 μg/dL among 1- to 5-year-olds. By 1999, the average had declined ~88% to 2.0 μg/dL, further fueled by bans on lead in paint. Grosse and colleagues estimate that children born in the 1990s had IQ points on average 2.2 to 4.7 IQ points higher than children born in the 1970s. The improvement in lifetime economic productivity due to these policy changes was estimated to be $110 to 319 billion annually,[65] an ongoing economic benefit that increases to this day as lead levels continue to diminish as lead-based paint hazards are eradicated. Reductions in criminality and increases in high school graduation rates have also been related to lower blood lead levels in children.[66]

Similar health and economic benefits can be traced to the 1990 Clean Air Act amendments, which strengthened federal government authority to enforce regulations that limit air pollution.[67] Between 1997 to 2008 childhood asthma morbidity declined substantially.[68] Premature births due to fine particulate matter are also likely to have declined.[69] Children from three cohorts of southern California in 2007 to 2011 were found to have greater growth in their lung function between the ages of 11 and 15 compared with similar aged populations followed between 1994 to 1998 and 1997 to 2001, due to increasingly stringent vehicle emissions limits and subsequent improvements in air quality.[70]

### *Ongoing Flaws in the Regulatory Framework*

In the United States, chemical regulation is administered by the Environmental Protection Agency (EPA) and the Food and Drug Administration (FDA). The Toxic Substances Control Act (TSCA) provides the EPA with oversight of most commercial uses of industrial chemicals, except for pesticides. Authority for pesticide regulation is provided to EPA under the Federal Insecticide, Fungicide and Rodenticide Act and the Federal Food Drug and Cosmetic Act (FFDCA). FDA has authority to regulate chemicals used in cosmetics and personal care products, food and food packaging, and pharmaceuticals under FFDCA.

TSCA does not address EDCs or require testing for endocrine disruption, despite a revision in 2016.[71] This is problematic, as understanding of EDCs continues to accelerate rapidly, with only ~5% of synthetic chemicals tested for their potential endocrine disruption. The US FDA, for example, has now identified more than 1800 chemicals that disrupt at least one of three endocrine pathways (estrogen, androgen, and thyroid).[72]

Even if testing data are available, EPA regulatory policies continue to adhere to the Paracelsian notion that "Solely the dose determines that a thing is not a poison."

Although this adage has been fundamental to toxicologic science and in shaping regulatory policy, EDCs have revealed the flaws in the Paracelsian paradigm. EDCs are often able to promote effects at concentrations below those traditionally examined in toxicologic risk assessments.[71] They can exhibit non-monotonic dose response curves, resulting in quantitatively and qualitatively different outcomes at low versus high concentrations.[73] Greater effects have been identified during critical windows of development, with disruption during these windows altering normal development and promoting disease.[34] There is clearly a need for a shift from a flawed, risk-based paradigm to one that proactively excludes chemicals with some evidence of hazardous properties.[74]

Flaws in FDA policy frameworks also limit the capacity to address EDCs using the latest endocrine science. For example, the Food Additives Amendment of 1958 exempted food additives from regulation "if such substance is not generally recognized, among experts qualified by scientific training and experience to evaluate its safety." The Generally Recognized as Safe (GRAS) exemption has resulted in greater than 10,000 additives allowable in US food through exemptions and limits on FDA authority.[75,76] The Federal Fair Packaging and Labeling Act of 1973 initially required cosmetics ingredients to be listed on product labels, but concerns over trade secrets led to the exemption of the term "fragrance," used to describe a combination of chemicals including phthalates, solvents, preservatives, UV absorbers, and other chemical constituents known or suspected to be EDCs.[77]

In the absence of strong FDA and EPA regulatory frameworks, new chemicals have been introduced as replacements for chemicals of concern without a regulatory framework that fully evaluates their potential effects on children:

- Chemically similar bisphenols (eg, bisphenol S, or BPS) have replaced BPA;[78–83]
- Organophosphate esters (OPE) have replaced PBDEs in electronics;[84]
- Diisononylphthalate (DINP), diisodecylphthalate (DIDP) and 1,2-cyclohexane dicarboxylic acid diisononyl ester (DINCH) are replacing di-2-ethylhexylphthalate (DEHP) in food packaging;[85]
- Neonicotinoids are emerging in use as insecticides, replacing OPs and pyrethroids[86]; and
- Short-chain PFAS are increasingly replacing their long-chain analogues.[87]

Unfortunately, regrettable substitutes have been identified to produce similar effects as the chemicals they replace in all the above examples. For example, the few studies that have studied BPA replacements such as BPS have identified similar genotoxicity and estrogenicity,[78–83] embryonal effects,[88] oxidative stress,[89] cardiotoxicity,[90] disruption of osteoblast function,[91] and greater resistance to environmental degradation.[92,93]

Comparing the costs of EDCs between Europe and the United States also illustrates the crucial role of regulatory policy in shaping exposures children experience in early life and their contribution to disease burden. For example, OP-related cognitive loss ($44.7 billion) was vastly lower in the United States compared with Europe ($121 billion).[94] This divergence is likely a byproduct of the 1993 Food Quality Protection Act in the United States (which required lower allowable residues of OPs in foods) in the absence of similar activity in Europe until recently.[95] The converse is true for PBDEs due to TB-117, a California law that required addition of PBDEs to furniture from the 1970s until 2013, when the requirement was withdrawn. In contrast, Europe banned PBDEs from use much earlier, reducing the costs of exposure drastically compared with the United States.[64]

Without effective federal regulations governing EDCs, individual states have undertaken more local efforts to restrict or ban individual chemicals or classes. New York

has passed a Consumer Chemical Awareness Act that notifies consumers about personal care products that contain one or more EDCs. New Jersey, New Hampshire, and Michigan have set regulations on PFAS levels in water that are considerably lower than federal limits.

### *Opportunities for Prevention in the Clinical Setting*

Intervention studies have promise in reducing EDC exposures. Though large-scale intervention studies have not yet been conducted, small-scale interventions have supported the feasibility of reducing EDC exposures (**Boxes 1** and **2**). Lu and colleagues reduced OP metabolites in the urine of children to nondetectable levels through an organic diet intervention.[96] Though concerns about the additional costs associated with organic food are appropriate, a more recent dietary intervention also produced similar reduction in pesticide metabolites in a low-income, agricultural population.[97] A recent intervention study in young girls found that choosing personal care products that are labeled to be free of phthalates, parabens, triclosan, and benzophenones can reduce personal exposure to these EDCs by 27% to 44%.[98] Another dietary intervention study, which replaced diets in a small sample of families with fresh foods, reduced urinary levels of phthalate metabolites and bisphenols by 53% to 56%.[99]

Household interventions can also reduce exposure. A recent study measured dust from offices, common areas, and classrooms having undergone no intervention (conventional rooms in older buildings meeting strict fire codes), full "healthier" materials interventions (rooms with "healthier" materials in buildings constructed more recently or gut-renovated), or partial interventions (other rooms with at least "healthier" foam furniture but more potential building contamination). Rooms with full "healthier" materials interventions had 78% lower dust levels of PFAS than rooms with no intervention ($P < 0.01$). Rooms with full "healthier" interventions also had 65% lower OPE levels in dust than rooms with no intervention ($P < 0.01$) and 45% lower PBDEs than rooms with only partial interventions ($P < 0.1$), adjusted for covariates related to insulation, electronics, and furniture.[100]

It should be noted that not all studies have achieved expected changes in EDC levels. One study reported an increase in urinary phthalate metabolites in the intervention group, which was determined to be due to substantial phthalate contamination in the coriander provided to participants.[101] Another more recent study attempted to create a BPA risk score based on characteristics of food containers and packaging, and was unable to reduce urinary levels.[102]

Though further research is particularly needed to generalize the interventions which have been shown to reduce exposure, the American Academy of Pediatrics (AAP) Council on Environmental Health has published multiple policy statements on pesticides[103] and chemicals intentionally and unintentionally added to foods.[35] The AAP guidance suggests reductions in exposure to pesticides in foods, and identifies steps including the consumption of organic produce, recognizing the nutritional, environmental, health and cost issues involved. It documents the variability of pesticide residues, as they are highest in leafy fruits and vegetables, and refers to various guides provided by Consumer Reports (Stop Eating Pesticides) and Environmental Working Group (Dirty Dozen and Clean Fifteen lists). Rinsing fruits can reduce residues but has not been proven to reduce exposure.[104]

### *The Importance of the Pediatrician Voice in Environmental Advocacy*

The medical professional community has called their members to action to protect their patients from EDC exposure, including (but not limited to) the American Academy of Pediatrics,[35] Endocrine Society,[33,34] and International Federation of Obstetricians

and Gynecologists.[36] This section describes patient- and government-level advocacy opportunities for pediatricians steeped in the latest scientific evidence.

The AAP Policy Statement on Pesticides recommends improved labeling on pesticide containers including inert ingredients and risks posed specifically to children. It also supports improved reporting requirements for poisonings, and the support of least toxic alternatives, including the use of integrated pest management in households and agricultural settings, both in the United States and abroad. The Policy Statement also endorses the notion that communities and its members have the right to know where pesticides are applied, so that modifications can be made to reduce exposures in vulnerable groups.[105]

The AAP Policy Statement on Food Additive Chemicals identifies multiple improvements needed in FFDCA reform, including:

- Revising the GRAS process permit independent scientific review, followed by FDA review of such evaluations, before approval;
- Eliminating conflicts of interest in toxicologic evaluations of food additives;
- Requiring FDA to consider vulnerable subpopulations and systems in evaluating food additive safety, and applying additional safety factors to account for this vulnerability;
- Considering cumulative exposure from all dietary sources, as well as other additives and contaminants that interact with the same biological pathways; and
- Expanded FDA authority to revisit safety of chemicals when concerns are raised.

The Endocrine Society has also called for a shift from a flawed, risk-based paradigm to one that proactively excludes chemicals with some evidence of hazardous properties until further detailed reassuring testing data become available.[74] This call is based upon growing evidence that EDCs can exhibit nonlinear and non-monotonic dose response curves, resulting in quantitatively and qualitatively different outcomes at low versus high concentrations.[73] This phenomenon means that effects of low-level exposures in humans cannot be extrapolated from high-dose experiments in animals, leaving to a false interpretation of safety.[34]

Health care facilities have also begun to support sustainability initiatives that reduce the use of plastic, particularly those with chemical hazards. Practice Greenhealth, a network of over 1,400 hospitals in the United States, has implemented sustainability initiatives and climate-smart strategies in their facilities. The network also includes industry partners (manufacturers, suppliers, service providers, and other supply chain partners). Health Care without Harm supports hospital partners in recommending safer medical products and other materials that health care organizations and hospitals should adopt.

## ADVOCATING FOR MEDICAL EDUCATIONAL CHANGE

Rapidly accelerating awareness about the threat of climate change, especially among medical students and residents, has brought to the fore the need for enhanced environmental health education in the medical curriculum. Given that many EDCs derive from fossil fuels, there are potential co-benefits to reductions in their production. Increasing awareness of these exposures among the public also raises the need for educational efforts that span the population of child health care providers from pediatric interns to senior practitioners.

The surveys of state chapter membership of the AAP in Michigan,[106] Minnesota, (Trasande L, Ziebold C, Schiff JS, et al. The environment in pediatric practice in Minnesota: attitudes, beliefs, and practices towards children's environmental health.

Minnesota Medicine, submitted. 2008.)Wisconsin[23] and New York,[21] which revealed strong self-efficacy in managing lead exposure, also identified a lack of self-efficacy in managing patients with pesticide and other EDC exposures (and supporting anticipatory guidance around prevention). These findings were also confirmed among obstetricians and gynecologists.[107] Gaps in provider self-efficacy related to managing EDCs should not be surprising given the limited amount of environmental health education in medical training.[108] A survey of pediatric residencies in 2003 revealed a modest (typically 1–6 hour) focus on environmental hazards across 3-year programs. Clearly, there is a need for updating medical school curricula.

To address gaps in active practitioners, the Endocrine Society has organized a series of educational videos for health care providers, now posted on YouTube and the Endocrine Society website (www.endocrine.org). The International Federation of Gynecologists and Obstetricians has also developed a series of patient-facing materials to guide families about safe and simple steps to reduce exposure. The Council on Environmental Health of the AAP has produced patient- and provider-facing educational materials linked to the pesticide and food additive statements. Each of these initiatives represents an important advance in our ability to protect children.

Pediatricians have long served as outstanding advocates, from childhood vaccines to injury prevention. Although EDCs and other environmental exposures compete for attention with other aspects of anticipatory guidance, as well as treatment for acute conditions, their increasing contribution to chronic diseases that increasingly affect youth cannot be neglected. The best treatment will ultimately come from primary prevention of toxic exposures, through the combination of individual- and population-level advocacy. The voice of the pediatrician remains extremely well-respected in both of these circles, and given the known contribution of these exposures to disease and disability across the lifespan, we all stand to benefit when pediatricians show true leadership on behalf of the most vulnerable.

## DISCLOSURE

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