Editorials

Potential Toxicity of Synthetic Chemicals: What You Should Know About Endocrine-Disrupting Chemicals

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A growing body of evidence suggests that many synthetic chemicals once considered safe can be harmful to the developing fetus, infant, and child. There is particular concern about the developmental effects of substances known as endocrine-disrupting chemicals (EDCs), which can mimic, block, or alter the synthesis, transport, binding, or metabolism of endogenous hormones.[1]

Just as the estrogenic effects of diethylstilbestrol affected the daughters and granddaughters of women exposed during pregnancy, exposure to EDCs during development has been found to interfere with physiologic signaling in experimental animals, permanently altering neurologic, reproductive, immune, and endocrine systems by disrupting thyroid hormones and sex steroid homeostasis.[2] Human evidence is largely consistent with animal data, linking developmental EDC exposure to: (1) neurodevelopmental effects, including lowered IQ and attention deficits; (2) reproductive effects, such as hypospadias, cryptorchidism, decreased fertility, and accelerated puberty; (3) immune dysfunction linked to asthma and allergies; and (4) hormonally mediated cancers.[3]

Family physicians have the opportunity—during preconception counseling or in routine prenatal and well-child care—to educate patients and reduce exposure when possible to environmental contaminants, including EDCs.[4]

Human Exposure to EDCs

Humans encounter EDCs daily in many forms, including:

- Polybrominated diphenyl ethers added as flame-retardants to computers, televisions, and furniture.
- Phthalates added to soften plastics (e.g., toys) and vinyl products or to carry fragrances in cosmetics and household cleaners.
- Bisphenol A, a component of hard plastics that leaches from some plastic containers and the linings of cans.
- Perfluorooctanoic acid, which forms nonstick, stain repellant, or waterproof coatings on cookware, carpets, and clothing.
- Organochlorines (e.g., polychlorinated diphenyl ethers), many of which are banned, but are still found in the environment.

All of these EDCs have been detected in the blood and urine of most U.S. children and adults in representative samples of the National Health and Nutrition Examination Survey cohort.[5] They, along with more than 100 other environmental contaminants, have also been detected in breast milk[6] and umbilical cord blood.[7]

Assessing Health Effects of Chemical Exposures

EDCs illustrate several concepts that physicians can use to evaluate emerging environmental health science.

Windows of vulnerability: In animal studies, even brief exposures to EDCs during critical developmental periods have produced direct health effects, as well as alteration in the response to future exposures. For example, although not a frank carcinogen, bisphenol A has been shown to increase animals' likelihood of developing breast cancer in response to subsequent estrogen exposure.[8]

Low-dose effects: Although classic toxicology asserts, "the dose makes the poison," most hormonally active substances affect physiologic signaling mechanisms at extremely low doses, usually below those used in standard toxicology testing. Like their endogenous counterparts, many EDCs show nonlinear dose-response relationships, which make extrapolations from high-dose studies inaccurate.[9]

Multigenerational effects: Many EDCs alter gene expression, producing heritable effects known as epigenetic changes, which can affect animal offspring three generations after a single in utero exposure.[10]

Chronic, mixed exposures: Unlike experimental animals, humans are exposed to a mixture of chemicals, some of which produce additive or synergistic effects.[11]

These concepts illustrate that the traditional tools of toxicology and epidemiology are unable to accurately characterize human exposures to, or potential health effects of, synthetic chemicals and pollutants. In addition, it is difficult to capture health effects in case-control studies of universally exposed populations. Observational studies can only establish association, but not causality, and retrospective studies are often limited by lack of exposure data.

Financially vested industry groups have historically undermined scientific evidence when the findings could implicate their products.[12] In the case of bisphenol A, 90 percent of government-funded studies found significant effects, whereas nearly all industry-funded

studies produced negative findings, attributable to nonstandardized experimental conditions, methodologic errors, and failure to use positive controls.[13]

In November 2007, an expert panel on bisphenol A convened by The National Toxicology Program expressed "some concern" for neurologic and behavioral effects of in utero and childhood exposure, but only "minimal concern" for its potential reproductive effects.[14] The panel's report was widely criticized for flaws and inconsistencies in its inclusion criteria and was investigated for its employment of consultants with ties to industry.[15] A draft revised report released in April 2008 incorporated evidence from hundreds of studies not included in the first report, and raised the level of risk, expressing "some concern" for reproductive effects in addition to the neurologic and behavioral effects in fetuses, infants, and children exposed to bisphenol A.[16]

Recently, legislative bills and reports in the popular press have targeted EDCs, such as bisphenol A and phthalates. Now, the United States has banned phthlates in children's products, and some sources suggest alternatives to food products most likely to contain EDCs. Although the U.S. Food and Drug Administration does not currently recommend against these products, a task force is reassessing the safety of one EDC, bisphenol A.

Precautionary Action

As physicians, we will never have perfect information. However, widespread exposure to EDCs, at doses linked to chronic health effects in animals, combined with significant barriers to establishing definitive evidence of human harm, warrant that physicians and their patients be educated about developmental exposure to EDCs. Given the ubiquity of EDCs in the environment, true risk reduction will ultimately hinge on our ability as a society to reduce or eliminate the production and use of the most hazardous substances.

Resources

The Collaborative on Health and the Environment
Searchable database of chemicals and diseases (http://database.healthandenvironment.org/index.cfm).

Center for Science in the Public Interest's Nutrition Action Health Letter
List of resources about bisphenol A (http://www.cspinet.org/nah/bpa.html#reducing).

Greater Boston Physicians for Social Responsibility
Fact sheets for patients and physicians, including the Pediatric Environmental Health Toolkit (http://psr.igc.org/hhep.htm).

Natural Resources Defense Council
Consumer guides and summaries of the science (http://www.nrdc.org/health/).

Women's Health & the Environment
Environmental health toolkit (http://www.womenshealthandenvironment.org/article.php?list=type&type=64).

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