The Exposure of Fetuses and Children to Endocrine Disrupting Chemicals: A European Society for Paediatric Endocrinology (ESPE) and Pediatric Endocrine Society (PES) Call to Action Statement

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Objective: During recent years, evidence has accumulated that both wildlife species and humans are exposed to ubiquitous endocrine-disrupting chemicals. Some are persistent in our bodies; others are nonpersistent but are produced in large quantities. Hitherto, the bulk of research in this area has been carried out by basic and experimental scientists and wildlife researchers. Relatively few clinical scientists have been engaged in research on this topic to date. The aim of this statement is to have pediatric endocrinologists consider the issue of endocrine disrupters in their clinical work and research.

Participants: Six pediatric endocrinologists who belonged to working groups on endocrine disrupters endorsed by the European Society for Paediatric Endocrinology (ESPE) and the Pediatric Endocrine Society (PES) participated, including three members from each society. Meetings were limited to the members of the working groups. No funding was associated with the work.

Evidence: Important data sources were publications from the World Health Organization, the European Science Foundation, and The Endocrine Society. Several of the participants have made long-standing contributions to the field of endocrine disruption. No unpublished work was considered.

Consensus Process: The statement was written by the committee members together, using e-mail and phone. A draft was submitted to the Boards of the ESPE and PES. After some changes, the draft was accepted by both Boards.

Conclusions: Pediatric endocrinologists are urged to be alert to the possible significance of endocrine-disrupting chemicals when assessing both clinical problems and research data where etiologies of endocrine symptoms or diseases are unknown. **(*J Clin Endocrinol Metab* 96: 3056–3058, 2011)**

In the past 10–15 yr, accumulating scientific evidence indicates that our populations are exposed to ubiquitous endocrine-disrupting chemicals (EDCs) through modern environments and lifestyles. Although some EDCs possess a similar chemical structure, many have quite different molecular structures. What groups them together is their ability to interfere with hormonal systems of living organisms, including humans. The World Health

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Abbreviation: EDCs, Endocrine-disrupting chemicals.

Organization definition of an EDC is "an exogenous substance or mixture that alters function(s) of the endocrine system and consequently causes adverse health effects in an intact organism, or its progeny, or (sub)populations" (1).

The chemicals include several of the so-called persistent EDCs that accumulate in fat tissue (*e.g.* dioxins, polychlorinated biphenyls, pesticides, and brominated flame retardants), whose production and distribution have been limited by legislation because of broad toxicological effects beyond endocrine disruption. Suspected persistent EDCs, some of which are still in production, include perfluorinated compounds, which do not accumulate in fat tissue but rather distribute to various organs where they are thought to bind to cell membranes. Characteristic of the persistent compounds is that they have very long half-lives in the body and the tendency to accumulate over years. Ironically, the most efficient mechanism of reducing the body's load of EDCs may be through pregnancy and breast-feeding, in that the compounds are transferred to the fetus and newborn child via the placenta and breast milk. Another group of chemicals are the nonpersistent EDCs, many of which are still being produced. In fact, some of them, like phthalates and bisphenol A, are manufactured at a global capacity of more than 5 million metric tons because they are used in modern industry as components of a large number of utensils. Some modern pesticides and surfactants also belong to the group of nonpersistent EDCs.

Large studies by U.S. and European authorities have shown that human fluids and tissues contain small concentrations of a high number of EDCs (2, 3). Many chemicals have been shown in animal studies to have endocrine disruptive effects at high concentrations, concentrations at which humans are not routinely exposed. The question remains as to whether the concentrations of EDCs present in humans contribute to disease. As reviewed in a recent statement from The Endocrine Society (4), there is a growing body of evidence from human epidemiological and animal studies to suggest that even small concentrations of EDCs at levels currently present in many humans cause endocrine disruption. Some animal experiments have demonstrated that low exposures to compounds affecting the same signaling route can cause an additive mixture effect. However, other epidemiological and animal studies do not demonstrate endocrine disruption at the small concentrations with single compound exposures. This lack of consensus from researchers impedes public health and government regulatory agencies in their efforts to allow production of chemical products that improve quality of life, whereas limiting production of chemicals that are harmful to the general public. A multidisciplinary effort among epidemiologists, basic scientists, public health officials, endocrinologists, chemical companies, and regulatory agencies is thus necessary to achieve the shared goal of public safety and quality of life.

The questions about EDCs would be theoretical and abstract if we were not presented with many unexplained endocrine phenomena among our patients. Careful cohort studies in the United Kingdom and Nordic countries have shown that 2–9% of newborns have cryptorchidism, and the trends may be increasing, mimicking well-established data on increasing trends in testicular cancer (5, 6). The latter is relevant from a pediatric perspective because more and more evidence suggests that testicular cancer is of fetal origin (7). New research has also linked poor semen quality to fetal exposures. Other common endocrine problems for which we lack explanations are widespread infertility, tendencies of early puberty, some cases of childhood obesity, as well as an increase in type 1 diabetes mellitus, thyroid diseases, and neuroendocrine problems. These unexplained trends in endocrine diseases spur the debate about EDCs from the public health and regulatory sphere into the realm of pediatric endocrinology.

Examining and addressing the public health effect of EDCs is an enormous challenge for both basic and clinical researchers and regulators. Recently, eight American Research Societies in a letter to *Science* (8) wrote: "Although chemical testing and risk assessment have long been in the domain of toxicologists, it is clear that the development of improved testing guidelines and better methods of assessing risks posed by common chemicals to which all Americans are exposed requires the expertise of a broad range of scientific and clinical disciplines." The boards of the European Society for Paediatric Endocrinology and the Pediatric Endocrine Society support this statement and urge their members to be alert to the possible significance of EDCs when assessing both clinical problems and research data about endocrine problems where disease etiologies are lacking. It is well documented that fetuses and children may be very sensitive to exposure from exogenous hormones. We urge participation of pediatric endocrinologists in international research networks for studies of EDCs and their effects on children as recently proposed in a publication from the European Science Foundation [Male reproductive health—its impacts in relation to general well-being and low European fertility rates. European Science Foundation Science Policy Briefing no. 40 (http://www.esf.org/publications/science-policy-briefings.html), 2010].

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