" Endocrine Disruptors: From Wingspread to Eco-Devo ".

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Abstract :

A massive introduction of man-made chemicals into the environment has taken place during the last 60 years. The first indication that these chemicals may be hormonally active was documented in a 1950 publication on the effects of the pesticide DDT. It soon became evident that environmental exposure to these chemicals was detrimental to wildlife species, in particularly, the bald eagle population in the US, which revealed eggshell thinning and failure of the eggs to hatch. Consequently, in the US, agricultural use of the pesticides DDT and kepone were banned in 1973, as were polychlorinated biphenyls in 1977. While this policy had the effect of normalizing eggshell development in the bald eagle population, it revealed the more subtle effects of DDT exposure, namely, the hatchlings showed a diversity of developmental malformations.

In 1991, the Wingspread Conference was held in Wisconsin to address this new development. The participants proposed that the developmental alterations observed in a diversity of wildlife species was due to exposure to multiple chemicals that, through different modes of action, disrupted the endocrine system of the developing organisms. They made the observation that some of the effects observed in the genital tract of wildlife were comparable to those seen in the daughters and sons of women who had been exposed during pregnancy to the synthetic estrogen diethylstilbestrol (DES). It was postulated that the DES syndrome was an extreme expression of the plasticity of the fetus to environmental cues provided by endocrine disruptors such as DDT and PCBs. They noticed that, in addition to the banned chemicals, other sources of endocrine disruptors were being introduced into the environment and human food. The anti-oxidant nonylphenol, which had just been shown to leach from laboratory plastic ware, was one such example and headed a growing list of chemicals that were identified subsequently as being endocrine disruptors; plasticizers, disinfectants, sunscreens and new pesticides were added to the list . The participants of the Wingspread Conference concluded that the developmental abnormalities observed predominantly in birds might portend what was happening in mammals, including humans.

BPA is a monomer used in the manufacture of polycarbonate plastics and epoxy resins from which food and beverage containers, and dental materials are made. BPA has been shown to leach from these materials under normal conditions of use. The actual levels of human exposure to BPA are unknown, however, developmental effects in rodents have been found at doses within those reported to be leaching from dental materials. These effects occurred at exposure levels several orders of magnitude lower than those needed to increase the wet weight of the uterus of prepubescent mice (uterotropic assay), an assay that is considered by toxicologists to be the “gold standard” for testing estrogenicity.

Exposure to environmentally-relevant doses of the xenoestrogen BPA during morphogenesis of estrogen-target tissues and organs results in changes that become fully manifested during adult life. The observed organizational and functional changes provide important pieces of evidence to the understanding of how BPA exposure effects male and female reproduction in mammals. This ongoing research has both practical and theoretical implications. The former is the realization that wildlife and humans are being affected by environmental exposure to endocrine disruptors at levels previously considered to be irrelevant. The latter is that the prevalent view that development is the unfolding of a genetically determined program is incorrect. Developmental biology now has the tools to successfully revisit the old tradition of ecological regulation of development. The emerging field of endocrine disruptors promises to provide new insights into the mechanisms underlying the development of hormone-target organs.