Our Stolen Future: A Review

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Abstract

The publication of *Our Stolen Future: Are We Threatening Our Fertility, Intelligence, and Survival? A Scientific Detective Story* by Theo Colborn, Dianne Dumanoski, and John Peterson Myers in 1996 created a stir in the scientific community. The controversy surrounding the endocrine disruption hypothesis introduced in *Our Stolen Future* rages on while researchers seek to establish clear causal relationships between endocrine disrupting compounds and human health effects. *Our Stolen Future* focuses on Colborn's investigation into how hormone signals required for normal fetal development are affected by exogenous chemicals, and on the effects of altered hormone levels on the health and reproduction of adult organisms. The evidence presented makes a strong case for the endocrine disruption hypothesis. Publication of *Our Stolen Future* has effectively raised public awareness of issues related to endocrine disruption and has prompted numerous studies. The U.S. EPA is responsible for identification and characterization of endocrine disrupting compounds, and the resulting regulatory action. The ultimate effects of *Our Stolen Future* and the endocrine disruption hypothesis on society are yet unknown.

Introduction

The 1996 publication of the book *Our Stolen Future* by Theo Colborn, Dianne Dumanoski, and John Petersen Myers introduced the endocrine disruption hypothesis and challenged conventional approaches to determining the impacts of chemical contamination. The endocrine disruption hypothesis essentially states that certain synthetic chemicals interfere with hormonal messages involved in growth and development. The chemicals implicated in endocrine disruption include persistent organohalogens, selected pesticides, phthalates, heavy metals and alkylphenols, and assorted other compounds. Uses of these chemicals are so widespread that they have become ubiquitous in natural environments (Crews et al. 2000). Many of the suspected endocrine-disrupting chemicals have been widely distributed throughout the global ecosystem by atmospheric and oceanic currents.

Our Stolen Future is a review of more than one thousand research articles and reports detailing birth defects, sexual abnormalities, reproductive failures, behavioral changes, declining sperm counts, and increased rates of hormone-related cancers. The book details the development of the endocrine disruption hypothesis from results obtained during field and laboratory studies. Colborn et al. begin their discussion of endocrine disruption with a series of brief accounts of anomalous behavior and reproductive problems in wildlife populations, which the authors refer to as “omens”.

Our Stolen Future describes Theo Colborn’s efforts to find links between environmental contamination in the Great Lakes region and cancer incidence. What emerged as Colborn continued her research was not a correlation between contaminants and cancer, however, but a pattern of aberrant behavior and physically deformed offspring among wildlife populations in the region. While the adult animals appeared healthy, offspring survival among the wildlife populations around the Great Lakes was low. Tissue analyses performed on wildlife from the Great Lakes region showed elevated levels of certain chemicals including polychlorinated biphenyls (PCBs) and the pesticides dieldrin, DDT, chlordane, and lindane (Colborn et al. 1996).

Recognizing that the observed abnormalities in wildlife could result from altered hormone levels, Colborn shifted the focus of her investigation to hormone disruption by chemical contaminants. *Our Stolen Future* focuses on Colborn's investigation into the role of hormones in fetal development and how the hormone signals required for normal fetal development are affected by chemicals, and on the effects of altered hormone levels on the health and reproduction of adult organisms.

Background

Hormones produced by the endocrine system are the chemical messengers that control normal functions, including sleep, appetite, temperature, growth and development, sexual maturation, and reproduction. Estrogen is a hormone primarily secreted by the ovaries that controls such functions as menstruation, fertility, and maintenance of a healthy pregnancy. In adults estrogen regulates ongoing physiologic processes, and it is essential for normal fetal development because estrogen affects gene expression in the developing fetus.

Many chemicals are able to cross the placental barrier, which means that a developing fetus can be exposed to the accumulated body burden of the mother (Smolen 2000). Nursing further exposes young to concentrated doses of lipophilic compounds bound to fats in breast milk. Exposure to chemicals during embryonic, fetal, and early postnatal development is of particular concern because many developmental processes are occurring during this time. Neural, reproductive, or immune system function may be compromised by exposure to certain chemicals. Development of different systems is known to occur at discrete intervals, thus timing of exposure may be as important as dose. The effects of endocrine disruptors may be magnified through subsequent generations, as the bioaccumulated endocrine-disrupting substances inherited from the mother influence the reproductive development and physiology of offspring as well as the offspring's' reproductive behavior as adults (Crews et al. 2000). Endocrine disruption during development permanently alters physiological processes.

Exogenous chemicals can alter endocrine function by mimicking or blocking the compounds produced by the body, thus altering hormonal levels and disrupting the functions controlled by these hormones. Some chemicals may have an indirect effect by altering the body's ability to produce hormones, interfering with hormone transport, or altering hormone receptors. These compounds that interfere with the role of natural hormones in the body are endocrine-disrupting substances. Most suspected endocrine disruptors are lipid soluble, which means they bioaccumulate in upper trophic levels of food webs (NRDC 1998). The studies described in *Our Stolen Future* that first led Colborn to suspect hormonal disruption were conducted on bald eagles, lake trout, herring gulls, mink, otter, double-crested cormorants, snapping turtles, common terns, and coho salmon, all top predators that fed on fish from the Great Lakes.

In *Our Stolen Future*, Colborn et al. chronicle reproductive failures and abnormal behaviors in wildlife populations and suggest that these problems are due to elevated levels of certain chemicals. Colborn et al. document reproductive failures in Greenland's polar bear population and alligators in Florida's Lake Apopka; abnormal sexual development in herring gull chicks; immune system deficiency in beluga whales living in the St. Lawrence River; declining populations of harbor, ringed, and gray seals in the Baltic Sea; physical deformities in bald eagle chicks, and more. Repeatedly, observations from field studies are supported with evidence from laboratory studies showing that the chemicals in question produce the observed effects.

The endocrine disruption hypothesis introduced in *Our Stolen Future* has had an impact on the regulation of chemicals in the environment. Since the publication of *Our Stolen Future* in 1996, Federal agencies have funded a multitude of research projects related to endocrine disruption, as well as research on the biochemistry of hormones and their regulation of physiological processes. The Food Quality Protection Act (FQPA) and amended Safe Drinking Water Act of 1996 mandated that the U.S. EPA develop a screening program for endocrine

disrupting substances and authorized the EPA to screen drinking water for endocrine disruptors. The EPA has recently begun implementing elements of the Endocrine Disruptor Screening Program, which was designed by an EPA advisory committee to provide methods and procedures to detect and characterize endocrine activity of pesticides, commercial chemicals, and environmental contaminants (EPA 2000). The information gathered by the EPA through this screening program will permit identification of endocrine disruptors and facilitate the enactment of appropriate regulatory action.

Discussion

Colborn et al. present a convincing case for their endocrine disruption hypothesis early on by presenting a brief discussion of the results of thalidomide and diethylstilbestrol (DES) use. The discussion of thalidomide serves a reminder that the placental barrier is permeable to many compounds, whereas the DES case study shows how the human body can mistake a foreign chemical for a hormone and details the significance of disrupting the processes occurring during fetal development. Most people are familiar with thalidomide, a drug first prescribed for pregnant women in Europe during the late 1950's to combat nausea and was later found to cause severe birth defects. The thalidomide tragedy illustrated how a substance that has no ill effects on adults can be unsafe for the developing fetus at the same dose.

Diethylstilbestrol, the synthetic estrogen mimic prescribed in the United States for more than 30 years to prevent miscarriages and premature births, has also been shown to have detrimental effects on fetal development. Unlike thalidomide, however, the effects of DES are not apparent at birth. DES exposure in the womb has been linked to cancer, vaginal tissue malformation, and reproductive tract deformities in young women whose mothers took DES during pregnancy. The severe long-term impact of DES coupled with the lack of obvious birth defects emphasizes the sensitivity of the developing fetus to foreign compounds.

One of the interesting aspects of the DES case is that negative effects of exposure to abnormally high levels of natural or synthetic estrogen in the womb were documented several years before DES was first synthesized. Female rat pups exposed to excess estrogen during fetal development exhibited structural defects of the uterus, vagina, and ovaries, and male pups showed genital deformities and stunted penises (Colborn et al. 1996). Another animal study in 1963 showed the development of cysts and cancers in mice receiving estrogen injections as newborns (Colborn et al. 1996). However, it was not until the early 1970's that DES was identified as a possible cause of clear-cell cancer of the vagina, as later linked to reproductive tract deformities.

Much of the controversy surrounding the endocrine disruption hypothesis set forth in *Our Stolen Future* has focused on the extrapolation of data from animal studies to explain observed human health problems or to predict human health risks. It is important to recognize that there is no fundamental difference between the cellular and molecular processes in animals and those in humans. The same processes that govern cellular communication, energy production, immune response, fetal development, etc., are active in animals and in humans. For this reason, animals have been used for decades to test the safety of consumer products. Why is it that when studies using the same animal species as used in product safety tests indicate a possible problem with certain chemicals, the reliability of data obtained in animal studies is questioned?

Critics also argue that there is not enough evidence to support the endocrine disruption hypothesis. In a June 2000 review published in *Environmental Health Perspectives*, Steven Safe presents data refuting the results of previous studies supporting the endocrine disruption hypothesis. Safe argues that the data collected to date are inconclusive and have been over-interpreted (2000). Others have questioned the experimental protocols used in studies whose data supports the endocrine disruption hypothesis (Ashby and Odum 1998).

While the debate over the validity of some experimental results may never be fully resolved, new research has been published supporting previous reports. A study by Zhan et al. (2000) documented altered levels of the sex hormones 17?-estradiol and 11-ketotestosterone in Crucian Carp (*Carassius auratus gibelio*) exposed to hexachlorobenzene (HCB). The authors noted that female carp were more sensitive to sex alterations caused by HCB exposure than males of the species (Zhan et al. 2000). One particularly interesting recent publication documents abnormally low hormone levels and malformed testicles in deformed frogs in New Hampshire (Sower et al. 2000). The authors rule out parasitic infestation and conclude that disrupted neuroendocrine system development is a likely cause of the frog deformities (Sower et al. 2000).

A study by Willingham et al. (2000) documented altered sex steroid profiles in red-eared slider turtles (*Trachemys scripta elegans*) exposed to three different endocrine-disrupting compounds. The turtles were exposed to chlordane, *trans*-nonachlor, or the PCB mixture Arochlor 1242 during embryogenesis. While the hatchling turtles appeared morphologically normal, sex steroid levels were significantly different when compared to untreated controls (Willingham et al. 2000). Arochlor- and chlordane-exposed male turtles had decreased testosterone levels, whereas chlordane caused reduced levels of testosterone, dihydrotestosterone (DHT), and progesterone in exposed female turtles (Willingham et al. 2000).

Much of the criticism of *Our Stolen Future* centers on the purported effects of endocrine disrupting substances on humans. Some of the more controversial topics discussed in *Our Stolen Future* include declining sperm counts in human males, increased rates of hormone-related cancers and reproductive abnormalities, immune system deficiencies, accelerated sexual development in children, and altered behavior and intelligence. Guo et al. (2000) analyzed sperm from adolescent males exposed prenatally to PCBs and polychlorinated dibenzofurans. The study showed no difference in semen volume or sperm count among

exposed males and unexposed males, but the sperm of the exposed males exhibited abnormal morphology and reduced motility and strength as compared to the control group (Guo et al. 2000). Thus, while the quantity of semen was not affected the quality was significantly different between exposed and unexposed males.

A recent study by Howdeshell et al. (1999) indicates that the plastic component bisphenol A increases the rate of sexual development in mice. Premature sexual development has also been observed in humans. Colón et al. (2000) analyzed blood serum of Puerto Rican girls with premature breast development to search for known endocrine disrupting substances. High levels of phthalate esters were detected in the blood serum of the majority of girls exhibiting premature sexual development, including phthalate esters shown to be estrogenic in recombinant yeast assays (Colón et al. 2000). The authors note that even compounds with weak estrogenic activity may cause disruption in biologic systems if exposure occurs during critical developmental periods (Colón et al. 2000). Recently, the U.S. Center for Disease Control reported that dibutyl phthalate and benzyl butyl phthalate cause reproductive tract defects by blocking androgen production (Renner 2000).

In *Our Stolen Future* Colborn et al. present the results of a study by Jacobsen and Jacobsen, in which the behavior and intelligence of children whose mothers consumed PCB-contaminated fish from the Great Lakes during pregnancy was analyzed. The study found evidence of neurological impairment in the children whose mothers ate Great Lakes fish (Colborn et al. 1996; *"Fooling With Nature"*). Tests at four years of age indicated that children whose mothers had the highest blood serum levels of PCBs had lower scores in verbal and memory tests as compared to a control (Colborn et al. 1996). A recent study by Hussein et al. (2000) showed that exposure to PCB 153 reduced long-term potentiation, a prolonged increase in synaptic responses that is believed to be essential for learning. Interestingly, PCB 153 is one of the most abundant PCBs in human blood serum, and is often considered relatively nontoxic (Hussein et al. 2000).

Although it is difficult to establish direct correlations between environmental contaminants and human health effects, recent evidence indicates that PCBs and related chemicals may weaken the immune system (Kaiser 2000). A study conducted in the Netherlands showed that children with high PCB exposures at age 3½ were more likely to have had chickenpox and ear infections than children with lower PCB exposure (Kaiser 2000). PCBs have also been implicated as causal agents of on-Hodgkin lymphoma. Rothman et al. (1997) found a strong correlation between PCB blood serum levels and incidence of non-Hodgkin lymphoma.

Conclusion

The case of DES is perhaps the most compelling piece of evidence for the endocrine disruption hypothesis, simply because the effects were so severe and occurred so long after exposure to the chemical. Animal studies had reported the detrimental effects of excess estrogen prior to the discovery of human health problems related to DES, but were either disregarded or went unnoticed until evidence was sought to prove the link between health problems and DES. Why did the animal studies fail to serve as a warning? How many people could have been spared health problems had DES been subjected to rigorous testing and its use discontinued earlier?

Critics of *Our Stolen Future* have argued that we lack sufficient evidence to impose regulations on suspected or known endocrine-disrupting substances. Steven Safe warns that it is "important to carefully validate and replicate findings before media announcements that may contribute to unnecessary fear and worry by the public" (2000). At what point do we have enough information to act? According to the precautionary principle, which has been widely accepted both nationally and internationally, if an activity poses a threat to human health or the environment precautionary measures should be taken, even if cause and effect relationships have not been fully established (Tickner 2000). Certainly enough scientific evidence has been

collected to date to indicate that endocrine-disrupting substances represent at least a potential threat to human and wildlife populations.

Establishment of clear causal relationships between endocrine disruptors and human disease may require many more years of research. It is difficult to establish causal relationships between chemical exposure and human health effects due to the complex mixtures of contaminants in the environment and the lack of analytical data documenting contaminant levels throughout the duration of exposure. Historically, wildlife population declines have foreshadowed negative effects on human health, such as the effects of DDT on raptor populations detailed in Rachel Carson's *Silent Spring*. Shouldn't we be concerned that wildlife populations are experiencing reproductive failures? Why do we only become concerned when we believe that human health may be threatened?

Perhaps the endocrine disruption hypothesis has sparked such controversy among the scientific community because it challenges conventional toxicological principles that the toxicity of a compound increases with dose, and that there is a threshold dose below which there is no observed adverse effect. It has been suggested that there may not be a threshold dose for endocrine disrupting compounds (Crews 2000). There is currently no criterion for regulating endocrine disrupting substances and no precedent for the regulation of substances with no threshold dose, which forms the basis of current safety limits. Regulating these compounds will especially difficult because they are widely dispersed in the environment.

There is some concern that the identification and regulation of endocrine disrupting compounds will be economically devastating to certain industries. The question we should ask ourselves, however, is not whether we can afford research and regulation of endocrine disrupting substances, but whether we can afford not to. Endocrine disrupting chemicals have the potential to permanently alter the physiological processes essential to life.

Several books about environmental pollution have been represented as a sequel to Rachel Carson's *Silent Spring*. *Our Stolen Future* lives up to this portrayal. *Our Stolen Future*

is a well-written, well-researched book that should serve as a warning to all of us, and as a call to action for scientists and regulators alike.

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