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Endocrine Disruptors - A Controversy in Science and Policy: Session III Summary and Research Needs

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SESSION SUMMARY

Building on the new synthesis of information introduced at the Wingspread Conference in 1991 (Colborn and Clement, 1992) participants helped frame the concept of “endocrine disruption”. The core observation upon which this concept was based was that some exogenous compounds of both natural and synthetic origin can interact with hormonal systems by one of several mechanisms, including mimicking or blocking receptor binding, altering the rates of hormonal synthesis or metabolism, or affecting receptor availability. Great progress has been made since the Wingspread Conference, but perhaps the greatest progress has been in clarifying the boundaries, and depth, of our ignorance. Five trends can be identified from the new research on endocrine disruptors: (1) exposure levels sufficient to produce profound physiological effects in laboratory experiments are dramatically lower than once thought; (2) endocrine disruptors are not just a small number of persistent bioaccumulative contaminants but rather are found in a broad array of chemical classes which had previously been thought to be devoid of hormonal activity; (3) human exposure to endocrine disrupting chemicals is ubiquitous; (4) every hormonal system examined has been found to be vulnerable to endocrine disruption by exogenous chemicals; (5) in utero exposure to a growing list of chemicals have been found to impact development in ways that may be present at birth, or may not be measurable until adulthood.

The thesis that some pharmaceutical, agricultural, and industrial chemicals can interfere with the hormonal signals in wildlife and humans has been discussed within the scientific community for two decades. The media has responded slowly to the hypothesis linking endocrine-disrupting chemicals to human and wildlife abnormalities until 1996 when the first mass-market book on the subject was published. Following the publication of *Our Stolen Future* (Colborn et al., 1996), there was extensive coverage of the issue in the major national dailies, regional papers, science magazines, and news weeklies. The images that most appealed to the media involved reproduction and sexuality, including the reduced phallus size of alligators and sperm count decline. Some of the science on neurobehavioral effects, which had some of the strongest data backing it, were underrepresented in the media. Loss of IQ and the possibility that in utero exposures to chemicals like PCBs and dioxins can result in ADHD in children were not given a significant presence in the stories. The major media presentations on TV consisted of two programs—an Emmy award-winning BBC documentary titled *Assault on the Male*, and a Frontline PBS Special called *Fooling with Nature*. The former documentary was designed as a strong argument that endocrine disrupting chemicals are hazards to wildlife and are strongly linked to human hazards. *Assault on the Male* was first aired on the Discovery Channel during Labor Day, and was trivialized by the New York Times and other publications. *Fooling with Nature* took a different approach in that it was designed to present both proponents’ and critics’ views of the environmental endocrine hypothesis and

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left the viewer the task of weighing the evidence. Overall, the media still has trouble interpreting and communicating the general hypothesis about chemicals interfering with the hormonal systems of humans and wildlife. First, the explanation embedded in the hypothesis is so wide ranging that it is difficult for most Journalists to follow. Second, the amount of information related to the hypothesis is so vast that it is a challenge for the media to place it in context. Third, journalists seem to be more comfortable with a single chemical, single disease outcome. Finally, the media looks for a blockbuster. It has no interest in the accretion of information. If the theory of endocrine-disrupting chemicals were more formalized as a scientific structure with specific testable hypotheses identifiable to the media, there would be a greater understanding of the progress that is made in either confirming or refuting parts of the theory.

An endocrine system essential for brain development and for which there is growing evidence that environmental chemicals may be interfering with its action is that of thyroid hormone. Thyroid hormone clearly plays essential roles in brain development, as exemplified by clear neurological impairments associated with cretinism and with congenital hypothyroidism. However, until the beginning of this decade, it was believed by some investigators that thyroid hormone only exerted effects on postnatal brain development, and that the fetus was refractory to its action. Because the effects of thyroid hormone are mediated by receptors that function as hormone-responsive transcription factors, the Zoeller laboratory identified a number of genes expressed in the fetal cortex that are selectively regulated by thyroid hormone before the onset of fetal thyroid function. Therefore, thyroid hormone of maternal origin can affect gene expression in the developing cortex. Identification of thyroid hormone-responsive genes in the fetal cortex will help lead us to identify the developmental processes regulated by thyroid hormone. Moreover, these findings suggest that any exogenous chemical that interferes with maternal thyroid function, or with thyroid hormone action, has the potential to interfere with thyroid hormone-responsive developmental processes in the fetal brain. The genes identified by the Zoeller laboratory will be useful biomarkers to test this hypothesis.

RESEARCH NEEDS

The summary of Research Needs in Session III for the Endocrine Disruptors: a Controversy in Science and Policy.

1. Further studies designed to test whether environmental chemicals can cause specific developmental defects by interacting with endogenous endocrine mechanisms.
2. Additional laboratory studies to characterize the low-dose, non-linear, and non-monotonic dose-response characteristics of endocrine disruptors.
3. Development of strategies to characterize the effects of chemical mixtures on endocrine-guided developmental events in both wildlife and humans.
4. Additional studies to define the mechanisms by which hormones can influence early events in the developing brain and in the developing immune system.
5. Continued laboratory research to determine the mechanisms by which classes of environmental chemicals can interfere with hormone action in the adult and during development.
6. Studies aimed at identifying markers of exposure to chemicals and markers of endocrine disruption capable of detection at the time of health impacts which may be decades after exposure.
7. Systematic characterization of human exposure patterns to hormonally-active compounds: what are the exposure pathways and what levels of contamination do they produce?
8. Mechanistic and epidemiological exploration of other systems vulnerable to hormonal disruption, with priority given to those potentially linked to important public health problems. Three examples are: learning disabilities and behavioral disorders; the hormonal control of body weight regulation; and immune system dysfunction.

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