Learning Disabilities Association-Sponsored Symposium on Chemical Hormone Impostors and Child Development

Jerry Heindel

Division of Extramural Research and Training, National Institute of Environmental Health Sciences, Research Triangle Park, North Carolina, USA

The Learning Disabilities Association (LDA) is a parent-run, all-volunteer organization started in 1960. It now numbers 50,000 members with affiliates in every state. The association is self-supported and undertakes advocacy initiatives in the areas of prevention, services, education, and research concerning learning and overlapping developmental disabilities. Originally, the total focus was remediation of specific academic learning disabilities, such as dyslexia, that were evident in the classroom. Over time, attention has broadened with the realization that behavior, social perception, functional coordination, etc. must be considered in the context of whole-person development. The LDA is especially interested in the areas of early assessment and intervention, behavior, social perception, and functional coordination as they pertain to outreach and education. The national LDA maintains 20 committees to cover the multifaceted concerns of members. The committees interact with a myriad of professional and lay sources of information to provide constructive directions and initiatives.

One of the LDA standing committees is the Research Services Committee. A current initiative of this committee is directed at the urgent challenge presented by the recognition that environmental chemicals may be altering hormones, especially those necessary for normal fetal development, and thus contributing to the perceived increase in developmental disabilities. In an effort to address the possible relationship of exposure to endocrine-disrupting chemicals and learning disabilities, the LDA sponsored a symposium, titled "Chemical Hormone Impostors and Child Development: Learning, Behavior and Function," at the LDA International Conference in Atlanta, Georgia, 24–25 February 1999. The Jennifer Altman Foundation, The National Institute of Environmental Health Sciences (NIEHS), The Agency for Toxic Substances and Disease Registry (ATSDR), The Physicians for Social Responsibility, and the U.S. Environmental Protection Agency (EPA) jointly sponsored the symposium.

There is growing evidence that hormonally active chemicals accumulating in the environment worldwide may adversely affect humans and wildlife. There is also evidence that alterations in thyroid hormone levels can compromise brain development from conception on, resulting in learning and functional decrements. Thus the goals of the symposium were to explore the available research data, identify research and policy gaps, identify steps to reduce exposures and motivate public awareness, and to define future directions. The symposium was attended by more than 100 scientists, teachers, and lay persons interested in learning about the current state of knowledge relating exposure to hormonally active compounds, particularly polychlorinated biphenyls (PCBs) and pesticides, with the resulting alterations in brain development, thyroid hormone status, and learning disabilities.

Seven lectures were presented at the symposium. The symposium began with an overview of the data linking exposure to endocrine-active chemicals to human health. Currently the best approach to this problem is to use weight of evidence in determining a possible role of hormonally active compounds; it is difficult to show cause-and-effect relationships between exposure and human disease. Recent laboratory, epidemiologic, and wildlife biologists' studies conducted in the Great Lakes Basin and elsewhere provide a strong weight of evidence for the hypothesis that some environmental chemicals may act as thyroid hormone disruptors. It was proposed that a research program in this area should use a framework of surveillance of populations at risk and an evaluation of the human and animal data, including exposure information. This information could then be used in prevention, risk communication, and education programs.

The next presentation discussed the role of thyroid hormones in development and the possibility that PCBs might exert their toxicity via alterations of thyroid hormone function during development. PCBs and dioxins are structurally related to thyroid hormones and there is a growing literature which suggests that one pathway by which PCBs may exert their neurotoxicity may be via interference with thyroid hormone metabolism. Thyroid hormones have profound effects on neurologic function in people of all ages. However, hypothyroidism during development caused by genetic or environmental agents produces irreversible neurologic damage ranging from behavioral problems, impaired learning, and memory to gross mental retardation. PCBs can interfere with the action of thyroid hormones during development at numerous stages, resulting in learning and memory disorders. However, data directly linking PCBs to alterations in thyroid hormones are scant.

The next presentation discussed the human data relating developmental exposures to environmental toxicants and learning disabilities. There are several studies sponsored by the NIEHS and the ATSDR that show the effects of eating PCB-contaminated fish from the Great Lakes. These studies showed that pregnant women who consumed several meals of PCB-contaminated fish per month during pregnancy gave birth to infants with small but detectable learning and behavioral deficits. When these children were 11 years of age, the intelligence quotient (IQ) scores of the children with the highest PCB exposures were on average 6 points lower than children exposed to PCBs at lower levels. Although this change in IQ would not normally be noticeable and is functionally not important to children with an average score, this exposure appears to increase the proportion of children performing in the low normal range who are likely to be struggling to keep up in a normal classroom setting. As important as these data and those of the other confirmatory studies are, they must be interpreted cautiously because the mechanism of the effects of *in utero* exposure to the PCBs has not been elucidated. At present, although it is possible that these PCB-related effects are due to altered thyroid hormones, endocrine modulation is only one of several possible mechanisms.

A discussion of the data showing a genetic mutation in the human thyroid receptor and its relation to attention deficit hyperactivity disorder (ADHD) followed the discussion on PCBs and thyroid function. ADHD is a childhood disorder characterized by impulsiveness, distractibility, inattention, and hyperactive behavior. Currently, the generally accepted prevalence estimates for ADHD range from 3 to 10% of all school-age

Address correspondence to J.J. Heindel, OSTB OPD DERT, NIEHS (EC-23), PO Box 12233, Research Triangle Park, NC 27709-2233 USA. Telephone: (919) 541- 0781. Fax: (919) 541-2843. E-mail: heindelj@niehs.nih.gov

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children. Four to eight times as many boys as girls have the disorder. An autosomal disease in which there is resistance to thyroid hormone (RTH) has been characterized as a mutation in the human thyroid receptor gene on chromosome three. Seventy percent of children with RTH also have ADHD. This single gene disorder represents a unique genetic model to study prospectively the neurodevelopmental manifestations of the disruption of thyroid hormone regulation. In addition to ADHD, other central nervous system manifestations of RTH include decreases in IQ (on average 10–12 points lower than unaffected siblings); abnormalities of myelin formation, as shown by smaller corpus callosum size; language disorders; and abnormalities of brain metabolism and brain morphology. To examine the details of this disorder, RTH transgenic mice have been created. They have a similar phenotype as humans with RTH, including increased locomotor behavior, memory impairment reversed by amphetamine, and smaller corpus callosum size. The convergence of studies that describe the neurodevelopmental consequences of moderate impairment of thyroid function, such as that in RTH in humans, with those of animal and human studies demonstrate the adverse behavioral effects of perinatal exposures to PCBs and other dioxin-like chemicals. These data also provide justification to measure thyroid and related hormones in newborns as well as to use brain imaging techniques to study humans exposed to these chemicals *in utero*.

A final scientific presentation showed that it is not just exposures to PCBs *in utero* that have been associated with learning and memory problems. Similar deficits have been noted after exposure to lead, methylmercury, and some pesticides. A study was discussed that examined farmers in Mexico who use pesticides on their crops and compared the health and behavior of their children to children from similar families who did not use pesticides. Because these are field studies, nonclassical methods have been developed to measure learning, memory, and physical ability. For example, children 4–5 years of age were asked to draw a picture of a person. The children from the area that never used pesticides drew a normal stick-type person whereas the children from the area that used pesticides could only scribble and showed no ability to draw anything resembling a person. The children of the pesticide users were also hyperactive, less coordinated physically, and had increased incidence of illness (more colds and infections and more stomachaches and vomiting). No measurements of pesticide residues in the parents or children have been made; therefore it is not possible to make a connection between *in utero* exposure to any pesticides and the learning and memory deficits measured in this study. Nonetheless, the difference in the health of the two populations, which are so similar in other respects, is striking and worthy of further research.

Both the NIEHS and the EPA have intense interest and significant research efforts in the area of endocrine-disrupting chemicals and the symposium closed after an overview of these agencies' interests. The EPA has been mandated by Congress to develop and implement a program to detect endocrine-disrupting chemicals. After more than a year of meetings, a committee formed by the EPA has developed a scheme to detect endocrine-disrupting chemicals, and it is currently being tested and validated. In addition EPA investigators are working to address issues of low-dose effects, international harmonization of guidelines, and the need for the evolution of a screen for developmental neurotoxicity. The NIEHS has a large portfolio of research grants and intramural research projects examining the question of the importance of exposure to endocrine disruptors to human health. These projects include studies on the role of *in utero* exposure to lead, methylmercury, PCBs, dioxin, and several pesticides in the development of the brain and subsequent learning disabilities including ADHD. Protecting children's health is a major area of emphasis of NIEHS research. Recent examples of the NIEHS commitment to this area are the funding of eight Children's Environmental Health Research Centers. The centers are funded jointly with the EPA and the Centers for Disease Control and Prevention. A recent request for applications in the area of developmental neurotoxicity and several intramural research projects examines the prevalence and causes of ADHD and the effects of PCBs on learning and memory.

The formal symposium was followed by a half-day roundtable discussion by presenters, sponsors, and distinguished invitees to decide future directions. There was considerable discussion on the need to support the studies that will show if indeed there is a cause-and-effect relationship among exposure to endocrine-disrupting chemicals such as PCBs, methylmercury, and some pesticides *in utero*, alterations in thyroid hormones, and alterations in learning and behavior. The best approach would be a coordinated effort of the LDA, ATSDR, EPA, and NIEHS to ensure funding for research that would answer this important question. There was also a resounding consensus that the compelling role for volunteers should be to concentrate on collaboration and cooperation among groups to create a more cohesive national movement to support increased research on the causes of learning disabilities and intervention and prevention strategies.

Speakers

Christopher DeRosa
Agency for Toxic Substances and Disease Registry
Atlanta, Georgia

Susan Porterfield
Medical College of Georgia
Augusta, Georgia

Joseph Jacobsen
Wayne State University
Detroit, Michigan

Peter Hauser
Baltimore VA Medical Center and the University of Maryland School of Medicine
Baltimore, Maryland

Elizabeth Guillette
University of Arizona
Tucson, Arizona

Lynn Goldman
Johns Hopkins University School of Hygiene and Public Health
Baltimore, Maryland

Jerry Heindel
National Institute of Environmental Health Sciences
Research Triangle Park, North Carolina

Audrey McMahon
Learning Disabilities Association
Pittsburgh, Pennsylvania