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Introduction

The Developing Brain and the Environment: An Introduction

Bernard Weiss[1] and Philip J. Landrigan[2]

[1]Department of Environmental Medicine, University of Rochester School of Medicine and Dentistry, Rochester, New York, USA; [2]Department of Community and Preventive Medicine, Mount Sinai School of Medicine, New York, New York, USA

Thalidomide, advertised in the 1950s as a safe drug for morning sickness in pregnancy and as a sedative, created an epidemic of 15,000 babies worldwide with missing limbs (*1*). As we discovered later, thalidomide also caused other developmental disabilities including mental retardation and autism (*2*,*3*). Graphic depictions of children deformed by thalidomide aroused the public and its elected representatives and provoked new laws and regulations designed to prevent a recurrence. A birth defects surveillance program was put into place at the Centers for Disease Control (CDC) in Atlanta, Georgia, and continues to this day. New drugs now undergo extended testing for their potential to induce birth defects.

Today, 40 years later, we are coming to realize that the thalidomide tragedy was not an exception, but, rather, a warning. We have come to understand that chemicals in the environment can cause a wide range of developmental disabilities in children, and that anatomic malformations are only the most obvious. Current concerns especially focus on the concept that certain chemicals can cause clinical and subclinical deficits in neurobehavioral development through injury to the fetal brain. The implications of small shifts in intelligence quotient score and a slightly increased tendency to aggression are not so easily conveyed or grasped as a picture of deformed limbs. However, recognition of the importance of such changes is gathering momentum and is documented in this monograph.

A prime motivating force is the realization that we know the causes of fewer than 25% of neurodevelopmental disabilities. These disabilities, including dyslexia, attention deficit hyperactivity disorder (ADHD), intellectual retardation, and autism, affect an estimated 3-8% of the 4 million babies born each year in the United States. Some of these disorders are of genetic origin; some are caused by chromosomal aberrations such as fragile X syndrome and Down syndrome; some are the consequence of untoward events in early life such as perinatal anoxia and meningitis; and some result from exposures *in utero* to drugs of abuse such as alcohol, cocaine, heroin, and probably nicotine. But for most neurodevelopmental disabilities, the cause remains unknown.

A diverse assortment of toxic chemicals in the environment is capable of causing neurodevelopmental disabilities. For example, elevated blood lead levels and lead poisoning still affect nearly 1 million children in the United States (*4*), and

prenatal exposure to even relatively low levels of lead result in lifelong reductions of intellectual function and disorders of behavior (*5*,*6*). Polychlorinated biphenyls (PCBs) are distributed widely in the environment and cross the placenta to cause *in utero* injury to the developing brain (*7*,*8*). Organic mercury compounds are among the most potent developmental neurotoxicants (*9*,*10*). Certain pesticides are documented to induce prenatal brain injury in rodent species and to result in functional deficits (*11*,*12*); the possibility that they produce similar effects in humans helped spur passage, in 1996, of the Food Quality Protection Act (*13*).

Little information on possible toxic potential is available for the 80,000 chemicals registered today with the U.S. Environmental Protection Agency (EPA). Of the 3,000 chemicals produced or imported at over 1 million pounds a year, only 43% have received even minimal toxicologic assessment, and a mere 23% have been tested to determine whether they have the potential to cause developmental damage (*14*). In the words of pediatrician Herbert L. Needleman, "We are conducting a vast toxicologic experiment in our society, in which our children and our children's children are the experimental subjects" (*15*).

We are faced with two major unanswered questions. First, to what extent do chemicals in the environment cause neurodevelopmental disabilities or other developmental disorders? Second, which chemicals in the environment in addition to lead, PCBs, and methyl mercury can cause neurodevelopmental disabilities? These are critical questions to address and resolve, because disabilities arising from exposure to toxic chemicals should be preventable.

The articles published in this monograph reflect the mounting concern that for too long we have neglected the possibility that environmental chemicals contribute to developmental disabilities in our children. Most of these reports are culled from two major conferences held in 1998 and 1999 devoted to the question of how children's neurobehavioral development is influenced by the chemical environment.

The first of these conferences, The Role of the Environmental Neurotoxicants on Developmental Disabilities, held at the University of Rochester in Rochester, New York, on 23-25 September 1998, arose from a desire to bridge the continuing disjunction between two distinct research areas, neurotoxicology and developmental pediatrics. Their literatures, practitioners, and approaches inhabit separate universes. The conference was designed to unite them. It convened a group of government and university scientists and clinicians to examine the scientific basis for relationships between exposure to environmental neurotoxicants and the incidence, prevalence, etiology, severity, and pathophysiology of developmental disabilities. It also strove to join these two disparate disciplines and perspectives to examine how they are intertwined, to identify gaps in our understanding of their relationships, and to recommend a program of research.

The Rochester conference represented the 20th in a series on environmental toxicity that began in 1968 with *Chemical Fallout* (*16*). The proceedings, published in 1969, linked two emerging environmental problems, contamination by organomercurials and organochlorines, with two groups of experts--ecologists viewing the problem from one angle and toxicologists and environmental health specialists from another. The 20th conference, like the first, used the power of binocular vision to view the problem, so to speak, in three dimensions. The proceedings were divided into four sessions: *a*) mental retardation: timing and thresholds; *b*) endocrine dysfunction and developmental disabilities: dose and target implications; *c*) attention-deficit disorder-ADHD and learning disabilities; and *d*)

new horizons: extending the boundaries.

Support for the Rochester conference came from both public and private sources. The National Institute of Environmental Health Sciences (NIEHS), the National Institute of Child Health and Human Development, and the EPA represented the federal government. The conference also received grants from several foundations: the Jennifer Altman Foundation, the Heinz Family Foundation, the National Alliance for Autism Research, the Violence Research Foundation, the Wacker Foundation, and the Winslow Foundation.

The second of these conferences helped launch a new Center for Children's Health and the Environment at the Mount Sinai School of Medicine. It was held in New York City on 24-25 May 1999, and was convened specifically to consider the intersection between neurodevelopmental impairment, environmental chemicals, and prevention. Over 300 health scientists, pediatricians, and public health professionals examined the growing body of evidence linking environmental toxins to neurobehavioral disorders. The conference title was Environmental Influences on Children: Brain, Development, and Behavior. The conference began by reviewing well-known examples of deleterious effects of environmental chemicals, including lead and PCBs, on children's brains. The conferees then considered the potential impact of environmental chemicals on neurological disorders with particular focus on ADHD, autism, and Parkinson's disease. The inclusion of Parkinson's disease was intended to signal the notion that exposures in early life may have an influence on the evolution of neurological disease in later life.

Support for the Mount Sinai conference came from the Superfund Basic Research Program (NIEHS); The Pew Charitable Trusts; the Institute for Health and the Environment at the University of Albany School of Public Health; the Agency for Toxic Substances and Disease Research (ATSDR); the Ambulatory Pediatric Association; Myron A. Mehlman, PhD; the National Center for Environmental Assessment (EPA); the National Center for Environmental Health (CDC); the National Institute of Child Health and Human Development; the Office of Children's Health Protection (EPA); Physicians for Social Responsibility; The New York Academy of Medicine; The New York Community Trust; and the Wallace Genetic Foundation.

The impact of environmental toxins on children's health has become a topic of major concern in the federal government. Eight new research centers in children's environmental health have been established in the past 2 years with joint funding from EPA and NIEHS. Clinical units that specialize in the treatment of children with environmentally induced illness have been developed across the nation with grant support from ATSDR. The American Academy of Pediatrics has just published its *Handbook of Pediatric Environmental Health* (*17*), the "Green Book," which is available to pediatricians throughout the Americas.

Children's environmental health has climbed to a critical position as we launch the new millennium. This monograph marks a significant milestone in the evolution of this emerging discipline.

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