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ABSTRACT. Recent public recognition that children are different from adults in their exposures and susceptibilities to environmental contaminants has its roots in work that began >46 years ago, when the American Academy of Pediatrics (APA) established a standing committee to focus on children's radiation exposures. We summarize the history of that important committee, now the AAP Committee on Environmental Health, including its statements and the 1999 publication of the AAP Handbook of Pediatric Environmental Health, and describe the recent emergence of federal and state legislative and executive actions to evaluate explicitly environmental health risks to children. As a result in large part of these efforts, numerous knowledge gaps about children's health and the environment are currently being addressed. Government efforts began in the 1970s to reduce childhood lead poisoning and to monitor birth defects and cancer. In the 1990s, federal efforts accelerated with the Food Quality Protection Act, an executive order on children's environmental health, the Agency for Toxic Substances and Disease Registry/Environmental Protection Agency Pediatric Environmental Health Specialty Units, and National Institute of Environmental Health Sciences/Environmental Protection Agency Centers of Excellence in Research in Children's Environmental Health. In this decade, the Children's Environmental Health Act authorized the National Children's Study, which has the potential to address a number of critical questions about children's exposure and health. The federal government has expanded efforts in control and prevention of childhood asthma and in tracking of asthma, birth defects, and other diseases that are linked to the environment. Efforts continue on familiar problems such as the eradication of lead poisoning, but new issues, such as prevention of childhood exposure to carcinogens and neurotoxins other than lead, and emerging issues, such as endocrine disruptors and pediatric drug evaluations, are in the forefront. More recently, these issues have been taken up by states and in the international arena. *Pediatrics* 2004;113:1146–1157; *child, child welfare, environmental exposure, environmental health, environmental pollutants, human risk assessment, public policy.*

ABBREVIATIONS. AAP, American Academy of Pediatrics; COEH, Committee on Environmental Hazards/Health; NICHD, National Institute of Child Health and Development; NIEHS, National Institute of Environmental Health Sciences; EPA, Environmental Protection Agency; CDC, Centers for Disease Control/Centers for Disease Control and Prevention; ATSDR, Agency for Toxic Substances and Disease Registry; NRC, National Research Council; FDA, Food and Drug Administration; PCB, polychlorinated biphenyl; HPV, high-production volume; HUD, Department of Housing and Urban Development; FQPA, Food Quality Protection Act; NCSL, National Conference of State Legislatures; CEC, Commission for Environmental Cooperation; WHO, World Health Organization; UNEP, United Nations Environment Program.

Pediatric environmental health, also known as environmental pediatrics, is an area that has gained prominence in recent years. Pediatric environmental health is based on the understanding that children have patterns of exposure and susceptibilities to toxic chemicals in the environment that have no counterparts in adult life. Corollary to this understanding is the recognition that pediatricians and others who care for children need to become more knowledgeable about environmental effects on children's health.

The American Academy of Pediatrics (AAP) has played a pivotal role in launching pediatric environmental health in the United States. Pediatricians have been centrally involved in the past 30 years in clinical practice, research, advocacy, and education in this relatively new field. This article reviews the history of pediatric environmental health and summarizes major pediatric environmental health achievements in public policy and legislation at the federal, state, and international levels.

EMERGENCE OF PEDIATRIC ENVIRONMENTAL HEALTH

The field of pediatric environmental health traces its origins to a decision made by the AAP in 1957 to establish a Committee on Radiation Hazards and Epidemiology of Malformations.[1] Fear of nuclear war was widespread, especially in regard to children, who had school drills in what to do in case of an atomic attack. In 1954, fallout from a nuclear weapons test on Bikini Island in the South Pacific caused Marshall Islanders to develop burns of the

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feet from β radiation, a prompt effect that is only skin deep. On Rongelap, the most heavily exposed island, 2 children who were exposed in the first year of life soon developed severe hypothyroidism. Among 18 children who were exposed under 10 years of age, 14 developed thyroid neoplasia (13 benign, 1 malignant) and 1 developed leukemia.[2] At approximately the same time, fallout in southwestern Utah from tests in Nevada apparently caused sickness in sheep; people who were exposed worried about late effects. Many news stories told of scientists who claimed that fallout, as it moved east, was causing increased leukemia, other childhood cancers, and perinatal mortality. In 1956 Alice Stewart, a British epidemiologist, published an observation of a possible linkage between diagnostic exposure to ionizing radiation and childhood leukemia.[3] That same year, expert committees of the National Academy of Sciences and the British Medical Research Council reported on their reviews of the biological effects of ionizing radiation in the human. They reported excessive exposure to medical radiographs, as in the use of fluoroscopy instead of films, and radiotherapy for benign disorders. This information led to a marked reduction in unnecessary exposures.

In 1961, the AAP's concern for the relationship between children and the environment in general was reflected by a change in the name to the Committee on Environmental Hazards (COEH). In 1991 "Health" was substituted for "Hazards" to emphasize prevention. In 1966, the time was right for an expert overview of radiation effects focusing on children, so the COEH organized a Conference on the Pediatric Significance of Peacetime Radioactive Fallout, held in San Diego, California. The participants included pediatricians, radiobiologists, scientists from government agencies, and Dr Benjamin Spock, who spoke on psychological effects in children. The proceedings were published as a supplement to *Pediatrics* in 1968.[4]

As chemicals increasingly permeated the environment, the COEH saw the need for a conference on the Susceptibility of the Fetus and Child to Chemical Pollutants, held in 1973 at Brown's Lake, Wisconsin.[5] Original thinking and approaches were sought by bringing together scientists who knew about environmental effects but not about child health and pediatricians who knew about child health but had not considered environmental effects. Among their observations were the following:

1. No federal health agency was responsible for research into the special exposures and susceptibilities of the fetus and child—the National Institute of Child Health and Development (NICHD) was thought to be a good candidate for this endeavor.
2. The COEH should add liaison members from NICHD, the National Institute of Environmental Health Sciences (NIEHS), the Environmental Protection Agency (EPA), and the Centers for Disease Control (CDC), a suggestion that was implemented.
3. The fullest possible use of registries should be made for monitoring congenital malformations, a suggestion that has been taken up by the CDC.
4. A greater interaction between COEH and AAP chapters should be encouraged by exchange of information with chapters and by inviting chapter representatives to meetings held near AAP headquarters.
5. Attention should be given to hazards in newborn nurseries, a suggestion that was implemented with regard to the possibility that the interaction of noise from the incubator and the aminoglycoside antibiotics administered to newborns results in deafness, that mercury from thermometers that are broken in incubators is toxic to newborns, and that skin temperature sensors in infant radiant warmers may come loose and measure the temperature of the air rather than the infant, resulting in death by hyperthermia.
6. At the end of the meeting, pediatrician and Nobel laureate Frederick C. Robbins gave a summary of the importance of environment on child health, as brought out by the conference. The meeting led to greater interactions between pediatric experts and federal agencies concerned with the environment. The proceedings, including the full discussions, were published as a supplement to *Pediatrics* in May 1974.[5]

Because of growing concern about chemicals and health,[6,7] in 1981 the Ross Conference on Pediatric Research focused on Chemical and Radiation Hazards to Children.[8] This conference led to additional interactions between the committee and federal environmental health agencies. A second Ross Conference on Environmental Health was held in 1995, and the proceedings were distributed to general pediatricians throughout the United States.[9]

For >40 years, the COEH has prepared evidence-based statements and technical reports to advise pediatricians about diagnosis, treatment, and prevention of environmental hazards (Table 1). COEH statements usually include recommendations to health care providers and to government.

An important step toward building a new field of knowledge was the preparation of a book that consolidates the body of knowledge in the field. In 1995, the COEH set out to prepare a manual for pediatricians on pediatric environmental health. The *AAP Handbook of Pediatric Environmental Health*, published in 1999, included 33 chapters of information for pediatricians and other child health providers about the identification, treatment, and prevention of environmental hazards.[1] This manual was distributed to >20 000 pediatricians. A second edition was published in 2003.

Reflecting the goal of broadening environmental educational efforts to pediatric trainees, the COEH sponsored yearly educational workshops for incoming pediatric chief residents at the meetings of the Pediatric Academic Societies in 2000–2003. In this activity, sponsored by the EPA Office of Children's Health Protection, residents created presentations about environmental health topics based on informa-

TABLE 1. Statements of the AAP

1960s
Radiation Hazards and Epidemiology of Malformations on Diagnostic Use of X-Ray (1961)
Statement on the Use of Diagnostic X-Ray (1961)
Hazards of Radioactive Fallout (1962)
Present Status of Water Pollution Control (1964)
Smoking and Children: A Pediatric Viewpoint (1969)
1970s
More on Radioactive Fallout (1970)
Pediatric Aspects of Air Pollution (1970)
Acute and Chronic Childhood Lead Poisoning (1971)
Neurotoxicity From Hexachlorophene (1971)
Earthenware Containers: A Potential Source of Acute Lead Poisoning (1972)
Lead Content of Paint Applied to Surfaces Accessible to Young Children (1972)
Pediatric Problems Related to Deteriorated Housing (1972)
Animal Feedlots (1973)
Noise Pollution: Neonatal Aspects (1974)
Effects of Cigarette Smoking on the Fetus and Child (1976)
Carcinogens in Drinking Water (1976)
Hyperthermia From Malfunctioning Radiant Heaters (1977)
Infant Radiant Warmers (1978)
National Standards for Airborne Lead (1978)
PCBs in Breast Milk (1978)
1980s
The Environmental Consequences of Tobacco Smoking: Implications for Public Policies
That Affect the Health of Children (1982)
Special Susceptibility of Children to Radiation Effects (1983)
Involuntary Smoking: A Hazard to Children (1986)
Statement on Childhood Lead Poisoning (1987)
Smokeless Tobacco—A Carcinogenic Hazard to Children (1985)
Asbestos Exposure in Schools (1987)
Radon Exposure: A Hazard to Children (1989)
1990s
Lead Poisoning: From Screening to Primary Prevention (1993)
Ambient Air Pollution: Respiratory Hazards to Children (1993)
Use of Chloral Hydrate for Sedation in Children (1993)
PCBs in Breast Milk (1994)
The Hazards of Child Labor (1995)
Environmental Tobacco Smoke: A Hazard to Children (1997)
Noise: A Hazard to the Fetus and Newborn (1998)
Risk of Ionizing Radiation Exposure to Children (1998)
Toxic Effects of Indoor Molds (1998)
Screening for Elevated Blood Lead Levels (1998)
Ultraviolet Light: A Hazard to Children (1999)
Thimerosal in Vaccines—An Interim Report to Clinicians (1999)
2000s
Chemical-Biological Terrorism and Its Impact on Children: A Subject Review (2000)
Irradiation of Food (2000)
Technical Report: Mercury in the Environment: Implications for Pediatricians (2001)
Technical Report: Pediatric Exposure and Potential Toxicity of Phthalate Plasticizers (2003)
Radiation Disasters and Children (2003)

tion in the *AAP Handbook of Pediatric Environmental Health*. All presentations were subsequently distributed to participants for use in teaching junior residents. Approximately 150 residents participated in these sessions over 4 years.

In 2001, the COEH held a workshop in Phoenix, Arizona, sponsored by the Agency for Toxic Substances and Disease Registry (ATSDR) titled "A Partnership to Establish an ''Environmental Safety Net' for Children." This workshop brought together representatives from each AAP chapter and representatives of the ATSDR and the EPA. The goal was to educate participants on key pediatric environmental health issues, enabling them to better identify, prevent, and treat environmental health hazards. The workshop also fostered communication between pediatricians and public health officials. The proceedings of that workshop were published in a supplement to *Pediatrics* in July 2003.[10]

Effort on pediatric environmental health has expanded beyond the COEH to other parts of the AAP and to other pediatric professional organizations. In 2002, the AAP formed a Nexus on Environmental Health. The Nexus is similar to AAP sections in that it has a primary focus on education and advocacy. It aims to build working ties with AAP chapters and districts.

The AAP established its Center for Child Health Research in 2000. This center has spearheaded the effort to make tobacco a pediatric issue by creating and implementing effective clinical and community-based anti-tobacco roles for pediatricians.

In 2002, the Ambulatory Pediatric Association launched the first fellowship program in pediatric environmental health.[11] This cross-disciplinary fellowship program provides 3 years of specialized postresidency training in environmental pediatrics at academic training sites.

AN EVOLVING ROLE FOR GOVERNMENT

The AAP COEH and other children's advocates have emphasized that government agencies must address the impacts of environmental toxicants on children's health. Considerations of children's risks need to be incorporated at all aspects of government, including regulatory policy, health promotion activity, public health surveillance, and research. At core, child protective standards need to account for unique aspects of children's risks. In 1983, in an attempt to standardize environmental health risk assessment, the National Research Council (NRC) proposed a 4-step risk assessment model that has been widely adopted and applied: 1) hazard identification, 2) dose–response assessment, 3) exposure assessment, and 4) risk characterization.[12] When evaluating whether and how children's risks are being considered, it is useful to ask several questions: Does the hazard assessment assess hazards that are likely to occur during fetal and childhood development? Does the dose–response assessment take into account these hazards for children? Does the exposure assessment incorporate knowledge about children's intake rates (of, eg, air, food, water) and the pharmacodynamics of chemicals at various stages of development? Does the risk characterization incorporate

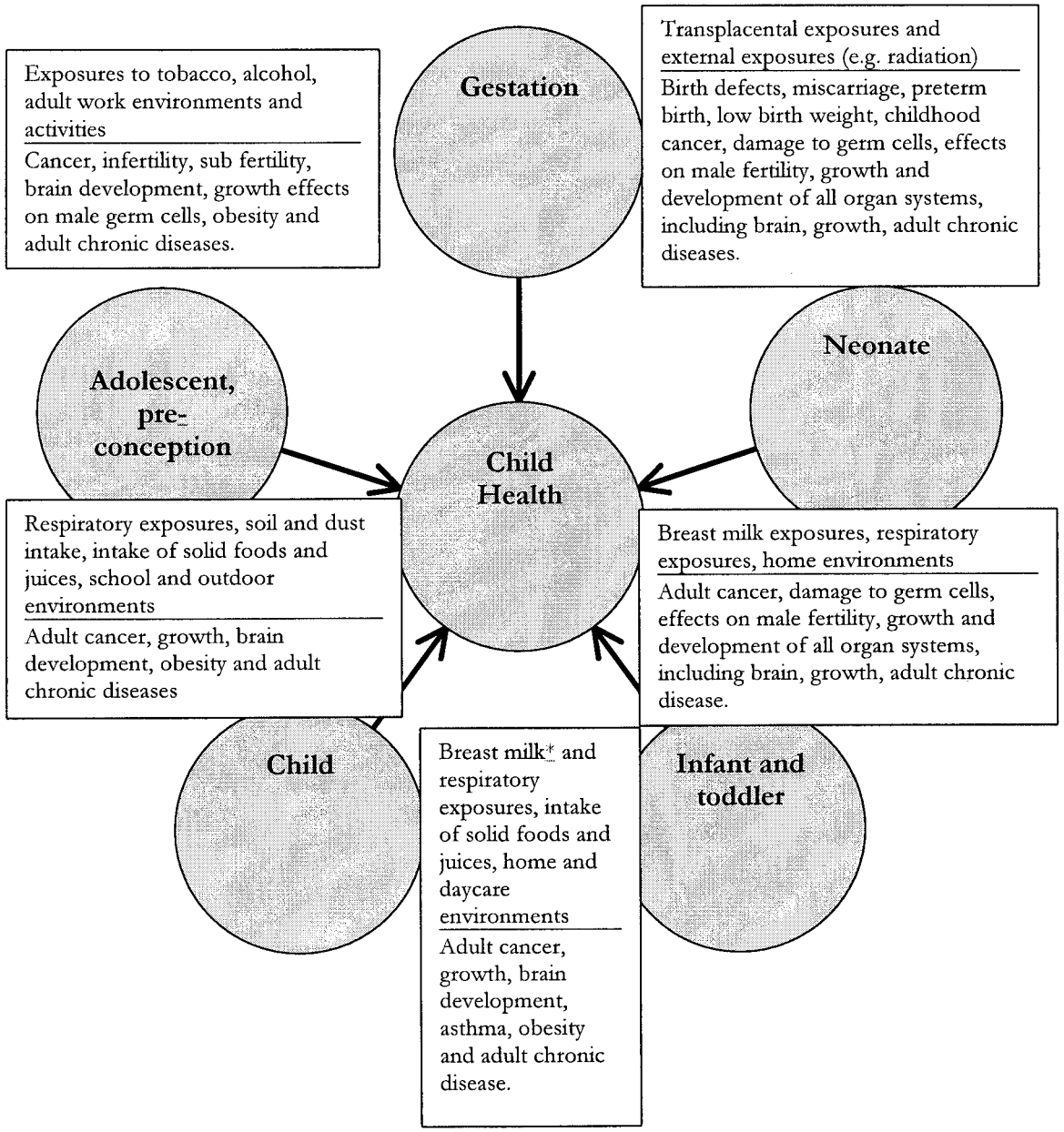

Fig 1. A proposed lifecycle approach for identifying exposure pathways of concern and windows of vulnerability for adverse health effects in childhood and adult disease.

reasonable exposure scenarios for children? Figure 1 shows a "lifecycle approach" that is proposed as a roadmap for risk assessment in the federal government, to ensure that children's risks are fully accounted for. It outlines a schematic for an approach to identify risks to children at various stages of development, known as "exposure windows." These are critical times during which development may be particularly susceptible to derangement by toxicants in the environment. Concern begins with exposures that might occur to parents before conception and continues with exposures and events during various stages of fetal and child development (gestation, neonate, infant and toddler, childhood, and adolescence) and completes the circle with exposures early in life that potentially have an effect on health in the next generation.

In consideration of how government addresses children's risks, several critical issues are in the forefront. First is that the majority of standards-setting activities in the United States are conducted by the federal government; thus, the focus of this discussion is on federal activities. Second is that the federal government not only sets standards but also plays the most significant role in funding research to provide the information that is required by the risk assessment process. Several areas have been the focus of federal activity over the years: cancer, birth defects, neurotoxic agents, and asthma. More knowledge is needed about these and other health hazards to children to identify preventable hazards in the risk assessment process. Likewise, the federal government funds or directly carries out most efforts that provide assessment of exposure to children. Exposure assessment needs to be done so that it is possible to distinguish exposures that may occur at these various life stages so that exposures and hazards can be linked together appropriately in the risk assessment process. This is a new paradigm for risk assessment. Only recently has the federal government begun to consider the unique exposure patterns of children, and it has yet to take the comprehensive approach that is portrayed in Fig 1.

Cancer

Two early events, the discovery of the link between prenatal radiation and childhood leukemia and the diethylstilbestrol disaster, generated early interest by risk assessors in the issue of susceptibility of children to carcinogens. Adding to the concerns raised by Dr Stewart's observations in 1956,[3] the studies of Japanese children who were exposed to A-bomb radiation have found that these children, as they grew, had higher rates of childhood leukemia than unexposed children.[13] Exposure to A-bomb radiation in childhood also was associated with higher rates of adult cancers, particularly cancer of the breast.[14,15]

The hormone diethylstilbestrol caused cancer in offspring of women who were given the drug during pregnancy.[16] In all, between 1 in 10 000 to 1 in 100 000 girls who were exposed in utero during the first trimester of pregnancy later developed vaginal cancer. (In addition, there was a high rate of teratogenicity observed in the offspring.) Increased cancer rates in male offspring have not been confirmed; however, follow-up studies are under way.[17]

Toxicology studies have shed some light on the issue of transplacental and childhood carcinogenesis. Although these studies have been limited, they suggest that adult carcinogens cause cancer when they are delivered in utero as well and that a greater frequency of tumors has been found. The design of these studies did not allow for a determination of whether this was because of increased susceptibility, increased dosing (the dose to the fetus was not measured), increased time to tumor (because of dosing earlier in life), or some combination of these factors.[18,19] For animals, there is evidence that mutagen exposures to germ cells can lead to an excess of tumors in offspring.[18–20] However, a recent review of the evidence for a number of paternal exposures and childhood cancers was inconclusive.[21] A number of factors that may be involved with the greater susceptibility of the fetus have recently been reviewed.[22] Although there is increased concern for exposure to carcinogens, particularly in utero and to the neonate, in practice, cancer bioassays that are conducted for regulatory purposes by the EPA and the Food and Drug Administration (FDA) have relied on testing of mature animals, and, in the past, susceptibility of the young has not been taken into account. There have been technical difficulties in the design of appropriate animal studies, and it has been difficult to monitor doses that are received by the fetus in utero. New models of whole-animal and in vitro germ cell and neonatal/perinatal carcinogenesis will need to be developed, models that can be conducted in a standardized way and with a minimum of burden on animals. As a means of establishing priorities for such research, known exposures to carcinogens (eg, using lists such as the ATSDR superfund list, biomonitoring of mothers and newborns) might be used as a starting point for design of new epidemiology and laboratory investigations.

Birth Defects

Birth defects are the number 1 cause of infant mortality in the United States and result in major costs to families and to the health care system. Birth defects have been a federal concern relative to environmental exposures ever since the epidemic of phocomelia (a limb malformation) that occurred with gestational use of the sedative thalidomide to control morning sickness.[23] Much later it was reported that there seemed to be an unusual incidence of autism among children with phocomelia, suggesting a common cause and window of vulnerability.[24,25] Although there was a major epidemic of phocomelia in Europe, fewer cases occurred in the United States as a result of the refusal of a single medical officer at the FDA, Dr Frances Kelsey, to approve thalidomide for morning sickness.[26]

A number of other episodes also brought government attention to the issue of birth defects and the environment. Children who were exposed to A-bomb radiation in utero had small head size and increased rates of mental retardation.[27] Children in

Minimata, Japan, who were exposed to very high levels of methylmercury were born with cerebral palsy–like syndrome.[28] Children in Taiwan with high gestational exposure to polychlorinated biphenyls (PCB)s were small and had cola-colored skin and a number of other abnormalities.[29] Vinyl chloride was also identified as a potential teratogen for those who resided in a highly exposed community, but this has not been characterized elsewhere.[30] These and other reports led to the establishment of birth defects registries by the federal and state governments and federal funding of research to identify preventable causes of birth defects. Although a number of leads have been identified by these studies, so far no new environmental causes have been established. However, these efforts have yielded important discoveries, such as the identification of the acne treatment Isotretinoin (retinoic acid) as a teratogen during pregnancy.[31,32]

More recently, there are questions about endocrine effects of chemicals on children who are exposed during critical periods of development as well as the causes of developmental disabilities in children[33] and whether certain malformations involving the reproductive system might be attributable to such effects.[34] The EPA is now developing an endocrine disruptor screening and testing process to identify such agents in the environment.

At this time, most of the information on teratogenicity for policy makers is derived from toxicity testing of animals. Food-use pesticides are required to be tested in whole animals for teratogenicity. Industrial chemicals are not. In 1998, there were 2863 high-production volume (HPV) chemicals that the United States imports or produces at >1 million pounds per year. In 1997 and 1998, Environmental Defense, the EPA, and the Chemical Manufacturer's Association (now the American Chemistry Council) concluded that insufficient information was available to determine whether basic screening-level data were available for HPV chemicals. The EPA found that 43% have no publicly accessible data on basic toxicity, and only 7% have a full set of basic test data available to the public and the research community. (It is important to note that although data may not have been publicly accessible, testing may nonetheless have been conducted by the chemical producers.) According to the EPA's information, for 78.2%, or 2240 HPVs, there was no available screening information for developmental toxicity. For 716 HPVs present in consumer products, nearly half (45.8%) were lacking screening developmental toxicity information. One fourth (23.8%) of the 239 HPVs for which the Occupational Safety & Health Administration had established permissible exposure levels and one fourth (23.6%) of the 251 HPVs listed in the Toxics Release Inventory lacked information about developmental toxicity. For non-HPVs, information is even more scarce.[35] In 1998, the American Chemistry Council and the American Petroleum Institute signed an agreement with the EPA to fill these data gaps on a voluntary basis.

Neurodevelopment

The federal government has increasingly been concerned about preventing exposure to agents that may cause impaired neurodevelopment, as low level exposures to lead, PCBs, and methylmercury were found to be associated with subtle impacts on IQ and cognition. The response of the government took a number of tacks. First, it should be noted that most of the relevant research has been funded by the US government, most notably, the NIEHS and the EPA but also the CDC, the ATSDR, and the FDA. Second, the government has had a role in monitoring exposure to these chemicals in the population. The third area is that of risk assessment; only recently has the government developed formal guidelines for assessing the hazards of developmental neurotoxicity. In a recent review, Rice and Barone[36] described several critical components of brain development that should be considered in the toxicologic evaluation of a potential developmental neurotoxicant, including growth (which occurs in utero and in the first 2–3 years of life); proliferation of neurons (which occurs during fetal development and continues postnatally); migration of recently proliferated cells from central to cortical regions (which occurs immediately after proliferation); differentiation of neuroblasts to mature forms; synaptogenesis, or formation of connections between neurons (which occurs through adolescence in humans); gliogenesis and myelogenesis, in which support cells and neuronal insulation are formed (which occurs through adolescence); and apoptosis, or programmed cell death, which also is critical for proper development of the nervous system. Timing is critical in that structures are developing at different rates at different times during gestation and early life.[36] This kind of analysis has clear implications for regulatory policy and for research recommendations. Only recently has the EPA begun to require the developmental neurotoxicity test for pesticides that are neurotoxic to adult animals.[37,38] The FDA does not yet have a standardized protocol for this endpoint to use for testing of drugs, food additives, and cosmetics. Moreover, there are questions about whether the current developmental neurotoxicity protocol is adequate for detection of disruption of all components of neurodevelopment and over the full developmental time span. (For example, dosing begins later and ends before full development of the nervous system.) Clearly, research efforts to develop better predictive models, as well as a better understanding of the fundamental mechanisms for neurotoxicity, are needed.

Asthma

Asthma is a chronic respiratory disease characterized by bronchial hyperresponsiveness, intermittent reversible airway obstruction, and inflammation of the airways and the lungs. It causes attacks of wheezing and shortness of breath. That there is a linkage between asthma attacks and outdoor air pollution has been demonstrated many times in the past several decades, and the protection of "susceptible populations" from such exposures was envisioned by

Congress, from the beginning, in the Clean Air Act, yet during the 1980s and most of the 1990s, asthma prevalence and deaths rose dramatically. Although these rates now seem to have leveled off, the current prevalence is nearly double the rates of the 1970s.[39] Why this occurred and how to intervene to lower asthma rates are unknown at this time. However, it has become clear that it is events in early childhood that are most predictive of asthma rates over a lifetime.[40]

Agents that cause asthma exacerbation are generally categorized into 2 groups: irritants and allergens. The 1999 Institute of Medicine report *Clearing the Air: Asthma and Indoor Air Exposures* reviewed the current state of our knowledge about the causes of asthma; it is not known whether outdoor pollutants cause asthma development.[41] They emphasized that asthma exacerbation is much better characterized than asthma development. Certain allergens as well as environmental tobacco smoke (in preschool-age children) have sufficient evidence of a causal relationship; allergens from dogs, fungi/molds, rhinovirus, and high indoor nitrogen oxides and NO_2 levels have sufficient evidence of an association with asthma exacerbation; infections with *Chlamydia pneumoniae*, *Mycoplasma pneumoniae*, and respiratory syncytial virus; environmental tobacco smoke (in school-age and older children and adults); and exposures to formaldehyde and fragrances have limited/suggestive evidence of an association with asthma exacerbation. Of this array of possible targets for prevention, the government has traditionally monitored outdoor air pollutants, including sulfur dioxides, ozone, nitrogen oxides, and particulate matter, all of which have been hypothesized to have some role in asthma exacerbation. EPA regulation has succeeded in reducing harmful levels of all of these outdoor pollutants, except nitrogen oxides. However, government at all levels has done little to prevent exposures to many of the other agents that are associated with asthma development and/or exacerbation.

FEDERAL POLICIES

The 1970s were a time of great advances in environmental legislation. Pediatricians and others played an important role in ensuring that children were protected in these efforts. In 1970, the CDC began its birth defect registries program, which sought to identify causes of birth defects in the environment. In 1971, the federal government initiated efforts to screen high-risk children for lead poisoning, and in 1976, the CDC began to support state-based programs. Also in the 1970s, numerous regulatory activities were undertaken to reduce lead in the general environment, including the EPA's phase-down of lead in gasoline; the banning of lead in interior house paint, children's toys, and a number of items by the Consumer Products Safety Commission; and reduction of lead in food cans and drinking water. In 1971, President Nixon announced a "War against Cancer," and Congress passed the National Cancer Act. As 1 of the many efforts involved in this "war," the federal government began to track cancer incidence through its Surveillance, Epidemiology and End Results program, which collected data for all cancer cases in specific regions of the United States. At the same time, the EPA and the Occupational Safety & Health Administration took action to reduce the population's exposures to a number of powerful carcinogens, such as benzene and asbestos.

In the early 1990s, AAP pediatricians helped to create 2 advocacy organizations that did much to bring children's environmental health to the forefront for policy makers: the Alliance to End Childhood Lead Poisoning (1990) and the Children's Environmental Health Network (1992).[42] Although children had been a major focus of concern about environmental hazards, these organizations helped to catalyze these efforts into a much larger movement. By 1992, 3 federal agencies (CDC, Department of Housing and Urban Development [HUD], and the EPA) had completed strategic plans to eliminate lead poisoning, a bolder goal than had ever been put forward. This was the first time that HUD was fully engaged in prevention of childhood lead poisoning. Congress enacted the Lead Poisoning Prevention Act of 1992, which directed all 3 agencies to address the abatement of lead in housing and other prevention goals. The federal efforts to eliminate lead poisoning have had great success. The most recent data from the CDC document that average (geometric mean) children's blood lead levels fell from 12.8 to 2.8 to 2.0 μg/dL between 1976–1980 and 1988–1991 and 1999.[43] Average blood lead levels among poor children, however, are 4-fold higher than levels among children who do not live in poverty.[44] This means that there are still hundreds of thousands of children with elevated blood lead levels in the United States. The federal government has crafted a strategic plan for "primary prevention," cleaning up the lead in the housing that continues to be contaminated by lead based paint before children are poisoned by it.

In 1993, the NIEHS with the Children's Environmental Health Network held the first scientific meeting on children's environmental health, the proceedings of which were published in a monograph.[45] This activity has over time led to research funding in this area. The EPA, the NIEHS, and the CDC joined together in 1998 to fund the first Centers of Excellence in Children's Environmental Health located at academic medical and public health centers across the country. In addition, the EPA directs competitive research grants via its STAR (Science to Achieve Results) program. The NIEHS supports a focus on children's environmental health, as a special aspect of its journal *Environmental Health Perspectives*, and the *Journal of Children's Health* was established in 2003 to publish papers in this area as well.

In 1993, the NRC published the report "Pesticides in the Diets of Infants and Children."[46] This committee was chaired by a pediatrician and included 3 other pediatricians and an obstetrician among its 14 members. The NRC report elevated concern on a broad national level about children's special vulnerabilities to environmental agents. It made clear that children are highly vulnerable to pesticides and other toxic chemicals and that protection of the health of vulnerable populations would require new

approaches to risk assessment and risk management. The NRC report recommended an approach that moved beyond consideration of "average" exposures based primarily on adult characteristics to one that accounted for the heterogeneity of exposures and for potential differential sensitivities at various life stages, particularly during prenatal development, infancy, and childhood.

The NRC Committee concluded, "In the absence of data to the contrary, there should be a presumption of greater risk to infants and children." To validate this presumption, the committee recommended, "The sensitivity of mature and immature individuals should be studied systematically to expand the current limited database as to relative sensitivity." To provide added protection to children during vulnerable periods of early development, the NRC Committee recommended that a child-protective "uncertainty factor" of up to 10-fold be considered in risk assessment of the effects of pesticides and other toxic chemicals "when there is evidence of developmental toxicity and when data from toxicity testing relative to children are incomplete."[46] This additional factor was deemed necessary because there were not adequate data about the effects of these chemicals on children. There was a great need for toxicology research to predict more accurately the risks for children. In consequence, the report concluded that the risk assessment procedures that were used by the EPA were inadequate and that reform was needed.[46]

In 1993, in response to the NRC report, numerous administrative reforms were undertaken, including improvement of dietary surveys, pesticide residue monitoring, and food intake models to assess better the dietary patterns of children, and the EPA moved to add child health endpoints to pesticide studies required of manufacturers for approval of pesticides. In 1996, the US Congress enacted the Food Quality Protection Act (FQPA).[47] The key element of this act is the requirement of a health-based standard for children. It is not subject to the "cost-benefit" analyses that have often served to thwart child protective regulations. It included a requirement for the additional 10-fold "margin of safety" to protect children. There were other innovative provisions (also recommended by the NRC), including the requirement for aggregate (all routes of exposure) and cumulative (all pesticides that share a common mode of action) assessment of pesticide risks to children. In the case of the EPA, the pesticide reassessments required by the FQPA have already resulted in cancellations of many of the household uses of organophosphate pesticides (eg, chlorpyrifos, diazinon), which were particularly risky for children because of the greater potential for exposure and the likelihood of cumulative impacts from all of the organophosphates. Likewise, uses on foods that children preferably eat (eg, apples) have been sharply curtailed (eg, chlorpyrifos, methyl parathion). However, cumulative assessments have yet to be completed, and it is difficult to predict at this time what the total impact of FQPA will be by the time of its completion (2006, as required in the statute). FQPA contained an additional provision requiring screening and testing of pesticides for potential to disrupt the endocrine system.[47]

Meanwhile, progress was made on other fronts. The EPA in 1996 published a white paper on children's environmental health that established a number of goals, most of which were eventually realized.[48] Following on this, the EPA established an Office of Children's Health Protection, which coordinates policies across all environmental areas and issues reports on the state of children's health and the environment. To guide its efforts and assist with establishing priorities, the EPA created a Children's Health Protection Advisory Committee.

In 1997, President Clinton issued an executive order on children's environment, health, and safety requiring that all federal agencies consider the risks to children in their actions.[49] The executive order also established the Task Force on Children's Environmental Health Risks and Safety Risks, co-chaired by the Secretary of Health and Human Services (Donna Shalala) and the EPA Administrator (Carol M. Browner). The Executive Order required that all agencies incorporate knowledge about exposures and susceptibilities to children in decisions. This resulted in policy changes in a number of areas, most notably, the FDA's policy on pediatric testing of drugs. The task force soon established a focus on 4 areas: childhood cancer, developmental disabilities, asthma, and injuries.[50] By 2000, it had brought about a number of changes, including the creation of a national childhood cancer registry, the development of an integrated federal strategy to eliminate lead poisoning, and a national plan of action to address the asthma epidemic. The task force also launched efforts to initiate an ambitious longitudinal cohort study called the National Children's Study. The study plans to recruit a national cohort of 100 000 births and study them during the next 2 decades. Clearly, if the study is fully funded, it will provide the opportunity to develop a better understanding of how chemical, drug, and physical insults affect the health of children over the full life cycle, along with social and behavioral issues that also are critical.

In 1996, the federal ATSDR established its efforts in children's environmental health and began to incorporate assessments of children's health in all of its health assessments of contaminated sites and in its toxicology profiles of hazardous chemicals. The ATSDR and the EPA in 1998 began to establish the Pediatric Environmental Health Specialty Units in medical institutions in each of the 10 federal regions in the United States to provide clinical consultation and referral services for evaluation of individual pediatric patients.[51]

The area of pediatric testing for pharmaceutical agents has been more difficult. In 1998, the FDA issued the so-called "Pediatric Rule," which required manufacturers to assess the safety and effectiveness of new drugs and biological products in children. This rule was challenged in court by manufacturers, and in 2002, the US District Court for the District of Columbia decided that the FDA did not have the authority to issue this rule; the decision was not appealed by the federal government. Instead, Secre-

tary Tommy Thompson announced an intention to seek new legislative authority for the needed assessments. Meanwhile, the FDA is engaged in a process to assess pediatric effectiveness and hazards associated with certain drugs that are already on the market. This activity is occurring under the Best Pharmaceuticals for Children Act (PL 107-109) that was enacted in 2002.

Even more difficult have been efforts to fill the gaps in knowledge about pediatric risks of chemicals found in humans. In 1998, efforts began to fill in the information gaps on the toxicity of HPV chemicals, including toxicity to children. In partnership with Environmental Defense and the EPA, industry volunteered to provide data on >2000 of the HPV chemicals. Industry already has made a large amount of the existing information more available to the public; it is expected that by 2005, most of the HPV chemicals will have a complete set of basic toxicology data available, including much screening information relevant to children but not necessarily including in-depth information on developmental toxicity. At the same time, there is a voluntary effort under way to do a pilot study of more extensive evaluations for chemicals to which humans have been shown to be exposed. This effort, the Voluntary Children's Chemical Evaluation Program, is under way but has not yet produced any new information. Finally, the EPA is engaged in efforts to develop endocrine disruptor screens and tests for its mandated Endocrine Disruptor Screening and Testing Program. At this time, these efforts involve research and validation of possible testing protocols.

In 1999, recognizing a need for additional information about children's vulnerabilities to chemicals, the EPA convened a workshop to identify critical windows of exposure to children's health. The proceedings of this workshop were designed to be useful to federal risk assessors.[22,36,52–55]

In 2000, Congress passed HR 4365, the Children's Health Act of 2000. This was an omnibus bill that contained a few aspects that are relevant to children's environmental health. The act authorized work in many areas that previously had been determined to be priority areas by the Federal Task Force on Environmental Health Risks and Safety Risks to Children. It specifically expanded services in lead poisoning prevention and childhood asthma and called for more research in these diseases as well as birth defects, childhood cancer, and developmental disabilities (most notably autism). It authorized development of the National Children's Study, a longitudinal follow-up study of environmental influences on children's health and development. The National Children's Study is now under development by a consortium of federal agencies, coordinated by the NICHD.

Asthma in children, identified by both the Federal Task Force and the Children's Health Act of 2000 as a priority, is receiving increased attention. No federal agency has the authority to regulate pollution in indoor air, although the associations are much more clearly established than for outdoor air. A priority for research is to identify preventable causes of asthma onset and exacerbation to decrease the prevalence and the severity of asthma. The CDC has a grants program that supports state efforts in asthma interventions and surveillance. It is interesting that HUD has recently become engaged via its Healthy Homes initiative, which, among other things, seeks to reduce conditions in federally funded housing that are conducive to asthma development and exacerbation, such as the presence of cockroaches, molds, and house dust.

Most recently, in 2003, the EPA released provisional cancer risk assessment guidelines that address risks to children.[56] This is the first time that a government regulatory agency has found that cancer susceptibility is increased when exposures occur early in development. If adopted as final guidelines, this policy would provide an extra measure of protection to children from exposure to known or suspected carcinogens.

STATE AND LOCAL POLICIES

Over the years, the states have also been engaged with children's environmental health. Two states have acted on children's environmental health per se. California's Children's Environmental Health Act in 1999 required the state government to assess its standards for air quality and toxics to assess whether they had accounted for children's susceptibility and exposures. The California Environmental Protection Agency found that current air standards do not adequately address risks to children and has begun to revise those standards accordingly. Maryland enacted House Bill 313 in 2000, creating a children's environmental health task force to review statutes, regulations, and proposed regulations with respect to children's risks. Four states have passed legislation to ban or reduce uses of mercury: Indiana, Maine, Maryland, and Minnesota.[57]

State and local governments have had a significant engagement in childhood lead poisoning prevention activities. These began in the 1960s and focused on identification and treatment of lead-poisoned children, mostly exposed to lead via deteriorating paint found on older housing. In the 1970s, the CDC provided states with categorical funding for childhood lead poisoning prevention programs, but by the early 1980s, when the federal "block grants" were created, many states shifted their attention to other priorities. However, a few states were in the vanguard, most notably, Massachusetts, which developed an aggressive approach that reduced the burden of childhood lead poisoning despite a large population living in high-risk contaminated housing. New York and California first developed state-based blood lead surveillance systems, which helped to track the prevalence of lead toxicity among children in local areas within states. Likewise, several cities (eg, Louisville, KY) developed innovative approaches. In the 1990s, the federal government undertook another wave of activity to reduce childhood lead poisoning. As funding became available, states began to develop their own policies in this area, allowing for tailored approaches to the problem. However, most states focused on the development of

standards and a well-trained workforce to identify lead paint hazards and remediate contamination in older housing. The diversity of approaches is evident in the list of state statutes that was identified by the National Conference of State Legislatures (NCSL) in 2001 (www.ncsl.org/programs/esnr/pbstlaws.htm).

The federal government in 1991 recommended universal screening of children for lead poisoning. However, states believed that this was impracticable, and in 1997, the CDC created a risk-based system to determine which communities had low enough levels of lead poisoning such that targeted, rather than universal, screening would be recommended.[58] A strength of state programs has been the ability to identify and address exposures that are unique to particular communities. Today, lead screening is recommended for all children who participate in the federal Medicaid program. Still, there are many Medicaid-covered children who are not screened. A recent NCSL survey of states found that the major reasons given for lack of screening were health care provider perceptions that there is "no problem" (21 of 43) or lack of awareness by health care providers (14 of 43; 7 states did not respond). Other major issues cited included reduced access to health care (10 of 43) and difficulty reaching transient populations (10 of 43). More than half of states (23 of 43) reported efforts to ensure provider compliance with screening recommendations, and 2 (Illinois and Rhode Island) required lead screening for admission to preschool or kindergarten. Alaska and Utah have sought waivers from the screening requirement on the basis of low prevalence of lead exposure in their states. States have been active in extending Medicaid benefits to cover aspects of the environmental interventions needed when lead toxicity is identified. According to the NCSL, 19 states use Medicaid for case management and 22 states for environmental assessment to identify sources of lead poisoning. Rhode Island, through a Medicaid Section 1115 waiver, pays for window replacement (but not other environmental interventions) in homes of lead-poisoned children.[59]

States have for many years been active participants in birth defects prevention efforts, and some states, most notably California, have invested significant resources in birth defects tracking and epidemiology. A recent review of state efforts by the Trust for America's Health found that 75% of births are now covered in state birth defects tracking programs. Of these, 22 states were given a good or an excellent rating for the quality of their efforts. Two thirds of states with registries were found to be unable to explore possible links between birth defects and the environment, however. The report cited state budget pressures as threatening the quality and continued improvement of state efforts to track birth defects.[60]

More recently, the states have become involved with efforts to prevent and better treat childhood asthma. Currently, 37 states participate in federally funded asthma prevention activities that largely consist of interventions to increase knowledge and awareness, improvements in quality of access to asthma treatments, and increases in asthma surveillance by states.

INTERNATIONAL EFFORTS

Multinational/Regional Efforts

This article covers agreements that involved the United States; however, there were other efforts (mostly in Europe) that are equally important and occurred during this same period. The Organization for Economic Cooperation and Development, a trade pact established after World War II and initially including the United States, Western Europe, Canada, Australia, and Japan, took some of the earliest actions to address children's environments when it adopted agreements regarding the need to limit levels of mercury (1973), PCBs (1987), and lead (1996) in the environment. These agreements were binding only on member states and reflected an early awareness of the need for international action to control toxic substances that are persistent and travel over long distances. In 1987, the United States and Canada signed the Great Lakes Water Quality Agreement, which pledged to virtually eliminate the discharge of persistent toxic chemicals in the Great Lakes region. This treaty recognizes the importance of the Great Lakes to human health (they contain 18% of the world's fresh surface water) and that cooperation between the 2 countries is required to protect it from toxic pollution. In 1993, the North American Free Trade Agreement was signed by the United States, Canada, and Mexico, along with environmental side agreements that created the North American Commission for Environmental Cooperation (CEC). In 1995, the CEC initiated a Sound Management of Chemicals to reduce the risks of persistent organic pollution in North America. In 1997, the Group of 8 (G8) nations adopted a commitment to address children's environmental health. Also in 1997, the United Nations Economic Commission for Europe and North America adopted the Persistent Organic Pollutants Protocol of the Agreement on Long Range Transfer of Atmospheric Pollutants. By adopting this protocol, Western Europe, the United States, and Canada agreed to add agreements to control a number of persistent toxic pollutants to air to an existing regional air pollution treaty. In 2002, the CEC initiated a cooperative agenda on children's health and the environment and called for the establishment of an expert advisory board to advise the council on issues of children's health and environment. In June 2002, the council adopted the Cooperative Agenda for Children's Health and the Environment in North America.[61] This agenda engages the United States, Canada, and Mexico in cooperative efforts to assess and prevent environmental hazards to children. Also in 2002, the European Environment Agency and the World Health Organization (WHO) Regional Office for Europe released in 2002 a new book: *Children's Health and the Environment: A Review of Evidence*.[62]

Global Efforts

In a sense, one could argue that efforts to protect the global environment will benefit children. How-

ever, here we focus on efforts that are more specifically directed toward risks to children. The UN Convention on Rights of the Child concluded that children have the right to a safe, clean environment; clean water; safe food; and clean air. Children are not able to make decisions about their environments independently but must rely on adults. Despite these commitments, it has taken a long time for the international community to take collective action to ensure safe environments for children. Another significant milestone was the adoption of the UN Conference on Environment and Development Rio Declaration, which included a strong commitment to addressing intergenerational equity as part of a global effort to ensure sustainable development over time. Principle 3 is, "The right to development must be fulfilled so as to equitably meet developmental and environmental needs of present and future generations." An additional milestone was the completion, in 1998, of negotiations for the Stockholm Convention on Persistent Organic Pollutants (which covers certain persistent toxic substances of particular concern to children, including PCBs and dioxins). Once in force, this treaty will have the effect of controlling releases of the top 12 of these substances worldwide, as well as providing an international mechanism for controlling similarly hazardous and persistent substances in the future. In 2002 in Bangkok, pediatricians from around the world convened at a conference sponsored by the WHO, the United Nations Environment Program (UNEP), and others, which culminated in the "Bangkok Statement," a powerful declaration calling on all nations to protect children against environmental threats to health and specifically supported the banning of lead from gasoline.[63] Also in 2002, the UNEP Governing Council adopted a resolution encouraging all countries to phase out the use of leaded gasoline. In 2002, Dr Gro Harlem Brundtland, Director-General of the WHO, launched a new initiative on Healthy Environments for Children at the Johannesburg "Rio + 10" global conference on sustainable development and health. In 2003, the WHO theme for World Health Day was Children and the Environment, and a monograph on the global implications of environmental threats to children was published jointly by the WHO, UNICEF, and UNEP. The monograph powerfully presents the major impacts of environment on the health of children in developing countries, where lack of sanitation, indoor air pollution from burning fuels, severe outdoor air pollution, and child labor pose risks that are even more severe and pressing than those in industrialized nations.[64] Also at the 2003 UNEP Governing Council meeting, it was decided that UNEP should move forward to develop global action to reduce the risks of mercury emissions to humans and wildlife.

CONCLUSIONS

Understanding of the impact of environmental factors on the health of children has grown in the past 40 years. This is attributable in large part to the clinical activities, research, education, and advocacy pursued by pediatricians, other child health providers, and scientists. There is substantial reason to believe that much more will be learned in the decade ahead. As more is learned, pediatricians and other health providers will need to continue to prevent, diagnose, and treat environmental health hazards that affect children and to work together with colleagues in the executive and legislative branches of government to formulate sound public policy.

Although progress has been made in promoting healthy environments for children, much more needs to be done. We still have not identified preventable causes of serious childhood diseases, including birth defects, developmental disabilities, asthma, and childhood cancer. Research efforts that are under way in academic institutions and government laboratories and planned, such as the National Children's Study, hold promise for the future. Some efforts, such as prevention of childhood lead poisoning and the establishment of Pediatric Environmental Health Specialty Units, continue to show remarkable progress, whereas others, such as the FDA Pediatric Rule, have experienced setbacks. Many other efforts, such as reassessment of pesticide standards under the FQPA; gathering new information on toxic chemicals; reform of pediatric drug approvals; setting of protective air standards; control of mercury in the environment; protection of children from carcinogens, developmental toxicants, and endocrine disruptors; and cleaning up unhealthy home environments for children are best understood as works in progress that need to be monitored carefully by those who are concerned about children's health. It is particularly encouraging to see the beginning of global progress with respect to children's environmental health. Despite some setbacks, it is clear that there is reason for optimism.

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