Child Health and the Environment

DONALD T. WIGLE, MD, PhD, MPH

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DONALD T. WIGLE, MD, PhD, MPH
R. Samuel McLaughlin Centre for Population Health Risk Assessment
Institute of Population Health
University of Ottawa
Ottawa, Canada

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To Beth,
children everywhere,
and Garreth,
who bravely fought non-Hodgkin's lymphoma
from age 10 to 19 years.

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Preface

The public health goal of collectively assuring the conditions in which people can be healthy[1] is particularly relevant to children as they are vulnerable to environmental hazards but have little or no control over their environmental conditions. Children differ profoundly from adults with respect to physiology, metabolism, growth, development, and behavior. By interfering with child growth and development during critical time periods, environmental hazards may cause structural and functional deficits and lifelong disability. The long life expectancy of children carries the potential for relatively high cumulative exposures and time to develop delayed adverse health outcomes; for instance, intense sun exposure during childhood is a major determinant of adult melanoma risk.

This book explores potential health outcomes of prenatal and childhood exposure to environmental hazards, particularly anthropogenic contaminants. Among the overarching themes are the susceptibility of the rapidly developing fetus and infant to early-life toxic exposures and the importance of modifying factors (e.g., poverty, genetic traits, nutrition) and timely intervention. Public health policy development in this field

[1]National Academy of Sciences. 1988. The future of public health. Washington, D.C.: National Academy Press.

must respond to high public concern about the safety and well-being of children but is complicated by the multiplicity of environmental contaminants, major knowledge gaps, the limitations of toxicologic and epidemiologic studies, and a lack of scientific consensus on causal relationships. Under the precautionary principle, lack of full scientific certainty does not justify postponement of cost-effective measures to prevent significant potential public health risks. This book documents several historic examples of environment-related child health disasters resulting from failures to apply the precautionary principle.

Chapters 1 to 3 present overviews of key children's environmental health issues and the role of environmental epidemiology and risk assessment in child health protection. Chapter 1 shows that international, national, and other bodies have identified asthma, air pollution (indoor and outdoor), lead, pesticides, water contaminants (chemical and microbial), climate change, hormonally active agents, and environmental tobacco smoke as important environmental health issues for children. Epidemiologic studies have identified adverse health effects during gestation, childhood, and adulthood arising from early-life exposure to diverse environmental toxicants such as ionizing radiation, lead, methylmercury, polychlorinated biphenyls (PCBs), environmental tobacco smoke, and outdoor air pollutants. Nevertheless, knowledge about the proportions of prenatal, childhood, and adult adverse health outcomes that are attributable to prenatal and childhood environmental exposures is very limited. Chapter 2 illustrates epidemiologic strengths with published examples and discusses their limitations such as problems in quantifying exposures, assessing delayed effects, and limited ability to detect relatively small risks.

When there is evidence that a particular environmental factor poses a threat to human health, regulatory authorities face the challenge of deciding how much population exposure should be permitted. Chapter 3 describes the role of the U.S. National Academy of Sciences risk assessment framework in quantifying health risks for the purpose of setting exposure limits protective of human health. Among the issues covered are processes used by national and international agencies to assess causal relationships, the assessment of dose–response relationships, uncertainties surrounding recommended exposure limits, and the need for improved premarket testing of commercial chemicals for early-life toxicity. The chapter also addresses key issues related to risk assessments of carcinogens, reproductive toxicants, developmental toxicants, and neurotoxins.

Lead and mercury are potent neurotoxins and the developing fetus and infant are especially sensitive to their effects. The role of social factors (especially poverty) in childhood lead exposure; the importance of

physiologic, nutritional, and developmental factors unique to childhood; possible developmental effects of prenatal parental lead exposure; the apparent absence of a blood lead threshold for hearing and cognitive deficits; and the persistent effects of childhood lead exposure on adolescent and adult cognitive performance are all discussed in Chapters 4 and 5. Major issues include controversies surrounding the efficacy of blood lead screening and lead abatement interventions, the possible neurotoxic effects of relatively low-level dietary methylmercury, and the need to further reduce the levels of population exposure to these toxicants. Sources and potential health effects of inorganic mercury, elemental mercury, arsenic, cadmium, and manganese are also discussed.

The disastrous health effects (intrauterine growth retardation, developmental delays, cognitive deficits, and chloracne) among infants of women highly exposed to PCBs are discussed in Chapter 6. Also covered are the possible health effects of early-life exposure to background levels of PCBs and related organochlorine compounds that share a common mechanism of toxicity, that is, activation of the aryl hydrocarbon receptor. This chapter documents the global dispersion and bioaccumulation of organochlorine compounds in aquatic and terrestrial food chains, and it flags such issues as uncertainties around the potential neurotoxic effects of relatively low-level lactational exposure to PCBs and related compounds, and the need to reduce human exposures.

About 3 million tons of conventional pesticide active ingredient chemicals are used annually worldwide, inevitably exposing the developing fetus and child to at least trace levels of currently used and persistent agents (e.g., DDT). Chapter 7 examines the known and potential health effects of pesticides, including acute poisonings, developmental effects, reproductive effects, neurotoxicity, and cancer. It addresses their potential to disrupt fetal and childhood growth and developmental processes and the inadequacy of premarket toxicity testing, as well as the potential role of pesticides in childhood cancer and the need to monitor population exposure levels.

Human experience with the drug diethylstilbestrol (DES) showed that prenatal exposure to this potent synthetic estrogen could cause reproductive tract abnormalities and vaginal cancer in offspring. Several environmental contaminants modulate endocrine function in experimental animals but their possible roles in human fetal and child development and health are unknown as very few epidemiologic studies have addressed these issues, and almost none have measured internal doses. Chapter 8 covers the potential roles of hormonally active environmental contaminants in the apparent trends toward reduced average age at menarche, reduced sperm quality, increased male reproductive tract birth

defects, and increased cancer incidence rates. The importance of monitoring population exposures to hormonally active contaminants and tiered toxicity testing of high-production volume chemicals for hormonal activity are noted.

Children prenatally exposed to atomic bomb radiation had substantially increased risks of microcephaly and severe mental retardation while those exposed as young children during the 1986 Chernobyl nuclear accident had increased thyroid cancer risks. Relatively low-level prenatal exposure to medical X-rays appears to increase the risk of childhood leukemia but the possible role of low-level environmental radiation in adverse developmental outcomes (birth defects, intrauterine growth retardation) and childhood cancer is poorly understood. These issues and those related to other types of electromagnetic radiation are presented in Chapter 9. After describing the mixed evidence of a link between power-frequency magnetic fields and childhood cancer, this chapter notes widespread exposures and uncertainties, and calls for precautionary measures such as minimizing exposure during pregnancy and childhood. This chapter documents the role of intense childhood sun exposure in malignant melanoma and its possible links to cataracts and immune suppression. Also addressed are uncertainties related to the efficacy of sunscreen use in preventing melanoma, the importance of multiple interventions in protecting children from intense sun exposure, and the need to monitor their exposures and sun-protective behaviors (including those of their guardians).

Environmental tobacco smoke (ETS) is a major indoor air contaminant with known adverse effects on child health, notably respiratory and middle ear infections, lung function deficits, and asthma. In addition, ETS appears to cause sudden infant death syndrome and is a possible cause of childhood and adult cancers. Biologic agents, toxic gases, and volatile organic carbons (VOCs) comprise the other indoor air pollutants reviewed in Chapter 10. The chapter addresses the roles of house-dust mite antigens and other aeroallergens in the onset or exacerbation of asthma, carbon monoxide poisoning from indoor combustion sources, the possible role of VOCs and nitrogen dioxide in childhood respiratory disease and cancer, and the virtual absence of national comprehensive prevention programs for indoor air health hazards.

Children are vulnerable to outdoor air pollution because they often engage in physical activities or play outdoors; also, they have relatively high air intake compared to adults. Chapter 11 describes the role of major outdoor air pollutants in adverse developmental outcomes (intrauterine growth retardation, preterm birth), respiratory tract inflammation and hyperreactivity, lung function deficits, and respiratory illnesses such as incident asthma. The need to minimize exposure of children and preg-

nant women to ambient air pollutant levels from major sources, especially motor vehicles and industry is noted. Evaluation of progress in this field requires monitoring personal exposures and prevalence/incidence rates of potential respiratory health effects.

An adequate supply of safe drinking water is an elusive goal in economically disadvantaged regions globally. Chapter 12 addresses waterborne microbial and chemical hazards, the latter including chlorination disinfection by-products (DBPs) and toxic chemical contaminants from hazardous waste disposal and other sources. Emerging evidence of developmental effects (spontaneous abortions, stillbirths, intrauterine growth retardation, and certain birth defects) related to first trimester maternal DBP exposure, the susceptibility of surface waters to high DBP levels, and economic barriers to DBP abatement, particularly in small water systems, are discussed. Hazardous waste disposal and storage often contaminate groundwater but the few existing epidemiologic studies preclude an adequate assessment of this child health hazard. Needs to protect source waters, reduce DBP levels, control hazardous waste disposal, and monitor water quality are noted.

Children develop enteric infections by ingesting fecally contaminated water and other substances (e.g., formula mixed with contaminated water) and by engaging in hand-mouth behavior. Although such infections are a leading cause of childhood deaths in economically disadvantaged countries globally, Chapter 12 focuses mainly on microbial threats in developed countries. *Escherichia coli 0157:H7*, a major cause of acute renal failure in children, can be transmitted through contaminated drinking water. Water appears to be a source of *Helicobacter pylori* infection during childhood; this organism causes chronic gastrointestinal infection and increased risks of peptic ulcers and stomach cancer during adulthood. The need to address both microbial and disinfection by-product hazards is a major risk management challenge.

This book will interest professionals and graduate students in the fields of public health, pediatrics, environmental health, epidemiology, and toxicology. The introductory and concluding segments of each chapter should interest a wider audience including health policy analysts in voluntary and governmental agencies. The final chapter summarizes the associations between environmental exposures and child health outcomes described in the previous chapters and calls for measures to create the evidence needed to enable public health decisions protective of child health. The five tables in this chapter are unique in that they summarize available information on the burden of child health adverse outcomes and the potential role of environmental hazards together with the level of epidemiologic evidence.

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Environmental Threats to Child Health: Overview

Control of childhood infections through sanitation, immunization, improved nutrition and housing, and antibiotics during the twentieth century greatly increased life expectancy at birth and dramatically changed patterns of childhood illnesses in developed countries. But there is growing evidence that global changes in atmosphere, terrestrial ecosystems, and climate, driven by population increase and consumption, pose threats to current and future human health. Children are especially vulnerable because they have no control over their prenatal and postnatal environments, including the quality of the air they breathe, the water they drink, the food they eat, and their place of residence. Exposure to environmental toxicants during prenatal and early childhood periods can disrupt developmental processes, causing structural and functional abnormalities that range from subtle to obvious, immediate to delayed, and transient to permanent. The leading health conditions that result in illness, disability, and death among children now include asthma, unintentional injuries, cancer, low birth weight, neurodevelopmental deficits, and birth defects. Apart from injuries, the proportions of these conditions attributable to environmental hazards are uncertain or unknown. By using a Delphi process and other sources to estimate attributable risks and economic impacts, a recent study concluded that 100% of lead poisoning, 30% of

asthma, 5% of cancer, and 10% of neurobehavioral disorders among children in United States are caused by environmental pollutants and impose an economic burden of about $55 billion annually (Landrigan et al., 2002).

Enteric and related infections caused by use of fecally contaminated water and respiratory conditions related to indoor and outdoor air pollution cause about 13% of all disability-adjusted life years (DALYs) lost globally, with considerably higher proportions in economically disadvantaged regions. Indigenous groups dependent on traditional foods may have increased risks of exposure to environmental hazards such as methylmercury in fish, organochlorine compounds in whale blubber, and lead in waterfowl. Even in developed countries, children in disadvantaged groups have higher levels of exposure to environmental hazards such as lead, environmental tobacco smoke (ETS), cockroach antigen, and outdoor air pollution and lower access to protective interventions such as sunscreens.

This book addresses the impacts of chemical, radiologic, and biologic environmental contaminants on child health and development from conception to early adulthood. Chapters 2 and 3, respectively, describe the roles of epidemiology and environmental risk assessment in providing an evidence base for public health policy and program decisions. Succeeding chapters review current evidence on major environmental hazards including lead, mercury and other heavy metals, dioxins, polychlorinated biphenyls, pesticides, radiation, hormonally active agents, indoor air, outdoor air, and drinking water. The final chapter summarizes known and suspected environmental threats to child health and policy issues arising from knowledge gaps. The present chapter deals with important issues related to child health, environmental hazards, vulnerabilities of the developing fetus and child, and the prevention and control of environmental hazards.

ENVIRONMENTAL HEALTH CONCERNS ABOUT CHILDREN

Leading Adverse Child Health Outcomes

Major pregnancy and child health outcomes (events per year in the United States) and their known or suspected environmental links are presented in Table 1–1. The very large annual number of fetal deaths (almost 1 million recognized events) and low-birth-weight infants (about 300,000) indicate the major impact of these conditions on population health. The reported number of fetal deaths is likely to have been substantially underestimated; longitudinal studies of women using biomarkers to detect

TABLE 1–1. Adverse Fetal, Infant, and Child Health Outcomes, United States

(a) Adverse pregnancy outcomes

Outcome	*Number of Events*
Fetal deaths[a]	983,000
Low birth weight[b]	
<1,500 g	57,477
1500–2499 g	243,706
Total	301,183

(b) Childhood diseases

	Deaths[c,d]			Hospitalizations[e]
	Age <1 Yr	*Age 1–14 Yr*	*Age <15 Yr*	*Age <15 Yr*
Perinatal conditions (low birth weight, complications of pregnancy, other)	14,084	135	14,219	170,000
Birth defects	5,473	977	6,450	130,000
SIDS	2,648	—	2,648	—
Respiratory disease—total	687	644	1,331	741,000
(asthma)	(5)	(153)	(158)	(190,000)
Cardiovascular diseases	667	591	1,258	25,000
Gastrointestinal diseases	500	249	749	221,000
Cancer and other neoplasms	126	1,594	1,720	36,000
Nervous system diseases	441	877	1,318	89,000
Certain infectious diseases	562	493	1,055	173,000
Injuries (including poisonings)	1,285	6,163	7,448	228,000
Other	1,464	1,121	2,585	645,000
Total	27,937	12,844	40,781	2,458,000

[a]Miscarriages and stillbirths, USA, 1996. Source: Ventura et al. (1999).

[b]USA, 1999. Ventura et al. (2001).

[c]USA, 1999. Hoyert et al. (2001).

[d]USA, 1999. Anderson (2001).

[e]USA, 1999. Popovic (2001).

early pregnancy have shown that 20%–40% of conceptions end in fetal death before 20 weeks' gestation but only a quarter to a half are clinically recognized. Among human early fetal deaths, about 10%–20% have autosomal chromosome aneuploidy and 10%–20% have congenital heart defects.

Leading causes of infant deaths include perinatal conditions (e.g., conditions related to complications of pregnancy, labor, or delivery, preterm birth, intrauterine growth retardation, birth trauma, or respiratory distress), birth defects, and sudden infant death syndrome (SIDS). Among

older children, the main fatal conditions are injuries, cancer, and birth defects. The main causes of childhood hospitalization are respiratory diseases (infections, asthma), injuries, and gastrointestinal conditions (infections, other). All of these conditions have known or suspected environmental links. Reported increases of birth defects and cancers among children and young adults and their known or suspected links to preconceptual, prenatal, and childhood exposures have raised public concern.

During the period from 1974 to about 1984 in Canada, incidence rates of overall childhood cancer increased by about 15%; since then, incidence rates of total and specific childhood cancers (leukemia, brain cancer, Hodgkin's disease, and non-Hodgkin's lymphoma) have been relatively constant. Childhood leukemia incidence rates increased in the United States during 1974–1991 but appear to have decreased slightly thereafter. Childhood brain cancer incidence rate increases have been reported in several countries; the U.S. increases occurred mainly during 1983–1986, possibly due to improved detection of low-grade cerebral and brainstem gliomas after the introduction of magnetic resonance imaging (MRI) (Smith et al., 1998). In sum, there is little convincing evidence of childhood cancer incidence rate increases since the late 1980s.

Incidence rates for several types of cancer have increased among young adults in Canada and some other countries during recent decades: melanoma, thyroid cancer (especially among females), testicular cancer, and non-Hodgkin's lymphoma. Intense sun exposure during childhood appears to explain most of the increase in melanoma. Some of the increase in non-Hodgkin's lymphoma among men was likely caused by human immunodeficiency virus (HIV) infection, but this cannot explain the striking global increases in this cancer across gender and age groups and beginning before the HIV epidemic. Infection with simian virus 40 was recently identified as a possible cause of non-Hodgkin's lymphoma among persons who received contaminated polio vaccines during 1955–1963 (Shivapurkar et al., 2002; Vilchez et al., 2002). Exposure to medical X-rays during childhood and youth may partially explain the increased thyroid cancer rates. Unexplained are testicular cancer incidence rates that increased twofold or more during the past three or four decades in several geographic regions, especially among more recent birth cohorts (see, e.g., Liu et al., 1999).

Recognized Children's Environmental Health Issues

There is considerable consistency in the children's environmental health issues identified as important by international and national agencies (Table 1–2). Six or more of the ten agencies acknowledged asthma, air (indoor and outdoor), lead, pesticides, and water contaminants (chemical

TABLE 1–2. Children's Environmental Health Issues Identified by International, National, and Other Organizations

Issue	*Number of Agencies*	*Issue*	*Number of Agencies*
Air—outdoor	9	Other metals (mercury, cadmium)	3
Water—infectious agents	9	Persistent organic pollutants	3
Lead	8	Acute respiratory infections	2
Asthma	7	Developmental disabilities (cerebral palsy, autism, learning disabilities, hearing loss)	2
Air—indoor	7		
Pesticides	7		
Water—chemical contaminants	6		
Environmental tobacco smoke	5		
Poverty	4	Injuries	2
Hormonally active agents	4	Radiation (ionizing)	2
Hazardous waste sites	4	Acute poisonings	1
Radiation (sunlight/ ultraviolet radiation)	4	Diarrheal diseases	1
		Food—contaminants	1
Birth defects	3	Genetically modified organisms	1
Cancer	3		
Climate change	3	Vectors of parasitic diseases (malaria)	1

Sources: World Health Organization (2001), European Centre for Environment and Health (1999), Lvovsky (2001) (note—the survey was not targeted to children, but the issues identified are strongly linked to child health), Pan American Center for Sanitary Engineering and Environmental Science (2001), G8 countries (1998), Commission for Environmental Cooperation (2000), U.S. Environmental Protection Agency (1996), Centers for Disease Control and Prevention (2000), U.S. Department of Health and Human Services (2000) (note: these are objectives for the entire U.S. population but relate directly to children's health), Council of State and Territorial Epidemiologists (2001) (note: these are objectives for the entire U.S. population but relate directly to children's health).

and microbial) as important issues directly relevant to children. The World Health Organization (WHO) Europe and the G8 nations (Canada, France, Germany, Italy, Japan, Russia, United Kingdom, United States of America) added three other issues—climate change, hormonally active agents (HAAs), and environmental tobacco smoke. An Environmental Protection Agency (EPA) advisory committee noted five areas where children's needs were not adequately addressed by existing EPA regulations: mercury emissions, farm worker protection, triazine pesticides (atrazine in drinking water), organophosphate and carbamate insecticides (neurotoxicity), and indoor and outdoor air quality and asthma.

Knowledge of Environmental Threats to Child Health

The relative importance of children's environmental health issues could be approached by measuring the frequency of adverse health conditions among children, identifying their causal factors, measuring exposure to

causal factors, and estimating attributable risks. In practice, this is only partially feasible because of major gaps in understanding the relationships between prenatal and childhood environmental exposures and adverse health outcomes. On the one hand, up to 60% of SIDS deaths may be caused by prenatal and postnatal tobacco smoke exposure. On the other hand, several epidemiologic studies have shown associations between childhood cancer and pesticide exposure indices, but causality is uncertain because of the lack of strong epidemiologic evidence, positive or negative.

Cancer incidence patterns among identical and nonidentical twins indicate that about 80% of cancers that occur commonly during childhood are attributable to environmental factors or gene–environment interactions, but these remain largely unknown. The U.S. National Academy of Sciences estimated that toxic chemical and physical agents cause about 3% of all developmental disorders and that a combination of genetic and nongenetic factors (including infections, tobacco, alcohol, and environmental hazards) may cause about 25% of these disorders (National Academy of Sciences, 2000). It is important to recognize that very few epidemiologic studies of adverse developmental outcomes with large sample sizes and rigorous exposure assessment have been conducted. It seems likely that future studies will reveal higher attributable risks of environmental factors than current estimates indicate. Although the impacts of environmental toxicants on child health have not been quantified systematically, succeeding chapters describe many important known links.

Some environmental hazards have been assessed in a least a few high-quality epidemiologic studies (e.g., childhood leukemia and power-frequency magnetic field exposures), but uncertainties related to exposure indices, mixed exposures, low frequency of highly exposed subjects, and inconsistent findings have complicated the interpretation of study results. Although there have been many studies of pesticides and childhood cancer, few have had strong statistical power and exposure assessment. Despite extensive research on the exacerbation of asthma by environmental exposures, there have been relatively few studies of causal factors for incident asthma. In addition to adverse health outcomes during childhood and youth, early-life exposure to environmental hazards may cause cancer and other adverse health effects during adulthood.

The childhood equivalent of the Framingham Heart Study or the U.S. Nurses' Health Study would be large longitudinal studies with intensive environmental exposure assessments beginning before conception or during early pregnancy with prolonged follow-up to identify health outcomes during pregnancy, infancy, childhood, adolescence, and adulthood. Such studies, initiated in Europe and at the planning stage in the United States, promise to provide much needed information on a wide variety of po-

tential health outcome and environmental exposure relationships (Golding et al., 2001; National Institute of Child Health and Human Development 2001).

Children's Vulnerabilities

The genome controls prenatal and postnatal growth and function but, as documented throughout this book, genes and the many molecular processes they control can be disrupted by environmental hazards. Inherited mutations and a wide range of social, behavioral, or other factors that increase exposure to environmental hazards can all increase a child's vulnerability. Sociodemographic subgroups of children may have both higher exposures related to older or deficient housing, residence in areas with high outdoor air pollution, dependence on contaminated drinking water, consumption of traditional foods, and the presence of household smokers and increased vulnerability because of maternal and childhood dietary deficiency and other risk factors.

The National Research Council report *Pesticides in the Diets of Infants and Children* documented age-related population heterogeneity with respect to exposure levels and toxicity (National Academy of Sciences, 1993). This report noted several unique aspects of children: (*1*) rapid body growth and development—the underlying molecular and cellular processes are vulnerable to disruption by toxicants, causing irreversible adverse effects on body structure (birth defects, reduced growth rates) and function, (*2*) the potential for relatively high exposures related to children's diet, behavior, and physiologic/metabolic differences from adults, (*3*) immature detoxification systems, and (*4*) inadequate toxicity testing of chemicals for developmental, neurobehavioral, immunologic, and reproductive system effects of perinatal exposures.

Disruption of Growth and Developmental Processes

Development has been described as evolution's foremost accomplishment in gene regulation, involving a complex orchestration of genes activated in specific cells at specific times (National Academy of Sciences, 2000). The cascades of genetically controlled molecular processes that underlie growth and development from fertilized egg to mature youth create periods during which toxic exposures can cause irreversible structural and/or functional abnormalities. Periods of vulnerability for adverse developmental outcomes depend on the mechanism of action of a given tox-

icant, the dose of toxicant taken up by the target tissue, the developmental timetable of the target tissue, and the age at evaluation of outcomes.

Birth Defects

Although there are known risk factors for birth defects (e.g., maternal smoking and alcohol consumption during pregnancy, relative folic acid deficiency, and use of certain pharmaceuticals), the attributable risks are generally low and the causes of most birth defects remain unknown. Research in this field is complicated by the fact that spontaneous abortion during the first trimester is quite common (20%–40% of all conceptions and about 10% of recognized pregnancies), and a high proportion of affected fetuses have birth defects and/or chromosomal abnormalities. Studies of birth defects among infants therefore include only a fraction of incident cases, that is, those prevalent at birth. Although molecular mechanisms of teratogens are poorly understood, rodent models indicate that many embryotoxins are proteratogens that are activated in vivo by enzymes including P450 cytochromes and peroxidases to electrophiles or free radicals that may damage DNA directly or indirectly through the formation of reactive oxygen species such as hydroxyl radicals. The embryo may be vulnerable to reactive intermediates because of immature detoxification systems. See later chapters for further discussion of potential environmental causes of birth defects.

Nervous System

The adult brain, a complex network of about 10^{11} neurons and 10^{14} synaptic connections, has a high metabolic rate, consumes about a fifth of the body's oxygen uptake, and is almost entirely dependent on glucose for energy. The development of the nervous system from the embryonic through the adolescent periods depends on genes and chemical messengers that guide a complex series of processes that occur at specific points in time and space. Development proceeds faster in some brain regions than others; for example, the growth rates of the human diencephalon and cerebellum, respectively, peak at birth and age 7 months. Although the neuronal population is complete by age 2 years, synapse formation and apoptosis continue until about age 5 years, and myelination continues through childhood and adolescence.

Periods of vulnerability during nervous system development include (Rice and Barone, 2000)

- Neural tube closure during early gestation
- Neuron proliferation, migration, synaptogenesis, gliogenesis, myelinogenesis, and apoptosis during gestation and infancy
- Brain remodeling during adolescence

The vulnerability of the developing brain to neurotoxins depends on access of the active agent to the nervous system and the timing of exposure in relation to developmental changes. The so-called blood–brain barrier is not fully developed until about age 6 months and, even then, it only partially protects the brain from environmental toxicants, especially lipid-soluble agents. Perinatal exposure to neurotoxins can disrupt subsequent cascades of developmental processes, greatly amplifying adverse effects, but later exposures may have little or no effect. Radiotherapy of brain tumors before age 4 years disrupts neuron proliferation and synapse formation and causes substantial cognitive deficits; treatment at age 4 to 7 years or later, respectively, causes mild or no detectable cognitive deficits.

Until the 1970s, concern about the impact of neurotoxins such as lead, mercury, and alcohol was almost entirely limited to adults. Frank mercury poisoning among infants ("pink disease" or acrodynia) was once thought to be an infectious disease; use of mercurous chloride in teething powder was not recognized as the actual cause until 1947, partly because the clinical signs differed from those of adult mercury poisoning. Perinatal exposure to methylmercury in Iraq and Japan during the 1950s and 1960s caused severe neurobehavioral deficits and deaths among offspring at exposure levels that caused minimal or no maternal toxicity. The use of lead in gasoline, paint, and other products caused widespread exposure of children and adverse effects ranging from subtle neurobehavioral deficits to severe and occasionally fatal childhood poisonings during much of the twentieth century. During the 1950s and 1960s, many newborn infants were washed daily with a 3% suspension of hexachlorophene; this practice was discontinued after discovery of a link to vacuolar encephalopathy of the brainstem reticular formation in preterm infants. Preterm human infants and young rats are far more susceptible than adults are to myelin degeneration caused by dermally absorbed hexachlorophene, a lipid-soluble substance with a very high affinity for myelin.

Animal studies have identified neurotoxic mechanisms relevant to humans. Ethanol and certain drugs (e.g., barbiturates) interfere with neurotransmitter activity at *N*-methyl-D-aspartate (NMDA) and γ-aminobutyric acid type A ($GABA_A$) receptors, the most ubiquitous receptor systems in the developing brain; exposure of rodents to such neurotoxicants during the neonatal brain growth spurt period causes widespread apoptosis of developing neurons. Neonatal exposure of rodents to pesticides that target neurotransmitter systems (e.g., chlorpyrifos) also disrupts brain development processes and triggers apoptosis (see Chapter 7, Pesticides). Further research is needed to assess the known and hypothesized links of environmental neurotoxins to schizophrenia, dyslexia, epilepsy, autism, mental retardation, attention deficit hyperactivity disorder (ADHD), learning disorders, and adult neurologic diseases.

Immune System

Known or suspected environmental immunosuppressants in humans include ultraviolet light (inhibits natural killer cell activity and contact hypersensitivity in adults), high-dose ionizing radiation, and 2,3,7,8-tetrachlorodibenzo-ρ-dioxin (TCDD). Rodent studies have shown that immune system development can be disrupted by perinatal exposure to relatively low doses of various toxicants (e.g., dioxin or dioxin-like organochlorines, polycyclic aromatic hydrocarbons, certain pesticides, heavy metals), with resultant persistent immunosuppression (Holladay and Smialowicz, 2000). These toxicants may interfere with hematopoietic cell proliferation, differentiation, and migration, expansion of lineage-committed stem cells, colonization of postnatal lymphopoietic compartments, cell–cell interactions, and maturation to immunocompetence. There is limited evidence that perinatal exposure of genetically predisposed rodents to immunotoxicants increases the risk of hypersensitivity responses and autoimmune diseases but little evidence from human studies. Adult humans exposed to contaminants in cooking oil and tryptophan supplements developed autoimmune connective tissue disorders, but the role of perinatal environmental toxicant exposures in autoimmune disease in humans is unknown.

Respiratory System

Development of the human respiratory system involves the differentiation, proliferation, and organization of multiple cell types into a complex system with over 300 million alveoli, the terminal gas exchange sacs (Pinkerton and Joad, 2000). Lung development begins at about 4 weeks' gestation, but alveolarization does not occur until the third trimester and the number of alveoli in a newborn's lungs is only 20% that of adults. Airway outgrowth, branching, and alveolarization continue until about age 18–20 years under the control of substances such as epidermal growth factor, transforming growth factor-α, and retinoic acid. Factors contributing to the susceptibility of the developing human respiratory system to environmental toxicants include the following:

- Several lung enzyme systems responsible for detoxification of xenobiotics are not fully developed at birth.
- Postnatal lung growth and development continues from birth until late adolescence, a period of 16–18 years during which children are exposed to airborne toxicants and aeroallergens.
- Polymorphisms in any of several candidate genes may increase susceptibility to asthma.

Perinatal exposure to ETS is associated with lung function growth deficits and incident asthma. The infant lung appears to be susceptible to idiopathic pulmonary hemosiderosis caused by combined exposure to the toxicogenic fungus *Stachybotrys chartarum* and ETS. Spores of *S. chartarum* are respirable and slowly release toxins that cause capillary fragility and suppress immune function; the ability of fungal toxins to inhibit protein synthesis in rapidly growing lungs may partially explain the susceptibility of infants to this disease.

Reproductive System

Experimental animal studies revealed vulnerable periods of exposure during reproductive system development including

- Spermatogenesis—preconceptual exposure of males to genotoxins can damage sperm DNA and cause early embryo death and birth defects
- Male reproductive development
  - Prenatal exposure of the male rat to androgen receptor antagonists (e.g., the pesticides vinclozolin, procymidone, linuron, and dichlorodiphenyltrichloroethane [DDT]) causes reduced anogenital distance and induces areolas at relatively low doses, hypospadias, agenesis of reproductive accessory tissues, and retained nipples at intermediate doses, and undescended testes and epididymal agenesis at high doses.
  - Immature and pubertal rats appear to be more sensitive than adults to testicular toxicity of phthalate esters and the pesticide, 1,2-dibromo-3-chloropropane.
- Ovarian development—neonatal exposure of female rats to androgens causes delayed puberty, irregular ovarian cycles, lower numbers of ovarian follicles, and premature cessation of ovulation.
- Puberty—exposure of experimental animals to certain neurotoxins (heavy metals, solvents, or pesticides) may accelerate or delay puberty.

Exposure

Behavior and Diet

Breast milk is a potentially important source of polychlorinated biphenyls (PCBs) and other fat-soluble contaminants for infants, especially those whose mothers consumed large amounts of contaminated fish or other foods. Infants and toddlers frequently mouthe or lick objects or surfaces; young children showed about 10 hand–mouth contacts per hour when videotaped while playing. Children often sit on floors or grass/soil while watching television, playing, or eating snacks, thus being exposed to tox-

icants in house dust, carpets, and soil via skin contact, ingestion, or inhalation. Compared to adults, 1-year-old infants consume (per unit body weight per day) twice as much tap water, total vegetables, and total citrus fruits and 10–20 times as many pears, apples, and total dairy products (Table 1–3); children aged 3–5 years consume 2–3 times as much tap water, total vegetables, and total citrus fruits and 7–8 times as many apples and total dairy products. These habits increase the risk of exposure to pesticide residues on citrus fruits and vegetables and to fat-soluble organochlorine compounds in dairy products.

Genetic Characteristics

Certain genetic traits interact with infectious, chemical, physical, nutritional, and other factors to cause adverse health effects. Diseases caused by single gene mutations may be aggravated by environmental contaminants; for example, cystic fibrosis is exacerbated by ETS. Genetic factors are also important in relatively common childhood conditions and diseases including birth defects, cancer, and asthma. Polymorphisms involve two or more distinct alleles at one genetic locus at stable frequencies in the population too large (usually defined as ≥1%) to be explained solely by recurrent mutation—the average heterozygosity per nucleotide site in humans is about 1:1000. Although persons with polymorphisms usually have no obvious health problems, they may be more susceptible to environmental and other hazards (see the examples in succeeding chapters). As the function of the human genome becomes better understood, the

TABLE 1–3. Ratio of Childhood to Adult Intakes (Amounts per Kilogram of Body Weight per Day) of Air, Water, and Selected Foods

Substance	*Age <1 Year*	*Age 3–5 Years*
Total tap water	2.1	2.4
Air—inhalation rates at rest	3.4	2.8
Total vegetables	1.8	1.9
Citrus fruits	2.2	3.0
Apples	14.2	8.4
Bananas	6.0	2.1
Peaches	9.5	3.1
Pears	20.7	2.3
Peas	3.5	2.4
Tomatoes	1.7	2.5
Total meats	1.7	2.3
Total dairy products	20.3	6.8

Source: U.S. Environmental Protection Agency (1997).

role of polymorphisms in susceptibility to environmental hazards will likely have major implications for disease prevention and control policies and programs. Existing environmental standards invoke uncertainty factors intended to protect susceptible subgroups; improved knowledge may show that current standards are inadequately protective of susceptible subgroups.

Physiology

Certain physiologic and metabolic characteristics during prenatal and postnatal development may increase the risk of adverse health effects from environmental toxicants. Compared to an adult, an infant has about twice the surface area per unit body weight and a correspondingly higher metabolic rate, a threefold higher intake of air per unit body weight per day, and an immature blood–brain barrier. The term *blood–brain barrier* encompasses multiple mechanisms that control access of blood components to the brain; fetal and neonatal blood–brain barriers are relatively impermeable to protein but are more permeable than adult barriers to small lipophilic molecules such as unconjugated bilirubin.

Metabolism

To varying degrees, toxicants absorbed into the body are detoxified in the liver, kidneys, and other tissues by xenobiotic[1] metabolizing systems. The metabolism of many lipophilic xenobiotics involves two phases: phase I—mainly oxidative reactions and phase II—conjugation with water-soluble moieties, a step that facilitates excretion. Phase I involves mixed-function oxidases (P450 cytochromes) that can (*1*) inactivate xenobiotics to less toxic derivatives amenable to conjugation and excretion or (*2*) activate them to strong electrophiles or unstable compounds that generate highly reactive free radicals. Phase I products may be conjugated during phase II with glucuronide, sulfate, acetate, glutathione, or other conjugating agents, reactions catalyzed by specific enzymes (e.g., glucuronyl transferase, *N*-acetyltransferase, glutathione *S*-transferase). Glutathione also scavenges electrophilic xenobiotics, thus protecting RNA, DNA, and other potential targets.

Humans display wide variations in susceptibility to xenobiotics, in part due to genetic polymorphisms in P450 cytochromes and other phase I and II enzymes. The genes that encode cytochromes are divided into

[1] A xenobiotic is any chemical not produced in vivo.

families and subfamilies, each with some degree of specificity for certain xenobiotics, including (*1*) *CYP1*—the *CYP1A* subfamily includes *CYP1A1* (encodes a cytochrome active in metabolism of benzo(a)pyrene; occurs in the liver, lung, and kidney), CYP1A2 (encodes a cytochrome that metabolizes acetanilide; found mainly in the liver) and (*2*) *CYP2*, which includes several subfamilies—*CYP2A1* and *CYP2A2* encode cytochromes that are active in metabolism of sex steroids (testosterone, progesterone, and androstenedione) and xenobiotics; *CYP2E1* is restricted to mammals and appears to encode a cytochrome that activates benzene, nitrosamines, and certain other xenobiotics, thereby contributing to their carcinogenicity. Children with polymorphisms for *CYP1A1*, *CYP2E1*, and other xenobiotic metabolizing enzymes appear to have an increased risk of developing acute lymphoblastic leukemia (Infante-Rivard et al., 1999; Krajinovic et al., 2002).

Immature Detoxification Systems

Pharmacokinetic studies of drugs used to treat newborn infants indicate that they can metabolize xenobiotics, but clearance is generally slow (Gow et al., 2001). Liver enzymes develop at different rates postnatally; for example, levels of glycine *N*-acyltransferase, involved in detoxification of drugs and other xenobiotics, are very low at birth and do not reach adult levels until about age 18 months. In a population exposed to air pollution, levels of polycyclic aromatic hydrocarbon (PAH)-DNA adducts, total aromatic-DNA adducts, and cotinine in cord blood were higher than those in maternal blood, suggesting reduced fetal detoxification capacity (especially since maternal exposure to PAHs exceeds fetal exposure) (Whyatt et al., 2001).

RISK MANAGEMENT ISSUES

Historical Perspective

The former belief that the placenta protects the fetus from toxic chemicals was shattered by repeated events during the mid-twentieth century involving serious and sometimes fatal effects of prenatal maternal exposures including ionizing radiation, methylmercury, diethylstilbestrol (DES), and thalidomide. Thalidomide, an antinausea drug once widely prescribed during pregnancy, caused severe birth defects in about 7000 infants during 1958–1962. This experience stimulated developmental tox-

icity testing of new commercial chemicals and birth defect monitoring in many countries, and it showed that:

- A chemical that was virtually nontoxic in mice and adult humans caused a markedly increased risk of severe birth defects when consumed during pregnancy.
- New commercial chemicals should be adequately screened for developmental toxicity in diverse experimental animals before humans are exposed (e.g., thalidomide is teratogenic in rabbits and primates, but rodents are generally resistant).
- International premarketing regulatory practices varied widely. The drug was available across the counter in Germany, the country with the highest number of affected infants; because of case reports of peripheral neuropathy in adult users, the U.S. Food and Drug Administration (FDA) restricted its use to clinical trials, saving many infants from devastating birth defects

Human Exposure Assessment

Children may be exposed to environmental contaminants in air, water, soil, dust, and food by ingestion, inhalation, or dermal contact. The potential anthropogenic sources of environmental contaminants include fossil fuel combustion, manufacturing processes, various uses of commercial products (pesticides, building materials, solvents), human activities (e.g., smoking indoors), waste disposal (hazardous waste disposal sites, incineration), and accidents. One of the major drivers is the vast and rapidly growing number of commercial chemicals. Over 70,000 commercial chemicals are registered for use in the United States, and the EPA receives about 1500 petitions annually to approve new chemicals or new uses of existing chemicals (U.S. Environmental Protection Agency, 2001a).

Few countries have assessed children's exposures to environmental contaminants through population-based biomonitoring. The United States has included children in the U.S. National Health and Nutrition Examination Survey (NHANES) surveys over the past 25 years and has assessed their exposure to contaminants including lead, other metals, ETS, phthalates, and organophosphate pesticides. The German Environmental Survey has been conducted three times since 1985–1986 and has included analyses of blood, urine, and scalp hair samples from children aged 6–14 years and environmental samples (house dust, drinking water, indoor and personal air, food) for metals, volatile organic chemicals (VOCs), and organochlorine compounds.

Recent Progress

Although much remains to be done to reduce children's exposures to known environmental hazards and to define the links between environmental factors and child health, there have been significant achievements:

- Blood lead levels declined sharply among children in all sex, age, ethnic, and income subgroups immediately after the introduction of lead-free gasoline in 1976.
- Population exposure to ETS has been reduced; median serum cotinine levels among nonsmokers in the United States decreased from 0.2 to 0.05 ng/mL between 1988–1991 and 1999.
- The U.S. 1996 Food Quality Protection Act requires that the unique exposures and susceptibilities of children be considered in pesticide risk assessment.
- Some countries have banned or restricted uses of a few pesticides mainly to protect children, such as daminozide and chlorpyrifos.
- Breast milk concentrations of PCBs, DDT/DDE (dichlorodiphenyldichloroethylene), and several other organochlorine compounds have decreased to varying degrees during recent decades.

Not all of these actions were targeted solely to children; the conversion to lead-free gasoline followed the introduction of catalytic converters by car manufacturers to reduce emissions under the 1970 Clean Air Act; lead inactivated the platinum catalyst in catalytic converters, necessitating the use of lead-free fuel.

Toxicity Testing of Commercial Chemicals

Volume. Regulatory agencies rely mainly on industry to conduct toxicity tests of new commercial chemicals. Extensive testing of pharmaceuticals, including clinical trials, has been required for many years and has shown that children's reactions often vary quantitatively and/or qualitatively from those of adults. The EPA estimated that up to a quarter of the approximately 70,000 commercial chemicals have neurotoxic potential, but only about 10% (excluding pharmaceuticals) have been tested for neurotoxicity. Most high production volume (HPV) chemicals (those produced in or imported into the United States in amounts of at least 500 tons per year) have not been subjected to the six basic toxicity screening tests prescribed by the Organization for Economic Cooperation and Development (OECD) for its 30 member countries. The U.S. National Toxicology Program, established in 1978 to coordinate toxicity testing on behalf of federal agencies, biomedical science communities, and the public,

is probably the largest chemical toxicity testing program in the world, but even it can provide complete toxicologic evaluations on only 10–20 chemicals per year.

Developmental toxicity. In addition to the sheer number of commercial chemicals, routinely required toxicity tests may not detect important developmental effects. Relatively little toxicity testing has been directed to early embryogenesis, that is, the period between fertilization and gastrulation. In experimental animals, the effects of mutagens vary during early embryogenesis (Rutledge, 1997):

- Germ cells and early multipotential embryonic cells—mutagens affect many cells and organ systems, causing pre- and peri-implantation deaths, balanced chromosomal translocations (causing sterility or reduced fertility of offspring), growth retardation, and moderately increased rates of structural anomalies (mainly anencephaly, cleft palate, and skeletal anomalies).
- Zygote—exposure to mutagens at this stage causes early, middle, and late gestation deaths, as well as high rates of a restricted range of structural anomalies associated with chromosomal breaks and other cytogenetic abnormalities (mainly skeletal, eye, and abdominal wall closure defects, but no increase in anencephaly, spina bifida, or heart or urinary tract malformations).
- Preimplantation conceptus—mutagens cause growth deficits, high rates of structural anomalies (anencephaly, skeletal abnormalities, cleft palate), and late fetal death.

Nonmutagenic teratogens produce a spectrum of structural anomalies specific to time periods as brief as 1–2 days. In a review of the mechanisms of developmental defects, the U.S. National Academy of Sciences concluded that (National Academy of Sciences, 2000) (*1*) the mechanism of developmental toxicity is partially understood for a few toxicants (e.g., retinoic acid, diethylstilbestrol, and TCDD) but is not completely known for any compound; (*2*) testing should be done across the entire developmental period, including early fetal loss; and (*3*) there is potential to rapidly and inexpensively screen many chemicals for the ability to disrupt signaling pathways central to normal development.

Neurotoxicity. The EPA-designated toxicants that require developmental neurotoxicity testing include (in descending order) central nervous system teratogens and their structural analogues, adult neurotoxins, adult neuroactive agents, hormonally active compounds, and develop-

mental toxicants. Much of the baseline evidence for triggers assumes that developmental and reproductive toxicity studies have been done, but the latter are required by the EPA only for registration of food-use pesticides and not for other pesticides or commercial chemicals (Claudio et al., 2000). Most of the 140 pesticides considered to be neurotoxic by the EPA have not been tested for developmental neurotoxicity, indicating that historic practices generally failed to trigger neurodevelopmental toxicity testing of known adult neurotoxins. An EPA advisory group recommended routine developmental neurotoxicity testing for registration of all food-use pesticides. Recommendations for neurotoxicity testing that address the need to protect child health include (International Programme on Chemical Safety, 2001) the following:

- Develop standardized test methods and norms to evaluate neurotoxicity in infants and children.
- Increase testing in animals involving perinatal exposure to chemicals and/or mixtures of chemicals to define the relative sensitivity of the developing nervous system to neurotoxic injury.
- Develop and validate efficient animal tests for developmental neurotoxicity for use in international collaborative studies.

Carcinogenicity testing. The Carcinogenic Potency Database contains the results of over 5000 carcinogenic bioassays on about 1300 chemical entities (Gold, 2001); in other words, only a fraction of the commercial chemicals have been tested for carcinogenicity in animals. An EPA review of animal carcinogenesis bioassay studies relevant to the issue of perinatal exposures found that lifelong exposure of animals beginning neonatally often produces a higher incidence of tumors with shorter latencies but seldom produces types of tumors not found in the standard bioassay; perinatal exposure alone to three known carcinogens did not consistently cause an increased incidence of cancer. The EPA review concluded that there is insufficient evidence to justify routine inclusion of a perinatal exposure component in the standard carcinogenesis bioassay, a conclusion endorsed by the EPA Scientific Advisory Panel. Notwithstanding this decision, carcinogens that are more potent or that cause unique types of cancer in rodents after perinatal exposure include cycasin (brain and jejunal tumors), DES (vaginal cancer and uterine adenocarcinomas in exposed females and testicular tumors among exposed males and the male offspring of perinatally exposed females), genistein (a natural phytoestrogen present in soy—uterine adenocarcinomas), and *N*-ethyl-*N*-nitrosourea (nephroblastoma and brain gliomas).

Toxicity testing priorities. The EPA Scientific Advisory Panel recommended that priorities for testing commercial chemicals for child health hazards should be based on criteria such as potential for children's exposures to exceed those of adults and should include those chemicals to which children are uniquely exposed or for which children have unique susceptibility rather than production volume alone. After excluding low-volume chemicals (less than 5 tons/yr) and high molecular weight, poorly absorbable polymers, there were about 15,000 chemicals produced or imported at levels above 5 tons/yr, including about 2800 HPV commercial chemicals. Since 1979, about 540 of the chemicals in the 15,000 chemical subset above have been tested within the EPA's Existing Chemicals Testing Program; these were mainly HPV chemicals. In 1990, the EPA developed a Master Testing List of over 500 existing chemicals (i.e., already used commercially) based on toxicity testing priorities of U.S. federal agencies and the OECD; as of 2001, testing actions were underway for almost 300 entities.

Despite this progress, only about 7% of HPV chemicals have been adequately tested; the remainder are missing one or more of the OECD Screening Information Data Set (SIDS) tests, and 43% are missing all SIDS tests (U.S. Environmental Protection Agency, 1998). Although the EPA is pursuing toxicity testing of HPV chemicals through voluntary agreements, it can require chemical manufacturers and processors to test existing chemicals that pose unreasonable risks to human health or the environment. Among the 491 HPV commercial chemicals to which children are likely exposed, only 25% have been adequately tested (U.S. Environmental Protection Agency, 2000). Under a voluntary EPA program, companies that manufacture or import 23 targeted chemicals are asked to sponsor a three-tier toxicity-testing program.

Strengthening Prevention

The Precautionary Principle

Modern use of the precautionary principle in environmental health can be traced to the 1992 United Nations Conference on Environment and Development that promulgated the Rio Declaration. Principle 15 of the Declaration states, "In order to protect the environment, the precautionary approach shall be widely applied by States according to their capabilities. Where there are threats of serious or irreversible damage, lack of full scientific certainty shall not be used as a reason for postponing cost-effective measures to prevent environmental degradation" (United Nations, 1992). Concern about the slow pace of efforts to address climate

change, ecosystem degradation, and resource depletion was a major driver of the Rio Declaration.

Policymakers generally encounter a high level of uncertainty about children's environmental health risks because of knowledge gaps concerning relevant exposures and dose–response relationships for individual toxicants and mixtures. In the face of such uncertainty, a requirement for scientific consensus on causality is not necessarily appropriate for management of children's environmental health risks. As stated elsewhere, "If exposure is widespread and the consequences [are] serious, a need for primary prevention may suggest that even a moderate degree of evidence justifies regulatory action. On the other hand, if the probability of human exposure is low and the adverse health effects [are] uncertain, then the best policy may be collection of improved data" (Hertz-Picciotto, 1995). Scientific uncertainty about child health and the environment relates to several factors:

- Absent or inadequate evidence—gaps in knowledge of the toxicology and epidemiology of potential environmental hazards
- Inconsistent results of toxicologic studies—use of different test animal species or strains, differences in purity, dose, and route of exposure of the test substance, small sample size
- Inconsistent results of epidemiologic studies—limited statistical power, inadequate exposure estimates, uncontrolled confounders
- Uncertainty about the shape of the dose–response curve at doses below those observed
- Doubt about the adequacy of uncertainty factors used in quantitative risk assessments to compensate for knowledge gaps including extrapolation of results from animal studies to humans and the distribution of exposures and susceptibility factors among children in the general population

To obtain an improved evidence base for future policy and program development in this field, current efforts in two areas require strengthening: (*1*) research to better define environmental hazards, susceptible populations, and dose–response relationships and (*2*) tracking systems to monitor population exposure levels. The EPA and the National Institute of Environmental Health Sciences (NIEHS) have funded 12 children's environmental health research centers to address priority issues including child health effects of various toxicants (lead, mercury, PCBs, pesticides) and the role of environmental exposures in cognitive deficits, autism, learning disabilities, ADHD, and asthma (U.S. Environmental Protection Agency 2002).

Tracking Systems

Systems that track the occurrence of health conditions and their determinants have greatly aided prioritization, planning, and evaluation of disease control and prevention programs in specific fields (infectious diseases, unintentional injuries, disability, occupation-related diseases) and in nationwide health objectives (see, e.g., Thacker and Stroup, 1994). A framework for environmental tracking systems might include hazards, exposures, health outcomes, and children's environmental health policies. Tracking systems for child-related aspects of outdoor air pollution, for instance, might address hazard occurrence (e.g., concentrations of priority contaminants in outdoor air), exposure levels (e.g., proportion of children exposed to ambient air contaminant levels above current air quality standards), health outcomes (e.g., incidence of emergency room visits for childhood asthma), and health policies (e.g., clean air policies, standards, guidelines). It appears that no jurisdiction has implemented comprehensive tracking systems to monitor needs and progress related to children's environmental health, but some elements exist:

- Hazards
  - Outdoor air—many developed countries have national and/or regional monitoring networks to measure ambient air contaminants including particulate matter and ozone.
  - Drinking water—drinking water facilities in developed countries generally monitor microbial contaminants and may monitor chemical contaminants such as chlorination disinfection by-products (total trihalomethanes) and lead.
  - Indoor air—some national health surveys and many occasional surveys have included questions on the smoking habits of household members; census data may include information on housing characteristics such as fuels used for cooking and heating.
  - Food contaminants—some countries have conducted limited sampling of foods for pesticide residues and other contaminants; the enormous variety and volume of foods and the practice of testing batches rather than individual portions preclude detection of low-frequency, high-pesticide residue levels before distribution and consumption. This issue is further complicated by sparse or absent data on food consumption patterns within narrow age ranges among children (needed because of the large variation in diet as an infant or child ages).
- Exposures and doses—*exposure* generally refers to the level of a contaminant in environmental media (air, water, food, soil) to which a person is directly exposed, while the *internal dose* is the amount of con-