Policy Study No. 283—Summary

Protecting the Children: Risk Assessment, Risk Management, and Children's Environmental Health

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Studies show that as the 21st century begins, the health and safety of children in America are better than at any time in recorded history. Mortality rates for all children from newborn to 19 years of age have dropped over 90 percent since the turn of the last century, contributing 60 percent of the 27-year increase in life expectancy since 1900. Children's health has improved especially during the last 20 years, indicating that children in particular have benefited from advances in medicine and social policy.

The extent to which exposures to occupational and environmental toxicants contribute to childhood mortality is unknown, but has been estimated to be 1 percent. By comparison, mortality for all age groups due to these same exposures is estimated to be 3 percent. Nonetheless, increasing attention over the last 10 years has been given to the potentially disproportionate impact that environmental chemical exposures might have on the health of children.

That concern led to the children's health provisions of the 1996 Food Quality Protection Act, to President Clinton's 1997 Executive Order Protection of Children from Environmental Health Risks and Safety Risks, to establishment of the United States Environmental Protection Agency's (EPA's) Office of Children's Health Protection and Children's Health Protection Advisory Committee, and to a renewed research focus through the EPA's voluntary children's Chemical Evaluation Program and the Child Health grants program administered by the EPA and the National Institute of Environmental Health Sciences (NIEHS). Programs in children's

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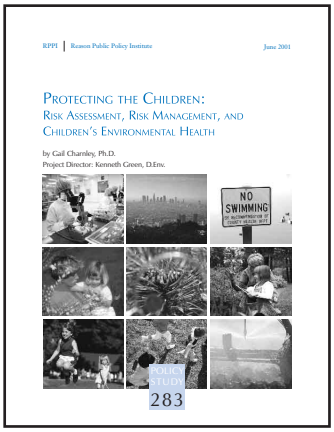

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environmental health also have been created at the Centers for Disease Control and Prevention and at the Agency for Toxic Substances and Disease Registry, and a national network of eight Children's Environmental Health Research and Disease Prevention Centers has been formed.

Much of the controversy over children's risk policy arises from uncertainty about the nature and extent of children's potentially disproportionate sensitivity to chemical risks. Sensitivity is determined by level, rate, and duration of exposure and by inherent biological susceptibility. There is general agreement that infants and children experience environmental chemical exposures differently from adults. Less certain is the extent to which children are of greater or lesser susceptibility to chemical toxicity than adults. This study provides an overview of what is known about differences in exposure and about differences in susceptibility, discusses how those differences are addressed when health risks are assessed, and draws conclusions about children's environmental health in the larger context of public health.

Age as a Factor in Chemical Exposures

Children's exposures to chemicals in their environment are qualitatively and quantitatively different from those of adults. For one thing, children are likely to be exposed to different levels of chemical contaminants in foods than adults because they consume more calories of food per unit of body weight, fewer types of foods, and more processed foods.

Normal childhood behaviors, such as hand-to-mouth activity and crawling on the floor or ground, can increase children's exposures to potential toxicants through contact with and ingestion of dusts and residues. Greater risk of lead poisoning from lead-based paint is a well-known example of this problem. Children breathe more than adults on a body-weight basis, so they also may be exposed to higher levels of air pollutants. Children consume more water than adults on a body-weight basis, so they may be exposed to higher levels of water pollutants. Infants consume breast milk, an important source of nutrition and immunological protection, but occasionally a source of fat-soluble contaminants such as PCBs that were originally ingested by the mother. Children also may not perceive hazards as quickly or effectively as adults, so may experience greater exposures by not avoiding them as readily.

As the types of children's chemical exposures are likely to differ from those of adults, so do their actual doses. In addition to level of exposure, the dose of chemical that is delivered to the target site for toxicity is a function of how well the particular chemical is absorbed into the body, how it is distributed in the body and metabolized, and the rate at which it is eliminated. Rates of absorption, distribution, metabolism, and elimination can vary with age.

Age as a Factor in Chemical Susceptibility

There are many physiological and pharmacological reasons why susceptibility to the impacts of chemical exposures may differ between children and adults. A developing fetus undergoes many complex, integrated processes that involve cell growth, differentiation, and morphogenesis. If mutation or altered cell division, enzyme function, or energy sources interfere with these processes, they can have significant adverse impacts on development. A number of environmental factors are known to have an impact on normal fetal development—including maternal nutrition, folic acid in the diet, prescription drugs, cigarette smoke, and alcohol consumption. Similarly, environmental factors can have an influence on normal childhood development, including ingestion of chemical contaminants such as lead (in paint), arsenic (in drinking water), and organic mercury (in fish).

Young children are more sensitive than adults to the toxic effects of some chemicals, such as lead and organic mercury. At the same time, children are less sensitive than adults to other chemicals. For example, unlike in adults, liver toxicity and death from acetaminophen poisoning is extremely rare in children. Reduced chemical toxicity in children generally is due to their more rapid rates of metabolism and elimination, resulting in lower body burdens of drugs or chemicals than adults for the same exposures. For example, as the table below shows, morphine is cleared about 50 percent faster by younger infants than by newborns, while older infants clear morphine about three times faster than newborns. Morphine clearance is slower in adults than in older infants and children, but approximately the same as in newborns and younger infants. The chemotherapy drug methotrexate is cleared six times faster by children less than 10 years of age than by adults. The antipsychotic drug Thorazine® (chlorpromazine) is cleared five times faster by children than by adults.

The more rapid metabolism and elimination by children of many drugs (chemically similar to many environmental chemicals) may compensate in part for any increased sensitivity during development.

Experiments using laboratory animals suggest that young animals are not generally more sensitive to chemical carcinogens than older animals. Studies of the effects of anti-cancer drugs, viral infections, and ionizing radiation demonstrate that both the young and old develop a similar spectrum of tumors. Rodent studies show that younger animals are less susceptible to chemical carcinogens in some cases and more susceptible in others, depending on the chemical. Taken together, those observations do not provide strong support for the idea that children are generally more sensitive to carcinogens than adults.

Charnley and Putzrath (2001) updated a 1993 study of rodent carcinogenesis included in the National Academy of Sciences (NAS) report *Pesticides in the Diets of Infants and Children*. They found that a similar number of studies show that younger animals are less susceptible (47 percent) than adults to chemically induced carcinogenesis as show that they are more susceptible (40 percent) under the conditions of the studies. A number of studies (13 percent) showed that age played no role at all in susceptibility. The NAS report concluded that the rodent bioassays (tests on the impact of a chemical or drug using rodents as experimental subjects) reviewed clearly demonstrate that age may be an important factor in susceptibility to chemically-induced carcinogenesis, but they do not support the conclusion that younger animals are always more susceptible than older animals. The data also illustrate the difficulty associated with assessing quantitatively the extent of the differences in susceptibility due to age. Virtually all of the studies evaluated used only one dose level, so the underlying dose-response relationships are unknown and comparison of sensitivities is possible only at the relatively high, single-dose levels. Generalizations about the effect of age on susceptibility to chemical carcinogens thus are difficult to make.

Data on acute chemical toxicity show similar results. A review of the data available on the lethal doses of a variety of chemicals (in laboratory animals) showed only small differences due to age. In some cases, infants were more susceptible and, in some cases, adult animals were more susceptible. In only a few cases did the differences exceed an order of magnitude; in many cases, there were no differences.

Data on the maximum tolerated doses (MTDs) of chemotherapeutic agents in humans show that MTDs were frequently higher for children than adults, indicating greater susceptibility of adults, although the differences between age groups were usually less than or equal to two.

Studies of pesticide acute toxicity also show variability. For 36 pesticides given orally to weanling and young adult rats, no more than two- to three-fold differences in sensitivity were observed, with the younger animals more sensitive

DRUG CLEARANCE RATES AS A FUNCTION OF AGE

Compound	Age	Clearance*
Morphine (ml/min/kg)	< 7 days	8.7 ± 5.8
	7 days – 2 months	11.9 ± 5.1
	2 – 6 months	28.0 ± 8.9
	Children	20.5 – 257
	Adults	6.2 – 15.6
Methotrexate (l/kg/h)	< 10 years	0.6
	10 – 15 years	0.2
	Adults (>15 years)	0.1
Thorazine® (chlorpromazine) (l/h/kg)	0.3 – 17 years	3.1 ± 0.6
	17 years and older	0.6 ± 1.2

Source: Adapted from A.G. Renwick, "Toxicokinetics in Infants and Children in Relation to the ADI and TDI," *Food Additives and Contaminants*, vol. 15S (1998), pp. 17-35. * Clearance rates (found under each chemical name) are as reported in the original literature. The units refer to the volume of the drug cleared per unit of body weight per hour. Absolute concentrations of the drugs delivered are not given, but the rates are primarily of interest for their variance with age.

to toxicity than older animals in only four cases. In contrast, 14 of 15 organophosphate pesticides showed greater acute toxicity to weanling rats than to adult rats. Newborn rats were more sensitive than adult rats to malathion poisoning, but less sensitive than adult rats to dieldrin toxicity.

The available evidence on age-related susceptibility of laboratory animals to the effects of chemical contaminants thus suggests that children may be more than, less than, or just as sensitive as adults, depending on the chemical and the exposure. Most of the available information on age-related differences in sensitivity comes from experiments using single, high doses of chemicals that produced short-term, acute toxicity, however. Those observations may be poor predictors of what occurs when low doses of chemicals are received over long periods of time or at key times during development. Long-term exposure to low doses of chemicals can produce different types of toxicity than short-term exposure to high doses—or no discernible toxicity. On the other hand, low environmental exposures to chemicals are less likely to overwhelm developing detoxification mechanisms, so age-related differences at low doses may be quantitatively less pronounced than at high doses.

Conclusions: Children, Public Health, and the Environment

No one argues against protecting children; the issue is how best to do so. Chemical contamination that occurs in utero or during childhood can have tragic consequences: stillbirths and spontaneous abortions, birth defects, greater likelihood of disease throughout childhood and adulthood, and/or early mortality. These place great demands on social and emotional resources. Although the proportion of birth defects and other problems attributable to environmental exposures to chemicals is likely to be small, it could constitute a public health problem by virtue of the numbers of people affected.

The evidence examined in this study demonstrates that evaluating the relative sensitivity of children and adults to chemical toxicity must be done on a case-by-case basis. It is not true that children are always more susceptible to chemical toxicity than adults; they may be more than, less than, or just as susceptible as adults. The only unifying principle that has emerged thus far is: "it depends."

The leading causes of childhood mortality (unintentional injuries, homicides, suicides, cancer, and congenital anomalies) are largely preventable. For example, 90 percent of children's unintentional injuries are preventable. According to the National Safe Kids Campaign, substantial progress is being made toward reducing the rate of childhood deaths due to accidents, in part due to increased use of seat belts, child safety seats, bicycle helmets, and smoke detectors. The Centers for Disease Control and Prevention have suggested that 70 percent of many kinds of birth defects are preventable through adequate folic acid consumption before and during pregnancy. Preventing fetal alcohol exposure would also substantially reduce birth defects, mental retardation, learning disabilities, and behavioral problems. While cancer and birth defects are important threats to children's health, environmental contamination has not been identified as a major risk factor.

The relationships between chemical exposures and health impacts are complex and poorly understood for people of all ages. Unless and until adequate data from basic research, environmental monitoring, and public health surveillance are available, conclusions about chemically-induced disease, the effect of age on risk, and the effectiveness of chemical regulation will remain speculative.

Some $100 to $150 billion are spent every year on environmental protection and compliance in the United States, but the impact that investment has on public health in general and on children's health in particular is largely unknown. The rhetoric, logic, and basic purpose of environmental health regulations are thoroughly grounded in the notion of improving public health. However, we have very little ability to measure our accomplishments or connect them with our aspirations. For example, asthma in children has shown an alarming rise, doubling in prevalence over the last decade, but scientists still fail to agree on its connection to environmental exposures or the best means of prevention.

According to a recent Pew Environmental Health Commission study, the United States is unable to mount effective prevention efforts for asthma, birth defects, developmental disabilities, cancers, and neurological disorders

such as Alzheimer's and Parkinson's, among other chronic diseases that are likely to have environmental components. Because the United States lacks a national disease surveillance network and the ability to track environmental exposures, we are unable to make meaningful connections between environmental exposures and public health outcomes. In its *America's Children and the Environment*, the EPA was limited to vague indices that conveyed no real information about actual health risks, such as "percentage of children living in counties where one or more of the six criteria air pollutants exceeded national air-quality standards."

In some ways, concern about the impact of the environment on health has become almost a religious issue. Without adequate data to support or refute suspected associations, risk decisions can be co-opted by vested interests of all stripes. The potential benefits and costs of more stringent regulation to protect children should be weighed carefully. More stringent regulation at this point appears to have little scientific justification and must be viewed as policy-driven. A precautionary approach that increases stringency on the basis that it is better to be safe than sorry implies that current regulatory strategies fail to protect children's health. However, there is little evidence that environmental exposures play a significant role in childhood disease, nor is there evidence that where such exposures do play a role, that more stringent regulation would be preventative. More targeted strategies that address known threats to children's health are likely to have more apparent benefits.

About The Author

Dr. Gail Charnley, President of HealthRisk Strategies, is an internationally recognized expert in environmental health-risk assessment and risk management science and policy. She was executive director of the Presidential/Congressional Commission on Risk Assessment and Risk Management, mandated under the Clean Air Act to evaluate the role that science and policy play in federal agency decisions about managing environmental health risks. Before her appointment to the commission, Dr. Charnley served as acting director of the Toxicology and Risk Assessment Program at the National Academy of Sciences/National Research Council. She has chaired and served on several EPA and FDA peer review committees related to environmental health risk research programs and decision-making. Dr. Charnley lectures frequently on risk science policy issues and is the author of numerous reports evaluating the toxicity of chemical exposures and their potential impact on public health, as well as on the social dimensions of risk management and democratic environmental decision-making. She holds an adjunct faculty position at the Harvard Center for Risk Analysis and has served as president of the International Society for Risk Analysis. She received her A.B. in biochemistry from Wellesley College and her Ph.D. in toxicology from M.I.T.

Related RPPI Publications

Kenneth Green, D.Env., *Seeking Safety in a Dangerous World: A Risk-reduction Framework for Policymakers*, Policy Study No. 261 (Los Angeles: Reason Public Policy Institute, August 1999).

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