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

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POLICY STUDY 283

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Executive Summary

Concern about the impact of the environment on health has become almost a religious issue in the United States, and one of the most controversial health issues is how best to protect children from environmental contaminants. Our ability to assess risks to children's health from chemical contaminants in the environment has become more sophisticated, as children's special behavior and consumption patterns are studied and factored in. Our understanding of the potential developmental toxicity of chemicals, especially developmental neurotoxicity, is incomplete, however, and should be improved. Surprisingly, data show that children generally are not more susceptible to chemical toxicity than adults, and that where differences do occur they are small, especially at low environmental exposures.

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.

Chemical contamination that occurs *in utero* or during childhood can of course have tragic consequences: stillbirths and spontaneous abortions, birth defects, greater likelihood of disease throughout both childhood and adulthood, and/or early mortality. These place great demands on social and emotional resources. The extent to which environmental chemicals—as distinct from other contaminations—contribute to such outcomes appears to be small, however. More stringent regulations, such as those required by the Food Quality and Protection Act to limit pesticide exposures, appear to be policy-driven, not science-based. Because the United States lacks both a public health surveillance network and the ability to track environmental exposures routinely, potential connections between environmental exposures and public health

outcomes are poorly understood for both children and adults. Without that understanding, the benefits or impacts of many environmental regulations limiting chemical exposures cannot be properly evaluated.

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Part 1

Introduction

A. Improvements in Children's Health and the Growth of Regulation

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.[1] 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.[2]

Overall, five causes account for 75 percent of the deaths in children: unintentional injuries, homicides, suicides, cancer, and congenital anomalies.[3] Major risk factors associated with mortality in children are alcohol use, drug use, motor vehicles, and access to firearms. By comparison, toxic agents and deficiencies in medical care—although they preoccupy national attention—are much less directly related to childhood mortality.[4] In fact, public opinion polls indicate that only a very small percent of the American public can identify the most serious childhood health problems. Most of those polled identified AIDS, infectious diseases, and drug abuse as the most serious problems faced by children today; in fact, those problems are responsible for only a small proportion of childhood morbidity and mortality.[5]

The extent to which exposures to occupational and environmental toxicants contribute to childhood mortality is unknown, but has been estimated to be 1 percent.[6] By comparison, mortality for all age groups due to these same exposures is estimated at 3 percent.[7] Nonetheless, increasing attention over the last 10 years has been given to the potentially disproportionate impact that environmental chemical exposures might have on the

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1 B. Guyer, M.A. Freedman, et al., "Annual Summary of Vital Statistics: Trends in the Health of Americans During the 20th Century," *Pediatrics*, vol. 108 (2000), pp. 1307–1317.

2 Public Health Policy Advisory Board, *Health and the American Child. Part 1: A Focus on Mortality Among Children. Risks, Trends, and Priorities for the21st Century* (Washington, DC, 1999).

3 United States Centers for Disease Control and Prevention, *Wonder Mortality Statistics* (Washington, D.C: 1998). (http://wonder.cdc.gov/)

4 Ibid.

5 R.J. Blendon, J.T. Young , et al., "Americans' Views on Children's Health," *Journal of the American Medical Association*, vol. 280 (1998), pp. 2122–2127.

6 Public Health Policy Advisory Board, *Health and the American Child. Part 1*.

7 J.M. McGinnis, and W.H. Foege, "Actual Causes of Death in the United States," *Journal of the American Medical Association*, vol. 270 (1993), pp. 2207-2212.

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 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.[8]

Much of the current concern surrounding children's health and risks from chemicals in the environment is attributed to the National Academy of Sciences (NAS) 1993 report *Pesticides in the Diets of Infants and Children.*[9] That report concluded that children may experience quantitatively and qualitatively different exposures to chemicals than do adults, that children may be more or less sensitive to chemically-induced toxicity compared to adults, and that standard approaches to risk assessment and regulation may not always account explicitly for potential age-related differences in exposure and toxicity. The report raised concerns that, at least in some cases, children may not be protected adequately by current regulatory policies.

Age-related effects on susceptibility appear to depend on the particular chemical, with children more sensitive than adults in some cases and less sensitive in others.

Response to the NAS report has been both scientific and political. Scientifically, many recognize that data are often inadequate to determine the extent to which children may or may not be experiencing disproportionate impacts from chemical exposures. Physiological and pharmacological differences due to age are poorly understood in many cases, as are age-related differences in chemical exposure patterns and levels. Age-related effects on susceptibility appear to depend on the particular chemical, with children more sensitive than adults in some cases and less sensitive in others. The new, children-focused research initiatives mentioned above are meant to address the paucity of information on age and risk by generating needed data.

Politically, however, the situation has polarized. Some are calling for precautionary "child-centered" risk evaluations and regulatory policies. The release of the EPA's revised cancer risk assessment guidelines has been delayed for at least a year due to pressure from some advocates to change its focus to children's risk assessment. Others argue that current regulatory practices are already adequate to protect children from environmental exposures, and they oppose more stringent regulation. Most agree that the regulatory changes instituted or contemplated will have an impact on product use and availability; few agree on whether those impacts will achieve the desired result of protecting or improving children's health.

Much of the controversy 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

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[8] P.J. Landrigan, "Risk Assessment for Children and Other Sensitive Populations," *Annals of the New York Academy of Sciences*, vol. 895 (1999), pp. 1–9.

[9] National Research Council, *Pesticides in the Diets of Infants and Children* (Washington, DC: National Academy Press, 1993).

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.

Part 2

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.[10] *Pesticides in the Diets of Infants and Children* concluded that differences in diet and thus in dietary exposure to pesticide residues account for most of the potential differences in pesticide-related health risks that may exist between children and adults (although the report did not find that children are at risk from pesticides in food).[11] The report found that both government and industry data on pesticide residue concentrations in foods reflected the regulatory emphasis on average adult consumption patterns, with foods eaten by infants and children under-represented in surveys of pesticide residues found in commodities.

A. Behaviors and Quantities

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. Occupational exposures—i.e. exposure to toxins in the workplace—would be greater for adults than children, but there are cases in which the children are exposed to residues unintentionally brought home by the parents. 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.

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[10] US Department of Agriculture, *Nationwide Food Consumption Survey: Continuing Survey of Food Intakes by Individuals, Women 19–50 Years and Their Children 1–5 Years* (Washington, DC: Human Nutrition Information Service, 1985).

[11] National Research Council, *Pesticides in the Diets of Infants and Children* (Washington, DC: National Academy Press, 1993).

As the types of children's chemical exposures are likely to differ from that 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. Part 3 of this report discusses the differences between children and adults that can affect dose.

B. Adjusting Estimations to Children

Current chemical risk assessment methods rely on retrospective estimates of exposures derived from animal-to-human extrapolations and mathematical modeling. Actual monitored human exposure data are rare, and thus accurate information about exposure is seldom available for either adults or children. Nonetheless, even poor exposure estimates can be improved to account for children's exposures. For example, adjusting exposure levels from adults to children may be appropriate when risk estimates are needed for less-than-lifetime exposures that occur during childhood. Data are available on air intake by age and activity level, on water intake by age, and on food consumption by age and ethnic group.[12] Adjusting exposure estimates to account for age-related differences in air, water, and food consumption and in behavior patterns has thus become routine, producing better exposure estimates.

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[12] A.M. Roseberry and D.E. Burmaster, "Lognormal Distributions for Water Intake by Children and Adults," *Risk Analysis*, vol. 12 (1992), pp. 99–104; D.S. Saunders and B.J. Peterson, *An Introduction to the Tolerance Assessment System* (Washington, DC: U.S. Environmental Protection Agency, 1997).

Table 1 shows examples of exposure factors for drinking water and breathing air over a range of age and population characteristics. Further research will produce more information about children's behavior patterns and their effects on exposures, along with more up-to-date food consumption information, for example. Such data continue to improve our ability to account for children's unique exposure characteristics when assessing chemical risks.

Table 1: Examples of Exposure Factors Recommended for Different Ages and Populations for Use When Assessing Risks From Drinking Water Contaminants

Age Group/Population	Mean Recommended Drinking Water Intake Rates (liters/day)	Mean Recommended Long-term Inhalation Rates (cubic meters/day)
< 1 year	0.30	4.5
< 3 years	0.61	—
1-2 years	—	6.8
3-5 years	0.87	8.3
6-8 years	—	10
9-11 years	—	14 males, 13 females
1-10 years	0.74	—
12-14 years	—	15 males, 12 females
15-18 years	—	17 males, 12 females
11-19 years	0.97	—
Adults	1.4	11.3 males, 15.2 females
Pregnant women	1.2	—
Lactating women	1.3	—
Active adults (temperate climate)	6	—
Active adults (hot climate)	11	—

Source: Adapted from U.S.EPA's *Exposure Factors Handbook* Volume 1 – General Factors, Chapter 3 ("Drinking Water") and Chapter 5 ("Inhalation"), August 1997.

Part 3

Susceptibility at Different Ages

A. Ingested Toxins

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.[13] 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 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 the situation in adults, liver toxicity and death from acetaminophen poisoning is extremely rare in children.[14] Reduced chemical toxicity in children is generally 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 Table 1 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.[15] 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 anti-psychotic drug Thorazine® (chlorpromazine) is cleared five times faster by children than by adults. Table 2 shows examples of some drug clearance rates at different ages.

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[13] J. Wilson, "Current Status of Teratology; General Principles and Mechanisms Derived from Animal Studies," in: *Handbook of Teratology; General Principles and Etiology*, ed. J. Wilson and F. Fraser (New York City: Plenum Press, 1977); E.M. Faustman, S.M. Silbernagel, et al., "Mechanisms Underlying Children's Susceptibility to Environmental Toxicants," *Environmental Health Perspectives*, vol. 108 (2000), pp. 13–21.

[14] A. Penna and N. Buchanan, "Paracetamol Poisoning in Children and Hepatotoxicity," *British Journal of Clinical Pharmacology*, vol. 32 (1991), pp. 143–149.

[15] In this context, "cleared" means "eliminated from the bloodstream."

Table 2: Drug Clearance Rates as a Function of Age			
Compound	Age	Clearance	Reference
Morphine (ml/min/kg)	< 7 days	8.7 ± 5.8	Pokela et al. 1993[16]
	7 days - 2 months	11.9 ± 5.1	
	2 - 6 months	28.0 ± 8.9	
	Children	20.5 - 25.7	Choonara et al. 1989, Lynn and Slattery 1987, Vandenberghe et al. 1983, Nahata et al. 1985[17]
	Adults	6.2 - 15.6	Choonara et al. 1992, Moore et al. 1984, Stanski et al. 1982[18]
Methotrexate (l/kg/h)	< 10 years	0.6	Donelli et al. 1995[19]
	10-15 years	0.2	
	Adults (>15 years)	0.1	
Thorazine® (chlorpromazine) (l/h/kg)	Children (0.3 - 17 years)	3.1 ± 0.6	Furlanut et al. 1990[20]
	Adults (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.

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.

The more rapid metabolism and elimination of many drugs by children (chemically similar to many environmental chemicals) may compensate in part for any increased sensitivity during development.[21]

16 M.L. Pokela, K.T. Olkkola, et al., "Pharmacokinetics of Single-dose Oral Ciprofloxacin in Infants and small children,". *Antimicrobial Agents and Chemotherapy*, vol. 36 (1992), pp. 1086–1090.

17 I.A. Choonara, P. McKay, et al., "Morphine Metabolism in Children," *British Journal of Clinical Pharmacology*, vol. 28 (1989), pp. 599–604; A.M. Lynn and J.T. Slattery, "Morphine Pharmacokinetics in Early Infancy," *Anesthesiology*, vol. 66 (1987), pp. 136–139; H. Vandenberghe, S. MacLeod, et al., "Pharmacokinetics of Intravenous Morphine in Balanced Anaesthesia: Studies in Children," *Drug Metabolism Reviews*, vol. 14 (1983), pp. 887-903; M.C. Nahata, A.W. Miser, and R.H. Reuning, "Variation in Morphine Pharmacokinetics in Children with Cancer," *Developmental Pharmacology and Therapeutics*, vol. 8 (1985), pp. 182–188.

18 C. Choonara, A. Lawrence, et al., "Morphine Metabolism in Neonates and Infants," *British Journal of Clinical Pharmacology*, vol. 34 (1992), pp. 434–437; R.A. Moore, D. Baldwin, et al., "Sensitive and Specific Morphine Radioimmunoassay with Iodine Label: Pharmacokinetics of Morphine in Man after Intravenous Administration," *Annals of Clinical Biochemistry*, vol. 21 (1984), pp. 318–325; D.R. Stanski, L. Paalzow, and P.O. Edlund, "Morphine Pharmacokinetics: GLC Assay Versus Radioimmunoassay," *Journal of Pharmaceutical Science*, vol. 71 (1982), pp. 314–317.

19 M.G. Donelli, M. Zucchetti, et al., "Pharmacokinetics of HD-MTX in Infants, Children and Adolescents with Non-lymphoblastic Leukemia," *Medical and Pediatric Oncology*, vol. 24 (1995), pp. 154–159.

20 M. Furlanut, P. Benetello, M. Baraldo, G. Zara, G. Montanari, and F. Donzelli, "Chlorpromazine Disposition in Relation to Age in Children, *Clinical Pharmacokinetics*, vol. 18 (1990), pp. 329–331.

B. Environmental (External) Toxins

Much attention has been focused on the susceptibility of children to chemical carcinogens in the environment. The EPA's cancer risk assessment guidelines conclude that "[m]ost often differences between carcinogenic effects in the young vs. adults can be traced to differences in the handling of chemical agents."[22] With notable exceptions, very few human cancers occur in children; cancer is a set of diseases that occur with advancing age. The incidence of cancer in children, like that for all ages, has shown a net increase of about 20 percent since 1975—although children's mortality from cancer has declined by almost 50 percent while mortality from cancer for all ages has remained unchanged.[23] A number of environmental exposures, including pesticides, parental occupational exposures, ionizing radiation (gamma rays, radon), non-ionizing radiation (power lines, electrical appliances), and infectious organisms, have been suggested as possible precursors to cancer in children; however, the considerable research conducted to date has yielded inconsistent or limited evidence linking those factors to cancer in children.[24]

The incidence of cancer in children, like that for all ages, has shown a net increase of about 20 percent since 1975—although children's mortality from cancer has declined by almost 50 percent while mortality from cancer for all ages has remained unchanged.

Experiments using laboratory animals suggest that young animals are not generally more sensitive to chemical carcinogens than older animals. The EPA's 1996 report, *Comparison of the Effects of Chemicals with Combined Perinatal and Adult Exposure vs. Adult-Only Exposure in Carcinogenesis Bioassays*, concluded that lowering the age of first chemical exposure in rodents to include the perinatal stage (from the 20th week of gestation to the 28th day of life) neither increased the sensitivity of the bioassays nor produced tumors of different types than did the standard bioassays.[25] That report also showed that increasing total doses by adding a perinatal stage can slightly increase tumor incidence and sometimes decrease tumor latency. Studies of the effects of anticancer drugs, viral infections, and ionizing radiation demonstrate that both the young and old develop a similar spectrum of tumors.[26] Taken together, those observations do not provide strong support for the idea that children are generally more sensitive to carcinogens than adults.

Rodent bioassays show that younger animals are less susceptible to chemical carcinogens in some cases and more susceptible in others, depending on the chemical. *Pesticides in the Diets of Infants and Children*

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21 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.

22 U.S. Environmental Protection Agency, *Guidelines for Carcinogen Risk Assessment*, July 1999 draft (Washington, DC: Risk Assessment Forum, 1999).

23 National Cancer Institute, "SEER Cancer Statistics Review, 1973-1998," L.A.G. Ries, M.P. Eisner, et al. (eds), (Bethesda, MD: National Cancer Institute, 2001).

24 Public Health Policy Advisory Board, *Health and the American Child. Part 1*.

25 U.S. Environmental Protection Agency, *Comparison of the Effects of Chemicals with Combined Perinatal and Adult Exposure vs. Adult Only Exposure in Carcinogenesis Bioassays* (Washington, DC: Office of Research and Development, 1996). A "bioassay" tests the impact of a chemical or drug using animals, bacteria, or other tissue cultures.

26 Ibid.

included a table summarizing the results of studies (performed through 1983) in which the effects of age on chemically-induced carcinogenesis in rodents had been evaluated.[27] Charnley and Putzrath (2001) updated those results to include studies performed since 1983.[28] The data indicate that there are a similar number of studies showing that younger animals are less susceptible than adults (47 percent) to chemically-induced carcinogenesis as there are showing that they are more susceptible (40 percent) under the conditions of the bioassays. A number of studies showed that age played no role at all in susceptibility (13 percent).

The NAS report concluded that the rodent bioassays 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.[29] 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 are thus difficult to make.

Experiments using laboratory animals suggest that young animals are not generally more sensitive to chemical carcinogens than older animals.

Data on acute chemical toxicity show similar results. A review of the data available on the lethal doses of a variety of chemicals for 50 percent of exposed laboratory rodents (LD_{50} milligram-per-kilogram body weight) showed only small differences due to age.[30] 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.[31] 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 to toxicity than older animals in only four cases.[32] In contrast, 14 of 15 organophosphate

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[27] National Research Council, *Pesticides in the Diets of Infants and Children* (Washington, DC: National Academy Press, 1993).

[28] G. Charnley and R.M. Putzrath, "Children's Health, Susceptibility, and Regulatory Approaches to Reducing Risks from Chemical Carcinogens," *Environmental Health Perspectives*, vol. 109 (2001), pp. 187–192.

[29] National Research Council, *Pesticides in the Diets of Infants and Children* (Washington, DC: National Academy Press, 1993).

[30] E.J. Calabrese, *Age and Susceptibility to Toxic Substances* (New York City: John Wiley & Sons, 1986).

[31] J.V. Bruckner, "Differences in Sensitivity of Children and Adults to Chemical Toxicity: The NAS Panel Report." *Regulatory Toxicology and Pharmacology*, vol. 31 (2000), pp. 280–285.

[32] T.B. Gaines and R.E. Linder, "Acute Toxicity of Pesticides in Adult and Weanling Rats," *Fundamental and Applied Toxicology*, vol. 7 (1986), pp. 299–308.

pesticides showed greater acute toxicity to weanling rats than to adult rats.[33] Newborn rats were more sensitive than adult rats to malathion poisoning, but less sensitive than adult rats to dieldrin toxicity.[34]

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 situation. 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.

[33] J. Brodeur and K.P. DuBois, "Comparison of Acute Toxicity of Anticholinesterase Insecticides to Weanling and Adult Male Rats," *Proceedings of the Society for Experimental Biology and Medicine*, vol. 114 (1963), pp. 509–511.

[34] F.C. Lu, D.C. Jessup and A. Lavallée, "Toxicity of Pesticides in Young Versus Adult Rats," *Food and Cosmetic Toxicology*, vol. 3 (1965), pp. 591–596.

Part 4

Formal Risk Assessment Factors

Some have accused EPA of failing to consider explicitly risks to children, but that accusation is not justified. Assessing health risks from chemical exposures involves reviewing all the toxicology testing data available for the chemical of interest. Thorough toxicity testing batteries include protocols designed to expose developing animals to test chemicals both before and after birth in order to detect any abnormalities. Chemicals regulated under the Toxic Substances Control Act or the Federal Insecticide, Fungicide, and Rodenticide Act, for example, must undergo such testing. Thousands of chemicals currently being screened under the high-production-volume chemical-testing initiative are being tested for developmental effects. When developmental effects have been detected, they have been considered in EPA risk assessments. Current efforts to extend and improve the ability of toxicity testing to detect developmental toxicants will increase the sensitivity of the testing batteries and strengthen the basis of risk assessment.

A. The Uncertainty Factor

EPA risk assessments include the use of uncertainty factors designed to account for differences in susceptibility within and among species (i.e. between rats and humans).[35] For example, if a chemical produces developmental abnormalities in rats, the lowest dose that produced those abnormalities is divided by an uncertainty factor of 10 when applied to humans because people might be more sensitive than rats. They are then divided by yet another uncertainty factor of 10 because some people are more sensitive than other people. The resulting exposure level—100 times lower than the level that produced toxicity—is considered to be "without an appreciable risk of deleterious effects during a lifetime," even to sensitive individuals.[36] Thus, if developing animals are found to be the group most sensitive to a chemical's toxicity, that fact forms the basis of any assessment of the chemical's risk and uncertainty factors are used to protect the most sensitive individuals. Studies that have evaluated risk assessments based on developmental toxicity in animals have shown that they are adequate to protect the human fetus.[37]

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[35] M.L. Dourson, S.P. Felter, and D. Robinson, "Evolution of Science-based Uncertainty Factors in Noncancer Risk Assessment." *Regulatory Toxicology and Pharmacology*, vol. 24 (1996), pp. 108-120.

[36] U.S. Environmental Protection Agency, Glossary of IRIS Terms, http://www.epa.gov/ngispgm3/iris/gloss8.htm.

[37] L.M. Newman, E.M. Johnson, and R.E. Staples, "Assessment of the Effectiveness of Animal Developmental Toxicity Testing for Human Safety." *Reproductive Toxicology*, vol. 7 (1993), pp. 359–390; J.L. Schardein, and K.A Keller, "Potential Human Developmental Toxicants and the Role of Animal Testing in their Identification and Characterization." *CRC Critical Reviews in Toxicology*, vol. 19 (1989), pp. 251–339.

The 1996 Food Quality Protection Act requires that an additional uncertainty factor of 10 be used in risk assessments of pesticides (for an acceptable exposure level 1,000 times lower than the toxic level) to account for potentially greater risks to infants and children, unless adequate evidence exists to show that there is no such greater risk. Debate about the need for that additional uncertainty factor is considerable. During the past 50 years of regulating thousands of substances, there is no known case of toxicity in children from the ingestion of pesticides that were used in conformity with established restrictions.[38] If one argues that children are not at risk from dietary pesticide exposures, as can be concluded from *Pesticides in the Diets of Infants and Children*, further restrictions on pesticide exposures by 10-fold has no apparent advantage.[39] If one believes—despite an apparent lack of evidence—that children experience unacceptable risk from dietary pesticides, whether another 10-fold factor will be sufficiently (or overly) protective depends on knowing the pesticide's dose-response relationship, or the dose at which toxicity is produced experimentally as compared to the exposure of interest. It also depends on knowing how the differences between the dose-response relationships for children and adults change with level of exposure.[40] If laboratory animals' pesticide exposures are similar to children's, such comparisons would be straightforward. However, doses used in the laboratory and actual human doses often vary by several orders of magnitude, making the likely effectiveness of the additional 10-fold uncertainty factor very difficult to evaluate.

A review of EPA pesticide risk assessments conducted between 1996 and 1998 indicates that in many cases, the additional uncertainty factor of 10 was not applied if two developmental toxicity studies and a rat multi-generational study (that tests for both developmental and reproductive effects) had been performed and were negative.[41] If such studies were missing, the additional uncertainty factor was applied. If such studies were performed and were positive, however, the additional uncertainty factor was also applied, constituting a precautionary approach that double-counts for uncertainties in the risk assessment process.

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38 R.J. Scheuplein, "Pesticides and Infant Risk: Is There a Need for an Additional Safety Margin?" *Regulatory Toxicology and Pharmacology*, vol. 31 (2000), pp. 267–279.

39 Ibid.; See also National Research Council, *Pesticides in the Diets of Infants and Children* (Washington, DC: National Academy Press, 1993).

40 G. Charnley and R.M. Putzrath, "Children's Health, Susceptibility, and Regulatory Approaches to Reducing Risks from Chemical Carcinogens," *Environmental Health Perspectives*, vol. 109 (2001), pp. 187–192.

41 J.C. Lamb, *Understanding Emerging Issues in Assessing Children's Health Risks*. Prepared by Jellinek, Schwarz and Connolly, Inc. for the American Industrial Health Council, American Petroleum Institute, Chlorine Chemistry Council, and American Chemistry Council (Arlington, VA, 1998).

Part 5

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 both 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 studies we've examined demonstrate that evaluating the relative sensitivity of children and adults to chemical toxicity must be done on a case-by-case basis.[42] 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 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.[43] 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. 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.

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. Concern about the impact of the environment on

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[42] International Life Sciences Institute, *Similarities and Differences Between Children and Adults: Implications for Risk Assessment* (Washington, DC: ILSI Press, 1992); National Research Council, *Pesticides in the Diets of Infants and Children* (Washington, DC: National Academy Press, 1993).

[43] 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; R.J. Scheuplein, "Pesticides and Infant Risk: Is There a Need for an Additional Safety Margin?" *Regulatory Toxicology and Pharmacology*, vol. 31 (2000), pp. 267–279.

health has become virtually a religious issue. Without adequate data to support or refute suspected associations, risk decisions can be co-opted by vested interests of all stripes.

According to a recent Pew Environmental Health Commission study, the United States are 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.[44] Because the United States lack a national disease surveillance network and the ability to track environmental exposures, they are unable to make meaningful connections between environmental exposures and public health outcomes. In *America's Children and the Environment,* EPA recently tried to convey information about trends in children's environmental health but was limited to vague indices that convey no 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."[45]

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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.[46] 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 has 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 relatively insignificant amount of federal support for health- and human services-related environmental agencies, coupled with the "command-and-control" tendencies of regulatory agencies, have weakened the ability of the federal government to effectively target public health improvements. Partnerships between the EPA and state and community public health agencies, the Centers for Disease Control and Prevention, and the NIEHS are needed to help develop the environmental health data and infrastructure that would provide a scientific basis for identifying, responding to, and preventing the components of chronic disease attributable to environmental exposures. 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.

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[44] Pew Environmental Health Commission, *America's Environmental Health Gap: Why the Country Needs a Nationwide Health Tracking Network* (Baltimore: Johns Hopkins School of Public Health, 2000).

[45] U.S. Environmental Protection Agency, *America's Children and the Environment: A First View of Available Measures* (Washington, DC: Office of Children's Health Protection and National Center for Environmental Economics, 2001).

[46] C.E. Koop, testimony to the Senate Labor and Human Resources Committee, May 1998; Public Health Policy Advisory Board, *Health and the American Child. Part 1: A Focus on Mortality Among Children. Risks, Trends, and Priorities for the 21st Century* (Washington, DC, 1999).

About The Author

Dr. Gail Charnley, President of Health Risk 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 is immediate past president of the International Society for Risk Analysis. She received her Ph.D. in Toxicology from M.I.T. and her A.B. in biochemistry from Wellesley College.

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