Children’s Vulnerability To Toxic Chemicals: A Challenge And Opportunity To Strengthen Health And Environmental Policy

ABSTRACT A key policy breakthrough occurred nearly twenty years ago with the discovery that children are far more sensitive than adults to toxic chemicals in the environment. This finding led to the recognition that chemical exposures early in life are significant and preventable causes of disease in children and adults. We review this knowledge and recommend a new policy to regulate industrial and consumer chemicals that will protect the health of children and all Americans, prevent disease, and reduce health care costs. The linchpins of a new US chemical policy will be: first, a legally mandated requirement to test the toxicity of chemicals already in commerce, prioritizing chemicals in the widest use, and incorporating new assessment technologies; second, a tiered approach to premarket evaluation of new chemicals; and third, epidemiologic monitoring and focused health studies of exposed populations.

Recognition of the unique vulnerability of children, infants, and fetuses to toxic chemicals in the environment was a watershed development for health and environmental policy.1 This discovery catalyzed two further insights: that early life exposures to toxic chemicals are important causes of disease and dysfunction in children and also in adults,2–4 and that diseases caused by chemicals can successfully be prevented, thus saving lives, enhancing the quality of life, reducing health care and education costs, and increasing national productivity. A notable example is the nation’s experience with removing lead from gasoline. This one change reduced lead poisoning by more than 90 percent5 and produced an estimated annual economic benefit of $110 billion to $319 billion.6

These insights have affected risk assessment, regulation, and law.7 In this article we explore the implications for health and environmental policy.

Children Are Vulnerable To Toxic Chemicals

The realization that children are uniquely sensitive to toxic chemicals was catalyzed by the publication in 1993 of a National Academies report, Pesticides in the Diets of Infants and Children.1 Studies cited in the report found that children are quantitatively and qualitatively different from adults in their sensitivity to pesticides and other chemicals.

Prior to the report’s publication, virtually all environmental policy in the United States had focused on assessment of risk to the “average adult.” Risk assessment had paid scant heed to exposures that diverged from the norm. Little attention was paid to the unique risks of infants, children, or other vulnerable groups within the population.

The report produced a paradigm shift in that approach to health and environmental policy. It led to new legislative and regulatory initiatives to better protect infants and children against environmental health threats and has been especially
influential in changing the regulation of pesticide and pharmaceutical chemicals.7

The report identified four differences between children and adults that contribute to children’s heightened susceptibility to chemicals in the environment.

First, children have greater exposures to toxic chemicals for their body weight than adults.1 A six-month-old infant drinks seven times more water per pound than an adult.6 Children take in three to four times more calories per pound than adults. The air intake per pound of an infant is twice that of an adult. These differences result in children being disproportionately exposed to toxic chemicals in air, food, and water. Children’s hand-to-mouth behavior and play on the ground further magnify their exposures.

Second, children’s metabolic pathways are immature,2 and a child’s ability to metabolize toxic chemicals is different from an adult’s. In some instances, infants are at lower risk than adults because they cannot convert chemicals to their toxic forms. More commonly, however, children are more vulnerable because they lack the enzymes needed to break down and remove toxic chemicals from the body.9

Third, children’s early developmental processes are easily disrupted.3 Rapid, complex, and highly choreographed development takes place in prenatal life and in the first years after birth, continuing more slowly throughout childhood into puberty. In the brain, for example, billions of cells must form, move to their assigned positions, and establish trillions of precise interconnections.10 Likewise, development of the reproductive organs is guided by a complex and precisely timed sequence of chemical messages and is shaped by maternal and fetal hormones.11

Recent research in pediatrics and developmental toxicology has elaborated the concept of “windows of vulnerability.”12 These are critical periods in early development when exposures to even minute doses of toxic chemicals—levels that would have no adverse effect on an adult—can disrupt organ formation and cause lifelong functional impairments.

If, for example, cells in an infant’s brain are injured by lead or a pesticide, the consequences can include developmental disabilities in childhood10,13 and possibly increased risk of neurological degeneration, such as Parkinson’s disease, in adult life.4 If inappropriate hormonal signals are sent to the developing reproductive organs by a synthetic chemical endocrine disruptor—such as certain chemicals commonly found in household products, plastics, and cosmetics (phthalates), and on clothing (flame retardants)—lifelong reproductive impairment may ensue.11 These windows of vulnerability have no equivalent in adult life.

Fourth, children have more time than adults to develop chronic diseases. Many diseases triggered by toxic chemicals, such as cancer and neurodegenerative diseases, are now understood to evolve through multistage, multyear processes that may be initiated by exposures in infancy.1,4 This insight has catalyzed new research to identify how early environmental influences may affect health in childhood and across the human lifespan. Notable research includes the US National Children’s Study,14 the Japan Environment and Children’s Study,15 and the International Childhood Cancer Cohort Consortium.16

Rates Of Chronic Diseases In US Children Are Rising

Today in the United States, the principal causes of sickness, disability, and death in children are chronic illnesses. Rates of many of these diseases are high and rising.2,3 Toxic chemicals in the environment are making important contributions to these disease trends.

Asthma is one of the most common chronic diseases in American children. The prevalence of childhood asthma has more than doubled over the past twenty years, and in 2008, 9 percent of all US children had asthma.17,18 Asthma is the leading cause of pediatric hospitalization and school absenteeism and a major driver of pediatric health costs.

Birth defects are now the leading cause of infant death and are associated with substantial health and education costs. Certain birth defects, such as those of the male reproductive organs19 and of the abdominal wall,20 appear to have increased in frequency.

Neurodevelopmental disorders, including dyslexia, mental retardation, attention deficit hyperactivity disorder, and autism, affect 5–10 percent of the babies born in the United States each year.21 Autism spectrum disorder is currently diagnosed in one of every 110 American children.22 The prevalence of attention deficit hyperactivity disorder has also risen, and today 14 percent of US children have been diagnosed with this condition; two-thirds of them also have learning disabilities.23

The incidence of leukemia and brain cancer in children younger than age eighteen increased steadily from the 1970s through the 1990s, despite declining mortality.24 Testicular cancer in males ages 15–30 has increased in incidence by more than 50 percent.24

Obesity in children has tripled in prevalence over the past twenty years, from 5 percent to
17 percent. One of its consequences, type 2 diabetes, is occurring earlier in life and at epidemic rates.

**Children And The Chemical Environment**

The environment in which American children live has changed greatly in the past fifty years, especially in terms of the chemicals to which they are routinely exposed. During this time, more than 80,000 new synthetic chemicals have been invented and are used today in millions of consumer products, ranging from foods and food packaging to clothing, building materials, cleaning products, cosmetics, toys, and baby bottles.

Some of these chemicals may pose risks for children’s health. The Environmental Protection Agency has identified 3,000 “high-production-volume” chemicals—chemicals produced in quantities of more than a million pounds per year—that are in widest use and therefore have the greatest potential for human exposure. Children are especially at risk for exposure to these chemicals.

In national surveys conducted by the Centers for Disease Control and Prevention, measurable quantities of 200 high-production-volume chemicals have been detected in the blood and urine of virtually all Americans, including pregnant women. The significance of this finding for human health is not fully understood. But it is worrisome, because most of these chemicals have not undergone even minimal assessment for potential toxicity, and only about 20 percent of them have been screened for their potential to disrupt early human development or to cause disease in infants and children. Even less is known about the potential effects of exposure to several of these chemicals simultaneously, or how they may interact with one another in the human body, possibly causing synergistic adverse effects on health.

The absence of information about the possible risks associated with routine exposure to untested synthetic chemicals is fraught with risk for disease and dysfunction. Unless studies are conducted to specifically seek ill effects associated with chemical exposures, dysfunctions can go unrecognized for many years.

The “silent epidemic” of childhood lead poisoning is a dramatic case in point. Millions of American children were exposed to excessive levels of lead from the 1940s to the 1970s, when lead was an additive to gasoline. Many suffered unrecognized brain injury before sufficient evidence could be marshaled to mandate removing lead from gasoline, household paint, and consumer products.

Failure to evaluate chemicals for potential toxicity reflects the failure of the Toxic Substances Control Act of 1976. At the time of its passage, the act was intended to be pioneering legislation that would require testing chemicals already in commerce for potential toxicity, and would also require premarket evaluation of all new chemicals. The act never fulfilled these intentions. A particularly egregious lapse was a decision by Congress to “grandfather in” 62,000 chemicals already on the market without any toxicity testing requirement. These chemicals were presumed to be safe and allowed to remain in commerce, unless and until the Environmental Protection Agency made a finding that they posed an “unreasonable risk.”

The “unreasonable risk” standard identified in the Toxic Substances Control Act has created a substantial barrier to the regulation of industrial and consumer chemicals. This standard has been so burdensome that the Environmental Protection Agency has not been able to remove chemicals from the market except when there is overwhelming evidence of potential harm. The result is that only five chemicals have been controlled under the act in the thirty-five years since its passage. These chemicals were polychlorinated biphenyls (PCBs), chlorofluorocarbons, dioxin, asbestos, and hexavalent chromium. Only two of these five were totally banned; PCBs, which were eliminated by an act of Congress and not because the Environmental Protection Agency exercised its authority, and asbestos, a chemical for which there is overwhelming evidence of serious hazard to human health.

Further barriers to enforcement of the Toxic Substances Control Act have resulted from the federal courts’ interpretation of the “unreasonable risk” standard. Thus, in a 1991 opinion on the asbestos ban in *Corrosion Proof Fittings v. EPA*, the Fifth Circuit found that the Environmental Protection Agency had failed to show that it was taking the “least burdensome” approach required under the act in formulating its final rule banning asbestos. The court thus overturned the agency’s rule. This interpretation has made it virtually impossible since 1991 for the Environmental Protection Agency to regulate dangerous chemicals under the act.

**Toxic Chemicals And Disease In Children**

Evidence is strong and continuing to accumulate that toxic chemicals are important causes of disease and dysfunction in children. This recognition first arose in studies of lead and mercury. In recent years, as research strategies in environmental pediatrics have become more refined, the...
pace of scientific discovery has quickened and a series of new associations has been discovered. Examples include the following.

Prenatal exposure to PCBs is associated with reduction in children’s intelligence.37 PCBs are an environmentally persistent class of chemicals that accumulate to high levels in certain species of fish. Human exposure is principally the consequence of maternal consumption of contaminated fish before and during pregnancy. Although PCBs are no longer manufactured in the United States, they were used extensively for many years in manufacturing electrical equipment such as transformers, and they continue to be important contaminants today because they are highly persistent in the environment and because they become concentrated in the tissues of organisms in the food chain.

Prenatal exposure to the commonly used insecticide chlorpyrifos is associated with reduced head circumference at birth36 and with developmental delays.39 Small head circumference at birth is an indicator of delayed brain growth during pregnancy. Chlorpyrifos is also linked to pervasive developmental disorder, a form of autism.39,40

Baby boys exposed in the womb to phthalates—a chemical compound found in plastics, cosmetics, and many common household products—appear to be at increased risk of behavioral abnormalities that resemble attention deficit hyperactivity disorder.41 Prenatal exposure to bisphenol A, a synthetic chemical used to manufacture polycarbonate plastics, is linked to behavioral abnormalities in girls.42 Prenatal exposure to brominated flame retardants is linked to cognitive impairments,43 and prenatal exposures to arsenic and manganese is associated with neurodevelopmental impairment.39,44

Rates of asthma are increased in children exposed to secondhand cigarette smoke and to fine particulate air pollution.17,18 Risk of respiratory death is increased in infants exposed to fine particulate air pollution.46

Prenatal exposure to phthalates has also been linked to shortening of the ano-genital distance in baby boys, a finding indicative of feminization.47 Prenatal exposure to perfluorinated chemicals (perfluorooctanoic acid and perfluorooctane sulfonate) used to make nonstick pans and stain repellents has been linked to decreased birthweight and reduced head circumference in newborn infants.48

**Diseases Associated With Chemicals Are Costly**

Preventing exposures to chemicals can yield great savings. To estimate the contribution of environmental pollutants to the prevalence and costs of disease in American children, investigators at Mount Sinai School of Medicine examined four categories of illness: lead poisoning, asthma, cancer, and neurobehavioral disorders.49 Based on prevalence, the environmentally attributable fraction of each disease, and national economic data, they calculated that the total annual costs of these diseases attributable to environmental exposures is $54.9 billion (range $48.8 billion to $64.8 billion): $43.4 billion for lead poisoning, $2.0 billion for asthma, $0.3 billion for childhood cancer, and $9.2 billion for neurobehavioral disorders. Because of the difficulties inherent in assessing the full economic consequences of neurobehavioral impairments, it is likely that these estimates are low.

Disease and dysfunction caused by toxic chemicals can be prevented. Prevention is most effectively achieved by assessing chemicals for toxicity through laboratory and human studies and using the data gained in those assessments to guide evidence-based prevention of exposure. Great cost savings can result.

Again, we use the example of phasing out the use of lead in gasoline. This phase-out began in the United States in 1976, was 50 percent accomplished by 1980, and virtually complete by 2000.5 Prior to 1976, 100,000 tons of tetraethyl lead was added to the US gasoline supply each year to improve engine performance and fuel efficiency. Widespread environmental contamination resulted.

The average US blood lead level peaked in the mid-1970s at 17 micrograms per deciliter, a level significantly above the current Centers for Disease Control and Prevention guideline of 10 micrograms per deciliter and now known to be associated with significant toxic injury to the developing brain. These elevated blood lead levels, found in epidemiologic studies, were associated with reduced intelligence, shortened attention span, and disruptive behavior in children.33,34 Each increase of 3 micrograms per deciliter in mean blood lead level was shown to be associated with a decline of 0.5–1.0 points in intelligence quotient (IQ).6 These effects occurred in the absence of any clinical symptoms or obvious illness and were thus termed “silent” lead poisoning.34

The discovery that lead could erode children’s intelligence even at relatively low levels was not the original justification for the Environmental Protection Agency’s decision to remove lead from gasoline. In fact, the decision to remove lead was made in the first instance to protect catalytic converters from damage by lead. However, the discovery did play an important role in reinforcing the decision and in sustaining it over
time. A result of the phase-out was that between 1976 and 1990 the mean blood lead level of American children decreased by more than 90 percent (to below 2 micrograms per deciliter today). The incidence of childhood lead poisoning also fell by more than 90 percent.

A further consequence of the reduction in exposure to lead was that the mean IQ of American children has increased. Children born in the United States today are estimated to have IQ scores that, on average, are 2.2–4.7 points higher than those of children born in the early 1970s. And because each 1-point gain in population mean IQ is associated with an estimated 2 percent increase in productivity over a lifetime, the gain in population IQ is estimated to have produced a national economic benefit of $110–$319 billion in each annual cohort of babies born in the United States since the 1980s.

Consequences For Environmental Policy

The recognition of children’s unique vulnerability to toxic chemicals has had far-reaching consequences.

**Legislative Consequences**

Recognition of children’s susceptibility to toxic chemicals strongly influenced the Food Quality Protection Act of 1996, the major federal law governing the use of pesticides. This act became the first federal environmental statute to contain explicit provisions for protecting children’s health.

This recognition led also to passage of the Best Pharmaceuticals for Children Act of 2002. This act requires that drugs labeled for use in children undergo studies to specifically examine children’s susceptibilities.

**Consequences for Risk Assessment and Regulation**

A key provision of the Food Quality Protection Act is a requirement that federal pesticide standards (“tolerances”) be health-based and that they explicitly consider the effects of pesticides on children’s health. This requirement represents a diametric change from the previous regulatory regime, in which the health risks of pesticides were balanced against the costs of regulation to agricultural producers in setting standards. This provision of the act forced reexamination of all extant pesticide tolerances to ensure that they met the standard of public health protection. As a result, many uses of pesticides were reduced or dropped altogether.

For example, agricultural use of organophosphate insecticides, a class of pesticide chemicals toxic to brain development, was reduced. The review led also to bans on residential applications of two widely used insecticides—chlorpyrifos and diazinon—that had been used for household pest control.

The Food Quality Protection Act mandates realistic consideration of exposures to multiple pesticides via multiple routes to assess potentially synergistic effects. The law also mandates consideration of exposures to pesticide chemicals that are endocrine disruptors. These are chemicals that exert their toxicity through interactions with the endocrine system, disrupting function of the thyroid or pituitary glands, the ovaries, or the testes, or changing levels of hormones by changing their metabolism.

The new approaches to risk assessment mandated by the Food Quality Protection Act have not yet extended beyond pesticides to include industrial or consumer chemicals.

**Consequences For Biomedical Research**

Recognition of children’s vulnerability led to establishment of the Office of Children’s Health Protection within the Environmental Protection Agency. It catalyzed a 1997 executive order requiring federal agencies to consider children’s special susceptibilities in all policy and rule making. And it led to the creation of a White House Task Force on Children’s Health and Safety.

Those programs have, in turn, stimulated substantial investments in children’s health research. The resulting initiatives include the following: a national network of Centers for Children’s Environmental Health and Disease Prevention Research, supported by the National Institute of Environmental Health Sciences and the Environmental Protection Agency; a network of Pediatric Environmental Health Specialty Units supported by the Centers for Disease Control and Prevention and the Agency for Toxic Substance and Disease Registry; fellowship training programs in environmental pediatrics; and the National Children’s Study, a prospective epidemiologic study that will follow a nationally representative sample of 100,000 children from early pregnancy to age twenty-one.

**Consequences For Health Policy**

The finding that children are uniquely vulnerable to synthetic chemicals indicates the need for fundamental revision of US chemical policy. By default, current policy presumes chemicals to be safe and permits them to enter and remain on the market with minimal evaluation of potential toxicity unless and until they are proved to be overwhelmingly hazardous by the Environmental Protection Agency, using the Toxic Substances Control Act’s standard of “unreasonable risk.” This policy is neither protective of human health nor consistent with current scientific
A New US Chemical Policy

The linchpin of a new, health-based chemical policy would be a legally mandated requirement that chemicals already on the market be systematically examined for potential toxicity. Such testing will not be an easy task, but it is necessary. It will be far more challenging than updating the tolerances for pesticides proved to be.

To evaluate tens of thousands of chemicals currently in commercial use would require new legislation that directed the Environmental Protection Agency to first address those classes of chemicals that are in the widest use and the most likely to confer risk. Data on the use of chemicals in consumer products, especially products used by young children and pregnant women; data on discharges of chemicals into the air and water; and data on chemicals already widely detectable in the bodies of Americans would help to target the chemicals that most urgently need to be evaluated.

Enhanced evaluation of chemical toxicity would require new, more efficient approaches to toxicity testing. Such approaches are already in development at the National Institute of Environmental Health Sciences and the Environmental Protection Agency. These approaches should incorporate new technologies identified through research in developmental toxicology and consider such complexities as which endpoints to assess, which doses to administer, and which mixtures to evaluate.

A second critical component of a health-based chemical policy would be a legally mandated, strictly enforced requirement that all new chemicals be assessed for potential toxicity before they enter the market. Such assessment could be undertaken in tiered fashion, making use of new rapid assessment methods in computational and in vitro toxicology, taking into account the proposed use patterns of new chemicals, and giving the Environmental Protection Agency latitude to require less extensive evaluation of chemicals and chemical uses judged to be less hazardous to health.

As has happened with pesticides, the new approach to the evaluation of industrial chemicals that we propose here would be more likely to result in continued approval for certain uses and withdrawal of approval for others, rather than outright bans of chemicals. For example, the United States, Canada, and the European Union have all recently taken action to ban polycarbonate plastics containing bisphenol A from baby bottles. However, in all of these regions, polycarbonates are still permitted in the manufacture of compact discs, eyeglasses, and other consumer products in which the potential for human exposure is judged to be lower than in uses where the bisphenol A can migrate into foods.

One model approach to health-based chemical policy can be found in the European Union’s Registration, Evaluation, Authorisation and Restriction of Chemical Substances legislation, enacted in 2007. This legislation, commonly referred to by its acronym, REACH, places the responsibility on industry to generate substantial amounts of data on potential risks of commercial chemicals and to register this information in a central database that is housed in the European Chemical Agency in Helsinki. The European Chemical Agency not only manages this central database but also coordinates the in-depth evaluation of suspicious chemicals. It is also developing a public database to house and make accessible hazard information relevant to consumers and health and environmental professionals. The first cycle of REACH registrations closed in January 2010 and in February 2011 the European Chemical Agency released its first list of six dangerous substances that are to be phased out by the European Union, through a process that involves scientific analysis and consultation with member states. The European Union is using this information to craft regulations that protect the health of European children, and it has led to bans and restrictions of certain potentially toxic products.

Much of the information collected by the European Chemical Agency will be available to the Environmental Protection Agency in the United States, allowing it to more efficiently conduct risk assessments and to target more effectively the industrial chemicals that are most hazardous to health.

The credible possibility exists that among the hundreds of untested chemicals currently in widespread commercial use, there are synthetic chemicals whose toxicity to early childhood development has not yet been discovered. The late David Rall, former director of the National Institute of Environmental Health Sciences, once stated, “If thalidomide [a drug widely used in the 1950s and 1960s to treat morning sickness in early pregnancy] had caused a ten-point loss of IQ instead of obvious birth defects of the limbs, it probably would still be on the market.”

To protect human health, and especially the health of infants and children, the paradigm for regulating industrial and consumer chemicals needs to become health-based. The Toxic Substances Control Act’s “unreasonable risk” standard needs to be replaced with a new standard that explicitly considers effects of industrial and consumer chemicals on children’s health. Such a move would align the strategy used to regulate pesticides under the Food Quality Protection Act to regulate industrial chemicals with the strategy used to regulate industrial chemicals already on the market.

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Vulnerabilities of Children

The argument will probably be made that any additional controls on chemicals would cost jobs and harm the economy. However, there is little evidence that environmental protection has to date been harmful to the US economy or to business. To the contrary, there is compelling evidence that the high costs of diseases caused by toxic chemicals are a major, but potentially avoidable, drag on the US economy.

Conclusion

Recognition of children’s unique vulnerability to toxic chemicals, a vulnerability that receives scant consideration in current US chemical policy, challenges existing policy and creates an opportunity for change.

Creating a new chemical policy explicitly protective of health could prevent disease and dysfunction in childhood and across the lifespan, reduce health and education costs, increase national productivity, and promote better health and well-being for all Americans. ■

NOTES


50 Salkever DS. Updated estimates of earning benefits from reduced exposure of children to environmental lead. Environ Res. 1995;70:1–6.


61 European Chemical Agency. ECHA
In Health Affairs this month, Philip Landrigan and Lynn Goldman review findings that children are far more sensitive to environmental toxins than are adults—and on that basis, the authors argue for an overhaul of our system for regulating chemicals. They call for a requirement that all chemicals be introduced into the market, as well as those already on the market, be tested for toxicity. What’s more, they argue that chemicals’ actual or potential impact on all exposed populations, including children, should be taken into account in the testing and review process.

Landrigan, who is also the subject of a “People and Places” article in this issue of Health Affairs, is an epidemiologist and pediatrician, and the Ethel Wise Professor of preventive medicine at the Mount Sinai School of Medicine. He is also the school’s dean for global health and the director of the Children’s Environmental Health Center. He has long been associated with research demonstrating that children are more susceptible than adults to environmental exposures, such as to lead and pesticides.

Landrigan is a recipient of the Meritorious Service Medal of the Public Health Service and a member of the Institute of Medicine. He received his medical degree from Harvard Medical School and a master of science degree in occupational medicine from the University of London.

Goldman is the dean of the George Washington University School of Public Health. Previously, she was a professor of environmental health sciences at the Johns Hopkins University’s Bloomberg School of Public Health. Before that, she served in the Clinton administration, as assistant administrator for toxic substances in the Environmental Protection Agency. During her time there, the agency overhauled the nation’s pesticide laws, expanded right-to-know requirements for release of toxins, reached consensus on an approach to testing chemicals with the potential to disrupt the human endocrine system, developed standards to implement lead screening legislation, and promoted children’s health and global chemical safety.

Goldman also worked in environmental health for the California Department of Public Health Services, where she managed a statewide environmental epidemiology program that focused on childhood lead poisoning, birth defects, and occupational health. She is a member of the Institute of Medicine and of the National Academy of Sciences Board on Environmental Sciences and Toxicology.

Goldman earned a master’s degree in health and medical science from the University of California, Berkeley; a master of public health degree in epidemiology from the Johns Hopkins University School of Hygiene and Public Health; and a medical degree from the University of California, San Francisco.