Growing Up Toxic

Chemical Exposures and Increases in Developmental Disease

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Top photo: Bradley Mason; Second from top: Ken Hammond, USDA; Bottom photo: John Stevens

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EXECUTIVE SUMMARY

Californians face increasing obstacles to healthy development, from the moment of conception until they themselves attempt to conceive. Problems like premature birth; male genital defects; learning, attention, and emotional disturbances; early puberty; obesity; and low sperm quality have been increasing in California and the nation as a whole over the past several decades, impacting every stage of growth from conception to adulthood.

While a range of factors, from lifestyle to heredity, may contribute to any one of these trends, a growing body of research suggests that toxic chemicals play a significant role. Studies are revealing chemical contamination in human bodies, finding associations between chemical exposure and human disabilities and disease, and demonstrating toxic effects at increasingly lower levels of exposure.

The findings of this report are by no means comprehensive. While well-known toxicants like mercury, lead, dioxin, and PCBs have been clearly linked to human health damage, thousands of other chemicals that people are exposed to in the home have never been studied for health effects. Here we focus on the most recent science surrounding several emerging chemical hazards—a growing body of evidence showing that chemicals found in the home and in common consumer products may hinder normal development.

Chemical exposure is widespread.

Human bodies are the repository for countless chemicals encountered in everyday experiences and found in common consumer products. Exposure to these substances during fetal development is unavoidable.

- Phthalates, used to "plasticize" some food containers, plastic wrap, toys, shampoos, perfumes, and beauty products, are among the most frequently found contaminants in human bodies.
- Flame retardants, added to foams, plastics, and electronics, have been found at exponentially increasing levels in women in California; levels in U.S. women have reached up to 75 times the levels found in Europe and Japan.
- Bisphenol-A, the main ingredient in hard polycarbonate plastics for baby bottles, drinking water bottles, and food containers, has been detected in pregnant women in Germany and Japan. It is one of the top 50 production-volume chemicals in the U.S., and exposure likely is widespread.
- Pesticides and their breakdown products are commonly found in people. In a recent study, the U.S. Center for Disease Control and Prevention found 13 different pesticides in the average American, out of 23 pesticides under consideration.

At each stage of life, toxic chemicals may hinder normal development.

Even before their first breath, insurmountable challenges, from premature birth to birth defects, await an increasing number of children.

Premature birth, which raises the risk for reduced intelligence and learning and attention problems throughout life, is 23% more frequent now than in the 1980s in the United States. One potential factor may be phthalates:

- Babies exposed to a common phthalate *in utero* are born a week earlier on average than babies without exposure.

Birth defects are the leading cause of infant death in the U.S. While the specific causes of most birth defects are unknown, they could be linked to a variety of chemical exposures, including:

- Phthalates. In male lab rats, phthalate exposure *in utero* leads to undescended testicles and malformed urinary tracts. The frequency of these conditions in baby boys doubled from 1970 to 1993 in the United States.
- Bisphenol-A. In experiments with mice, bisphenol-A can induce the genetic defect that causes Down's syndrome, at levels comparable to those found in women tested to date.
- Pesticides. One study found an association between miscarriages caused by birth defects and commercial pesticide applications within a nine square mile area around the home. Another study found that boys conceived during the period of most intense application of the herbicide 2,4-D were five times more likely to have a birth defect than boys with no unusual exposure.

Infancy and early childhood is a time marked by rapid growth and learning. However, a growing number of California children are suffering from developmental disorders that impair their ability to learn normally.

Photo: Gail Kewney

Neurodevelopmental and mental health disabilities are rapidly rising in California. Autism cases in California have more than tripled since 1994, and the number of students in public schools with learning disabilities increased 65% from 1985 to 1999. No one cause has been implicated, but scientific evidence raises questions regarding numerous potential factors, including exposure to toxic flame retardants, bisphenol-A, perchlorate, pesticides, and the well-established culprits of lead, mercury, dioxin, and PCBs. Consider:

- Flame-retardant chemicals given to newborn mice in small doses permanently impair their learning and behavior, and small doses of bisphenol-A produce hyperactivity.
- The rocket fuel component perchlorate, found in the drinking water sources of 16 million Californians, affects the thyroid hormone system at very low levels of exposure. Children born to mothers with thyroid problems have higher rates of learning disabilities.

Photo: Teri Olle

- Children exposed to agricultural pesticides show deficiencies in intellectual development, stamina, balance, hand-eye coordination, and short-term memory.

As children develop into young adults, they struggle with the rapid changes in their bodies that lead to sexual maturity. However, several unexplained trends suggest that children face additional health challenges at this stage of life, including early puberty and obesity.

In the last four decades, the number of obese adolescents in the U.S. has quadrupled, and girls in the U.S. appear to be reaching puberty six months to one year earlier than in the past, with a small number of girls developing breast tissue when they are as young as three years of age. Both trends could be tied to endocrine-disrupting chemical exposures in utero.

- Rodents exposed to bisphenol-A give birth to female offspring that grow faster, weigh more, and enter puberty earlier. If applicable to humans, these effects could predispose exposed children toward obesity and early puberty.

Finally, upon reaching adulthood, many people choose to have children of their own. However, chemical exposures may be contributing to infertility and other reproductive difficulties.

Sperm density has declined 40% in the U.S. since World War II. Exposure to phthalates, pesticides, and flame retardants may be contributing to this trend.

- Men with high levels of phthalates or pesticides in their urine (including diazinon, heavily used in California agriculture) tend to have low levels of sperm production.
- Male rats exposed to even a single low dose of PBDE flame retardants while in the womb have significantly decreased sperm counts.

Reducing exposure can prevent harm.

Several instances where regulatory agencies took action demonstrate the value of reducing exposure for human health:

- The EPA banned household uses of the pesticides chlorpyrifos and diazinon in 2001. It appears that this

health-protective action had a nearly immediate effect. After 2001, mothers in New York City had lower levels of these compounds in their bodies and, remarkably, gave birth to heavier and longer babies than those born before the pesticide ban.

- The phasing out of leaded gasoline and other efforts to reduce lead exposure have reduced the number of children with toxic levels of lead by half over the last decade.

Policy Reforms

The newly discovered connections between chemicals and disease outlined here just begin to scratch the surface of the potential impact of chemicals on public health. Tens of thousands of industrial chemicals on the market have not been tested for developmental health effects at low doses. No public health information exists for close to half of the high production-volume chemicals. Moreover, where significant evidence of harm to public health already exists, inadequate resources and legal authority often prevent regulatory agencies from taking protective action.

In order to protect children from toxic exposures, we must take firm steps to remedy the ignorance about health effects of widely-used chemicals and empower regulatory agencies to ensure that consumer products do not contain dangerous chemicals. These steps include:

1) Phasing out chemicals that persist in the environment, accumulate in organisms, or for which evidence of potential harm to human health exists from exposure.
2) Requiring chemical manufacturers to develop analytical techniques to detect the chemicals they produce, and relevant breakdown products, in environmental media and organisms, and to submit these techniques to the state. Currently, taxpayers pay for scientists to guess at what emerging chemical threats may be present in our environment and bodies and then develop the testing methods to detect them. This causes significant delay in determining which chemicals pose the greatest threat to public health.
3) Requiring chemical manufacturers to supply the state and federal government with toxicity data for their products, including low-dose effects on development and reproduction. The European Union recently developed a model policy, known as Registration, Evaluation and Authorization of Chemicals (REACH), that would vastly increase the amount of information available to determine the safety of chemical products.
4) Encouraging the federal government to stop lobbying heavily against the new European Union chemicals policy on behalf of U.S. industry, and to take a stronger stand for public health.

INTRODUCTION

In August of 2003, California passed legislation banning the sale of two types of toxic chemicals. These chemicals, used as flame retardants in furniture and plastics found in every California home, illustrate the dilemma society is facing when it comes to evaluating the safety of industrial chemicals.

On one hand, the ban represents the triumph of a basic principle of government: individual states have a duty to protect the health and well-being of their citizens.

On the other hand, this action reveals a profound failure. By the time the evidence of harm was strong enough to motivate action, exposure had become widespread. Flame retardants were already widely distributed in homes. In fact, the chemicals were widely distributed across the planet, from the blubber of Arctic seals to the breast milk of mothers in California. Product manufacturers had become accustomed to using the chemicals and the chemical industry was reliant on the profits from their sale.

Although the first evidence that flame retardants could be found in the environment surfaced as early as the 1980s, the problem did not attract widespread attention until 1997, when Swedish scientists found the chemical in human breast milk. As evidence of harm accumulated, worry began to mount. Policymakers chose to act when the evidence of harm was strong, with scientists finding exponentially rising concentrations of flame retardants in people and animals across the country, and evidence that small doses—below levels already documented in the breast milk of some California mothers—could cause permanent neurological damage in infant mice.

Flame retardants reveal a pattern of widespread exposure before regulatory action, a pattern that could be played out repeatedly with dozens, if not hundreds, of chemicals commonly used in consumer products. Flame retardants are just one class of over 75,000 industrial chemicals on the market in the United States. The health effects of almost half of the major industrial chemicals have not been studied at all.[1] Of those that have been studied, approximately 1,400 chemicals with known or probable links to cancer, birth defects, reproductive impacts, and other health problems are still in use today.[2]

All of these chemicals may pose serious risks for future generations while substantially affecting the health of today's children. As outlined in this report, the rates of many childhood diseases are rising. More children are suffering from asthma, allergies, autism, learning disabilities, attention deficit disorder, and certain types of birth defects than ever before. More children are developing cancer as well, although rates have leveled off in the last few years.[3] No one fully understands what is happening to this generation of children. However, the mounting number of sick kids takes a toll on parents, families, schools, communities, local and state resources, and society as a whole.

The federal government is hoping to mount the largest study of children's health in U.S. history to unravel this mystery. If Congress grants funding for the project, known as the National Children's Study, researchers will spend $2.7 billion dollars over the course of 20 years tracking the health of 100,000 children from womb to adulthood. The researchers will examine numerous po-

tential factors in childhood illness: genetics, chemical exposures, eating habits, home lives, and more.

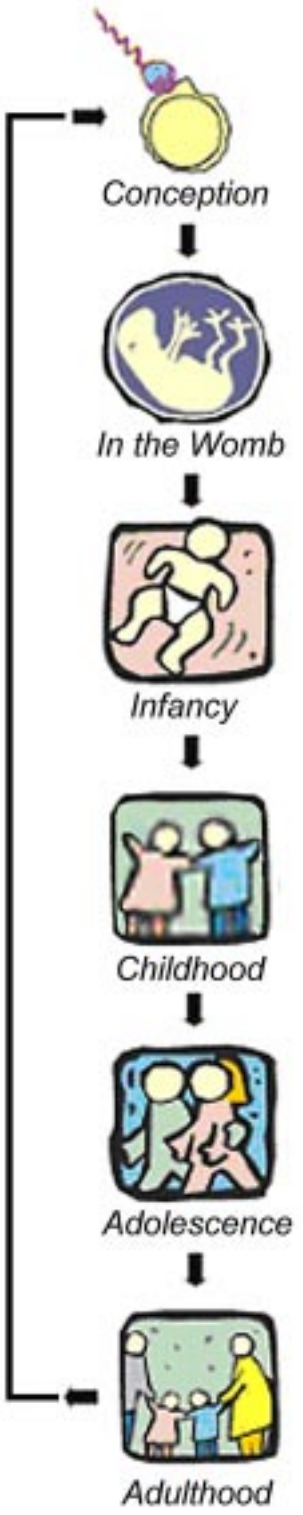
Studying the issue on this grand scale will provide more answers than are available today. What it will not provide is assurance to parents that we are taking all reasonable and timely steps to prevent illnesses in children that may be caused, at least in part, by exposure to toxic chemicals.

Without a concerted effort by regulators and manufacturers to ensure that information is available to make responsible choices as a society about what chemicals we choose to include in our lives—and our bodies—future hazards will be unavoidable. Society may not discover the next toxic flame retardant until twenty years from now, after exposure has once again become commonplace and irreversible. Already, people everywhere are exposed to thousands of potentially dangerous chemicals that may be harming our health without our knowledge or consent.

The evidence connecting chemical exposures to developmental disease—while not yet foolproof—is strong enough to justify a larger effort to prevent harm to children's health. Parents deserve the assurance that everyday consumer products are safe to bring home from the store and to use in feeding, clothing, and caring for their families.

Photo: Shawn Sutherland

Figure 1: Timeline of Human Development and Summary of Disease Trends[4]



Conception

- Genetic damage to a mother's egg or a father's sperm can cause birth defects.

In the Womb

- The most vulnerable period for chemical exposure.

Infancy

- Premature birth has risen 23% in the U.S. since the 1980s.[5]
- Although rates of birth defects related to nutritional deficiencies have fallen, other types of birth defects have increased.
- The CDC reported an increase in deaths from birth defects caused by chromosome sorting errors in sperm or egg cells from 1980 to 1995.[6] These errors are the cause of Down's Syndrome.
- The frequency of baby boys born with undescended testicles (cryptorchidism) or a malformed urethra (hypospadias) doubled from 1970 to 1993.[7]

Childhood

- Neurodevelopmental disabilities that impair normal learning and social skills are rising. Autism cases tracked by the state of California have more than tripled since 1994.[8] In California public schools, learning disabilities increased 65% from 1985 to 1999, rising from 5% to 6% of all students.[9]
- The prevalence of children with asthma doubled between 1980 and 1995, reaching 7.5% of all children.[10]

Adolescence

- Scientists are noticing changes in the timing of puberty that could signal an underlying developmental problem. Caucasian girls in the U.S. appear to be developing on average 6 months to one year earlier than previous studies suggest, with African-American girls developing earlier at every stage.[11]
- In the last four decades, the number of obese adolescents in the U.S. has quadrupled.[12]

Adulthood

- Parents may face more obstacles when attempting to have children. Scientists have found that sperm density has declined 40% in the U.S. since World War II, and that there are differences in male reproductive health in different regions of the country.[13]
- Sperm density deficits could be related to male genital birth defects and testicular cancer, both of which have been rising and could be linked to similar types of chemical exposures. Men born in 1960 face 2.5 times the risk of developing testicular cancer as men born in 1940.[14]
- Endometriosis – a painful condition in women where uterine lining tissue grows in inappropriate places – appears to be increasing as well. The Endometriosis Association estimates that over 5 million U.S. women and girls suffer from the condition. Before 1921, only twenty reports of the disease existed in the worldwide medical literature.[15]
- Breast cancer rates are increasing around 0.6% per year, and prostate cancer rates have climbed 150% over the last three decades.[16]

How Chemical Exposures May Be Harming Development

A human being begins existence as a single cell formed by the union of a mother's egg and a father's sperm. Within this one cell lie all of the ingredients required to produce a full-grown person. The process of growth and development unlocks this potential, leading from the first few cell divisions in the womb, to the birth of an infant, to learning and physical growth in childhood, to sexual development in adolescence, to full reproductive maturity in adulthood.

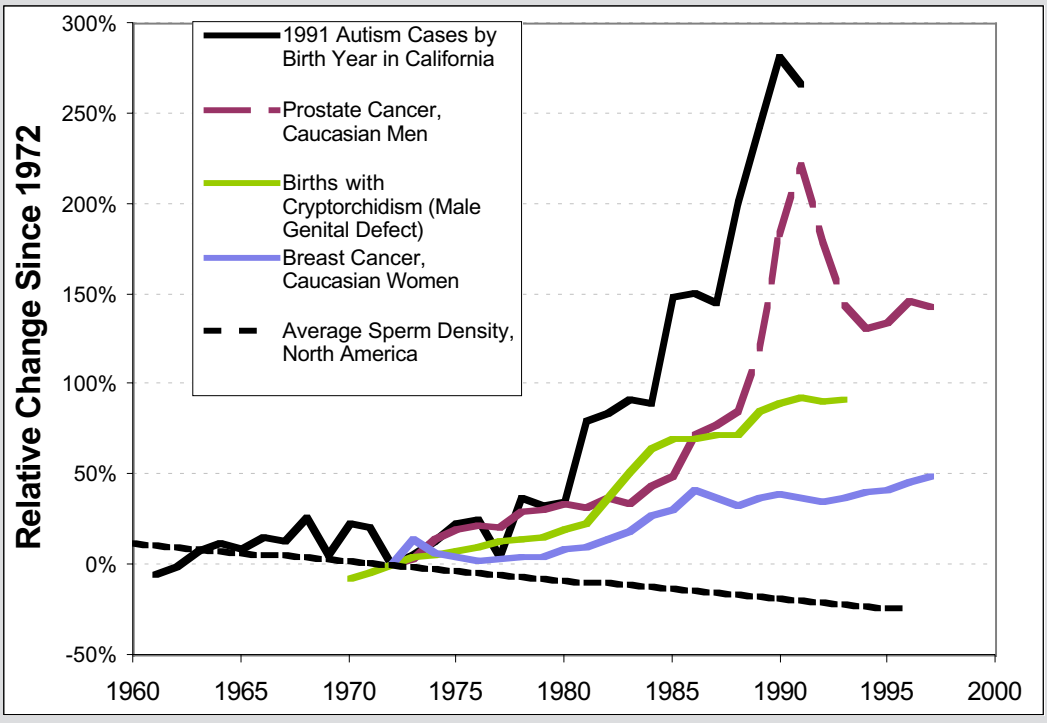
Unfortunately, the process of growth and development does not always occur flawlessly. Errors in the human blueprint in the egg or sperm may cause improper physical or neurological development. Problems can also occur when signals that guide the process do not happen as they should.

Public health researchers and agencies track the occurrence of some of these disorders. Although disease tracking capabilities are not nearly comprehensive enough in California or the U.S. as a whole, several alarming trends are arising from the data we do have. Taken together, they suggest that something is causing changes in fundamental processes of development. From conception to adulthood, many types of developmental disorders are rising, as summarized in Figures 1 and 2.

We have no completely satisfactory explanations for these rising trends in disease. Many different factors likely interact to produce these patterns, from heredity to changes in culture and lifestyle.

However, some scientists are testing the idea that exposures to synthetic

Figure 2: Relative Increase in Disease Incidence Rates Over the Last 40 Years



chemicals form a significant piece of the puzzle. Scientists are building evidence that toxic chemicals can interfere with the process of development in animals and people in ways that could lead to disease. First, they are discovering that chemicals can interfere with signal transmission in the body. Second, they are demonstrating toxic effects in animals given small doses of chemicals. Third, they are finding a variety of toxic chemicals in the blood and tissues of mothers at levels that could be contributing to health problems in their future children.

Increases in learning disabilities could be linked to chemicals that interfere with brain development, including brominated flame retardants (used in home furnishings and a huge variety of plastics), perchlorate (rocket fuel found in California drinking water and in produce), and plastic ingredients like bisphenol-A (used in food containers and plastic baby bottles). Increasing genital birth defects in males could be linked to chemicals that interfere with reproductive development, including pesticides (widely used in California agriculture and neighborhoods), and phthalates (used in PVC plastics and a wide variety of personal care products like perfume). Increasing rates of premature birth and earlier puberty in girls could be linked to chemicals that interfere with the reproductive system, including the plastic ingredients bisphenol-A and phthalates. Chemical exposures could even be playing a role in trends towards increased obesity in children today.

All of these contaminants and more can be found in products used in every California home. Most or all of them can be found in the body of the average California woman as well (see Table 1). When she becomes pregnant, they pass on to the developing fetus. For example, according to a 2000 study, approximately one in three pregnant women in the Los Angeles area had known endocrine-disrupting chemicals in their uteruses at levels approaching those that cause statistically significant damage to developing mice.[17]

Photo: Teri Olle

The science of developmental toxicology is still relatively young. While the chemical industry often points to this fact as a reason not to worry, it only signals massive ignorance, not safety. There are still tens of thousands of chemicals on the market that we know little or nothing about. These chemicals acting alone, may cause effects at extremely low doses. In addition, the chemicals may be mixing together in our bodies and interacting with each other in complex ways that produce effects invisible when tested individually.

Emerging evidence suggests that toxic chemicals play an important role in the genesis of some types of developmental diseases. In the following sections we take a walk through the course of human development, outlining the evidence supporting the role toxic chemical exposures may play in current public health trends.

Table 1: Partial Summary of Chemicals, Exposures, and Effects

Chemical	Human Contamination Levels	Low Dose Effects
Bisphenol-A	1 to 105 ppb in German placenta, average 8.3 ppb in Japanese amniotic fluid.[18]	A 20 ppb dose per day for 6-8 days causes chromosome sorting errors in mice.[19] A 2-3 ppb dose given to rats during pregnancy yields female offspring that tend to grow larger and menstruate earlier.[20] A 0.3 ppb dose in cell culture replicates the estradiol signal, important in brain development.[21] A single dose as low as 2 micrograms given to 5-day old male rats causes hyperactivity.[22]
Phthalates — DEP	The metabolite of diethyl phthalate (DEP), monoethyl phthalate (MEP), was present in urine at levels over 2,000 ppb in 5% of test subjects in the U.S.[23]	Levels within this range are associated with DNA damage in human sperm.[24]
Phthalates — DBP	The metabolite of dibutyl phthalate (DBP) was present in urine samples at levels above 149 ppb in 5% of test subjects.[25]	Levels within this range are associated with reduced sperm quality in adult men.[26] Larger doses cause male genital defects in rats.[27]
Phthalates— DEHP	The metabolite of diethylhexyl-phthalate (DEHP) was found above 21.6 ppb in the urine of 5% of women tested.[28]	Young girls in Puerto Rico with premature breast development had 450 parts per billion DEHP in their blood.[29] Larger doses cause male genital defects in rats.[30]
PBDE Flame Retardants	10 to 1080 ppb in fatty tissues of U.S. mothers.[31]	A dose leading to ~5000 ppb fat in infant mice leads to permanently impaired learning and behavior.[32] A single dose *in utero* can delay onset of puberty in both males and females and impair development of reproductive organs in laboratory animals.[33]

The Home as A Toxic Environment

Not all toxic chemicals enter the environment dripping from a factory waste pipe, leaking from a hazardous waste dump at the edge of town, or billowing into the air from an incinerator smokestack. Products made in factories and shipped to homes and offices around the state also contain hazardous materials, where they become an intimate part of the life of every Californian.

Many times more chemicals are shipped from factories to homes, contained within consumer products, than are spilled or dumped into the environment. Massachusetts, one of the few states where companies are required to report the amounts of chemicals they use and ship in products, provides a good illustration. In Massachusetts in 2001, for every one pound of chemicals released or disposed of, eight pounds were distributed in manufactured products.[34] Companies shipped thousands of times more of certain toxic chemicals—especially ingredients in plastics and personal care products—than they released into the environment.[35]

As a result, children today grow up surrounded by chemicals that did not exist a hundred years ago. Their food containers are made with plastic, from reusable bowls to throwaway wrapping. Their homes and yards are treated with chemicals designed to kill: pesticides. Their families use cosmetics and personal-care products that contain hundreds of synthetic chemicals. The furniture and electronics in their homes contain flame retardant chemicals. Many of these chemicals escape from products and end up in household dust and in household air.[36] The chemicals have become such a close part of our lives that now they can be found in the blood and bodies of every mother and child.[37]

Some common household items contain developmental toxicants, chemicals that can alter the sequence of events that brings forth healthy lives. For example, bisphenol-A can be found in plastic food containers and water bottles; phthalates are common in everything from vinyl flooring to food wrappings to beauty products; and flame retardants can be found in electronics and furniture. Developmental toxicants are capable of causing diseases, creating birth defects, reducing the mental or physical abilities of children, and altering normal behavior patterns.[38] Although it is usually impossible to connect a single chemical to a broad health trend, the evidence continues to mount that toxic chemicals may play a significant role in the health problems of today's children. The National Academy of Sciences estimated that toxic exposures play a role in at least one in four cases of developmental disorders.[39]

Although the amounts of chemicals found in a typical person are relatively small—on the order of grains of salt in an Olympic size swimming pool—these levels matter. Scientists are showing that chemicals that act as signals within the body can disrupt the process of growth and development in levels found in some people today. See Appendices A and B for a discussion of the rise of chemical use in the U.S., and scientific support for the hypothesis that low-level exposure to certain chemicals may be linked to developmental disorders.

Conception Through Infancy

The course of human development begins at the moment a father's sperm merges with a mother's egg. The single cell that results from this union contains all the information required to produce a miniature human being. As the embryo grows within the woman's uterus, cells develop specialized characteristics and functions, becoming limbs, hearts, eyes, brains, and all of the critical organ systems that make life possible. From the time parents realize they are going to bring a new life into the world, they wait with anticipation for the first outlines of shape and the first signs of movement.

After approximately 38 to 40 weeks of dramatic growth and development, babies are born and enter into direct contact with the world. However, for some parents, pregnancy might bring unexpected and possibly heartbreaking complications, from miscarriages to birth defects.

Inexplicably, a growing number of children are entering the world earlier than normal or with some types of birth defects. Pre-term birth is becoming more frequent in the U.S. Premature babies, defined as babies born more than three weeks early, face a higher risk of disrupted cognitive development or behavioral problems later in life. Male infants have a higher frequency of reproductive birth defects than they did thirty years ago. Infant boys with birth defects such as undescended testicles (cryptorchidism) and malformed urinary tracts (hypospadias), face an increased risk of testicular cancer and reproductive dysfunction. While a variety of factors could be responsible for this trend, scientists are discovering that chemical exposures – involving the parents' sperm or egg cells, or the developing fetus – may play a major role.

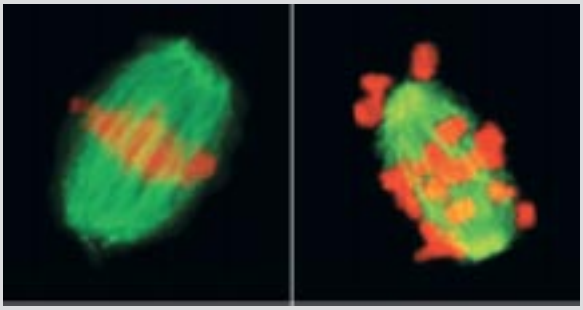
Miscarriages, Birth Defects and Plastic

Even before conception occurs, genetic damage to an egg or sperm can cause developmental problems for the resulting embryo. Severe genetic defects can lead to miscarriage before a woman even knows she is pregnant. For example, when chromosomes sort incorrectly in a father's sperm or mother's egg, diseases—or, more often, miscarriages—result. Incorrect sorting of chromosomes leads to diseases like Turner's syndrome, in which a female has only one X-chromosome and never develops ovaries; Klinefelter's syndrome, in which a male has one or more extra X-chromosomes and develops sterile; Down's syndrome, in which a child has an extra copy of chromosome 21 and suffers multiple mental and physical impairments; and sometimes miscarriages, when genetic problems disrupt development too drastically to make life viable. According to the *Los Angeles Times*, roughly 10% to 25% of human embryos have an incorrect number of chromosomes. Almost all of these end in miscarriage early in pregnancy.[40]

Bisphenol-A, a chemical found in many household items including plastic baby bottles and compact discs, recently burst onto the scene as a potential factor in inaccurate sorting of chromosomes. In 2003, Dr. Pat Hunt and her colleagues at Case Western Reserve University made an accidental but dramatic discovery: bisphenol-A can cause chromosomes to sort incorrectly in mouse eggs, even at very low doses.[41] While a variety of possible events could also lead to the same genetic outcome, the fact that a common chemical can cause this effect is cause for concern.

Dr. Hunt's research team was not studying bisphenol-A at the time the discovery was made. The lab was using

Figure 3: Bisphenol-A Causes Chromosomes to Sort Incorrectly During the Development of Egg Cells[42]



In normal development (left), eggs and sperm develop when a germ cell splits in two, giving an equal set of chromosomes to each germ cell. The chromosomes (red) line up on the spindle (green) to ensure equal separation. However, bisphenol-A prevents the chromosomes from lining up correctly (right), resulting in chromosome sorting errors like the kind that cause Down's Syndrome.

mice for their research, and lab staff kept the mice in plastic cages and fed them water from plastic water bottles. The staff were shocked when they discovered severe chromosome sorting problems in developing egg cells of mice they were expecting to be normal. Dr. Hunt faced the question of how untreated mice developed such striking damage to their egg cells.

The answer to the mystery turned out to be contamination from the plastic cages and the plastic water bottles. Bisphenol-A leached out of these items into the diet of the mouse in appreciable quantities. Lab staff were able to replicate the effect in several ways: by feeding mice with plastic bottles purposefully washed to accelerate leaching of bisphenol-A, and by directly administering small doses of pure bisphenol-A to the mice.

Even at the lowest dose tested (20 nanograms/gram weight for 6-8 days), bisphenol-A caused significant and observable damage to developing eggs (Figure 3). Germ cells normally split into two cells when forming eggs, separating chromosomes equally into each daughter cell. These cells then enter the reproductive process, and when fertilized by sperm, develop into new organisms.

Interviewed by Marla Cone and the *Los Angeles Times* about this finding, Dr. Frederick vom Saal at the University of Missouri, a leading bisphenol-A scientist, noted that "these effects in the Hunt study and other studies happen at lower doses than what is actually found in human fetal blood—umbilical cord blood."[40]

In fact, tests of placental tissue and amniotic fluid of women in Germany and Japan found bisphenol-A at high levels—from 1 to 105 parts per billion, which is in the range of the doses that caused chromosome sorting errors in mice.[43]

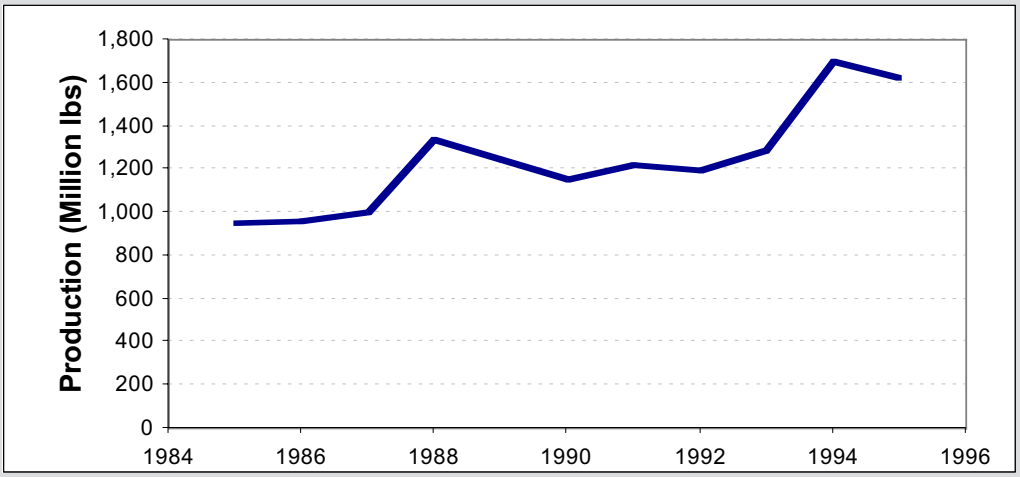
Bisphenol-A is Everywhere

Scientists first learned that bisphenol-A could act a synthetic substitute for the female hormone estrogen in the 1930s, close to 30 years after its invention.[44] However, in 1953 chemists discovered that bisphenol-A could be made into polycarbonate plastic. Despite the fact that bisphenol-A was known to be active in the human body, it went on to become commonplace in the manufacture of a variety of materials not meant to be drugs.

Dozens of common household items contain this chemical. Some of the most easily recognizable products include Nalgene drinking water bottles, hard plastic baby bottles, and CD and DVD disks. In addition, bisphenol-A is used to make the plastic found in some types of reusable and microwaveable food and drink containers, electrical and electronic equipment, automobiles, sports helmets and pads, eyeglass lenses, and more. Bisphenol-A is also useful in making epoxy resins, found in printed circuit boards, paints, glues, protective coatings—and more worrisome, in the lining of metal cans containing food and drink.[45]

Bisphenol-A is one of the top 50 products produced by the chemical industry, generating revenues on the order of $6 million per day in the U.S., Europe, and Japan.[46] In 1999, manufacturers in these regions produced 2 million metric tons of the chemical, with consumption expected to reach 2.6 million metric tons in 2004.[47] U.S. industry produces over one billion pounds of this chemical a year (Figure 4).

Figure 4: Production of Bisphenol-A in the United States from 1985 to 1995[48]



All of these products, the Rubbermaid "Dip 'n Snack Tray," the 5 gallon water jug, and the 9oz baby bottle from Avent, are made with polycarbonate plastic containing bisphenol-A. Plastic items made from polycarbonate can sometimes be identified by the recycling code "7," although the code represents a few other types of plastic as well.

Birth Defects, Plastic Additives, and Personal Care Products

Mutations in important genes, or the genetic blueprint of a human being, can also lead to birth defects. Mutations can be caused by a variety of factors, including exposure to reactive chemicals. For example, if signals required during the development of bone and muscle structures are disrupted by a mutation, defects like cleft palate or dwarfism can result.

Phthalates are a family of chemical 'plasticizers,' added to PVC plastics to

Trends in Birth Defects

The incidence rates of many birth defects in the U.S. have been declining with better nutrition and medical care. For example, adding folic acid to cereal in the 1990s has appeared to reduce the number of spina-bifida defects. However, birth defects remain the leading cause of infant death, and the specific causes of most birth defects remain a mystery. [49] According to the CDC, infant deaths due to birth defects have not declined as fast as other types of infant death over the last three decades.[50]

Moreover, the CDC reported an increase from 1980 to 1995 in the number of fetal deaths from trisomy 13 and 18 (defects that could be caused by errors in chromosome sorting), reduced brain volume, and respiratory system defects.[51] However, scientists face challenges in untangling the influences of increasing maternal age, increasing prenatal diagnosis of birth defects and elective termination, and other trends affecting infant death rates. While overall infant death rates are declining, important questions still remain to be answered about the origin of many birth defects. A national health-tracking network, which would systematically track the incidence rates of birth defects while controlling for changes in diagnosis, medical practice, and maternal age, could provide a lot of useful clues.

make them more flexible, and also added to personal care products such as perfumes, lotions, and nail polish. One type of phthalate may be linked to DNA damage in human sperm.[52] Although no studies have yet confirmed a link between phthalates and a specific birth defect, this mechanism suggests that phthalates could be associated with genetic damage leading to birth defects.

Dr. Susan Duty and her colleagues at the Harvard School of Public Health looked at DNA damage in the sperm of healthy men with no unusual exposure to phthalates in the Boston area. They found that levels of diethyl phthalate (DEP) and its breakdown products were associated with damage to the DNA in sperm cells.[53] In other words, men with high phthalate levels were more likely to have signs of DNA damage to their sperm. The plastics industry uses DEP to make PVC plastics more flexible in tools, automotive parts, toothbrushes, and food packaging; as well as adding it to cosmetics and insecticides. The levels of phthalate exposure seen in this study are common in American men.

Miscarriages, Birth Defects and Pesticide Exposure

Pesticides, which include insecticides, herbicides, fungicides, and rodenticides, are commonly used in agriculture, landscaping, and in and around the home. These chemicals are the only chemicals in this discussion that are created and used with the specific intent to kill something, be it weeds, insects, fungus, or rodents. However, the human organism is not so different.

Dozens of pesticides and their breakdown products can readily be found in people. In a recent study, the U.S. Center for Disease Control and Prevention found at least three different pesticides in one hundred percent of the people tested for pesticides in both blood and urine. Out of 23 different pesticides under consideration, the average person had 13 in their body.[54] These pesticides may be contributing to a variety of adverse health effects, including miscarriage.

One study found an association between pesticide use in California and an increased risk of miscarriage caused by birth defects. Dr. Erin Bell of the University of North Carolina and her col-

leagues showed that mothers who live within a 9-square mile area in which commercial pesticide spraying takes place during pregnancy are 40% to 120% more likely to suffer miscarriages due to congenital defects.[55] Risk is greater during gestation weeks 3-8, the critical period when many organ systems first begin to take shape. Associations were apparent for five major classes of pesticides: organophosphates, carbamates, pyrethroids, and endocrine disrupting pesticides, but strongest with halogenated hydrocarbons (examples of halogenated hydrocarbons include endosulfan, lindane, and pentachlorophenol).

In addition, studies of the herbicide 2,4-D (used in agriculture and for home lawn care) have linked exposure to reduced litter size in animal experiments and birth defects in people. Dr. Warren Porter at the University of Wisconsin discovered that rodents exposed to low doses (commonly found in the environment) of a commercial herbicide mixture including 2,4-D have reduced litter sizes.[56] This experiment is striking in that very low doses—as low as one seventh of the drinking water standard set by the EPA—produced the greatest effect.

Dr. Dina Schreinemachers at the U.S. EPA found that human babies born in wheat-growing areas of the western U.S. (where chlorophenoxy herbicides like 2,4-D are used in large amounts) are more likely to have birth defects than babies in non-wheat-growing areas of the West.[57] She found that:

- Children born in high-wheat areas were 60% to 90% more likely to have birth defects in the respiratory system, circulatory system, and in the muscles and skeleton (fused digits, clubfoot, extra digits, etc.).
- The frequency of birth defects were highest for babies conceived in the spring, when herbicide spraying is most intense. Boys conceived in high-wheat counties in April and May were almost five times more likely to have a birth defect than boys conceived in low-wheat counties at other times of the year.
- Infant death due to congenital abnormalities was more frequent for boys in wheat-growing counties compared to low-wheat counties.

In addition to agriculture, herbicides like 2,4-D are used in home lawn care and grounds maintenance. Common lawn care products, including Scotts and Weed-B-Gon weed killers and Miracle-Gro Weed and Feed contain 2,4-D.[58] In 2002 herbicide applicators used close to 470,000 pounds of 2,4-D and related herbicides across California.[59]

Premature Birth is Becoming More Frequent

Rates of pre-term birth (defined as giving birth after 37 or fewer weeks gestation) rose in the latter part of the 20th century in the U.S. From 1975 to 1995, preterm delivery increased 22% among Caucasian women, from 6.9% to 8.4% of births.[60] The increase among African American women was smaller, 3.6%, but the percentage of pre-term births among African Americans is very high already, accounting for 16% of all births in 1995. The increase appears to be continuing. Researchers at the CDC observed the same trend from 1981 to 1998, independent of maternal age.[61] Premature labor, which does not always result in pre-term birth, occurs in about 20% of all pregnancies in the U.S.[62]

Photo: John Stevens

A variety of factors, including an increase in the age of childbearing women, could explain part of this trend. However, exposure to chemicals in the environment such as phthalates (used in some cosmetics and plastics – see box on Page 23) and pesticide residues could also be contributing to the trend toward shorter pregnancies.

Chemical Ties to Premature Birth

New evidence ties leftover residues of the pesticide DDT, banned in the U.S. in 1972, to earlier births. In 2001, a research team led by Dr. Matthew Longnecker at the U.S. National Institute of Environmental Health Sciences reported that women with the highest levels of DDT in their blood were more than three times more likely to give birth to a premature child.[63]

Chemicals still in widespread use today may also affect delivery timing. For example, a group of Italian scientists found phthalates and their breakdown products in the blood of newborn infants, with higher levels leading to a higher incidence of premature delivery.[64] They report that on average, babies exposed to common phthalates enter the world a week earlier than babies with less exposure.

If chemical exposures are causing earlier birth times, it could have serious consequences for the health of children later on in life. Children born prematurely and undersized face more challenges than the average child growing up, including a greater risk for reduced intelligence and behavioral problems, including attention deficit hyperactivity disorder (ADHD).[65]

Moreover, new research suggests that medication commonly used to halt preterm labor and stave off birth could be making children more vulnerable to damage from other common chemicals. Dr. Theodore Slotkin and colleagues at Duke University Medical Center found that rat fetuses exposed to the pre-term labor drug terbutaline were more vulnerable to damage from the pesticide chlorpyrifos.[66] The damage affected regions of the brain associated with learning and memory, offering an explanation for previous studies that showed children whose mothers are administered terbutaline suffer cognitive defects.[67] According to the research team, over one million women per year in the U.S. receive terbutaline or related drugs.

Birth Defects of the Male Reproductive System are Increasingly Common

Genital defects in males are increasing. Although no researchers have precisely determined the cause, toxicants that affect the development of the reproductive system are a plausible factor.

The number of children born with hypospadias (a birth defect causing the opening of the urinary tract to develop on the underside of the penis), and with cryptorchidism (a birth defect disrupting the

Phthalates Everywhere You Look

Phthalates are a family of chemicals, including diethyl phthalate (DEP), diethylhexyl phthalate (DEHP), dibutyl phthalate (DBP), and many other distinct types. The polyvinyl chloride (PVC) plastic industry uses large amounts of phthalates as additives to improve the flexibility of their products, including home siding, flooring, furniture, food packaging, toys, clothing, car interiors, and medical equipment including IV bags. In addition, other manufacturers use phthalates in personal care products such as soaps, shampoos, hand lotion, nail polish, cosmetics, and perfumes, as well as industrial products like solvents, lubricants, glues, paints, sealants, insecticides, detergents, and inks.[68] The Worldwatch Institute estimates global phthalate production at roughly 5.5 million tons per year.

Scientists are finding phthalates everywhere they look. This class of chemicals is one of the most widespread contaminants in the environment today. In fact, according to EPA scientist Robert Menzer phthalates are so common that, "It has become very difficult to analyze any soil or water sample without detecting phthalate esters."[69]

The human body has not escaped contamination. In 2000, Dr. Benjamin Blount at the U.S. Centers for Disease Control and Prevention (CDC) found high levels of phthalates and their transformation products (known as metabolites) in every one of 289 adult Americans tested, including women of childbearing age.[70] The CDC confirmed widespread exposure with a larger study in 2003, finding disturbing levels of phthalates in practically every person they tested.[71] The metabolite of diethyl phthalate (DEP) was present in urine at levels over 2,000 ppb in 5% of test subjects.[72] The pattern of contamination reflected exposure to phthalates used mainly in personal care products. Children in California are contaminated as well. Dr. John Brock at the CDC found phthalates at average levels over 500 ppb in 19 children in the Imperial Valley.[73] The patterns of contamination suggested exposure from plastics, perhaps toys, as well as personal care products.

Plastics labeled with the recycling code 3 are made from polyvinyl chloride (PVC), and may likely contain phthalates.

Scientists began studying the toxicity of several phthalates as early as the 1950s, and discovered significant evidence of environmental and human contamination in the early 1970s, including the leaching of phthalates into human blood from PVC bags used in hospitals.[74] As noted by the Worldwatch Institute, NASA scientists were already warning against the use of PVC in the space program in 1971, because of poor physical properties and the presence of phthalates.[75] They noted that "substitute polymers . . .are available and in many cases they have far superior physical properties at a small sacrifice in immediate cost."[76]
However, phthalates remain in wide use today.

descent of the testicles into the scrotum) has doubled in the last three decades.[77] In the early 1990s, these problems affected about four children in 1,000 births, up from two in 1,000 in 1970 (Figure 5).

Exposure to chemicals in the environment could explain at least part of this trend. Scientists at Copenhagen University Hospital who study male defects note that in "perhaps the majority of newborns with malformations of genitalia, no chromosomal or other genetic defect can be demonstrated with our current knowledge."[78]

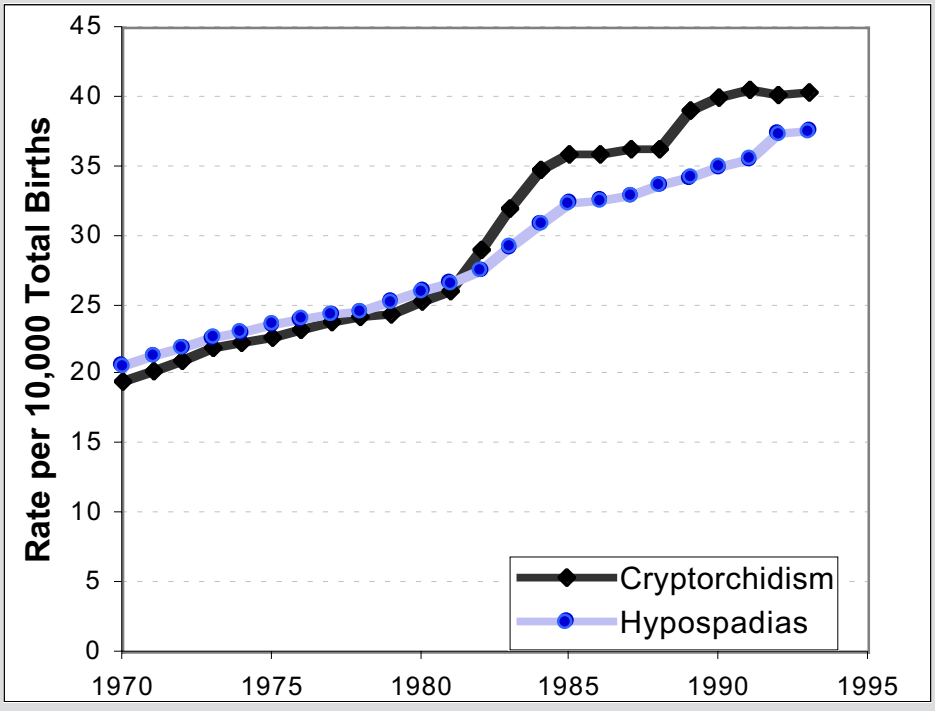
Reproductive Defects, Plastic Additives, and Personal Care Products

Phthalates from PVC (polyvinyl chloride) plastics and personal care products can cause reproductive defects in male rodents.

In 2000, Dr. L. Earl Gray and his colleagues at the U.S. EPA reported that three types of commonly used phthalates (DEHP, BBP and DINP) disrupt sexual development in the male rat.[80] When female rats were fed these phthalates during pregnancy, they gave birth to male pups that weighed less and showed symptoms of hypospadias, cleft phallus, reduced testes weight, and other reproductive malformations, including undescended testicles (cryptorchidism). Apparently, DEHP reduces testosterone production in the developing testes, interfering with the signals that direct normal male reproductive development.[81] A maternal dose of 750 mg/kg/day of DEHP after the second week of pregnancy reduces testosterone levels in male testes to the same level as in female rodents.

In 2004, Dr. Gray and others at the EPA followed up on this finding, showing that the phthalates DEHP, BBP, and DINP reduce the levels of insulin-like hormone #3.

Figure 5: Trends in Defects in the Male Reproductive System in the U.S., 1970-1993.[79]



Reduced activity of this hormone is another known cause of undescended testicles in mice.[82]

Other research groups have implicated another common phthalate (dibutyl phthalate or DBP) as a direct cause of hypospadias and cryptorchidism in rodents. When female rats are fed DBP at 500 mg/kg bodyweight during the third week of pregnancy, 60% of their male offspring suffer cryptorchidism, hypospadias, infertility, and/or other testicular defects.[83]

The similarities between the male reproductive defects induced by phthalates in rodents and the features of male birth defects seen in humans are strong.[84] Although phthalates have not been proven to cause birth defects in human males, the evidence suggests that phthalate exposures are cause for concern.

Parallel evidence for other chemicals harming reproductive development in the female was published in 2002 and 2003. In this case, the culprit appears to be the plastic ingredient bisphenol-A and PBDE flame retardants.[85] Pregnant rats given 0.1 mg/kg/day of bisphenol-A gave birth to female offspring with vaginal deformations, apparently caused by a disruption of the estrogen signal required for normal development. Females exposed to PBDEs *in utero* develop structural defects in their ovaries.

Reproductive Defects and Pesticides

Pesticide exposures could also be contributing to an observed upward trend in male reproductive birth defects.

At exposure levels far beneath those found in lakes, rivers, streams, and even drinking water, the pesticide atrazine causes male frogs to develop ovaries, abnormal testicles, or a mixture of ovaries and testicles; and to become demasculinized. These effects occur at exposure levels more than 10,000 times lower than those previously identified as non-toxic to frogs, as low as 0.1 ppb.[86] Atrazine contamination in California routinely exceeds this amount.

Photo: Bradley Mason

Atrazine is one of the most common water contaminants in California. In 2002, farmers used 58,939 pounds of atrazine in the state, mostly on crops such as trees, grasses, and corn. The top five counties for application were Imperial, Sacramento, Tuolomne, Humboldt, and Modoc.[87] After application the pesticide contaminates drinking water sources through runoff. In the mid 1990s, the U.S. Geological Survey looked for pesticide contamination around Los Angeles and through the Central Valley as a part of the National Water Quality Assessment. They found atrazine at levels between 1 and 73 parts per billion in dozens of groundwater and surface water locations across the state, up to 730 times higher than the levels associated with reproductive development problems in frogs.[88] In some areas, atrazine was detected in more than half of all surface water samples.[89]

Atrazine appears to affect the testosterone signaling pathway by promoting the conversion of testosterone to estrogen. Adult male frogs exposed to 25 ppb atrazine show a ten-fold decrease in testosterone levels compared to controls – effectively lowering testosterone to female levels.[90]

Childhood

As infants grow into children, they reach a number of traditionally celebrated milestones: taking their first steps, speaking their first words, and going to their first day of school. Parents often look forward to these moments and remember them with fondness. Parenting books describe the typical timelines of cognitive and physical development so that parents know when to look for the signs of proper growth in their children. For some parents, delayed or disrupted development will require minor adjustments in lifestyle and support from the community and schools. For other parents, more serious developmental disorders will mean years of testing, diagnosis, medication, and special education.

During their first few years, healthy children learn rapidly in a supportive, nurturing environment. However, if something goes wrong with brain development, the effects begin to manifest themselves during this period.

Inexplicably, a growing number of California children are suffering from autism and greater numbers of students are requiring special attention at school because of learning disabilities. While a variety of factors could be responsible for this trend, scientists are building evidence that chemical exposures in the womb may play a critical role.

Learning Disabilities and Autism are Growing More Frequent

California's Autism Epidemic

Autism cases have increased dramatically in California since 1980, without any generally agreed-upon explanation. In the past decade, autism cases tracked by the Department of Developmental Services have tripled (Figure 6).

Children born with autism face a lifelong inability to form social relation-

Figure 6: Rising Numbers of People with Autism in California[91]

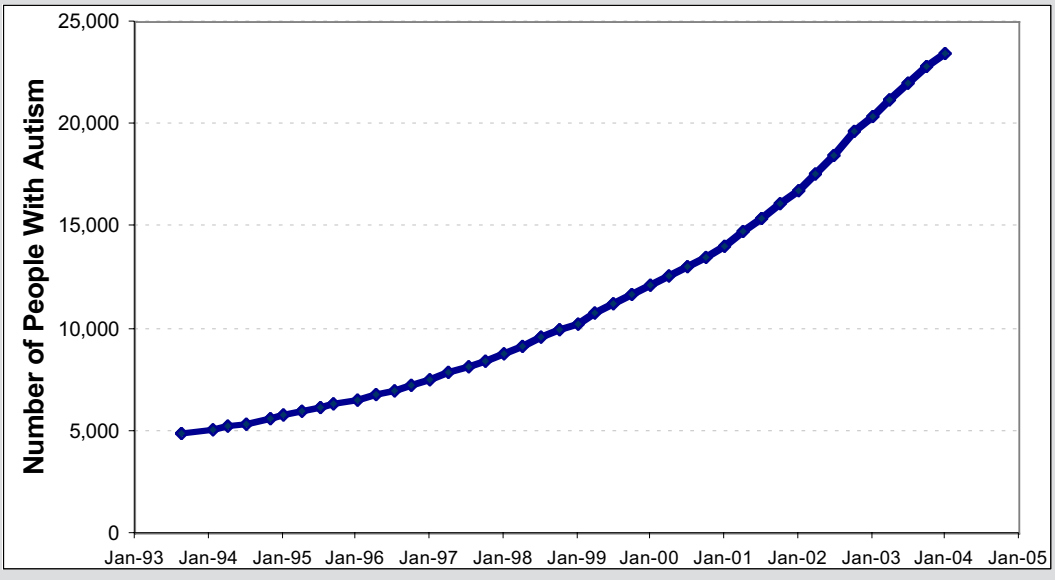
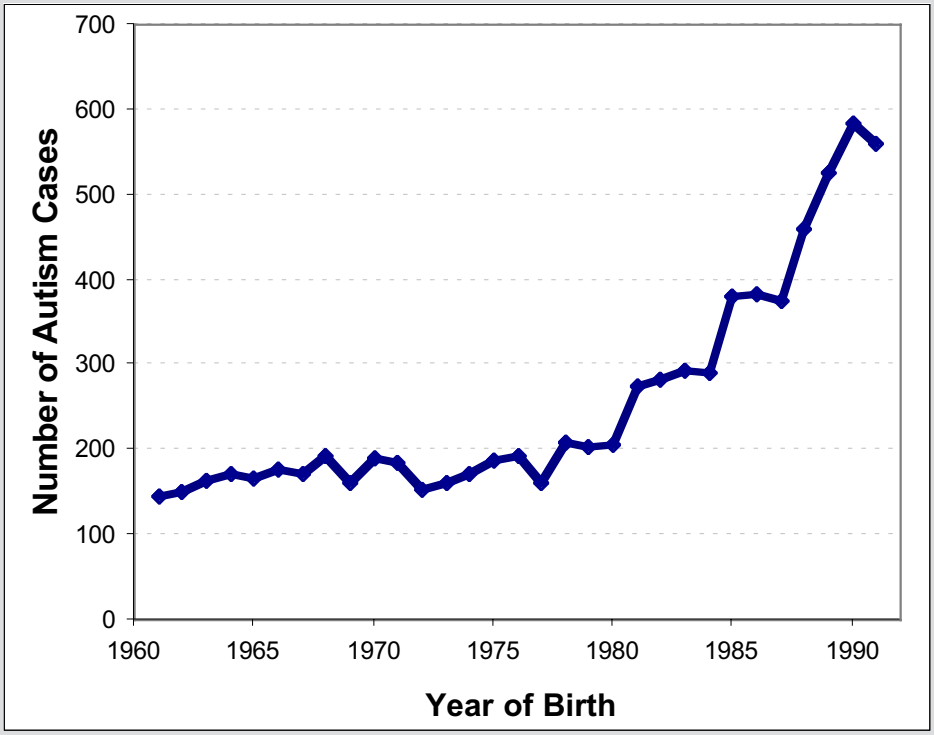


Figure 7: Year of Birth Distribution of the 1991 Autistic Population (7,915)[92]



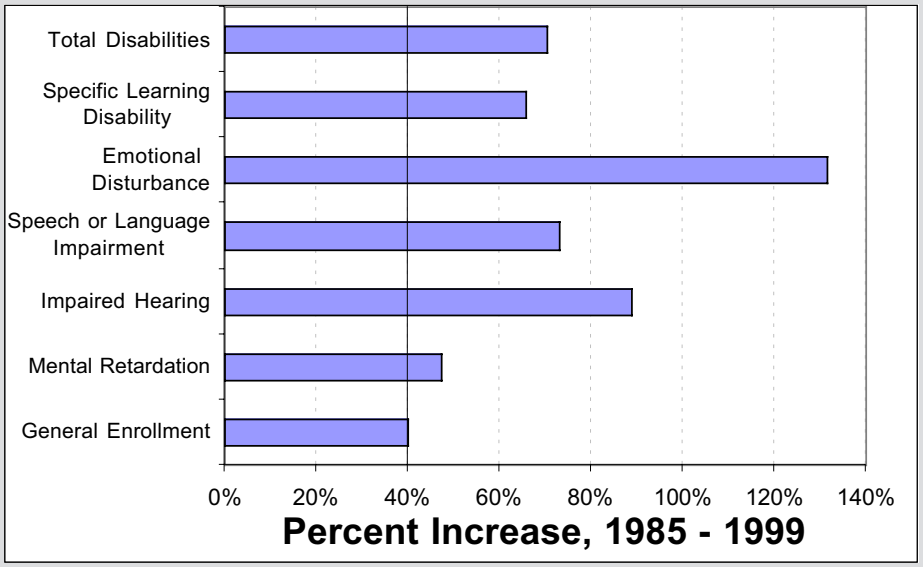
ships and an obsession with repetitive behaviors. As time passes, parents face a higher risk of having a child with autism, according to department statistics originally released in 1999. Figure 7 shows the dramatic increase in the number of autism cases tracked by the state for children born after 1980.

When these trends were first publicized, some doctors questioned whether they were real or caused by confounding influences. In October 2002, researchers at the University of California at Davis laid these doubts to rest. They ruled out population increases, trends in diagnosis, and other potentially misleading factors for the observed increase in autism cases, reporting that "some, if not all, of the observed increase represents a true increase in cases of autism in California."[93]

Learning, Attention and Emotional Disorders on the Rise

Learning disabilities have been increasing in California schools as well. The enrollment of children with specific learning disabilities has increased faster than the general student population in the last two decades (Figure 8). From 1985 to 1999, students enrolled in special education due to a learning disability increased 65%, while overall general enrollment increased 40%. Students with learning disabilities now make up roughly 6% of all students in the state.[94] In addition to learning disabilities, enrollment of children with emotional disturbance, speech or language disorders, and hearing impairment increased faster than general enrollment.

Figure 8: Change in Enrollment in California Schools by Type of Disability, 1985-1999[95]



Children with learning disabilities suffer from an impaired ability to concentrate, conceptualize, organize, and memorize. These impairments make it difficult for the child to perform basic school tasks, like reading, writing, spelling, and math. Memory deficits may affect rote, sequential, short- and long-term memory. Problems with speech development, language learning, and motor skills often co-exist. As a logical result, children with learning disabilities are not able to keep up with other children in their classes. Despite average or greater intelligence, students with learning disabilities are predisposed to dropping out of school and having social and employment problems throughout adulthood.[96] Children with learning and attention disorders can show common characteristics at birth, including low birth weight and reduced head circumference.[97]

This increase appears to be happening across the United States as well:

- Cognitive development experts report that learning disabilities in the U.S. have risen 191% between 1977 and 1994.[98]
- Estimates of the number of school children across the U.S. suffering from attention deficit hyperactivity disorder (ADHD) range between 3% and 6%, up to as high as 17%.[99]
- In 1985, there were 650,000 to 750,000 people diagnosed with ADHD. By 2000, that number had risen to 4-5 million, mostly school-aged children.[100]
- Scientists at the University of Washington found that visits to physicians resulting in a diagnosis of ADHD rose by 2.7 times for girls and doubled for boys from 1990 to 1998.[101]
- Dr. Kathy Kelleher at the University of Pittsburgh School of Medicine surveyed pediatricians about the frequency of psychosocial problems in their patients. She found that these types of problems increased from

6.8% of all visits among 4- to 15-year olds in 1979 to 18.7% of all visits in 1996. Attention deficit problems increased from 1.4% to 9.2% of all visits.[102]

Autism and ADHD Appear to Arise During Fetal Development

The brain is the most complicated and delicate organ in the human body. Nestled within the skull, the brain consists of a vast collection of nerve cells designed to pass messages to one another, with more complexity and adaptability than any computer.

The development of the brain is a complex and lengthy process. Starting in the third week of pregnancy, the tissue destined to become the brain and spinal cord begins to differentiate from the rest of the embryo. This tissue curls into a tube during the fourth week. By the fifth week, this tube begins to divide into the different regions of the brain. Beginning in the eighth week, the brain tissue develops rapidly into the complicated structures that give children the capabilities to perceive and organize information, learn, remember, and grow into fully functional people. Most of the cognitive capability of the brain develops between the eighth week of pregnancy and the second year of life.[103] During this period, the developing brain is most vulnerable.

During this intensive period of development, nerve cells replicate, grow, and even die in response to chemical signals. These signals tell cells when and where to connect to other cells, what proteins to put on their surface, and when to die when their function is complete. Many types of chemical signals, including those provided by the thyroid hormone system, help direct brain development.[104]

Thyroid hormone signals are particularly important. Scientists know that disruptions in thyroid levels as early as week eight in the womb through the second year of life can disrupt children's normal brain development and impair their intelligence and coordination. Too much or too little thyroid hormone during brain development can decrease the number of cells in the mature brain, impairing neurological development, with consequences including learning disabilities, speech and memory problems, poor coordination and balance, or – in severe cases—mental retardation. Mothers with thyroid problems during pregnancy give birth to children suffering from varying degrees of these defects.[105] Reduced thyroid levels in the first few weeks of life for pre-term and low birth-weight babies are associated with increased risk of neurological disorders, including the need for special education by age nine.[106]

Scientists and doctors do not really know what causes autism, ADHD, or other learning disabilities. However, there are strong indications that the cause is an event during fetal development, and that genetic makeup may affect people's vulnerability.

Signs of autism exist in the womb, even though behavioral symptoms normally do not become fully apparent until well after birth. Children with autism show delayed brain growth *in utero* and accelerated brain growth in the months after birth.[107]

Early signs of ADHD exist as well, independent of any medication, indicating that increasing ADHD rates cannot be fully explained by cultural changes in society. Dr. Francisco X. Castellanos at the New York University Child Study Center found that the brains of children diagnosed with ADHD, whether receiving drugs for treatment or not, lagged behind their classmates in growth over ten years.[108] Children with ADHD had brains on average 3.4% smaller than

normal children, and the differences remained fixed. Dr. Castellanos believes that the fact that differences remain unchanged over time suggests that ADHD begins in the prenatal period or early in life.[109]

Evidence exists that changes in thyroid hormone levels may be part of the cause of ADHD. Dr. Peter Hauser at the National Institutes of Health found that families with a genetic problem that reduces the function of the thyroid hormone system were more likely to have symptoms of ADHD. In the study, 70% of children from families with genetic thyroid problems had ADHD, while the disorder affected 20% of children in normal families.[110] In another experiment, Dr. Michael McDonald at the National Institute of Mental Health showed that mice with the same genetic defect in their thyroid hormone systems developed symptoms of ADHD, including hyperactivity and impaired learning ability.[111]

One study claiming no link between thyroid hormone levels in infants and learning-type disorders was performed by Consultants in Epidemiology and Occupational Health, Inc., a group that has done work for perchlorate manufacturers like Lockheed-Martin, as well as the American Wood Preservers Institute, an organization that promotes arsenic-treated wood products used in playgrounds.[112] Research funded by companies with a financial interest in vindicating their products tends to be less reliable than research without such conflicts of interest.[113]

Chemical Ties to Autism, Learning Disabilities and Behavioral Problems

Many different factors are likely contributing to the prevalence of diseases related to abnormal brain development in California. There is ongoing debate in the medical community about the role of environmental triggers in the development of autism and similar diseases. However, given the increasing trends of neurodevelopmental disorders, the potential role of exposure to chemicals widespread in the home environment cannot be ignored.

Strong evidence exists that certain chemicals can impair the development of the brain, both in humans and in animals.

Chemicals can disrupt the thyroid hormone system.

Studies with wildlife show that certain synthetic chemicals can disrupt thyroid function. Studies also show impacts on human fetuses – especially in terms of cognitive function later on in childhood.[114]

Chemicals can affect the behavior of animals.

Monkeys exposed to lead and PCBs during development show symptoms similar to those of ADHD in humans, including an inability to plan and perform tasks in an efficient or sensible sequence, a short attention span, and deficiencies in learning.[115]

Chemicals can damage the development of human children.

Humans have been exposed to some chemicals at levels proven to cause harm. Among the most well known of these chemicals are lead, mercury, dioxin, and PCBs (chemicals used as an electric insulator in transformers and other items until they were banned in 1976).

The CDC estimates that at least a half million children in the U.S. suffer from irreversible neurological damage from lead poisoning.[116] According to the U.S.

Environmental Protection Agency, one in six U.S. women has enough mercury in her body to risk brain damage in her children.[117] Scientists are still discovering effects in the average population caused by PCBs and dioxin.

The Legacy of PCBs

The story of how scientists gradually and painstakingly revealed the toxic legacy left by manufacturers of PCBs is particularly revealing. Children born to mothers exposed to PCBs by accidental poisoning in 1978 showed signs of irreparable damage associated with developmental toxicants: immune suppression, altered sexual development, delayed brain development and increased social dysfunction like hyperactivity and behavioral problems at school.[118]

Over the next two decades, these results were confirmed at far lower levels of exposure by studies in North Carolina, Michigan, upstate New York, and the Netherlands: as the level of PCB exposure before birth rose, the mental and physical abilities of infants after birth declined. Even at very low levels, prenatal PCB exposure contributed to hyperactivity and attention problems discovered later in childhood.[119]

As recently as 1994, scientists found that the levels of PCBs in the general population were still high enough to affect thyroid hormone balance in mothers and their nursing infants.[120]

Lead, mercury, dioxin, and PCBs are just four of many different threats that children are exposed to daily in modern society. New evidence about chemicals used in commonplace household items reveals that a variety of exposures could be causing increased incidence of abnormal brain development and related diseases.

Endocrine Disruption, Neurological Harm, and Plastics

Many items in every California home are made from plastic. Some of the chemicals used to make plastic, including the main ingredient in polycarbonate, can interfere with the transmission of signals in the body. In addition, some additives designed to confer properties like flame-resistance to plastic also show endocrine-disrupting effects.

Flame Retardants

Household products made from flammable materials, such as polyurethane foam in furniture and plastics in computers and electronics, contain chemicals designed to reduce the spread of fire in the event of an accident. Three of the most common such additives are polybrominated diphenyl ethers, or PBDEs, tetrabromobisphenol-A, or TBBPA, and hexabromocyclodecane, or HBCD. North American industry produced and used close to 130 million pounds of these chemicals in 1999.[121]

First introduced 30 years ago, these types of flame-retardant additives are now widely used, despite minimal health testing. The testing that has been done indicates that PBDEs are toxic to development, and the levels found in some mothers and fetuses are rapidly approaching the levels shown to impair learning and behavior in laboratory experiments.[122]

PBDEs build up in fatty tissue and do not readily leave the body. As a result, these chemicals are building up rapidly in the tissues of women across California. Contamination levels in the breast tissue of California women and in the breast milk of women throughout America are up to 75 times higher than those found in European countries.[123]

Flame retardants have been shown to alter thyroid hormone levels, an effect

similar to that caused by PCBs. Tetrabromobisphenol-A and pentabromophenol (a related flame retardant and pesticide) are better able to bind to a part of the thyroid system than the natural hormone itself.[124] Metabolites of PBDEs have the same effect. When rodents are exposed to PBDEs, they show depressed thyroid hormone levels and physical changes in the thyroid gland.[125] These effects occur in mice when exposed to a common PBDE at single doses as low as 0.8 milligrams per kilogram of body weight.[126] These effects appear to be additive with the effects of PCBs and dioxins on thyroid hormone levels.[127]

Flame retardants also cause irreversible neurological damage to infant mice. Mice exposed to PBDEs as newborns develop learning and movement problems that worsen as the animals grow older, an effect similar to that seen with PCBs.[128]

Evidence in animals suggests that exposure will have the same effect in humans. In the case of PCBs, humans were actually more sensitive than rodents used in experiments by at least 1,000 times.[129]

To date, less attention has been paid to TBBPA and HBCD. TBBPA can be found in the blood of electronics workers, although it does not appear to bioaccumulate.[130] In contrast, scientists in Sweden recently discovered HBCD in the shells of peregrine falcons, suggesting that HBCD is climbing the food chain.[131] Both TBBPA and HBCD can prevent the uptake of neurotransmitter molecules important in delivering messages between nerve cells in the brain. These two chemicals, PCBs, and the drug ecstasy have the same effect at similar concentrations.[132] Potential developmental consequences of this effect are not fully known.

Bisphenol – A

Recent work by Dr. Angel Nadal and colleagues at Miguel Hernández University in Spain demonstrated that the chemical bisphenol-A can mimic a signal that regulates how cells in the brain develop.[133] Their experiment showed that bisphenol-A is biologically active at extremely low levels, and that it has a potency and effect similar to that of the hormone estradiol.

Estradiol plays an important role in the development of connections between nerve cells in the brain and long-term memory formation. It controls the process of cleaning out unnecessary cells when nerves are making connections between each other. Known as controlled cell death, this process is a crucial part of development. For example, controlled cell death transforms webbed hands and feet into functional appendages with separate digits by freeing each finger and toe. A similar process helps the brain to become functional as well.

Bisphenol-A is able to mimic the effects of this hormone at levels as low as 0.3 parts per billion (ppb). Although very few tests have looked for bisphenol-A in pregnant women, results suggest widespread contamination of fetuses at or above this level.

The discovery that bisphenol-A can interfere with estradiol signals raises the possibility that bisphenol-A could be triggering steps important in the development of the brain at the wrong times, or encouraging improper connections to be made. Unfortunately, scientists do not yet know what happens to the developing brain when an external contaminant interferes with how nerve cells are connecting with one another.

Evidence is beginning to gather that bisphenol-A damages brain development in animals. Dr. Masatoshi Morita and his colleagues at the Japanese Na-

tional Institute for Environmental Studies recently studied the effects of bisphenol-A on rat development.[134] They found that a single dose given to a 5 day old rat lead to significant levels of hyperactive behavior, with greater hyperactivity resulting from higher doses of the chemical. They also found that bisphenol-A exposure changed how the dopamine signaling system developed in brain cells, resulting in less dopamine receptors and transporters. Dopamine is an important transmitter of nerve signals in the brain. Other Japanese laboratories recently showed that mice exposed to bisphenol-A in development and infancy were temporarily more aggressive and had smaller brains, kidneys, and testes than unexposed mice.[135]

These results suggest that bisphenol-A could be a serious factor in increasing rates of neurobehavioral disease.

Thyroid Disruption and Perchlorate in Drinking Water

Otherwise known as rocket fuel, perchlorate is a workhorse of the defense industry. Beginning in the 1950s, large amounts of the chemical were made at factories owned by American Pacific and Kerr-McGee corporations outside Las Vegas, in an area draining into Lake Mead and the Colorado River.[136] The chemical was used by numerous aerospace contractors, road-flare manufacturers, and pyrotechnic companies throughout the state. Perchlorate now pollutes the source of drinking water for over 16 million Californians, as well as much of the water used to irrigate the nation's winter produce.[137]

Perchlorate inhibits the uptake of iodine into the thyroid gland, reducing the production of thyroid hormone at very low levels of exposure.[138] Rats exposed to perchlorate at levels as low as 10 nanograms per kilogram body weight per day show changes in thyroid hormone levels, brain structure, thyroid structure, and behavior.[139] Interference with thyroid hormone in pregnant women and bottle-fed infants can lead to long-term brain development impairment.[140]

Photo: Teri Olle

These studies suggest that perchlorate could be playing a role in increased rates of learning disabilities in California. Only two studies not funded by corporations with a financial stake in the results have looked for evidence of these effects in people actually exposed to perchlorate. First, the Arizona Department of Health Services found differences in thyroid hormone levels among infants whose mothers were exposed to perchlorate-contaminated drinking water from the Colorado River and those who had not been exposed to perchlorate while pregnant.[141] Second, Jackie Schwartz, then a public health graduate student at U.C. Berkeley, found that infant thyroid hormone levels were significantly lowered when mothers were exposed to drinking water contaminated with perchlorate at levels as low as 1 to 2 ppb, with stronger effects at higher doses.[142]

Perchlorate levels in the Colorado River have been measured as high as 24 parts per billion, in Lake Mead.[143] Water taken from the river by the Metropolitan Water District of Southern California contains somewhere between 4 and 6 parts per billion perchlorate.[144] Perchlorate also concentrates in leafy vegetables like lettuce, which creates a concern for consumers of Imperial Valley crops irrigated with Colorado River water. Tests by the Environmental Working Group, an independent advocacy organization, found perchlorate in lettuce at levels more than 100 times higher than what the EPA considers safe in a liter of drinking water.[145]

Neurological Damage and Pesticides

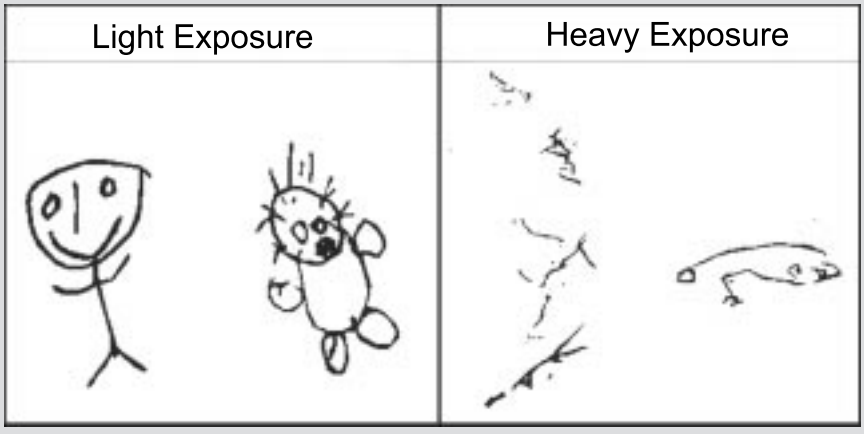
Hundreds of different herbicides and insecticides are used daily to control weeds, cockroaches, flies, rodents, and other common pests across California, in agricultural areas, homes and schools.

Evidence from rodent studies shows that certain types of pesticides can harm brain development. Infant mice exposed to neurotoxic pesticides early in life develop irreversible defects in learning and hyperactivity.[146] However, even more dramatic evidence that chemical mixtures in use today are already affecting human cognitive development come from an agricultural area in Mexico, where two groups of children grew up separated by a small difference in geography, and in their exposure to pesticides.

Dr. Elizabeth Guillette at the University of Arizona and her colleagues in Sonora, Mexico looked at the effect of pesticides on preschool-age children in the Yaqui Valley, Mexico. Farmers in the community had used pesticides in the valley since the 1940s, while farmers in the foothills avoided pesticide use. Dr. Guillette compared children from both areas, and discovered dramatic functional differences.

While the children did not differ in physical growth patterns, children exposed to high levels of pesticides were less mentally able to perform basic tasks and showed behavioral problems. For example, Dr. Guillette asked 4-year olds to draw a picture of a person. Less-exposed children were able to produce recognizable drawings, while children with high levels of pesticides were not (Figure 9). Heavily exposed children were also deficient in stamina, balance, hand-eye coordination, and in short-term memory compared to their less-exposed counterparts.

Figure 9: Drawings of People by 4-Year-Old Children Exposed to Pesticides in Mexico's Yaqui Valley[147]



Adolescence

During adolescence, children become young adults. They grow taller. They enter junior high school and high school, often awkwardly filling out the boundaries of their future selves. Children at this age develop the secondary sexual characteristics that will eventually bring them to sexual maturity, including pubic hair, active menstrual cycles, and other signs of reproductive development. Eventually, they develop the ability to have children of their own. Developmental textbooks generally describe this as the period between 10 and 15 years of age.

This time of a child's life can be confusing and challenging, but with the guidance of trusted adults, it can also be one of exciting change as the child begins to transition into adulthood.

Unfortunately, several unexplained trends suggest that children face growing challenges in their health and development at this stage of life. First, girls appear to be reaching puberty at an earlier age than in the past. In some cases, girls develop breast tissue as early as three years of age. Second, increasing numbers of youth in California are becoming obese. Obesity is now one of the most serious public health problems facing the state, and the nation.

Although changes in nutrition, lifestyles, and genetics certainly play a role in the development of these trends, scientists have recently discovered evidence that toxic chemicals in the environment may also be contributing factors.

Chemical Exposure Could Be Causing Changes in the Timing of Puberty

Girls in the U.S. appear to be undergoing puberty at an earlier age than in the past. In a 1997 study of tens of thousands of girls visiting pediatricians, Caucasian girls appeared to be developing 6 months to one year earlier than previous studies suggest is normal. Even at three years of age, 3% of African-American and 1% of Caucasian girls showed breast and/or pubic hair development in this study. By seven years of age, the numbers increased to 27.2% and 6.7%, respectively.[148]

Dr. Anne-Simone Parent at the University of Liege in Belgium and other scientists have suggested that exposure to hormone-like chemicals in the environment could partially explain this trend.[149] A tragic accident exposing thousands of Michigan residents in the 1970s to polybrominated biphenyl (PBB), a now banned flame retardant chemical, proves that chemical exposures can cause earlier menstruation and pubic hair development in humans.[150] Girls exposed *in utero* to meat and dairy products contaminated with PBB, which was accidentally added to cattle feed in the place of a nutritional supplement, started menstruating a year earlier than normal. Other chemicals in wide use today may also have this effect.

Early Puberty, Plastic Additives, and Pesticides

Plastic ingredients bisphenol-A, phthalates, flame retardants, and several types of pesticides have been shown to alter the timing of puberty in rodents. Although there is little evidence in humans, girls with early breast development in Puerto Rico have high levels of certain types of phthalates in their blood.

Bisphenol-A from polycarbonate plastics can alter the timing of puberty in experimental animals. When given in an extremely small dose (2-3 ppb) to a pregnant mouse, female offspring tend to grow larger and menstruate earlier.[151] A Japanese lab confirmed these findings in 2002.[152] Rats fed doses as low as 20 ppb bisphenol-A during the third week of pregnancy gave birth to daughters that had earlier vaginal opening (a developmental marker of sexual maturity in rodents), lower body weight at this point in maturity, and earlier menstruation than unexposed rats. A lower 2 ppb dose was also associated with significant difference in body weight at this point in maturity.

A variety of other chemicals have also been found to alter the timing of puberty in rodent experiments, although most chemicals in use today have not been tested for this effect (Table 2).

No firm links have been made between chemical exposures and earlier puberty in humans, because of the large number of variables and difficulty of sound experiment design. However, one study of Puerto Rican girls suggests that phthalates may be playing a role in trends toward earlier sexual maturity.

Puerto Rican girls suffer from the highest rates of premature breast development ever recorded. Dr. Ivelisse Colon at the University of Puerto Rico and her colleagues searched for a link between chemical exposures and this phenomenon. They looked for foreign chemicals in blood samples from a set of very young girls with premature breast development, girls with an average age of 31 months. They found high levels of phthalates in these girls compared to normal children.[154] In particular, the phthalate DEHP was seven times higher in girls with premature breast development than normal girls. It is unclear where the exposure was coming from, but potenial sources could be food and drink contaminated by contact with plastic wrappings and containers and chewing or mouthing of plastic toys and pacifiers.

The Obesity Epidemic and Plastics

Obesity and Bisphenol-A

More California children are becoming obese, and growing up into obese

Table 2: Toxicants that Affect the Timing of Puberty in Rats and Mice (partial list)[153]

Chemical	Affects Timing of Sexual Development?
Pesticides (Aldrin, Atrazine, Chlordecone, DDT and metabolites, Linuron, Methoxychlor, Vinclozolin)	YES
Phthalates (Dibutyl Phthalate, Diethylhexyl Phthalate)	YES
Bisphenol-A	YES
Dioxin, Polychlorinated Biphenyls, PBDE Flame Retardants	YES

Figure 10: Rising Obesity Trend in Adolescents[157]

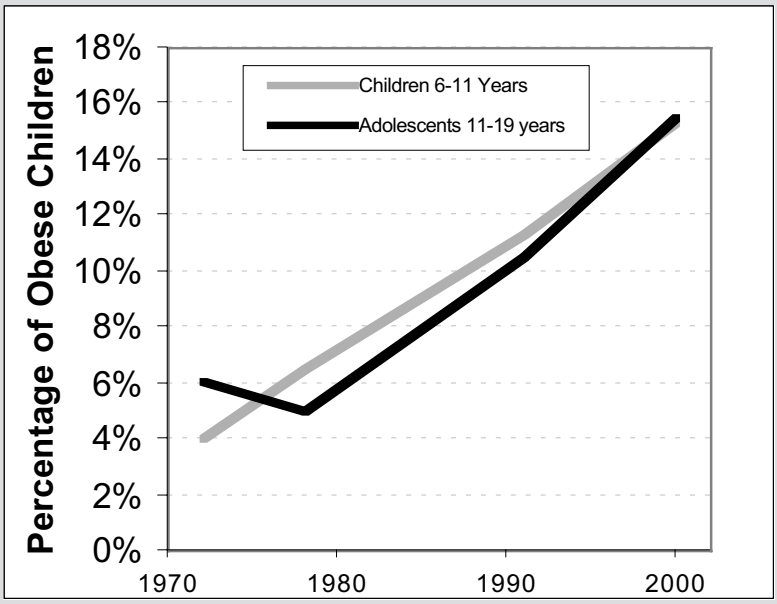
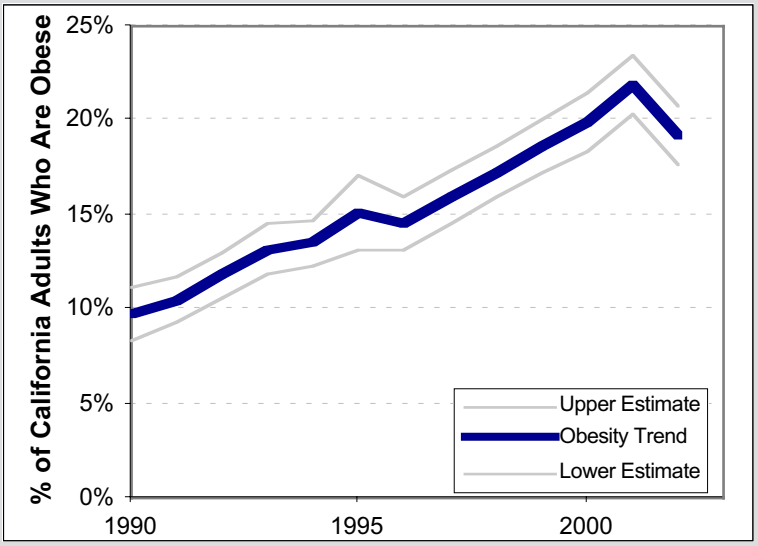


Figure 11: Rising Obesity in California[159]



adults. Even children less than four years of age are becoming overweight at higher rates.[155] In the United States overall, the number of overweight children between 2 and 5 years of age grew from 7.2% in the late 1970s to 10.4% in 2000. The overall prevalence of this condition in children and adolescents quadrupled in the past four decades (Figure 10).[156]

As defined by the U.S. Centers for Disease Control, close to 20% of adults in California were obese as of 2002, double the number in 1990 (Figure 11). Diseases associated with obesity are rising as well, especially type II diabetes.[158]

In 1995, just over 5% of Californians reported having diabetes. By 2002, over 30% more Californians suffered from the disease.

The increase in obesity rates is happening faster than changes in human genetics can fully account for, while human culture and environment are changing faster now than at any time in history.[160] The causes of obesity are many and intertwined. Dependence on automobiles, sprawling development patterns, increased television watching, decreased exercise, and changes in diet all contribute to the problem of obesity.

But the fact that obesity is increasing in very young people as well as adults points to events in child development that could predispose people towards obesity. Starting in the womb, chemical signals direct the development of fat tissues that take up and store energy in the body.

Scientists are beginning to look beyond the usual suspects of diet and behavior–in February of 2004, the National Institute of Environmental Health Sciences (NIEHS) and the Duke University Integrated Toxicology Program sponsored a symposium titled Obesity: Developmental Origins and Environmental Influences. Presenters discussed recent data that support the hypothesis that in utero exposures to environmental chemicals, particularly endocrine disruptors, could play a role in predisposing children toward obesity later in life. (See *Environmental Health Perspectives* Volume 112, Number 6, May 2004)

In 2002, a team of researchers at the Ehime College of Health Science in Japan first discovered that bisphenol-A can trigger the conversion of fiber cells into fat storage cells.[161] In the body, this effect could result in larger numbers of fat cells developing. In addition to converting to fat cells, treated cells increased their fat content by 150% over 11 days. Combined with insulin, bisphenol-A increased the fat content of cells by 1,300%. In other words, this experiment documented that bisphenol-A could trigger and promote the two main processes in developing obesity. In 2004, another Japanese laboratory confirmed these findings, showing that bisphenol-A alone and with insulin increased the uptake of sugar into fat cells.[162]

In 2001, Dr. Beverly Rubin at Tufts University Medical School in Boston and her colleagues showed that bisphenol-A makes rodents grow larger after they are exposed in the womb, confirming similar findings from Frederick vom Saal's laboratory.[163] When pregnant rats were fed 100 ppb bisphenol-A during pregnancy through lactation, their offspring were notably heavier after birth and into adulthood. The fact that the effect persisted long after exposure suggests that bisphenol-A may increase the number of fat cells in the rats and predispose them towards heavier weight through life.

Although these findings are just the beginning of the work that needs to be done to definitively show whether or not obesity is partially due to exposure to chemicals like bisphenol-A, they do challenge the traditional understanding of obesity. In addition to significant changes in our culture and our built environment, we must consider toxic exposures as we attempt to solve this public health crisis.

Becoming a Parent

By the time a child has become an adult, most growth and development is complete. The child is now fully developed, with bones that have stopped growing. All of the grown-up child's organs are fully functional, including the reproductive system.

Many adults choose to have children of their own, starting the process of child development all over again. However, the influence of chemical exposures, beginning perhaps even before they themselves were born, may extend to their ability to reproduce.

Parents in the modern industrial world may now face more obstacles when attempting to have children. Over the past century, sperm production has declined in the average U.S. or European male. Regional differences in sperm health suggests an environmental influence may be responsible.

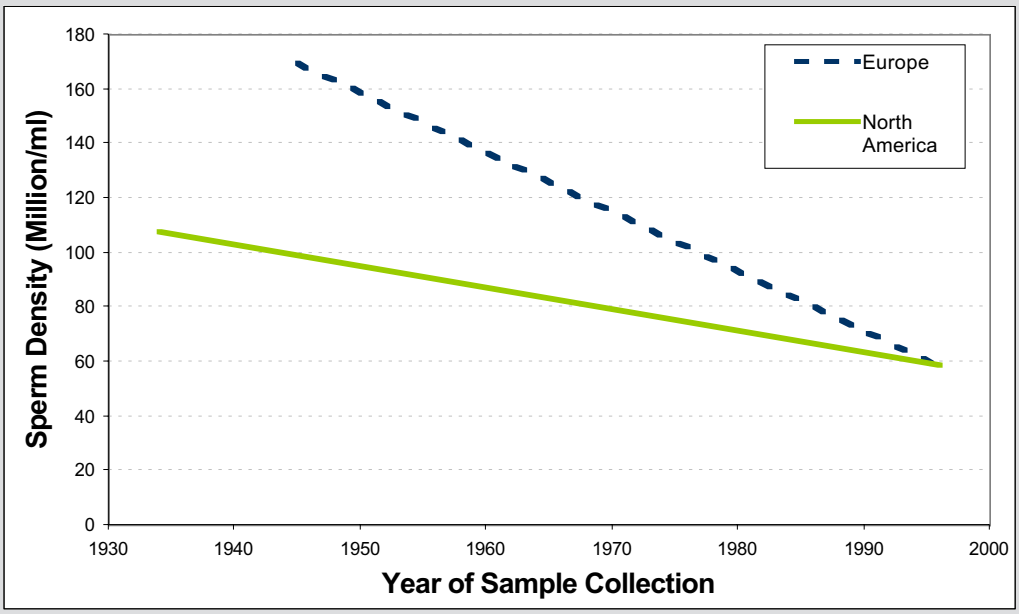
Declines in Male Reproductive Health

Sperm quality has declined in industrialized nations over the latter half of the 20th century. In 2000, Dr. Shanna Swan at the University of Missouri found a statistically significant decline in mean sperm concentration in U.S. and Europe, based on studies published between 1934 and 1996.[164] In the U.S., data showed an average decline in sperm density of about 1% per year during this period (Figure 12).

By 1996, the average sperm density had fallen to 60 million per milliliter (ml). This raises the possibility that impaired sperm quality is leading to infertility problems in parts of the U.S. population. When sperm density falls below 40 million per ml, couples begin to have difficulty in becoming pregnant.[166]

One study in Scotland found a trend toward lower sperm quality for people born more recently.[167] This suggests that

Figure 12: Average Decline in Sperm Density Across North America and Europe in the 20th Century[165]



deficiencies in sperm production could be caused during the development of the reproductive system, in addition to being influenced by external factors later in life. It also suggests that growing exposure to an environmental contaminant during this period could be responsible for the decline in sperm quality.

Decreased Sperm Quality and Pesticide Exposures

Dr. Swan also found that there are regional differences in sperm quality across the U.S. These regional differences could offer clues as to why sperm quality overall has shown a decline.

Dr. Swan demonstrated in the spring of 2003 that men from Columbia, Missouri have lower sperm counts than men from Minneapolis, New York or Los Angeles.[168] She wondered if this could be due to higher levels of agricultural pesticide use in Missouri, with exposure potentially resulting from drinking contaminated groundwater.

Dr. Swan subsequently showed that in fact, men with high exposure to pesticides, especially alachlor, diazinon, and atrazine, were much more likely to have poor semen quality than men with lower levels of these pesticides in their urine.[169] These pesticides are also heavily used in California's agricultural areas, including the central valley. In 2002, California farmers applied 28,000 pounds of alachlor, 59,000 pounds of atrazine, and 680,000 pounds of diazinon on fields in the state.[170]

Decreased Sperm Quality, Plastics, and Personal-Care Products

Scientists have linked both Phthalates and bisphenol-A to sperm defects.

In 2003, Dr. Susan Duty and Dr. Russ Hauser of the Harvard School of Public health published one of the first studies linking phthalate exposures with harm to human reproductive health.[171] They analyzed semen and urine samples from over 150 men in the Boston area. Men who had monobutyl or monobenzyl phthalate in their urine tended to have lower sperm counts, with the highest concentrations leading to the lowest sperm counts. These two chemicals are produced in the body from parent phthalates added to PVC plastics, food wrappings, nail polish, and a variety of other common items. Tests by the U.S. Centers for Disease Control and Prevention show phthalate levels in the average U.S. population in the same range associated with sperm damage in this study (see box on phthalates on page 23.)

In 1998, Dr. Frederick vom Saal at the University of Missouri at Columbia published one of the first studies linking reduced sperm production with bisphenol-A exposure. He and his colleagues fed bisphenol-A to female rats at a dose of 20 nanograms per gram (ng/g) of body weight for six days during pregnancy. They found that males born to exposed rats produced 20% less sperm after they matured than normal males did.[172] They also found that treated offspring had physical changes in hormone-secreting glands not found in untreated mice, even at a dose ten times smaller.

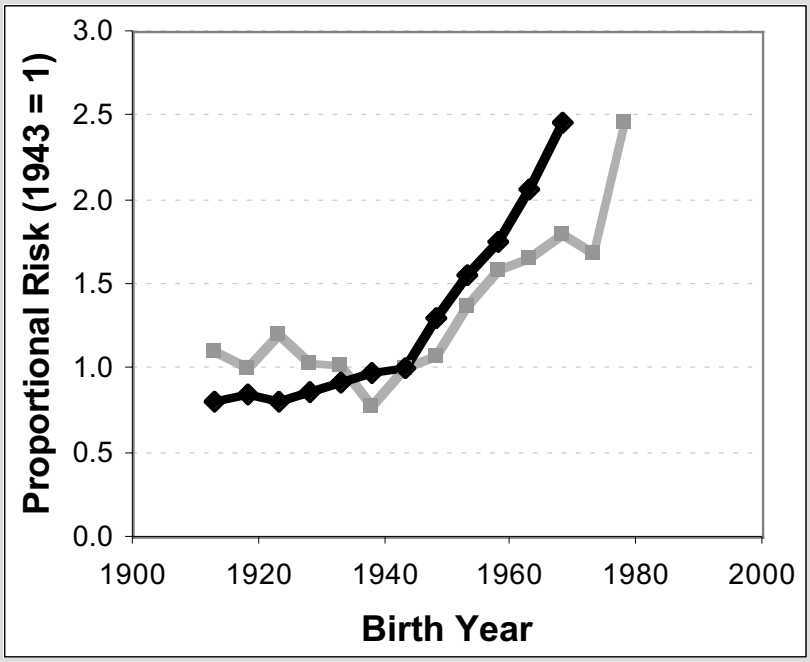
In 2001, Dr. Motoharu Sakaue and his colleagues in Japan added to these findings, discovering that bisphenol-A reduces the number of sperm in rats, even when given doses after puberty.[173] After feeding small doses to rats (20 ng/g for six days at week 13 of life), they noted a generalized decline in the ability of treated rats to produce sperm. Dr. Sakaue concluded that bisphenol-A retarded the development of germ cells

that normally takes place as the male rat reproductive system matures from week 14 to week 18. In 2003, another Japanese lab demonstrated that fetal exposure to bisphenol-A led to reduced testes weight at concentrations found in humans.[174]

A Connection Between Low Sperm Quality and Increased Testicular Cancer?

Impacts on reproductive health may all be related, from declining sperm counts to increased male birth defects to testicular cancer. The unifying factor lies in the process of sexual development *in utero*. The cells and processes that result in healthy males are all formed during this window of time, when they are most vulnerable to disruption.
From 1973 to 1995, incidence of testicular cancer in the U.S. increased 51%.[175] Additionally, the increase is correlated to year of birth – in other words, people who share a common time period of birth share a common risk of disease – suggesting that some early developmental event or prolonged exposure to an environmental contaminant may be the trigger for developing disease (Figure 13).[176]

Figure 13: Rising Risk of Two Types of Testicular Cancer in the U.S. by Time of Birth[177]



Cancer, Plastics and Pesticides

Testicular cancer could be linked to phthalate exposure from PVC plastics and personal care products, as well as organochlorine chemicals such as pesticides and PCBs.
The cause of testicular cancer is unknown. The only known risk factor is cryptorchidism, (undescended testicles).[178] Because phthalates can cause cryptorchidism in rats, it could be involved in creating pre-cancerous cells in the testes as well. Additionally, phthalates could be acting after development to promote the growth of latent cancer cells. Dr. Carl-Göran Ohlson and Dr. Lennart Hardell of the Orebro Medical Centre in Sweden found that men with testicular cancer had a significantly increased likelihood of having worked in the production of PVC plastics.[179] Organochlorine pesticides and PCBs could be linked to testicular cancer as well. A 2003 study by Dr. Hardell and his colleagues showed a strong correlation between maternal levels of PCBs, hexachlorobenzene, and chlordanes and testicular cancer in their sons.[180] For each chemical, mothers with high levels were about four times more likely to have sons affected by testicular cancer.

Success Stories: Reducing Exposure, Protecting Health

In the last four decades, regulatory agencies have occasionally taken action to reduce or eliminate exposure to a toxic substance after evidence of harm was discovered. Many of these efforts have successfully reduced human contamination and produced real improvements in human health.

Most recently, the U.S. EPA banned household uses of two pesticides, chlorpyrifos and diazinon. As these products were phased out of residential use in Manhattan, exposures in expecting mothers declined and they gave birth to larger and healthier babies. In the 1970s, the EPA phased out leaded gasoline. As a result, the number of children in the U.S. with lead levels higher than the EPA health target of 10 micrograms per deciliter of blood has fallen by half since the early 1990s. Finally, efforts to reduce the use of toxic flame retardants in Sweden resulted in a reversal of rapidly increasing levels in breast milk. Forthcoming efforts to reduce the use of toxic flame retardants in California should have the same effect, especially when questions about the unregulated "Deca" flame retardant are resolved.

Unfortunately, in two, if not three, of these cases, human exposures were allowed to reach the point where harm to human health was unavoidable before action was taken.

Increased Birth Weight After Ban of Two Pesticides

After the U.S. EPA banned household uses of two pesticides, chlorpyrifos and diazinon, in 2001, women in New York City gave birth to larger babies.

Until 2001, the pesticides chlorpyrifos and diazinon were commonly used to kill insects in homes, schools, gardens and agricultural crops. The EPA banned chlorpyrifos at the end of 2001 and diazinon at the end of 2002, due to significant evidence of harm to children. Products containing these ingredients began to dwindle on shelves while commercial applicators switched to new pesticides. (The products are still used in agriculture and can still be found on some produce, except for certain crops that kids often eat, such as tomatoes and apples).

In March of 2004, Dr. Frederica Perera, Dr. Robin Whyatt, and their colleagues at Columbia University studied the connection between exposure to these two pesticides and birth weight.

The researchers reported that pregnant women in upper Manhattan who had higher exposure to two common pesticides had smaller babies than women with less exposure.[181] Women with the highest pesticide exposures had babies that were more than 0.4 lb lighter and 0.33 inch shorter than babies from women with the least exposure. These findings suggested harm to the health of exposed children not just in the womb, but later in life as well. Interviewed in the *New York Times*, Dr. Perera noted that "birth weight is a very good predictor of later health and development of children, including physical development, mental development, and school performance."[182]

But the most striking finding of the work was the immediate benefit of the phase-out of chlorpyrifos and diazinon from household uses. The scientists noted that after the ban, women had much less chlorpyrifos in their blood. Before the ban, one third of children fell

into the high exposure group. From 2001 on, just one in 77 fell into that group. Remarkably, as pesticide levels fell, birth weight and body length rose.

The scientists were astounded that such an effect was visible so soon, since the phase-out of the pesticide products was not immediate. Surveyors still found remaining stocks of products containing chlorpyrifos and diazinon on the shelves of some stores in Manhattan as late as mid-2003.[183] Accordingly, exposure levels should continue to decline as the products become more scarce. In the *New York Times*, Dr. Whyatt noted that "the exposure levels are still going down… We may continue to see added benefits of this ban over time."[184]

Declining Lead Levels in Children after the Phase-Out of Leaded Gasoline

The story of lead in the United States is one of success, but also one of profound failure.

In the 1920s, oil companies decided to put tetraethyl lead into gasoline to keep car engines from "knocking." Emitted from the tailpipes of millions of cars, lead contaminated the blood of millions of mothers and children to the point where developmental damage, including brain damage, were unavoidable. Industry continued to promote the use of lead for decades, opposing efforts by the public health community and regulatory agency staff to ban lead in gasoline. Finally in the 1970s, advocates were successful in overriding industry concerns and winning a phase-out. The U.S. EPA began with mandated reductions of lead in gasoline and enforced a total ban in 1986. Other EPA actions eliminated lead from house paint. As a result, average blood lead levels for both children and adults have dropped more than 80 percent since the late 1970s.[185]

In 1997, then EPA administrator Carol Browner said, "The ongoing reduction in blood lead levels is a great American success story of environmental and public health protection. Years of aggressive action against lead exposure, particularly EPA's banning of lead in gasoline two decades ago, is yielding a brighter future for our children."[186]

However, the efforts of the EPA and countless public health agencies to reduce lead exposure would not have been necessary had the oil companies chosen ethanol, a relatively safer compound, to add to their fuel. Oil companies forced lead on the American public partially because of fears over competition with ethanol as an alternative fuel. They vigorously defended their product for decades against mounting evidence of harm to children's health. Lead was a known poison before it was introduced: lead manufacturers were aware of health risks and the U.S. public health community was clearly communicating such risks over 80 years ago. The introduction and widespread use of lead, plus delay in eliminating it, unnecessarily exposed roughly 68 million children to toxic levels of lead from gasoline from 1927 to 1987.[187]

Although exposure is much lower today than in 1970, toxic lead levels still persist in close to half a million children—far too many to claim victory over this pervasive health threat. Efforts must be aimed at eliminating the threat to children in low-income housing developments and older housing, where lead exposure is still high. Hopefully, individuals making decisions about the use of potentially hazardous chemicals in the future can learn from the story of lead in the U.S.

Declining Breast Milk Contamination in Swedish Mothers Following Decreased Use of Flame Retardance

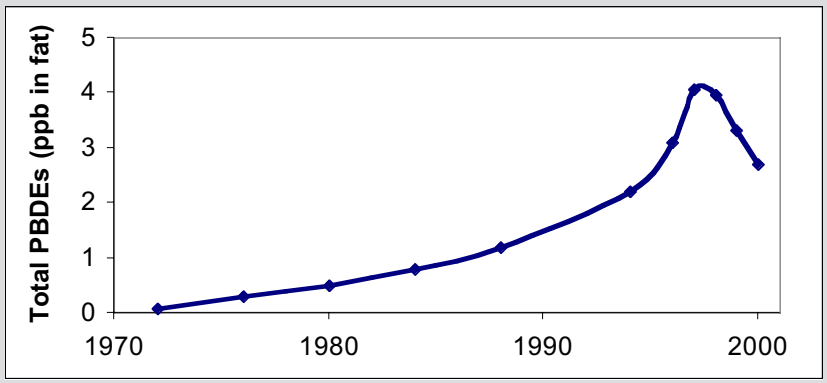
Sweden and Germany were the first countries in the world to scale back the use of the toxic flame retardants known as polybrominated diphenyl ethers, or PBDEs.

Swedish scientists were also the first to detect the exponential increase in contamination soon found to be sweeping the world. Dr. Ake Bergman and his colleagues at the University of Stockholm took advantage of Sweden's breast milk monitoring program, which enabled them to look back in time and document rising levels of toxic flame retardants in the breast milk of Swedish mothers [188] The group discovered that samples of milk from Swedish mothers in 1972 had PBDE levels of about 0.072 parts per billion in fat. In 1997, levels had increased about sixty-fold to 4 ppb in fat, doubling every 5 years.

This finding caused a stir in the scientific community, especially since the flame retardants were not readily leaving the body and showed similar structural features to polychlorinated biphenyls (PCBs), a well-known public health tragedy. Public concern about the potential health consequences of this trend led to sharply decreased usage of products treated with PBDEs in European countries. Germany had banned PBDEs in 1989 because of concern that they could form dioxins when burned. Sweden had scaled back the use of one type of flame retardant in the mid 1990s. In addition, from 1997 to 1998, the EU cut down on PBDE use by two thirds, or 180,000 pounds. Toward the late 1990s, levels of contamination in the breast milk of Swedish mothers began a consistent decline (Figure 14). Although it is unclear whether a particular action triggered the decrease, it occurred following a reduction in flame retardant usage.

In 2003, California passed a ban of two types of PBDEs mainly used in furniture foam. One manufacturer of these chemicals made an agreement with the EPA shortly thereafter to phase out national production of the two chemicals. As these actions take effect, California should see a similar decline in human contamination levels. Lingering questions over a third type of flame retardant (known as "Deca"), used in high volumes and shown to degrade in the environment to form the banned substances, could delay or reduce the response.[190] Full phase-out of all three chemicals would likely result in the swiftest reduction in exposure.

Figure 14: Recently Declining Toxic Flame Retardant Levels in Breast Milk from Swedish Mothers. [189]



The amount of synthetic chemicals manufactured in the United States has increased dramatically over the past half-century. In the U.S., over 75,000 industrial chemicals are on the market. Unfortunately, regulators have very little information to determine the danger posed by these chemicals. Tens of thousands of industrial chemicals on the market have not been tested for developmental health effects at low doses. No public health information exists for close to half of the high production-volume chemicals.[191] The newly-discovered connections between chemicals and disease outlined here just begin to scratch the surface of the potential impact of chemicals on public health.

Scientists at major universities and government agencies valiantly try to fill the void of information. Over the past several decades, they have accumulated significant knowledge of the potential for toxic chemicals to harm human health. Recently, scientists have paid particular attention to the ability of chemicals to interfere with human growth and development. From PCBs to pesticides, the work of these scientists has yielded several general lessons: [192]

1) Once a developmental toxicant is identified, further study almost always identifies more subtle health effects at lower levels of exposure;
2) The idea that the "dose makes the poison," or that certain chemicals dangerous in large amounts are safe in small amounts, is overly simplistic. Sometimes, small doses are more potent than large ones, and exposures can led to profound effects during some developmental periods, but no effect at other times;

Photo: Jeff Osborn

3) Mixtures of chemicals, which people are most likely to encounter in the real world, can have cumulative effects or effects that individual chemicals don't have on their own; and
4) Ending or preventing exposure is the quickest way to reduce harm.

Unfortunately, current chemical regulatory policy in California and the U.S. as a whole does not reflect these lessons. When the federal government created the Toxic Substances Control Act in response to the PCB crisis 30 years ago, the chemical industry succeeded in making sure there were no new testing requirements placed on the tens of thousands of chemicals already in use. For new chemicals, the law required only a rapid pre-market screening based on existing information, and did not require any additional toxicity testing for health effects. This approach runs directly counter to other regulatory frameworks, such as the way pharmaceuticals

Photo: Nik Frey

are evaluated by the Food and Drug Administration.

As a result, U.S. chemical regulation stumbles blindly, using an "innocent until proven guilty" model, allowing widespread exposure to toxic chemicals before they have been tested for safety, and often before methods have even been developed to test for the chemical's presence in our bodies, air, and water. The burden of proving harm remains on those who suffer the harm—the public. Moreover, where significant evidence of harm to public health already exists, inadequate resources and legal authority often prevent regulatory agencies from taking protective action.

This state of ignorance and inaction is unacceptable in a society suffering from the burden of so many public health crises.

Policymakers in the European Union have designed a draft policy known as REACH, or Registration, Evaluation, and Authorization of Chemicals. This policy would require safety testing for thousands of chemicals that are already on the market. Although lobbying by the U.S. State Department on behalf of the U.S. chemical industry recently succeeded in weakening the overall proposal, the idea remains sound.[193] The policy would dramatically increase the ability of regulators to identify and eliminate chemical threats to public health, and encourage manufacturers to replace dangerous products with safer alternatives.

Similar reforms in California and at the federal level would give regulators more tools to protect children from chemical threats to their health. Chemical policy reform would enable regulators to require the full spectrum of information necessary to ensure that consumer products are safe. Accompanied by efforts to eliminate the worst toxic chemicals and to develop safer alternatives, chemical policy reform can lead to a safer and healthier world for our children.

In order to protect children from toxic exposures, we must take firm steps to remedy the ignorance about health effects of widely-used chemicals and empower regulatory agencies to ensure that consumer products do not have dangerous chemicals in them. These steps include:

1) **Phasing out potentially harmful chemicals from uses leading to human exposure.** Although complete toxicity information is not available for most chemicals, evidence of potential harm exists for thousands of chemicals. These chemicals should not be allowed for uses that lead to human exposure. For example, the recent U.S. EPA action phasing out household uses of the pesticides chlorpyrifos and diazinon has been successful at reducing human exposure and improving infant health. When strong potential for harm exists, chemicals should be completely removed from the market and manu-

facturers should seek and switch to alternatives. Chemicals known to persist in the environment, accumulate in the food chain, or harm human health and development fall into this category. Additionally, toxicity exposure standards for chemicals like perchlorate that have already contaminated the environment should be set at levels that will definitively protect developing fetuses from harm, and cleanup to those levels should be required of those who caused the contamination.

2) **Requiring chemical manufacturers to develop analytical techniques to detect their chemicals in environmental and tissue samples, and supply those techniques to the state.** U.S. and California chemicals policy should ensure that manufacturers and industrial users provide regulatory agencies and the public with adequate information about their products so that agencies can act to protect public health from potentially dangerous substances before damage is done. Currently, manufacturers can put chemicals on the market before detection methods have even been developed to test for the presence of the chemical in air, water, soil, or our bodies. Scientists then guess at what chemicals are present in our environment and bodies and then develop these analytical methods—an expensive and time consuming process ultimately paid for by taxpayers. The costs of developing analytical methods as well as methods to test for a chemical's safety should fall to the manufacturers who stand to profit from the product.

3) **Requiring chemical manufacturers to supply the state with detailed toxicity data from independent laboratories for every chemical on the market, including low-dose effects on development and reproduction.** In the case of toxic flame retardants, harm may have been more avoidable had regulators known the potential hazards associated with the chemicals before exposure became widespread. Manufacturers can contribute to preventing public health damage in the future by testing their products for toxicity, and substituting dangerous substances with safer ones. California and federal chemicals policies should require testing information for every chemical on the market, beginning with high production-volume chemicals and ingredients in consumer products.

4) **Encouraging the federal government to stop lobbying against the new European Union chemicals policy on behalf of U.S. industry.** The European Union recently developed a chemicals policy with thorough testing requirements that will vastly increase the amount of information available to determine the safety of chemical products (REACH). The goal of the policy is not zero risk, but to restructure regulations to determine how much risk is avoidable from the start. The federal government has been lobbying against the new EU chemicals policy, working behind the scenes with the U.S. chemical industry.[194] The federal government should acknowledge significant concerns about the environment and public health and take a more preventive approach to public health. California leaders should encourage the White House to change its stance and advocate in favor of policies that will protect public health.

APPENDICES

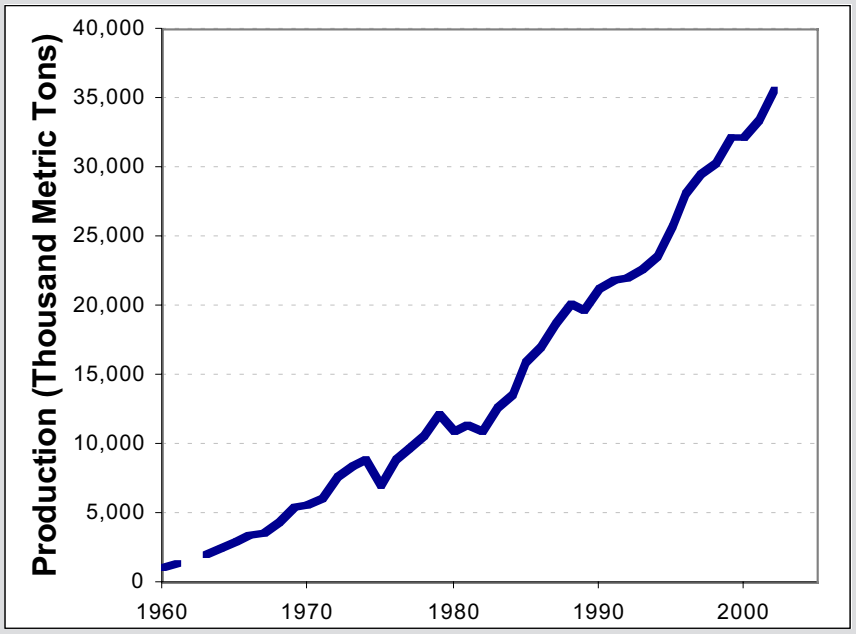
A. Exposure to Synthetic Chemicals Has Skyrocketed in the Last Half-Century

In the last 50 years, people have been exposed to rapidly growing amounts of man-made chemicals. Since World War II, annual chemical production in the United States has grown more than 15-fold. Today, U.S. companies are the world's largest chemical producers, generating 1.2 billion tons of chemicals each year and earning after-tax profits of $44.6 billion on $439 billion worth of sales.[195]

Over the last half-century, the chemical industry introduced thousands of new products – chemicals that did not exist anywhere on the Earth before the industrial revolution. From plastics to pesticides, the modern world contains potentially hazardous substances in far greater amounts than at any time in human history.

Today, plastics can be found in every home and pesticides in every supermarket. After 1960, growth in plastics production grew exponentially, with over 35 million metric tons produced each year by 2002 (Figure 15). Since 1960, U.S. industry has produced over 622 million metric tons of plastics like polystyrene and polyvinyl chloride, over two metric tons of plastic per person in the U.S. Pesticide synthesis and use grew dramatically as well. Since the mid-1940s, pesticide production increased by over 40 times, from 60,000 tons in 1945 to roughly 2.5 million tons in 1995.[196] While these chemicals have had many undeniable benefits for society, from improved medical care to increases in economic productivity made possible by electronics, the benefits may have come with unintended side effects.

Figure 15: Growth in U.S. Plastics Production Since 1960[197]



B. Small Exposures and Large Impacts: The Theory of Endocrine Disruption

In the past two decades, scientists have built a theory explaining how some synthetic chemicals can interfere with communication between cells in the body, sometimes leading to permanent damage during irreversible steps in growth and development. Scientists dub this process "endocrine disruption," and new evidence supporting the idea mounts daily.

The human body depends on accurate and timely exchange of information in order to function correctly. Chemicals produced by the body carry information from one cell to another. For example, chemicals called hormones direct growth and development, regulate mood and behavior, adjust the flow of energy and nutrients, and time the menstrual cycle, among many other important functions.

The levels of hormones are finely controlled in the body. During development, changes in the levels of signaling molecules trigger important steps, from the folding of cells into tissue that will become the brain to the organization of cells into what will become the reproductive system. Hormones transmit signals at very low concentrations, equivalent to grains of salt in an Olympic-size swimming pool.

Hormones transmit messages by physical contact. Hormones are released from one cell and bind to receptors inside or on the surface of other cells like a key fitting into a lock, triggering chemical reactions that lead to physical responses. Rising hormone levels function like a finger flipping a switch. For example, during the development of a male, the presence of testosterone tells the brain and body to develop male characteristics.

Some synthetic chemicals can act as signals within the body, in much the same way as hormones. In some cases, they have a similar structure to a hormone and can bind to a receptor – in other words, they fit in the lock. In other cases, they modulate hormone levels by interfering with how the hormone is made or by blocking the signal at a different point. These types of chemicals are known as endocrine disruptors.

The effects of endocrine disruptors are difficult to detect because signaling systems are complex. Exposure to an endocrine disruptor can cause profound changes during specific windows of time, but have different or no effects at other times. Chronic exposures to low levels can have different effects than short exposures to high levels. As a result, scientists face enormous challenges trying to untangle all of the factors that can harm the normal course of development.

Low Doses Matter

Any chemical that can interfere with signal transmission can cause harm at potentially tiny doses. Signals begin with tiny changes in the concentrations of hormones. Accordingly, exposure to low levels of contaminants can have significant effects, particularly during critical developmental windows.

In a recent paper, Dr. Frederick vom Saal at the University of Missouri demonstrated how chemicals can affect signaling at very low doses, while much higher doses are required to have toxic effects.[198] Dr. vom Saal and his colleagues measured the ability of a hormone, estradiol, to make cancer cells grow in a dish. Doses as low as 10 parts per quadrillion begin to increase cell growth, and reach their maximum effect at around 1 part per trillion (Figure 16). These levels are roughly parallel to

a few hundred postage stamps on a letter the size of California and Oregon. Most of the normal functions inside the human body happen with tiny signals in this concentration range. In contrast, hormone doses over a million times higher are required to kill the cell.

If an endocrine-disrupting chemical is present at physiologically relevant levels, it will prevent the accurate transmission of the signal. For example, when Dr. vom Saal added DES (a synthetic estrogen hormone that caused reproductive defects in daughters of mothers who were treated with it while pregnant) to the cancer cells in the experiment above, adding the hormone estradiol produced no effect until it reached doses toxic to the cell (Figure 17). In other words, the signal pathway was already activated when the hormone was added, and the cells were not able to respond normally.

Most toxicity tests of chemicals are not designed to detect low-dose effects. Many tests do not test a wide enough range of doses, and many do not control adequately for the possibility that contaminants are present in all samples. As a result, many tests are more likely to detect toxic effects and not signaling effects, and therefore are predisposed to overestimate exposure levels that are safe.

Figure 16: The Response of Cancer Cells to the Signaling Hormone Estradiol[199]

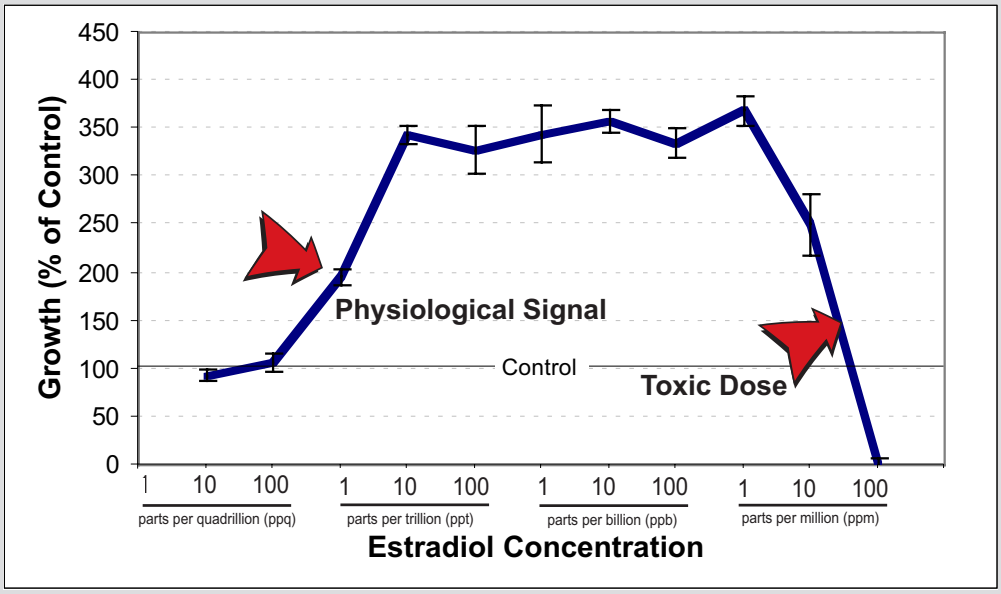
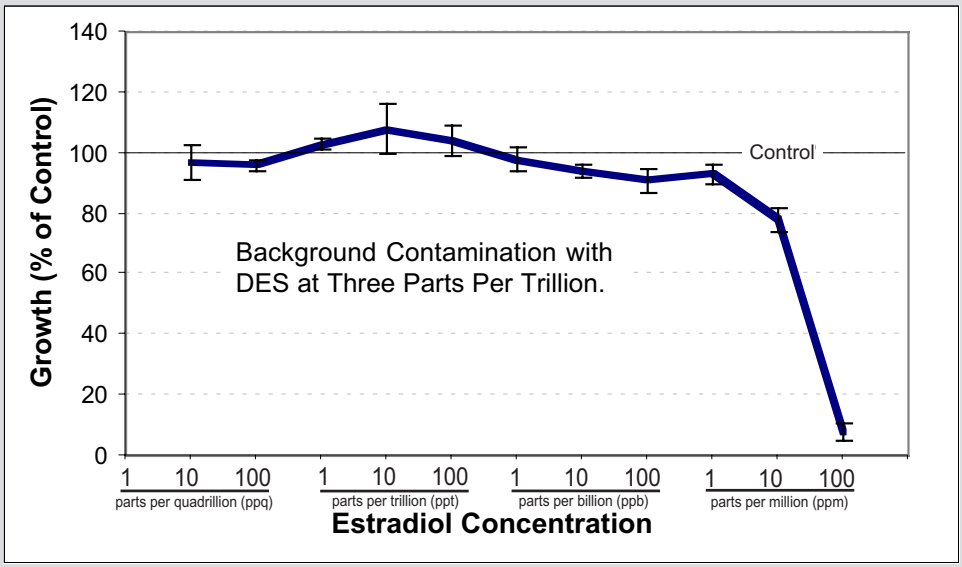


Figure 17: DES Disrupts the Function of Estradiol[200]



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