



EXPERIMENTAL
SUBJECT

HUNDREDS OF MAN-MADE CHEMICALS—

IN OUR AIR, OUR WATER, AND OUR FOOD—COULD BE DAMAGING THE MOST BASIC BUILDING BLOCKS OF HUMAN DEVELOPMENT BY GAY DALY

EVERYONE KNOWS THAT WORLD WAR II LEFT US, AS A LEGACY, THE ATOMIC BOMB. FAR FEWER PEOPLE ARE AWARE THAT THE WAR ALSO LEFT US A CHEMICAL BOMB, SILENTLY, INEXORABLY TICKING AWAY, THAT MAY THREATEN OUR HEALTH, OUR INTELLIGENCE, AND EVEN OUR ABILITY TO REPRODUCE. IT MAY BE EXPLODING AS YOU READ.

BEFORE THE WAR, ONLY A FEW SYNTHETIC CHEMICALS—LABORATORY-MADE COMPOUNDS THAT DO NOT EXIST IN NATURE—HAD BEEN INVENTED. WITH THE ONSET OF THE WAR, CHEMISTS EAGER TO HELP THEIR COUNTRIES ACHIEVE VICTORY BEGAN INVENTING PLASTICS, PESTICIDES, SOLVENTS, DEGREASERS, INSULATORS, AND OTHER MATERIALS THAT COULD BE USED TO MAKE MORE EFFECTIVE WEAPONS, INCREASE CROP YIELDS, AND FEED MORE SOLDIERS. THEY WERE, UNDERSTANDABLY, MORE FOCUSED ON SUCCESS THAN ON SAFETY.

In peacetime, these same labs helped fuel the economic boom of the second half of the twentieth century, formulating new chemical manufacturers needed to create cheaper, smarter products.

Federal regulation was fragmentary at best, and manufacturers were allowed to provide their own proofs of safety, a situation that remains true today. There are now more than 100,000 synthetic chemicals on the market, and these chemicals are everywhere. They enter our bodies and those of other animals through every possible route of transmission. They are in our food supply, so we eat them. They drift in the air, so we breathe them. (Carried on thermal currents, they have long since reached the Arctic, so polar bears breathe them too.) Present in landfills, they leach into the water supply, so we drink them. Released as effluent into lakes and rivers by factories, they affect the habitat of fish, frogs, and all aquatic life, right down to plankton. Ubiquitous in cosmetics, they are absorbed through our skin. Pregnant women pass them to their fetuses; mothers feed them to their newborns when they breastfeed. A large, uncontrolled scientific experiment has been in progress for the last 60 years, and the question now is: Can we figure out what the results are? And if those results show we are in danger, what we can do about it at this late date?

FOR ALMOST TWO DECADES AFTER THE WAR, OUR GREAT FAITH IN THE NEW CHEMISTRY WENT UNTESTED. IT SEEMED AS IF ONE MIRACLE AFTER ANOTHER EMERGED FROM THE LABS, PROVIDING ABUNDANT, CHEAP FOOD, DRUGS TO CURE DISEASE, AND TECHNOLOGY THAT MADE LIFE EASIER AND MORE PLEASURABLE: TELEVISIONS, DEPENDABLE CARS, INEXPENSIVE, RELIABLE REFRIGERATORS TO REPLACE THE ICEBOX.

Rachel Carson pushed Americans to question these miracles when she published *Silent Spring* in 1962, and legislation was passed to address concerns she and others raised about environmental toxins. By the early 1970s, more warning signs had showed up on the radar. DDT, the pesticide that had saved American soldiers who fought in the South Pacific from malaria and been sprayed on millions of acres of cropland, was fingered as a killer of birds, especially the beloved bald eagle. Eggshells thinned by exposure to the compound meant fewer hatchlings survived. DES, a drug believed to prevent miscarriage, was found to cause cancer in the young women whose mothers took it during pregnancy; emergency hysterectomies saved many of the daughters' lives, but at a terrible cost. PCBs, highly effective lubricants and insulators used in electrical capacitors, transistors, hydraulic fluids, plasticizers, inks, waxes and adhesives, were deforming and killing birds and fish; by 1971, Monsanto had voluntarily stopped making them. Each of these problems was seen as an isolated case: A few rogue chemicals had wreaked havoc, but havoc could be contained. Ban DDT, ban DES, ban PCBs—perhaps we couldn't undo the damage already done, but we thought we could stop it in its tracks and breathe a sigh of relief.

The average person still thinks about chemicals as single entities, and our system of federal regulation still decides on a case-by-case basis whether chemicals are safe enough to circulate in our world. But a paradigm shift is underway among some scientists, who have

over the last 30 years quietly begun to wonder: By introducing so many substances that did not evolve along with living organisms over hundreds of millions of years, have we unwittingly initiated changes in our biology that may be damaging it profoundly?

SHE WENT LOOKING

One of the researchers most responsible for raising this question and pressing to find answers is Theo Colborn, a woman whose career path has been anything but conventional. Colborn got her Ph.D. at 58, an age at which most people are beginning to think about retirement. By then, she had raised four children while working as a pharmacist, a job that required her to know a great deal about chemistry, biology, and health. In the 1970s she began to see disturbing patterns of illness in the six Colorado communities where she worked as a pharmacist. Eventually, she hypothesized that everybody drank from the local creek or river and each water source had its own unique set of toxins. She went to a number of conferences on water in the Western states and was shocked to find that all anybody talked about was the quantity of water—and who owned it.

Divorced, without a mortgage, her children grown and gone, Colborn decided to go back to school to make herself an expert on the quality of water. A master's degree in freshwater ecology led to a doctorate in zoology, then two years as a Congressional Fellow in the Office of Technology Assessment in Washington.

Then, in 1987, she landed at the Conservation Foundation, where her new boss asked her to take on a survey of research on the impact of pollution in the Great Lakes, a study that determined the course of her life's work. A younger scientist would probably have wanted to make her own mark rather than reading over other people's work. There is little glory in this kind of analysis, no tenure. One of Colborn's gifts was that she enjoyed looking for patterns. She was, and is, one of those rare people who can hold thousands of details in her head, shuf-

Theo Colborn, 78, has worked for almost 20 years to understand endocrine disruption. "Theo is a Rachel Carson of our day," says Gina Solomon, an expert in the field. "She has none of the trappings of a hero, but she is one."



fling and reshuffling them, able to tolerate the uncertainty of not knowing where they will take her. For six months, she worked seven days a week, reading more than 2,000 research papers and 500 government reports. She developed a primitive filing system: 43 boxes of documents, one for each species that had been studied.

At first, Colborn went looking for increases in cancer, but she found, instead, other problems that disturbed her. Where hundreds of bald eagles had nested on the Great Lakes' shorelines, only 45 pairs remained. Inland, these birds had rebounded in the years since DDT had been banned; near cleaner lakes they also flourished. But on the shores of the Great Lakes, deformed birds were showing up across species with missing eyes, crossed bills, clubfeet. A startling number of gull and tern nests sheltered twice the number of eggs they should, which suggested that females were sharing nests, apparently for lack of a male companion. Many males were not mating or not parenting. Some birds were abandoning their nests altogether. Chicks seemingly born healthy quickly developed a wasting disease and died. Creepy stuff, but what did it mean? She sought out wildlife biologists who told her that they, too, sensed something was wrong, but none of them could put a finger on what it was. Tissue analyses of the animals kept turning up the same chemicals, including DDT, dieldrin, chlordane, lindane, and PCBs. Everyone knew that hundreds of chemicals had been discharged into the lakes, many of them persistent but impossible to measure with methods available at the time.

To tame the data, Colborn made an electronic spreadsheet for species that were most profoundly affected to figure out where the patterns lay. Before long, she realized that something fundamental had to be happening to explain such a wide range of symptoms: reproductive failures, genital deformities, thyroid malfunctions, behavioral abnormalities, and immune suppression. Eventually she decided the most likely probability was endocrine damage.

Her knowledge of endocrinology was sketchy, so she set herself the task of mastering it. Endocrinology is the science of hormones, the chemical signals that, in myriad delicate and subtle ways, manage an organism's most vital functions. Hormones tell the ovaries and testes how to make eggs and sperm, tell the lungs how to breathe, the intestines how to digest, and the heart how to pump; they direct neurons in the brain. The way they do their work is an extraordinarily complicated dance that scientists are still working to comprehend. Estrogens, the female sex hormones, have been accorded the most attention so they are best understood; the male hormones, androgens, run second; and the thyroid, which controls brain development, is a distant third. If hormones cannot do their job properly, the consequences are legion—some subtle, some disastrous. The wrong balance of estrogens and androgens, for instance, can lead to reproductive failure. If a fetus suffers even a small drop in thyroid hormone levels, learning disabilities may be the consequence, IQ points may be lost.

Colborn drew up a list of world-class scientists from different fields—endocrinology, biology, immunology, toxicology, psychiatry, ecology, anthropology—whose work gave them, collectively, the expertise to test her suspicions, and invited them to the Wingspread Conference Center in Racine, Wisconsin, in the summer of 1991. "I was scared to death! There I was, a brand-new Ph.D. who knew only a handful of wildlife biologists." She did her best to set up conditions in which this wary bunch could find common ground. "I kept them working from morning till night so they had to get to know each other," she says. "Thank God there were no cell phones back then." Right away, people began to see surprising connections be-



Biologists knew something was wrong when they began to see too many eggs in a single nest; this one was shared by two female Western gulls.

tween their work. They stayed up talking into the small hours.

The term endocrine disruption was coined at the meeting. As the fruit of their work, the group issued a consensus statement that has stood up well to the test of subsequent research. The participants agreed that many man-made chemicals had the potential to disrupt the endocrine system of animals, including humans, by mimicking the activity of a hormone, by blocking it, or through other mechanisms, and that many wildlife populations had already been affected. Even more disturbing, they emphasized that the fetus and newborn are at greatest risk, and that the effects might not be manifested until the animal was mature. Perhaps the greatest bombshell was the statement that "the concentrations of a number of synthetic sex hormone [disruptors] measured in the U.S. human population today are well within the range and dosages at which effects are seen in wildlife populations." Suddenly, this was not about cleaning up a few lakes; the health of all the creatures in our care was at stake—including the health of our unborn children.

MOUNTAINS OF DATA

In the years since that conference, research on endocrine disruption has picked up speed; Colborn and her staff have built a database of 33,000 articles to make that research accessible. Chemical manufacturers have funded many studies that have almost uniformly concluded that endocrine disruption does not occur or, if it does, is not harmful. This is hardly surprising because a great deal of money is at stake. (To offer just one example: In 2002 U.S. companies produced 2.8 million tons of bisphenol A [BPA], a synthetic estrogen used to make baby bottles, plastic water bottles, dental sealants, and resin liners for metal food cans. At 94 cents a pound, this translates to sales of more than \$5.3 billion in that year alone.) By contrast, federally funded academic researchers, who have no financial stake in the outcome of their work, have found much compelling evidence that synthetic chemicals, including BPA, do cause endocrine disruption and that the damage can be serious.

One discovery in particular changed the ground of all endocrine disruption research. Frederick vom Saal, a reproductive endocrinol-

ogist at the University of Missouri, established in 1997 that significant effects can be seen at extremely low levels of exposure, parts per billion and even per trillion. These levels are present in the blood of humans as well as animals.

The next logical step would be to expose human subjects to these chemicals, but it is considered unethical to subject humans to substances that might damage their endocrine function. So rats and mice have had to stand in for humans, just as they do in cancer research.

Over the last 10 years, vom Saal has studied the effects of BPA on mice, and others have followed his lead. Collaborating with Wade Welshons, a veterinary medical researcher also at the University of Missouri, he established in 1997 that male mice whose mothers were exposed to BPA during gestation routinely developed enlarged prostates. Further research found that BPA has many other impacts. In male offspring, exposure of the mother results in decreased sperm counts, decreased motility of sperm, an increase in malformed sperm, and smaller testes. In females, researchers have observed early onset of puberty, larger uteri, polycystic ovaries, deformed and incomplete vaginal structures and tissues, enlargement of mammary ducts and milk glands in the breast, and an increase in miscarriages. Damage by BPA, vom Saal notes, is not limited to reproductive effects. Structural changes in the brain; immune-system damage; learning problems; hyperaggression; and changes in sexual behavior, social interactions, and play behavior have also been documented.

Chemical manufacturers have worked hard to counter this academic research, hiring chemists to study and discredit the results. Vom Saal and others have had to spend enormous amounts of time and money defending their work, resources better devoted to moving forward onto new ground. Researchers funded by industry, curiously, tend to find that every chemical is safe. In 2004, vom Saal tallied up results of all the studies he could find on BPA. He discovered that of 104 studies done by independent researchers, 94 found adverse effects and 10 found no effects. Of the 11 studies conducted by industry-supported researchers, zero identified adverse effects. Marian Stanley, a spokesperson for the American Chemical Council, which represents the interests of chemical manufacturers, says, "We are unaware of any big discrepancies between the experimental research supported by industry and by others. Animal studies—that is, credible experimental research—from all sectors show basically the same results across the board."

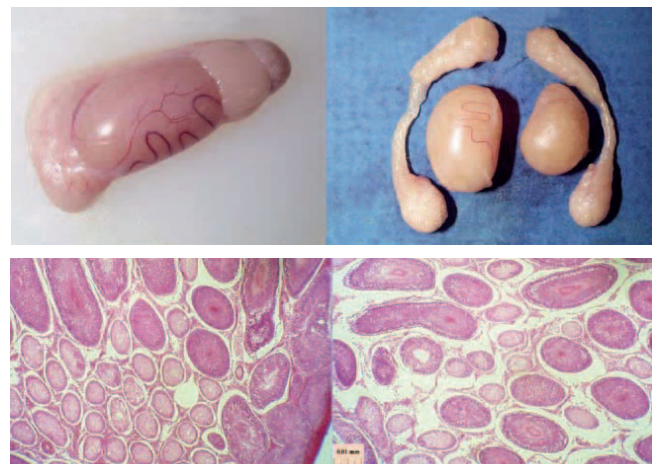
In fact, Colborn observes, academic researchers have been able to demonstrate the effects of chemicals at very low doses, but industry labs have not been able to replicate their work, and use their lack of results to claim that the chemicals are safe. Colborn says that independent researchers have identified possible causes of these discrepancies. Diet is key; animal chow that has more soy, which itself is mildly estrogenic, may skew results. Housing rats in plastic cages or stainless steel may throw things off since some plastics disrupt endocrine levels but metal does not. Intrauterine position can affect results: For instance, a male rat that grew in utero between two female rats will be born with higher levels of estrogen in its blood than one that grew between two male rats. Controlling for all these variables is hard and expensive. The most contentious variable has been breed of rat. Early in the process, researchers determined that the Charles River Sprague Dawley rat was so tough that it barely responded to estrogenic compounds. Many scientists whose work is funded by chemical manufacturers have continued to use this strain, a practice deplored by Colborn and other independent researchers.

Pat Hunt, a geneticist at Washington State University, was shocked when she discovered how great a difference a worn-out plastic cage could make. Suddenly, 40 percent of the healthy control mice in an experiment began to make eggs with grossly abnormal chromosome behavior where she expected to see a rate of 1 to 2 percent. She traced the problem back to BPA they were exposed to when it leached out of their cages and water bottles. She spent five years on the problem, making certain of her results before publishing "because I was going to say exposure to this chemical used in plastics can cause miscarriages." Today, at conferences, Hunt urges fellow scientists to take endocrine disruption seriously. "The mouse is an incredibly robust breeder while we humans are, comparatively, so fragile." She is concerned about delay. "If we wait till we see an increase in chromosomally abnormal [human] miscarriages or a sharp drop in sperm count, by the time that big an effect comes up on the radar screen, we need to ask ourselves if we are going to be reproducing as a species or not."

RESEARCH ON MALE SEX HORMONES, OR ANDROGENS, HAS SHOT FORWARD IN THE PAST DECADE, AND THE MAN MOST RESPONSIBLE FOR THIS PROGRESS IS EARL GRAY, A TOXICOLOGIST WHO WORKS FOR THE ENVIRONMENTAL PROTECTION AGENCY IN RESEARCH TRIANGLE PARK, NORTH CAROLINA. IN 1995, HE STARTED BY ADMINISTERING VERY LOW DOSES OF THE FUNGICIDE VINCLOZOLIN TO PREGNANT RATS.

Vinclozolin was widely used until 2002, when the EPA began to restrict it because of its potential health effects. Gray found that the rats' male offspring were born with nipples, malformed scrota and testes, vaginal pouches, and cleft phalluses with hypospadias (urethral openings in the wrong place, along the shaft of the penis or in the scrotum). This finding is particularly resonant for human health, since the rate of hypospadias in human infants doubled for no known reason between 1968 and 1993. The animals in this experiment also displayed

The rat testis (upper right) exhibits signs of atrophy and malformation after exposure to diisononyl phthalate (DINP); the undissected testis of a healthy control animal is at left. Micrographs (below) of the exposed rat's testes show reduced sperm; the right testis is more damaged than the left.



delayed puberty, lower sperm counts, and reduced fertility.

Gray went on to examine trenbolone acetate, a synthetic steroid used as a growth promoter in beef cattle in the United States and as a performance-enhancer by athletes who purchase it illegally over the Internet. Trenbolone, excreted in animal waste, shows up in rivers and streams where, Gray believes, it may affect aquatic animals. After experiments on the fathead minnow, Gray concluded that trenbolone was a powerful androgen: Female offspring of mothers exposed to the compound grew tubercles, part of the reproductive system usually seen only in males, and had fewer babies. Observers of wildlife are beginning to report similar effects around the world. Effluents from pulp and paper mills are sufficiently androgenic to sex-reverse female fish in Florida, the Baltic Sea, and New Zealand.

Gray is an extraordinarily productive researcher, at the top of his field. One can only wonder how much more he might discover if he had more resources. Because of a hiring freeze at EPA, Gray's staff of technicians has shrunk from three to one, limiting the number of experiments he can do.

THREATS TO OUR HEALTH

It is extremely difficult to obtain direct evidence that endocrine-disrupting chemicals cause reproductive damage in humans, for reasons beyond the ethical one. For instance, determining the effect of any particular chemical on an individual is nearly impossible because it is so difficult to figure out which chemicals the individual's mother was exposed to during pregnancy. However, Shanna Swan, director of the Center for Reproductive Epidemiology at the University of Rochester School of Medicine and a researcher who is at the forefront of this effort, published last May the first study to link prenatal exposure to phthalates to outcomes in offspring.

She had recruited a group of pregnant women and measured nine phthalate metabolites in their urine. This chemical group had already been shown to disrupt the endocrine system in rodents and is ubiquitous in our world—in plastics, nail polish, perfumes, toothbrushes, pesticides, paint, and the coating on time-release pills. Then Swan asked pediatricians who knew nothing about the maternal exposure levels to measure the distance between the genitals and the anus in the male babies. Then this distance was divided by the infant's weight to establish an anogenital index (AGI), a biomarker animal researchers have long used because it is predictive of the healthy development of the genitals in rodents. Short AGI correlates with smaller penises, smaller, ill-defined scrota, and incomplete testicular descent.

Swan found that a boy born to a mother with a high exposure to dibutyl phthalate (DBP), for example, was 10 times more likely to have a short AGI than a child of a mother with a low exposure to DBP. Swan points out that this was a small study of 85 infants; she has proposed a larger study of 600 families to investigate these effects further. She believes the research is necessary because the mothers of babies with short AGIs had been exposed to levels of phthalates that, according to estimates from the Centers for Disease Control and Prevention, are present in the bodies of one-quarter of all American women.

It is already clear that synthetic chemicals can also powerfully affect the thyroid gland, which is critical to brain development and function, according to Thomas Zoeller, an endocrinologist at the

University of Massachusetts Amherst. But work is still in an early stage; much remains to be understood about how the thyroid functions and how that functioning can be disrupted. Zoeller's lab works with PCBs even though they were banned in 1979, largely because the behavior of these chemicals is well understood, which makes it easier both to predict their behavior in the lab and to interpret it. Moreover, although PCB levels dropped at first after the ban, these chemicals have such a long half-life that the rate of decline leveled off in the mid-1990s, which means they will belong to our bodies' burden of toxins for a long time to come.

Zoeller has determined that exposing a fetus to PCBs leads to profound changes in the brain. "The corpus callosum is a big bridge of white matter that connects the two hemispheres, and in our experimental animals, the PCBs cause a reduction in the size of the corpus callosum," he says. This may prove to be a very important finding, he explains, because "a number of neuropsychological diseases in humans have been linked to the development of the corpus callosum—for example, autism and Tourette's." However, he emphasizes that we don't know yet if the link is causative. Zoeller also suspects that disruption of the thyroid may be contributing to the sharp spike in learning disabilities observed over the past two decades, a spike that cannot, he says, be explained away by improvements in diagnosis.

A careful study published in 1996 by Joseph and Sandra Jacobson suggests Zoeller is right to be concerned. Testing children of mothers who ate Great Lakes fish contaminated by PCBs, they found that children whose mother's blood and breast milk, along with umbilical cord blood, showed the highest concentrations of PCBs had lower IQs—on average six points lower—than children of mothers with the lowest concentration. Joe Jacobson points out that what he and his wife documented was a correlation between exposure and a drop in IQs rather than proof that PCBs caused the drop. The children with greatest exposure also exhibited memory and attention deficits and were twice as likely to be at least two years behind kids in the lowest exposure group in reading comprehension. None of these impacts sounds catastrophic, but they could mean more kids who can't sit still in class and are miserable in school. The Jacobsons followed these children only until they were 11 so they do not know how those exposures affected them later in life. But children who have difficulty in school may well grow up less able to read, write, or think clearly.

TWO BROODING QUESTIONS HAVE HUNG OVER ENDOCRINE-DISRUPTION RESEARCH. ONE: ARE THE EFFECTS OF ENDOCRINE-DISRUPTING CHEMICALS ADDITIVE—IF YOU ARE EXPOSED TO MANY OF THEM, WILL THEIR EFFECTS ADD UP TO PRODUCE GREATER CHANGES IN HORMONAL ACTIVITY? AND TWO: ARE THE EFFECTS HANDED DOWN FROM ONE GENERATION TO THE NEXT? THE FIRST ATTEMPTS TO STUDY THESE QUESTIONS SUGGEST THAT THE ANSWERS ARE LIKELY TO BE: YES AND YES.

In 2005 Kevin Crofton, a neurotoxicologist who works for the EPA at Research Triangle Park in North Carolina, published a finding that helped to confirm many researchers' worst fears. Crofton gave rats

different doses of mixtures of three classes of chemicals—dioxins, PCBs, and dibenzofurans—at concentrations ranging from approximately those that would be found in humans to levels 100 times higher. The chemicals in the mixture were chosen because they are found in foods people eat, from fish to breast milk. The highest dose he used for each chemical was still so low that he had seen no endocrine-disrupting effects for that chemical at that level. At the lower doses, Crofton found that the effect of the mixture was additive and that it significantly reduced the animals' level of thyroxine, the most common thyroid hormone. At higher doses, he observed that the mixtures reduced thyroxine synergistically so that the sum of their effect was slightly greater than simple addition. A fetus must have enough thyroxine for the brain to develop properly; adults need thyroxine to regulate metabolism and heart rate.

This and many other recent studies of mixtures up the ante considerably. They cut right through the endless debates about whether the levels of exposure to a chemical in any given experiment accurately reflect the levels at which humans or animals are actually exposed to that compound in the environment. These studies suggest that we can't solve the problem by taking a handful of the most dangerous chemicals off the market; instead, we will have to consider whether all endocrine disruptors need to go. The European Union has already begun to move in this direction.

The second question, whether effects are handed down from one generation to the next, got an answer almost by accident. Michael Skinner, a molecular and cellular biologist who focuses on reproductive biology at Washington State University, wanted to look at how cells communicate during the development of ovaries and testes. He dosed a group of pregnant rats at mid-gestation with vinclozolin, an anti-androgen (a substance that blocks androgenic hormonal activity), and another group with the pesticide methoxychlor, which is estrogenic, to see if either would alter the development of their off-

spring. A research fellow in his lab bred that first generation of babies, which was not part of the plan. She apologized, but Skinner told her not to worry, to seize it instead as an opportunity to examine the impact on a second generation. Everyone in his lab was stunned when they found that both chemicals wreaked significant damage. According to Skinner, of those exposed to vinclozolin, "greater than 90 percent of the males developed subfertility with a dramatic increase in developing sperm undergoing cell death" for not one but four generations. Further analysis established that the rats in both experiments had suffered germ-cell defects, the result of a chemical modification of their DNA. Both males and females developed various diseases as they aged. For example, female offspring of the first generation developed a condition equivalent to pre-eclampsia in human mothers, which can result in severe complications for the baby and death for the mother. In humans, incidence of pre-eclampsia has risen sharply over the last 20 years, and no one knows why. Skinner points out that he used a level of toxins higher than what people would be exposed to in ordinary circumstances, but he believes that "women in their mid-gestation pregnancies should be very cautious about their environmental exposures."

WE ARE UNPROTECTED

Fewer than a thousand of the 100,000 synthetic chemicals have been tested for endocrine disruption by anybody, but even the little we know is alarming. Sadly, the government's effort to mount a response has been checked continually by insufficient funding for research and regulation, by the complexity of the science that must be done, and by industry's well-funded efforts to delay the EPA's plans to test chemicals.

After the Wingspread conference, Colborn worked to raise awareness of endocrine disruption in citizens and legislators. With two gifted collaborators, John Peterson Myers and the science writer Dianne Dumanoski, Colborn wrote *Our Stolen Future*, a book for the lay reader. In 1996, the year it was published, Congress passed ambitious legislation mandating the testing of all synthetic chemicals to determine whether they cause endocrine disruption. The Endocrine Disruptor Screening and Testing Advisory Committee (EDSTAC) was charged to recommend a testing protocol within two years.

From the start, EDSTAC faced considerable obstacles. One was its size: 39 members, including chemical company representatives and environmental activists, but only five bench scientists. Gina Solomon, a Harvard-trained physician who had just started work at the Natural Resources Defense Council (NRDC), where she is now a senior scientist, remembers, "It was often hard to get a word in edgewise, let alone talk through anything." She adds, "These were public meetings with audiences of up to 100, held in anonymous airport hotels around the country so there could be local participation and comment, which is a good thing, but it created a disconnect. The committee was charged to do a very technical scientific task."

Discussions were contentious. Representatives of some chemical manufacturers were accompanied by teams of lawyers who had to consult on every issue. At one point, the committee reached a seemingly hopeless impasse on how to define an endocrine disruptor. A compromise was finally achieved when Colborn suggested that they "describe" rather than "define" the term. How to define an adverse effect of an endocrine disruptor also ate up

WHAT YOU CAN DO

In the fight to rid the environment of endocrine-disrupting chemicals, your purchasing power is your greatest weapon. You can start to make informed choices about what to buy only after you identify the sources of exposure—not an easy task.

For baby products, take a look at www.oeonline.org/kidshhealth/tinyfootprints. Cosmetics are a tough area because the federal government doesn't require that manufacturers list all ingredients. But the Environmental Working Group's website, www.ewg.org/reports/skindeep, is a good place to start. For pesticides, log on to www.pesticide.org. If you would like a fuller list of websites that have been vetted by Theo Colborn and her staff, send an email to tedx@tds.net asking for their self-help list. Manufacturers fear what they call product deselection. If you write to tell them why you have stopped buying a product, you exercise even greater power in the marketplace. You can also multiply that power by telling your relatives and friends what you're doing and why; at the same time, you will be helping to protect them.

To learn more about the science and politics of endocrine disruption, go to www.ourstolenfuture.org, the work of John Peterson Myers, one of the coauthors of Colborn's book.

oceans of time. The law required an investigation of estrogenic effects of synthetic chemicals but did not limit the investigation to estrogen alone. Industry wanted to look only at estrogens, while Colborn and others believed all hormones should be studied. Eventually androgens were included, and later thyroid hormones were added as well, but it took months to reach these agreements. (Other hormonal systems that are not yet part of the testing include the pancreas, where malfunction can lead to diabetes or obesity; the pituitary gland; the pineal gland, which controls sleep; and the thymus, critical to the immune system.)

The committee was also divided about whether the goal was to protect human health or the health of wildlife. Colborn considered this a false dichotomy because she does not see animals and humans as two groups with separate fates. If wildlife suffers, so do humans. Yet, while evidence of harm to wildlife was mounting, how to pin down causal connections to human health remained a vexed question. Representatives of industry were quick to exploit the dilemma inherent in the research: They argued that anything less than the gold standard of experiments conducted with human control groups would be “unsound science,” experiments that everyone agreed could never be conducted for ethical reasons.

Despite these difficulties, EDSTAC met its deadline: In August 1998, its final report recommended 14 assays, or tests, and a plan for making decisions about how many of these tests a chemical had to pass before it could be deemed safe.

NOT EVEN ONE ASSAY HAS BEEN APPROVED AS WE GO TO PRESS. BEFORE TESTING CAN BEGIN, PROTOCOLS HAVE TO BE AGREED UPON FOR CONDUCTING EACH ASSAY AND THEN EACH ASSAY HAS TO BE VALIDATED BY RUNNING TRIALS IN MULTIPLE LABS TO PROVE THAT RESULTS ARE REPRODUCIBLE FROM ONE LAB TO THE NEXT. ESTABLISHING PROTOCOLS AND VALIDATING THEM HAS PROVED TO BE EXTRAORDINARILY DIFFICULT AND TIME-CONSUMING.

But the work is all the more important because the chemical companies themselves will be responsible for conducting these tests. Still, the process of validating the government’s battery of assays has eaten up seven years. Colborn says that lack of resources has been the biggest deterrent to progress: “With the lack of funding and the limited staff provided to the EPA, we could not have expected much more.” Solomon of the NRDC is cautiously optimistic but warns that validation has seemed within reach several times before, only to be disrupted by unforeseen difficulties. Colborn fears that money and time will be thrown away testing high doses instead of low doses, on adult rats rather than embryos, on Charles River Sprague Dawley rats that won’t react.

Gray is, like Colborn, keenly impatient with the delays, but he believes the proposed assays will tell us what we need to know. “We have reliable screening assays for identifying estrogens and anti-estrogens and androgens and anti-androgens that have been used in the scientific community for decades,” Gray says. “These assays are reproducible, and they’re diagnostic of endocrine effect. They produce valid, interpretable results.”

SHOW US THE MONEY

Given the strength of the science and the risks in play, it would seem that it is time to spend the money to do the testing and move the regulatory process forward. Unfortunately, the reverse seems to be happening. In 2003, 2004, and 2005, the Bush administration tried to cut all EPA funding for independent scientists who do endocrine-disruptor research. While these efforts failed, the total budget for those three years was still less than \$15 million. (By contrast, Japan recently spent \$135 million on a research program and has identified some 70 chemicals as endocrine disruptors.)

Spokespeople for chemical companies maintain that the levels at which humans are exposed to endocrine disruptors are not dangerous. Marian Stanley at the American Chemical Council states: “The consensus of the research is clear that there is no evidence that humans have been adversely affected by environmental exposures to endocrine active substances...and there is not convincing evidence of a growing human health issue.” Still, there are signs that manufacturers have read the handwriting on the wall and are making changes to avoid liability suits down the line. Procter & Gamble has removed dibutyl phthalate (DBP) from all products that it sells around the world. Unilever, Revlon and L’Oréal have pledged to take chemicals banned in Europe out of any products they sell here. Baxter International is developing an alternative to phthalates for its medical bags and tubes. And methoxychlor, one of the pesticides Michael Skinner tested that showed endocrine damage through four generations, quietly disappeared from the U.S. market last year when Drexel Chemical failed to re-register it with the EPA.

Colborn is encouraged by these developments, but she is still extremely worried because these few withdrawals “don’t begin to clean up the womb environment.” Solomon worries, too, particularly with regard to food production and supply. “Every time a pesticide is re-registered by the EPA, the registration contains a boilerplate statement that there is no evidence that this chemical causes endocrine disruption, but that after tests are approved there may need to be additional testing. In the meantime, that chemical may be affecting the health of hundreds of thousands of farm workers or millions of people who eat the crops that are sprayed with that chemical.”

In addition to the chemicals already released into the environment, 2,000 new chemicals go to market every year, and each may have the potential to be another DDT, a DES, a PCB, all of which turned out to be powerful endocrine disruptors. The biggest hurdle to solving the problem is funding. Colborn and others have proposed that those who profit from these chemicals be made financially responsible for determining the environmental safety of their products. Money could be paid by manufacturers into a trust, or directly to the government, so that manufacturers could not influence the outcome of the testing.

Instead of drifting along for years, nibbling away at the problem of how to remove endocrine disruptors from the environment, Colborn hopes we will throw our collective will and enough resources into finishing the job as quickly as possible. “Think of how many billions we’ve spent on cancer research. If these chemicals threaten our ability to reproduce, then we ought to be spending at least as much money on understanding how they work and whether we need to get them out of our environment,” she says. “If we can’t reproduce, whether we get cancer or not will be a moot point.”