Hormone Hell

By

Catherine Gold

Industrial chemicals--from plastics to pesticides--paved the road to modern life. Now it appears

that these same chemicals, by mimicking natural hormones, can wreak havoc in developing

animals. And the road we once thought led to material heaven is heading somewhere else

entirely.

Biologist Charles J. Henny reaches into a plastic bag and pulls out eight long, slender structures

that look something like old chicken bones. He carefully places them side by side on his desk and

then points out the obvious. “See how they get smaller and smaller,” he says, waving a hand over

the lineup. “It’s right in correlation with the contaminants.” The evidence, thus laid out on the gray

metal desktop, seems clear. Otters living in the lower Columbia River area near Portland, Oregon,

have a serious problem.

The thin sticks in question are not chicken bones but baculums, the bony part of a river otter’s

penis. Those on the left side of the lineup once belonged to otters number 28 and 29, “reference”

animals that were taken from a less contaminated river habitat miles away from the Columbia. At

nearly six grams each, they are significantly larger than the remaining six baculums, which were

taken from Columbia River otters. These Columbia specimens average just 2.62 grams, with the

smallest weighing a measly 1.92 grams. The otters’ testes, says Henny, show a similar range in

size, all the way down to one poor otter that didn’t appear to have any testes at all.

To the naked eye, all eight animals had seemed healthy--all were just under a year old and about

the same size, around 15 pounds. They had all been caught by fur trappers, who then froze and

kept the skinned carcasses until Henny could collect them and bring them back to his office at the

National Biological Service in Corvallis, Oregon. When he and a veterinary pathologist examined

the otters, the only significant difference they detected--besides the weight and size of the

reproductive organs--was in the levels of industrial chemicals and pesticides in the animals’ livers.

Time after time, when they analyzed the tissues for pcbs, heptachlor, mirex, or one of several

dioxin-like compounds, the relationship was clear: the higher the concentration of chemicals, the

smaller the reproductive organs.

“It was unbelievable to see those baculums line up the way they did,” Henny remarks a short time

later as he steers his pickup along the banks of the Columbia River. At river mile 119, a few miles

east of downtown Portland and 119 miles inland from where the Columbia finally empties into the

Pacific Ocean, he pulls off the highway. “This is near the famous spot where Lewis and Clark shot a

condor,” he says. Looking at the wild, wide Columbia River, whipped with rain under a steel gray

sky, it’s easy to imagine the legendary explorers scouting around the river and the dense forests,

maybe even trapping a few otters themselves.

Looks can be deceiving. Although the Columbia doesn’t much resemble eastern rivers that fairly

scream pollution, with smoking factories lined up toe-to-toe on their banks, it is polluted

nonetheless. Heavy metals, dioxins, furans, pcbs, ddt, and other pesticides are all there. Some

came from local industry and farm runoff; some were probably transported on air from other parts

of the globe. Some of the pollutants exceed allowable levels; some don’t. For some chemicals,

permissible levels have not been set. Most of the pollutants tend to accumulate in animal fat, and

the otters, eating at the top of the local food chain, seem to be getting plenty.

Thirty-four years ago Rachel Carson’s Silent Spring alerted the world to the dangers of pesticides.

Chemicals such as ddt were recognized to be fatally toxic to some species and to cause

widespread reproductive failure among others. Now scientists are finding that these same

chemicals, at lower concentrations, can have an array of unexpected effects. Acting in the earliest

stages of an animal’s development, these chemicals are believed to play havoc with hormonal

systems, leading to abnormal reproductive organs, skewed sex ratios, odd mating behavior, and

animals that seem to be neither entirely female nor entirely male.

The Columbia River otters are obviously affected. And many other species--from alligators in

Florida to beluga whales in the St. Lawrence River--are showing similar problems. It seems

reasonable to wonder, then, if these chemicals pose a threat to humans also. After all, we are not

so different from other animals, and some researchers think these same chemicals might well be

pushing our sperm counts down and our cancer rates up. Added to this worrisome possibility is

recent evidence that points to what could be an even more insidious effect: some of these

endocrine- disrupting chemicals appear to be altering the behavior of children. And they seem to

be doing it at relatively low levels--levels that many of us already carry in our bodies.

Hormones, for all their notoriety in shaping sexuality, are little more than the messengers of the

endocrine system. Hormones released by the pituitary gland trigger the appropriate release of

hormones elsewhere in the body, such as in the ovaries or adrenal glands. These hormones, in

turn, travel to other parts of the body to tell cells what to do and when to do it. In a woman, for

example, the hormone estrogen tells the uterus to get ready to receive a fertilized egg;

adrenaline tells the heart to beat faster.

In the fetus, however, hormones do more than orchestrate activity. They perform complex

developmental tasks, tasks that require precise dosage and exquisite timing. They tell tissues

whether they should become female or male reproductive organs, nerve cells, muscle cells, or

even eyelash cells. Hormones set off this differentiating process by binding to a specialized

molecule--a receptor--on the surface or in the interior of a cell. The hormone-receptor complex

then informs the cell’s dna which genes need to be turned on, and the genes, in turn, tell the cell

which proteins and other substances it needs to make to take on the structure and function of the

cell it’s fated to be. Hormones are what tell the fetal cell what it will be when it grows up.

But what if chemical impostors interfere with these carefully articulated messages? Many

researchers now believe that a small army of common chemicals can somehow imitate natural

hormones, binding to receptors on fetal cells and scrambling the genetic instructions. By causing a

cell to turn on the wrong gene, or effectively turn off the right one, or even turn up the “volume” of

a gene, these mimics can derail an animal’s development, permanently distorting its reproductive,

immune, and neurological systems. There are more than 50 of these endocrine-disrupting

chemicals, as they have come to be called, most of them ubiquitous in our environment. Some,

such as ddt, alachlor, atrazine, chlordane, dieldrin, heptachlor, and mirex, are pesticides. Others,

such as pcbs, endosulfan, bisphenol-A, dioxin, and heavy metals, are chemicals that have been

used in, or created as by-products in, the manufacture of such everyday products as paper and

plastics.

In the United States the use of some of these chemicals was restricted decades ago. Still, they

persist in the food chain because of the way they accumulate in animal tissue: the chemicals,

which the body cannot degrade, tend to lodge in fat; animals feeding at the top of the food chain

usually have higher levels because they absorb the chemicals that have accumulated in their prey.

Moreover, many of these chemicals continue to be used in developing countries. The ultimate

result is that these substances can be found nearly everywhere on Earth. Black-footed albatross on

Midway Island in the middle of the Pacific Ocean are contaminated with ddt, pcbs, and dioxin.

Beluga whales in the St. Lawrence River have pcb levels so high they must be treated as

hazardous waste when they die. Even marine mammals and people living in remote Arctic regions

carry ddt, pcbs, dioxins, and other chemicals, transported around the world in the atmosphere.

“We have no evidence that there are any populations that don’t have these chemicals--fish,

wildlife, or people,” says Linda Birnbaum, director of experimental toxicology at the Environmental

Protection Agency. Ninety to ninety-five percent of the suspected endocrine-disrupting chemicals

that we absorb, she adds, are thought to come from the food and water we consume.

Fetuses--of any species--are particularly sensitive to exposure. When a pregnant female breaks

down her fat reserves, the chemicals migrate into the fetus, accumulating at concentrations many

times greater than daily adult exposures. Once there, they may unleash far more powerful effects

than in an adult, some of which may not become apparent until sexual maturity.

One serious abnormality after another has been reported in wildlife that have been exposed to a

highly contaminated environment. Alligators in Lake Apopka, Florida--the site of a cleaned-up

toxic spill-- have tiny penises; male fish in polluted English rivers are producing a protein normally

found only in fish eggs; beluga whales seem to be having fertility problems. In the case of the

Columbia River otters, scientists found a clear dose-response curve--as the levels of contaminants

increased, the size of the reproductive organs decreased. In most wildlife cases, however,

investigators have simply noted gross reproductive abnormalities associated with high levels of

chemicals. It has not been possible to show dose-dependent relationships, nor, because these are

wild populations and not controlled experiments, has it been possible to show definitive cause-

and-effect relationships. Even in the case of the otters, it is impossible to say which of the

contaminants are the problem. The researchers know they have a lot to learn.

Laboratory studies are starting to fill in the gaps. Controlled experiments have shown, for

example, that pcbs applied at just the right time during development can change male turtles and

alligators into females or “intersex” individuals. Exposing male gull embryos to ddt can cause

them to develop ovarian tissue. Giving tiny amounts of dioxin to rats before birth can sharply

reduce sperm generation, “feminize” male mating behavior, and decrease the size of male sex

organs. Most of these chemicals were thought to act through the estrogen receptor, but recent

studies have turned up other routes. A derivative of ddt known as dde was recently found to

interfere with normal male development by binding to receptors for androgens--that is, “male”

hormones, such as testosterone--and blocking their effects. Other chemicals have been found to

attach themselves to “orphan” receptors, molecules whose intended function is unknown. To make

matters worse, animal studies have recently turned up evidence of an awful chemical synergy:

evidently, two hormone-mimicking chemicals can exert far more powerful effects than either

chemical alone.

Still, much of the field remains a mystery. “We don’t really understand why these chemicals are

capable of mimicking hormones,” says Frederick vom Saal, a biologist at the University of Missouri

who studies the effects of estrogenic chemicals on mice. “They don’t look anything like

estradiol”--the most potent form of natural estrogen. What is not mysterious, though, is the

potential for damage across a wide range of species. Estradiol, vom Saal explains, is “the same

estrogen that is present in the body of a fish, frog, reptile, human, or bird. It hasn’t changed in

the course of 300 million years of evolution. The receptor hasn’t changed, either.” Other hormonal

systems have not been as thoroughly studied, but they, too, probably evolved from some

common ancestor and are at least similar among vertebrates today.

All of which leads vom Saal and others to ponder, “Why should humans respond any differently to

endocrine-disrupting chemicals?”

“If you look at the developing embryo right after conception, whether it’s a rat or a human or an

alligator, they are all very similar,” says Theo Colborn, a senior scientist with the World Wildlife

Fund who has taken the lead in publicizing the growing body of evidence on endocrine disrupters.

“It is during these stages of development, before specialization, that they are all vulnerable.”

Critics of the endocrine-disrupting theories say that synthetic chemicals are “weak” and not nearly

as potent as natural estrogen and thus not likely to produce ill effects in humans. “Arnold

Schwarzenegger is weak relative to Superman,” counters vom Saal. The real question, he says, is

whether these chemicals are present in concentrations high enough to elicit a response.

“Human cells or rodent cells respond to estrogen at approximately one ten-trillionth of a gram per

milliliter of blood,” says vom Saal. “What if a synthetic chemical is 10,000 times less potent than

that? Then the prediction would be that a chemical present at only one part per billion could exert

a biological response. It turns out that a can of peas contains as much as 30 micrograms of

bisphenol-A.” (This compound, a powerful estrogen mimicker, is found in the plastic coating in

cans.) “That is 30 parts per million, 300 million times higher than the natural action of estradiol.

The people who are running around saying these are weak chemicals don’t tell you that.”

In his own laboratory, vom Saal is looking at the effects of what he calls environmentally relevant

amounts of chemicals. Rather than seeing how much exposure will kill an animal, he says, “we ask

how the system functions normally and how much of this chemical would be required to cause

problems. Then we look at the literature and see how much humans are eating. Are the amounts

that induce changes in animals relevant to what is seen in the environment? The answer is often

yes.”

Ethically, of course, it is impossible to do controlled dosing experiments on humans. But,

tragically, there are cases of accidental contamination that provide evidence of effects in humans.

In Japan in 1968, and again in Taiwan in 1979, women ingested rice oil that was contaminated

with pcbs. The children born to those women have suffered from physical and mental

developmental delays, behavioral problems including hypoactivity and hyperactivity, abnormally

small penises, and iq scores five points below average.

The clearest evidence of endocrine disruption in humans, however, comes not from accidental

exposure but from a reportedly “safe” synthetic estrogen that doctors prescribed to as many as 5

million pregnant women from 1945 to 1971. The drug, diethylstilbestrol (des), was thought to

prevent miscarriage. It is now recognized as an endocrine disrupter that can distort fetal

development.

“We have seen all kinds of structural changes in the vagina, cervix, and uterus,” says Raymond H.

Kaufman of the Baylor College of Medicine, who has studied adult women who were exposed to

des in the womb. These women are also at risk for an uncommon cancer of the vagina and cervix,

some immune system disorders, ectopic pregnancy, and premature birth. des-exposed men have

a slightly higher risk for some genital abnormalities and decreased sperm counts. Experimental

studies of rats and other animals exposed prenatally to des have found similar abnormalities.

The question, of course, is whether hormone-disrupting chemicals now found in the environment

can also produce such dramatic alterations in human sexual development, and many

investigations into that possibility are under way. But even more worrisome are reports showing

that the chemicals may already be producing subtle changes in memory and behavior in children

exposed to them before birth.

The first studies of this type were launched more than 15 years ago. Joseph and Sandra Jacobson,

husband-and-wife psychologists at Wayne State University in Michigan, decided to look at the

babies born to women who had eaten trout and salmon caught in Lake Michigan. Fish from

polluted lakes, rivers, and coastal waters are a well-known source of pcbs and other contaminants;

they soak up so many toxins, in fact, that some states warn women to avoid eating sport fish not

only during pregnancy but at any time during their childbearing years. The Jacobsons asked

several thousand new mothers about their fish-eating habits and eventually studied the children of

more than 200 of them. What they found, says Joseph Jacobson, is “the clearest evidence yet that

pcbs are causing neurobehavioral problems.”

The Jacobsons analyzed the pcb levels found in the blood of each baby’s umbilical cord, which

gives an indication of prenatal exposure. At birth, they found, children who had higher exposures

to pcbs had smaller heads and lower weights. At seven months, they tested the babies for

cognitive function by showing them two identical photos for about 20 seconds. One of the photos

was then paired with a new photo and shown to the baby again. The normal response for an infant

is to spend more time looking at the new picture, indicating that it recognizes the familiar one.

The babies who had the highest exposure to pcbs, however, spent as much time looking at the old

photo as the new one, suggesting either deficits in short-term memory or attention problems.

When the children were four years old, they were given a battery of cognitive tests. Again the

highly exposed children showed memory impairments, this time in tests that asked them to recall

progressively longer strings of words and numbers. The differences in scores between unexposed

and the highest-exposed children, says Joseph Jacobson, “would be like ten points on an iq test.

We’re not seeing mental retardation, but we are seeing that the children are just not doing as

well.” Jacobson suspects these problems may affect the children’s ability to master reading and

arithmetic skills.

These children were not living next to a toxic waste dump, nor had their mothers eaten pcb-laden

fish every day during pregnancy. Their exposure to pcbs, while high, is still considered to be within

the range of normal background exposure levels, says Jacobson. Other possible causes, such as

lead exposure or the mother’s intake of tobacco or alcohol, were ruled out.

Two other studies of children have found similar problems. In the Netherlands, researchers found

that 18-month-old children born to women who carried relatively high but still “normal” levels of

pcbs were more likely to be neurologically “nonoptimal.” In fact, the higher their exposure to pcbs,

the lower their neurological scores. In that study the mothers had eaten normal diets; they got

their contaminants through their food and probably from water and air. Meanwhile, back in the

United States, researchers at the State University of New York at Oswego have found that babies

born to “high fish eaters”--women who in their lifetimes had eaten at least 40 pounds of fish from

Lake Ontario--tested worse on several scales than did babies born to “low fish eaters” and

“non-fish eaters.” Fish in Lake Ontario are highly contaminated with pcbs, dioxin,

hexachlorobenzene, dde, mirex, and other chemicals.

“We looked at the kind of stuff a pediatrician assesses in a newborn,” explains Edward Lonky, a

developmental psychologist at the university. “One of our main findings was in regard to

habituation, which is a measure of neurological intactness. It’s one of the tests we use to assess

fetal alcohol babies, crack cocaine babies, and babies exposed to environmental contaminants.

You shine a light through the eyelids of a lightly sleeping newborn and you get a startle response.

When the body settles down, you repeat the light. The startle response should habituate, or

diminish, over repeated administrations.” Normally an infant will show better habituation on the

second day of testing. Lonky and his colleagues found that infants from the high-fish-eater group

showed poor habituation responses as well as a greater number of abnormal reflexes and stress

responses.

Lonky doesn’t know what his findings might mean for the children as they grow. But he notes that

rats fed fish from the lake have been shown to react abnormally strongly to fearful and frustrating

events. His habituation studies suggest, but do not prove, that chemically exposed human infants

may also overreact.

Chemical exposure appears to be the culprit in these behavioral studies, and though there is as

yet no direct proof of that, researchers agree that the correlations are significant. But if chemicals

are to blame, how might they be scrambling messages in the brain? One theory is that pcbs and

dioxins are mimicking or blocking the action of thyroid hormones. These hormones help organize

the fetal brain and promote the growth of neurons, the nerve cells that transmit information;

severe disruptions in thyroid levels can even lead to mental retardation.

Whatever the cause, such effects may not be rare. “These were not people who were eating fish

every day,” stresses Linda Birnbaum of the epa. “I believe the data suggest there are subtle

changes going on in at least a portion of our population.”

Not all scientists, of course, embrace the theory that synthetic chemicals are disrupting fetal

development. Stephen Safe, a toxicologist at Texas A&M University, has often questioned some of

the studies cited. The hypothesis that synthetic chemicals are mimicking hormones is

“reasonable,” he says, given some of the evidence in wildlife. But that doesn’t mean they must

have the same effects in humans. “Our diet is chock-full of huge concentrations of natural

endocrine disrupters,” says Safe, adding that we consume only “trace amounts” of synthetic

chemicals by comparison. Although Safe acknowledges that the synthetic chemicals tend to

accumulate in the human body while the natural chemicals are quickly metabolized and excreted,

he argues that the natural chemicals still have an opportunity to take action. “How much is active?

We really don’t know. But we’ve got to take into account the fact that we take in huge quantities of

endocrine disrupters.”

Indeed, naturally occurring chemicals, such as phytoestrogens in plants, are known to disrupt

animal reproduction. They have typically arisen through an ongoing evolutionary battle between

plants and animals. If a plant happens to produce an estrogenic chemical that renders cows

infertile, cow herds decline, and presumably populations of that now- uneaten plant flourish. Over

time, though, cows that can somehow degrade the chemical will outbreed the infertile cows, and

the plants will have to come up with a new defense. Humans, like cows and other animals, have

evolved similar defenses against plant chemicals, says Louis Guillette, a reproductive biologist at

the University of Florida who first reported the reproductive problems in alligators. We can usually

make enough enzymes to degrade natural endocrine disrupters with little or no effect on bodily

processes. But Gillette points out that the human species hasn’t had time to evolve similar

defense mechanisms against something cooked up in a test tube only 30 or 40 years ago.

While some researchers are trying to understand just how endocrine-disrupting chemicals act in

animals, others are finding even more common chemicals to add to the growing list of estrogen

impostors. Laboratory studies in England have shown that two phthalates, common chemicals in

the manufacture of plastics, can mimic estrogen. These chemicals are used in many types of

plastic food wrappings and may well be leaching into foods. Meanwhile a food coloring known as

Red Dye No. 3, which lends color to hot dogs and a host of other common foods, has also been

identified as an estrogen mimic and a possible carcinogen.

The epa is paying close attention to hormone-disruption studies. “I take the wildlife findings very

seriously, and I think they should serve as a warning for humans,” says Lynn Goldman, the

agency’s assistant administrator for prevention, pesticides, and toxic substances. The epa is now

developing a national research strategy as well as new guidelines for screening chemicals.

Unfortunately, notes Goldman, its efforts have already been hindered by congressional budget

cuts. The National Academy of Sciences, for its part, recently convened a panel of scientists to

assess what is known about endocrine disrupters.

Much of the credit for an increased awareness of the potential dangers of endocrine-disrupting

chemicals must go to Theo Colborn, who has more than once been called the next Rachel Carson.

“Carson focused on cancer,” says vom Saal. “Theo Colborn has now shown us that there is a whole

other set of information out there that was right in front of us and nobody saw it.” Colborn

downplays any comparisons. Carson struggled alone to get her message across, Colborn says,

while she has had nothing but tremendous support from the scientific community. She does,

however, hope that the studies of endocrine-disrupting chemicals will have as big an impact on the

world as Silent Spring has.

Since World War II, production of synthetic chemicals has risen over 350-fold. No one is seriously

proposing that all such chemicals be banned, of course. Some of them are invaluable for

controlling pests and keeping water clean. As Colborn sees it, the answer to worrisome

“environmental hormones” lies in screening all synthetic chemicals for developmental effects and

creating chemicals that won’t persist in the environment.

“You can’t go back and rebuild a brain,” Colborn says. “You can’t go back and put more sperm

cells in a male. But the beauty of this is that it’s not the result of genetic damage. The blueprint

for the normal individual is still there. What we have to do is make sure that while that blueprint is

being followed, while the chemical messengers that tell this individual how to develop are doing

their job, we’re not introducing more chemicals into the environment of the womb.”

Article: Hormone Hell

Author: Catherine Gold

Topic Area: Biology & Medicine

Issue: September 1996