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In Feast of Data on BPA Plastic, No Final Answer
By **DENISE GRADY**

The research has been going on for more than 10 years. Studies number in the hundreds. Millions of dollars have been spent. But government health officials still cannot decide whether the chemical [bisphenol-A](#), or BPA, a component of some plastics, is safe. The substance lines most food and drink cans, and is used to make hard, clear plastic bottles, containers and countless other products. Nearly everyone is exposed to it.

Concerns about BPA stem from studies in lab animals and cell cultures showing it can mimic the hormone [estrogen](#). It is considered an “endocrine disruptor,” a term applied to chemicals that can act like hormones. But whether it does any harm in people is unclear.

Where science has left a void, politics and marketing have rushed in. A fierce debate has resulted, with one side dismissing the whole idea of endocrine disruptors as junk science and the other regarding BPA as part of a chemical stew that threatens public health.

About half a dozen states have banned BPA in children’s products, and Senator [Dianne Feinstein](#) hopes to accomplish the same nationwide, with an amendment to [the food safety bill](#) scheduled for a vote in the Senate next week.

This year, a [presidential panel on cancer and the environment](#) said there was a “growing link” between BPA and several diseases, including [cancer](#), and recommended ways to avoid BPA, like storing water in bottles free of it and not microwaving food in plastic containers. Some cancer experts said the report overstated the case against chemicals, but the concerns it raised seemed to reflect growing public worries.

Consumer fears have made the words “BPA-free” a marketing tool. Wal-Mart, Whole Foods, Sears, CVS and other retailers have said they will stop selling baby bottles made with BPA, and major formula and baby-bottle manufacturers have also scrapped it. Worried people have purged their homes of plastics labeled 7. (Products are numbered for recycling; those with BPA carry a 7, but not everything with a 7 contains BPA). Nalgene, which makes popular water bottles, quit using BPA when customers began complaining about it. Sunoco, one of the companies that makes BPA, said it would sell the chemical only to buyers who guaranteed that they would not use it in food or drink containers meant for children.

In May, a [White House task force on childhood obesity](#) issued a report suggesting that BPA and certain other chemicals might be acting as “obesogens” in children — promoters of [obesity](#) — by increasing fat cells in the body and altering metabolism and feelings of hunger and fullness.

Perhaps not surprisingly, the issue of whether BPA is safe has become highly partisan.

[Environmental groups](#) and many Democrats want BPA banned, blaming it for an array of ills that includes cancer, obesity, infertility and behavior problems. Environmentalists think the United States should adopt the “precautionary principle,” a better-safe-than-sorry approach favored in the [European Union](#). The principle says, in essence, that if there are plausible health concerns about a chemical, even if they are not proved, people should not be exposed to it until studies show it is safe. The United States takes the opposite approach: chemicals are not banned unless there is proof of harm.

Many Republicans, anti-regulation activists and the [food-packaging](#) and [chemical industries](#) insist that BPA is harmless and all but indispensable to keeping canned food safe by sealing the cans and preventing corrosion, and to producing many other products

at reasonable prices. They argue that the chemical has been demonized, and that adopting the precautionary principle would lead to needless and ruinously expensive bans on safe and useful products. Both sides are closely watching the issue unfold, because BPA is widely seen as a test case in an era of mounting worry about household chemicals, pollution and the possible links between illness and environmental exposures, especially in fetuses and young children.

“This isn’t the only endocrine-disrupting chemical on the block,” said Patricia Hunt, a biologist at [Washington State University](#), in Pullman. “It’s just the one that’s captured the attention, because researchers like me have gotten into the field and gone, ‘Holy cats! We’re all exposed to this.’ There’s been a heavy industry response, and we’ve gathered our forces together a little more strongly to shine a light on it. This is the poster child for this group of chemicals. Academic scientists are saying we need to do something, and we need to do it fast.”

Linda S. Birnbaum, director of the National Institute of Environmental Health Sciences (part of the [National Institutes of Health](#)), said that a new round of government-financed studies with uniform methods, now under way with animal subjects, should help to resolve unanswered questions. In the meantime, Mrs. Feinstein’s ambitious plan to ban BPA from baby bottles, sippy cups, baby food and formula was blocked by partisan battling. She had hoped that the ban would be included in the [food safety](#) bill, not merely in an amendment to be considered separately.

But after months of wrangling, she gave up. The food industry, mostly supportive of the food bill, threatened to oppose it if the BPA provision got in. So did many Republican senators. In August, Mrs. Feinstein’s Democratic colleague Representative [John D. Dingell](#) of Michigan made public a letter in which he urged her to back off on BPA for the sake of the bill, which will broaden the authority of the [Food and Drug Administration](#).

over the food supply — a measure widely seen as essential to reducing food-borne illnesses like the recent [salmonella](#) outbreak from eggs.

In a statement released in August, Mrs. Feinstein said, “The [Food Safety](#) Bill was the logical place for this legislation, and I have been working hard to reach a compromise, but unfortunately BPA language is not included.”

As an amendment instead of being part of the bill itself, the ban is far less likely to pass the Senate and become law. Last week, the legislature in Mrs. Feinstein’s state, California, rejected a BPA ban like the one she is proposing.

Buried in an Avalanche of Data

The mountains of data produced so far show conflicting results as to whether BPA is dangerous, in part because different laboratories have studied the chemical in different ways. Animal strains, doses, methods of exposure and the results being measured — as crude as body weight or as delicate as gene expression in the brain — have all varied, making it difficult or impossible to reconcile the findings. In science, no experiment is taken seriously unless other researchers can reproduce it, and difficulties in matching BPA studies have led to fireworks.

John A. Katzenellenbogen, a chemistry professor at the [University of Illinois](#) in Urbana, and an expert on how hormones works in cells, does not work with BPA but said he had seen researchers who study it argue bitterly at conferences, over supposedly identical experiments that had somehow yielded opposite results.

At one such meeting, scientists in the audience said, “We don’t want to hear you two speak until you get this straightened out,” he recalled.

“I’m interested, and despite the fact that I know a lot about this, somewhat bewildered at the discordances in reports,” Dr. Katzenellenbogen said.

Dr. Birnbaum said, “I think we need to lower the tenor of the discourse and look at what the research really is,” and added that researchers who clash over conflicting results may actually have done different experiments.

The new, government-financed studies will try to determine whether BPA can play a role in obesity, [diabetes](#), breast and [prostate cancer](#) and disorders of the developing immune, cardiovascular and nervous systems. Dr. Birnbaum said researchers would be looking for effects on learning and behavior, and also trying to find out whether there are “multigenerational” effects, meaning that exposure in a pregnant animal can affect her offspring and the next generations as well.

How could one substance possibly have so many different effects?

“What’s estrogen associated with?” Dr. Birnbaum asked. “[Breast cancer](#), [uterine cancer](#), obesity, behavior, the immune system. If BPA can have some estrogeniclike properties, it is scientifically plausible that it might have a wide spectrum of effects. We need to move beyond the idea that an environmental chemical or a drug is only going to do one thing, and need to understand that what happens to an infant may be different from what happens to an adult.”

The results from the new round of studies are not expected for at least two years. “We are in some ways using BPA as a model for an endocrine-disrupting compound,” she said. “What can happen when you perturb fundamental homeostatic processes in the body?”

Impersonating Hormones?

The idea that drugs or chemicals could act like hormones has been around for decades, but advocacy campaigns in the 1990s drew public attention to the issue. Such effects can be subtle and delayed. Hormones act on receptors in cells, structures to which they attach — the standard comparison is lock and key — and orchestrate growth, differentiation and all sorts of biochemical activities. Many cells have receptors for estrogen, and BPA can bind to those receptors, though far less strongly than the body's own estrogen can.

R. Thomas Zoeller, a biology professor at the [University of Massachusetts](#), Amherst, said BPA could also bind to receptors for male hormone and thyroid hormone.

“I don't know of a single other molecule that does this,” Dr. Zoeller said.

In people, the most notorious example of an endocrine disruptor is the drug diethylstilbestrol, or DES, which was given to pregnant women in the 1950s in the mistaken belief that it could prevent [miscarriage](#). The drug turned out to be a disaster, causing vaginal cancers and reproductive problems in some of the women's daughters, and abnormalities in the reproductive organs in some sons. But DES is a far stronger estrogen mimic than is BPA, and women were exposed to much higher levels of it.

Animal studies during the past decade or so began raising concerns about BPA, which is used to harden polycarbonate, a clear plastic that makes nice-looking food containers, bottles and sippy cups. It has been widely used since the 1960s and is also in some medical devices, dental sealants, thermal paper for cash register receipts and the epoxy resin that lines most food and drink cans. The United States produces about a million tons of it a year.

BPA is in people, too. Small amounts leach out of plastics and seep into the body. In

2008, a government study of 2,517 people age 6 and older found that 93 percent had BPA in their urine. Children had higher levels than adults, and other studies have detected the chemical in umbilical [cord blood](#) in newborns.

Studies show that in adults, BPA is eliminated from the body in hours; children take longer to get rid of it. But scientists say that finding it consistently in so many people suggests that the public is being exposed continuously. The main route by which people are taking it in is not known.

Just finding a chemical in people does not mean it is doing any damage, and there is no definitive proof that BPA harms humans. Research in adults has found that higher BPA levels in urine are associated with an increased risk of heart and [liver disease](#), but the studies do not prove cause and effect, because they merely observed correlations, which could have been coincidental.

It would be unethical to experiment on people by giving them BPA, so researchers use rodents, and say the results are relevant to people. Dr. Daniel R. Doerge, who studies BPA at the National Center for Toxicological Research in Jefferson, Ark. (part of the F.D.A.), says, “Animal studies are the cornerstone of all our drug and environmental risk assessment for humans.”

The animal studies have led the National Toxicology Program and the [Food and Drug Administration](#) to express “some concern about the potential effects of BPA on the brain, behavior and prostate gland of fetuses, infants and children.” (“Some” concern is the midpoint on a five-level scale, ranging from “negligible” to “serious.”) The [National Toxicology Program](#) also says, “The possibility that [BPA may affect human development](#) cannot be dismissed.” The [Environmental Protection Agency](#) says, “There are questions about its potential impact, particularly on children’s health and the environment.”

The F.D.A. says that infants are “a potentially sensitive population for BPA” because their brains and endocrine systems are still developing, and their livers are less efficient than adults’ at detoxifying and eliminating foreign substances. The drug agency has taken a seemingly paradoxical position, on the one hand saying there is no evidence of harm in humans, and on the other supporting industry actions to get BPA out of baby bottles and feeding cups, and to find alternative liners for food and formula cans. Bottle-makers have found substitutes, but can producers say there is nothing like BPA. Only a few companies are offering BPA-free cans.

Reconciling Disparate Studies

Most of the evidence against BPA comes from studies that find harmful effects in rats and mice at low doses comparable to the levels to which people are exposed. Sometimes the results seem downright weird, indicating that low doses could be worse than higher ones. There is sharp disagreement among scientists about how to interpret some research. The disputes arise in part because scientists from different disciplines — endocrinologists versus toxicologists, academic researchers versus those at regulatory agencies — do research in different ways that can make findings hard to reconcile.

The biggest unanswered question is whether low doses — the kind to which most people are exposed — can have lasting, harmful effects in fetuses and young children. Dr. Birnbaum said it was crucial to find out for sure whether the low-dose effects in animals really occur. “We have hundreds of studies that show they do, and then some that don’t,” she said.

She and other scientists said studies by university labs tended to find low-dose effects, and studies by government regulatory agencies and industry tended not to find them. The split occurs in part because the studies are done differently. Universities, Dr.

Birnbaum said, “have moved rapidly ahead with advances in science,” while regulators have used “older methods.” Some researchers consider the regulatory studies more reliable because they generally use much larger numbers of animals and adhere to formal guidelines called “good laboratory practices,” but Dr. Birnbaum described those practices as “good record-keeping” and said, “That doesn’t mean the right questions were being asked.”

The low-dose studies are newer and have raised safety issues that need to be resolved, she said. Last year, a scientific group called the Endocrine Society issued a 34-page report expressing serious concerns about endocrine-disrupting compounds, including BPA, dioxins, PCBs, DDT, the plasticizers known as phthalates and DES.

The society has about 14,000 members from more than 100 countries, who work in medicine, biology, [genetics](#), immunology, industry and other areas.

The report said there was strong evidence that endocrine disruptors could harm the reproductive system, causing malformations, infertility and cancer. It noted that the chemicals could affect all endocrine systems, and said there was mounting evidence for effects on the thyroid gland, brain, obesity and metabolism, and the body’s ability to regulate insulin and glucose levels. It also said that fetuses exposed to chemicals in the womb could experience effects later in life, and pass those abnormalities to future generations.

Scientists call such effects “the fetal basis of adult disease,” and say they probably result from epigenetic changes — meaning that the chemicals alter the functioning of genes, turning them on or off, but do not cause mutations, which are changes in the actual structure of the genes. Some scientists said that they had doubted that low doses could cause harm, but changed their minds after seeing the data.

“I was skeptical that there were effects that were repeatable,” said Gail S. Prins, a professor of physiology at the University of Illinois at Chicago, and an author of the Endocrine Society’s report. But in 2001 she was part of a panel that analyzed dozens of BPA studies for the National Toxicology Program. The panel had its own statistician reanalyze raw data from the studies to find out if the claims based on it were valid.

“I could see there was some consistent data,” Dr. Prins said. “I started thinking, ‘Hmm, maybe there could be something there.’ It was still curious to me. This is not a regular toxicant. It’s acting like a hormone, and hormones can act at extremely low doses. If you think the dose makes the poison, it doesn’t make sense. But if you think about it as a hormone — and I’m an endocrinologist — it does make sense.”

Her lab is one of the 10 that have received government grants under the economic Recovery Act to study BPA. She is analyzing its effects on the prostate in young mice and rats, and also in rats that have been implanted with human prostate cells. The work is being conducted under strict guidelines set by the National Institutes of Health, to make sure that the results of different groups will be reconcilable.

“This time N.I.H. said, ‘You all have to do oral exposures, and we’ll give you BPA from one source,’ ” Dr. Prins said. “We’re all working with one batch. We all have to measure free and conjugated BPA levels in our model systems, and it has to be done in a certified lab so that our data will be more aligned. It does make a lot of sense to go about doing it this way, and it hasn’t compromised anything I’m doing.”

There is no practical way to do these studies except in rodents, she emphasized. “I can’t look at early-life exposures and prostate risk in humans,” Dr. Prins said. “I can’t do it in my lifetime even if I start now. Likewise I can’t take men who currently have prostate cancer and see what their BPA levels were when they were born.”

Over the next few years, researchers hope to bring coherence to this confused and troubled field.

“This is a chemical we’re all exposed to, and I think that makes it incumbent upon us to study it,” Dr. Birnbaum said. “We really need to know what it might be doing, if anything.”