NEWS

Getting It Right: BPA and the Difficulty Proving Environmental Cancer Risks

By Mike Fillon

Science still has no answer on whether bisphenol A (BPA) has carcinogenic effects in humans, even as the U.S. government and retailers have banned products containing it. BPA has become the unofficial poster child for several compounds found in products that some researchers claim may be health hazards, including cancer. But critics of the BPA–cancer link say that most studies have used only animals, making extrapolating findings to humans difficult. And too often, studies that find BPA safe have been ignored.

First appearing in products in the 1950s, BPA is a common chemical in homes today. It is the chemical building block for clear polycarbonate plastic, which is used in bottles, in the linings of metal food cans— including cans containing infant formula, and in other food storage containers. It is also found in paper receipts. And it’s getting into our bodies. The 2003–2004 National Health and Nutrition Examination Survey (NHANES III) conducted by the Centers for Disease Control and Prevention (CDC) found detectable levels of BPA in 93% of 2,517 urine samples from people aged 6 years and older.

Although the practical implications of such a mechanism remain unknown and may be speculative at best, some experts say that the effects of environmental exposures have been widely underestimated. To date, more than 150 studies have shown that BPA disrupts the hormone system and causes changes that mirror properties of cancer cells. One recent example is a study in the Sept. 1, 2011, issue of Carcinogenesis, which found that breast cells exposed in vitro to BPA undergo structural changes that enable them to proliferate like cancer cells. Exposure to BPA affects the mTOR pathway, which regulates cell growth, proliferation, motility, survival, protein synthesis, and transcription. When the mTOR signal is turned off, cancer cells do not survive, but once mTOR is activated, cells can proliferate.

“It is a sort of switch that turns things off and on at the cellular level,” said lead author William Goodson, M.D., senior clinical research scientist at the California Pacific Medical Center Research Institute in San Francisco, adding that although cells exposed to BPA won’t necessarily become cancer, any chemical that can prompt healthy cells to act like cancer cells is worrisome. However, Goodson admits that it’s impossible to say yet whether the same effect occurs in humans.

Many researchers believe the dearth of studies on humans complicates interpretation of the findings. In general, researchers understand that animal studies are not always reliable precursors to human studies. “The answer is, it varies,” said David L. Eaton, Ph.D., associate vice provost for research at the University of Washington in Seattle. Eaton, who has written a great deal on toxicology and risk assessment, said when no good human data on a chemical exist, the question becomes how reliable the animal data are for predicting human response. “Sometimes they’re very good and sometimes they’re not. And it’s hard to tell which is the case with BPA.”
Environmental Causation

According to the 2008–2009 President’s Cancer Panel annual report, Reducing Environmental Cancer Risk: What We Can Do Now, 98% of the 80,000 chemicals on the market in the U.S. are “understudied and largely unregulated.” The report singled out BPA as particularly worrisome because of “the growing link between BPA and several diseases, including various cancers.” Although people lauded the report when it was first released, critics pounced on it, noting that many of the agencies responsible for studying and regulating the chemicals did not participate in the hearings.

Taking a more cautionary tack, an Institute of Medicine report in December 2011, Breast Cancer and the Environment: A Life Course Approach, noted that insufficient evidence exists to determine whether many chemicals—including BPA, pesticides, ingredients in cosmetics and dietary supplements, and other substances—alter the risk for breast cancer. (The report did conclude that women may lower their risk of breast cancer by avoiding exposure to benzene, 1,3-butadiene, and ethylene oxide.)

According to Eaton, who was a member of the IOM committee, one key attribute of animal testing is to identify hazard, a substance’s potential to cause a particular type of harm. So, when studying BPA or any other chemical in laboratory animals, researchers may look at health effects such as the development of a birth defect, cancer, or toxic effects on the liver.

“We just don’t know at this time whether the levels people are exposed to today are biologically significant or not.”

Eaton said although that approach addresses the question of hazard, researchers must use the dose response (the amount of the compound people are exposed to) to determine the risk. Doing so, he said, is often challenging, as is true with BPA. “We just don’t know at this time whether the levels people are exposed to today are biologically significant.”

A few public health organizations and political entities aren’t waiting and have reversed their former “wait-and-see” positions regarding BPA, particularly in products for children. In September 2010, Canada became the first country to ban BPA in baby bottles. In the European Union, all member countries had to remove baby bottles containing BPA from store shelves by June 1, 2011.

Although the U.S. Food and Drug Administration (FDA) ruled in 2008 that BPA is safe even for infants, in 2010 it said that “on the basis of results from recent studies using novel approaches to test for subtle effects, both the National Toxicology Program and FDA have some concern about the potential effects of BPA on the brain, behavior, and prostate gland in fetuses, infants, and young children.” Although the FDA’s National Center for Toxicological Research conducts studies to answer key questions and clarify uncertainties about the risks of BPA, the FDA is “taking reasonable steps to reduce human exposure to BPA in the food supply.” These steps include the following:

• Supporting the industry’s actions to stop producing BPA-containing baby bottles and infant feeding cups for the U.S. market
• Facilitating the development of alternatives to BPA for the linings of infant formula cans
• Supporting efforts to replace BPA or minimize BPA levels in other food can linings

Disputable Evidence

But some experts believe the government is generally overprotective about unproven environmental toxins. A series of recent columns in Forbes magazine questioned the results of BPA studies showing health risks, including Goodson’s. In a column appearing in the Nov. 14, 2011, issue, frequent contributor Trevor Butterworth wrote, “Overly simplistic studies advancing alarming hypotheses have been relentlessly reported, while the regulatory studies by agencies such as the CDC, FDA, EPA and their international equivalents that are designed to try and find out whether these simple studies are true or not, have been almost completely ignored.”

When a reader questioned their conclusions, asserting that 150 studies linked BPA to cancer and other diseases, Butterworth responded: “These 150 ‘governmental studies’ you allude to were disowned by the body that funded them—the National Institute of Environmental Health Sciences. Two years ago, it admitted that they were inadequate for risk assessment. Moreover, they do not show adverse health effects in humans.”
Suzanne Fenton, Ph.D., an epidemiologist at the National Toxicology Program Laboratory at the National Institute of Environmental Health Sciences in Chapel Hill, N.C., said this rebuttal is misleading, explaining that at a Board of Scientific Health meeting on BPA, board members decided that because results were based largely on animal studies, they could not make the connections between internal dose and different routes of exposure in humans. To fill in the gaps in these data, a new set of studies have been funded. Part of the problem, said Fenton, is that conducting clinical trials that expose humans to potentially hazardous materials is impossible, so science is limited to observational studies. “They want to corroborate existing data and be certain it has human relevancy. They certainly did not say the data were faulty.”

In another Forbes column on Sept. 21, 2011, titled “Breast Cancer Fund Study: Science or Class Warfare?” Butterworth wrote, “the Breast Cancer Fund has just published [a report] claiming that there’s BPA in canned food marketed for kids. Well, of course there is. The BPA is there to protect the seals in the cans from failing and allowing the food to become contaminated, you know, with things like...
botulism—the second most deadly naturally occurring toxin.”

Sandra Steingraber, Ph.D., Distinguished Scholar in Residence in the department of environmental studies and science at Ithaca College in Ithaca, N.Y., views that comment as a false dichotomy. “So, is that the only choice consumers have, tight cans or botulism? Surely those are not our only two choices. Steingraber, who also wrote Living Downstream: An Ecologist Looks at Cancer and the Environment, said the environmental sciences are always being accused of doom and gloom yet, “No one does gloom and doom more than industry.”

**Greener Solutions?**

Several corporations have already started using BPA alternatives, including stainless steel and glass containers. Although remaining mum on specifics, they are also looking at other materials as alternatives. Kabat said one concern companies have is that the alternatives might be harmful. “You always have to be sure about the safety of what you are substituting with versus the thing you’re indicting.”

According to a cover story in the June 6, 2011, Chemical and Engineering News, one idea has been to turn to chemicals that already have FDA approval for food-contact uses. These chemicals include isosorbide and isoidide, which are bicyclic sugars derived from sorbitol, and the compounds used as diuretics. Nitrated versions are also used to treat angina. So far, the article states, potential alternatives don’t yet match certain alternatives to BPA for qualities such as rigidity.

The onslaught of measures that agencies and companies are taking leads to the question, will BPA be banned? Since 1976, only five chemicals substances have been banned under the Toxic Substances Control Act. With enormous pressure from industry, much additional evidence would probably be required to ban BPA. Eaton said the issues surrounding BPA are far from resolved but that he is optimistic that research tools being developed using three-dimensional in vitro models of tissues will help predict how a human organ system might respond to chemicals. “These should make these evaluations easier in the future.”

Kabat, author of Hyping Health Risks, said politics poses another risk. Regardless of methods, he said, people who have no agenda must look critically at all the evidence. “That’s what science is all about. However, too often if one is critical of the data, one is tarred with being ‘pro-industry’ or ‘a denialist.’ It becomes more political than scientific.”

© Oxford University Press 2012. DOI: 10.1093/jnci/djs237