

Bisphenol-A (BPA)

WHAT IS BISPHENOL-A?

Bisphenol-A (BPA) is a high-volume production chemical used to make epoxy resin and polycarbonate plastic products, including some kinds of water bottles, baby bottles, and food storage and heating containers.¹ It is also used in the lining of metal food cans and in dental sealants, and is an additive to certain plastics used in children's toys.^{1,2} The chemical was first developed as a synthetic estrogen and was later polymerized to produce polycarbonate.^{3,4} Bisphenol-A mimics estrogen activity and is known as an "endocrine disruptor," a chemical that interferes with the hormonal system in animals and humans and contributes to adverse health effects.¹ New scientific evidence is emerging that demonstrates that exposure to bisphenol-A may affect multiple organs and systems within the bodies of animals and people.

HOW ARE WE EXPOSED TO BISPHENOL-A?

Humans are exposed to bisphenol-A on a daily basis through consumption of food and beverages contaminated with bisphenol-A, as well as environmental contamination. Polycarbonate plastic can become unstable over time and with use, allowing bisphenol-A to leach into material in contact with the plastic.⁴ Additionally, bisphenol-A is now found nearly everywhere in the environment and commonly found in dust particles, surface water and drinking water, as over 6 billion pounds are produced worldwide each year⁵ and the production of bisphenol-A releases

approximately 2 hundred thousand pounds of the chemical into the atmosphere annually.⁶

BISPHENOL-A IN OUR BODIES

A recent study by scientists from the U.S. Centers for Disease Control and Prevention found that 92.6% of Americans now carry bisphenol-A in their urine at an average level of 2.6 µg/L.⁷

Although the United States Environmental Protection Agency (EPA) considers exposure to 50 µg/kg/day of bisphenol-A safe, this standard was set in 1993 and is based on studies from the 1980s.⁸ In a review of scientific literature on BPA conducted in 2005, researchers found numerous studies indicate a wide range of health effects from exposure to bisphenol-A at much lower doses (as low as 2 parts per billion in some studies) than considered "safe" by the EPA.⁹ In August 2007, over 30 scientific experts on bisphenol-A, known as the Chapel Hill panel, published a consensus statement in the peer-reviewed journal *Reproductive Toxicology*, stating significant evidence indicates adverse health effects occur in animals at levels within the range of exposure that is typical for humans living in developed countries.¹⁰

In 2007, the Canadian Government began several studies of the effects of bisphenol-A on human health and the environment. They found that newborns and infants up to 18 months of age were exposed to levels of BPA similar to exposure levels that showed

effects in laboratory animals.¹¹

More recently, the US National Toxicology Program (NTP) Center for the Evaluation of Risks to Human Reproduction (CERHR) released the *NTP-CERHR Monograph on the Potential Human Reproductive and Developmental Effects of Bisphenol-A* which contributed significantly to the discussion of bisphenol-A's health effects. This report identified evidence from animal studies which raised "some concern" that current exposure levels to bisphenol-A to human infants, fetuses, and children may result in developmental changes to the prostate gland and brain.¹² Due to the panel's concern about the effects of bisphenol-A on children under six, the NTP has teamed up with the CDC to investigate further the effects on bisphenol-A on young children, infants, and neonates.¹³

WHAT DOES EXPOSURE TO BISPHENOL-A MEAN FOR OUR HEALTH?

While the majority of research on bisphenol-A has been conducted on animals and cell cultures, there is strong evidence that similar effects occur in humans. The Chapel Hill panel concluded in August 2007, "Based on existing data we are confident ... the similar effects observed in wildlife and laboratory animals exposed to bisphenol-A predict that similar effects are also occurring in humans." Moreover, research on estrogenic compounds all over the world is finding consistently that "animal studies of the effects of estrogenic substances are highly predictive of human impacts."¹⁴

Recent research has linked bisphenol-A to the following health effects:

Endocrine disruption:

As early as 1936, bisphenol-A was shown to be an environmental estrogen. Compared with natural estrogen, bisphenol-A is a less potent activator of the classic estrogen receptor, but in recent years it has been recognized that "BPA is equipotent with estradiol in its ability to activate responses

via recently discovered estrogen receptors associated with the cell membrane," as found in several studies on cell culture and laboratory animals. In addition to being shown to attach to estrogen receptors, evidence suggests that bisphenol-A also can change endogenous hormone synthesis, hormone metabolism and hormone concentrations in blood. Exposure to bisphenol-A has been shown to cause changes in tissue enzymes and hormone receptors as well as interacting with other hormone-response systems.



Recurrent miscarriage:

Researchers found that women with a history of recurrent miscarriage had average blood serum levels of bisphenol-A at 2.59 ng/ml, more than three times higher than women with successful pregnancies,¹⁵ a finding predicted by previous animal studies.¹⁶

Altered mammary gland development:

In a laboratory study, mammary gland development was significantly altered in mice exposed to 250 ng BPA/kg body weight/day of bisphenol-A,¹⁷ which is 2000 times lower than the EPA's safety standard for bisphenol-A (0.5 mg/kg/day). Scientists suggest that this study's implications for human health include increased susceptibility to breast cancer after perinatal exposure to bisphenol-A.

Low doses of bisphenol-A have also been shown to decrease the effectiveness of chemotherapeutic agents used for breast cancer.¹⁸

Prostate cancer:

Research using cell cultures showed that a concentration of bisphenol-A of 1 nM made

prostate cancer cells less responsive to the hormone treatment used to control prostatic adenocarcinomas into remission.¹⁹

Whether this cell culture impact also occurs in people is uncertain, but the concentration is lower than the average level of bisphenol-A found in Americans, as reported in 2008.⁷

Altered brain development and behavior: Scientists found that bisphenol-A exposure in the womb changes sexual differentiation of the brain and behavior in rats at only 30 µg/kg/day,²⁰ lower than the dose considered safe by the EPA.⁸ For some behaviors tested, results suggest that bisphenol-A exposure was linked to both demasculinization of males and defeminization of females.

At doses considered safe by the EPA, bisphenol-A blocked the synapse of estradiol in the hippocampus and prefrontal cortex of rodents and non-human primates.²¹ This signaling pathway may play a critical role in mood and cognition for humans.

Insulin resistance and cardiovascular diseases:

A recent study in adult mice provided evidence of a link between bisphenol-A exposure and increased risk of type II diabetes, hypertension and dyslipidemia.²² In this study, scientists found that chronic exposure to low doses of bisphenol-A leads to insulin resistance in adult mice. Doses used in their experiments were 5 times lower than the dose considered safe by the EPA.⁸

Based on population-wide exposure data from 2003-2004, scientists examined links between urinary bisphenol-A levels and chronic diseases in adults between the ages of 18 and 74.²³ They found high urinary levels of bisphenol-A are linked to cardiovascular diagnoses. Adults in this study who had high urinary levels of BPA were also more likely to have diabetes.

Developmental origins of adult health and disease:

The 2007 "Chapel Hill Bisphenol A Expert Panel Consensus Statement: Integration of Mechanisms, Effects in Animals and Potential to Impact Human Health at Current Levels of Exposure" states that enough evidence exists to suggest that adverse health outcomes may not become apparent until after exposure during critical developmental periods has happened. Especially of concern is that "these developmental effects are irreversible and can occur due to low-dose exposure during brief sensitive periods in development, even though no BPA may be detected when the damage or disease is expressed."

Disruption of hormone signaling pathways by BPA during critical periods of development also may lead to obesity.²⁴

REGULATIONS FOR BISPHENOL-A

Federal regulation of toxic chemicals is an important part of protecting public health. However, according to the Environmental Working Group, "The nation's system of regulations for industrial chemicals like [bisphenol-A] are embodied in the Toxic Substances Control Act, a law passed in 1976, and the only major environmental or public health statute that has never been updated."²⁵ Furthermore, "under this law, companies are not required to test chemicals for safety before they are sold, and are not required to track whether their products end up in people or the environment at unsafe levels." To date, the U.S. Food and Drug Administration has not performed a standard toxicology study or determined an Acceptable Daily Intake (ADI) for bisphenol-A.²⁶

Policies are currently being considered on a federal level that prohibit the sale of products that contain bisphenol-A.²⁷ On March 13, 2009, leaders from the House of Representatives and the Senate announced legislation which would ban the use of

bisphenol-A in all food and beverage containers.²⁸

Several states have also introduced legislation which would limit the sale of bisphenol-A, especially in children's products. In 2008, Maine enacted the Toxic Chemicals in Children's Products Act which

will phase out the use of chemicals, including BPA, that have been scientifically proven to cause cancer, reproductive toxicity, developmental toxicity, or endocrine disruption.²⁹ In March 2009, Canada became the first nation to restrict the use of bisphenol-A in children's products.³⁰

REDUCING YOUR EXPOSURE

You can prevent or minimize exposure to bisphenol-A in the following ways:

- Use glass, stainless steel, or polyethylene bottles (PETE, PET, or #1; HDPE or #2; LDPE or #4) instead of polycarbonate (PC or #7) bottles.²⁴
- Avoid using polycarbonate containers to store hot foods or to heat foods in microwaves, as bisphenol-A tends to leach faster with higher temperatures.²⁵ Use glass or ceramic containers instead.
- Cut back on consumption of canned foods to reduce exposure to bisphenol-A contamination from the interior coating of the container. Also, avoid canned foods with higher fat content, which may have higher levels of bisphenol-A.²⁵
- Before getting dental sealants, check with your dentist about the ingredients in the products they use, as some formulations may leach bisphenol-A.²⁵

¹ National Institute of Environmental Health Sciences (NIEHS). 2006. Endocrine Disruptors. Available: <http://www.niehs.nih.gov/oc/factsheets/pdf/endocrine.pdf> [Accessed 25 June 2007].

² Maffini MV, Rubin BS, Sonnenschein C, Soto AM. 2006. Endocrine disruptors and reproductive health: The case of bisphenol-A. *Molecular and Cellular Endocrinology* 254-255:179-186.

³ Colborn T, Dumanoski D, Myers JP. 1996. *Our Stolen Future: Are We Threatening Our Fertility, Intelligence, and Survival?—A Scientific Detective Story*. New York: Dutton.

⁴ Myers JP (Ed). *Our Stolen Future: Background on BPA: What is it, how is it used and what does science say about exposure risks*. Available: <http://www.ourstolenfuture.org/NewScience/oncompounds/bisphenola/bpauses.htm> [Accessed 9 July 2007].

⁵ Susiarjo M, Hassold TJ, Freeman E, Hunt PA. 2007. Bisphenol A exposure in utero disrupts early oogenesis in the mouse. *PLoS Genetics* 3(1):63-70.

⁶ Markey CM, Michaelson CL, Sonnenschein C, Soto AM. 2001. Alkylphenols and bisphenol A as environmental estrogens. In: Metzler M (Ed.), *The Handbook of Environmental Chemistry*. Part L, Endocrine Disruptors—Part I, vol. 3. Springer-Verlag, Berlin Heidelberg, pp. 129–153.

⁷ Calafat AM, Ye X, Wong LY, Reidy JA, Needham LL. 2008. Exposure of the US population to bisphenol A and 4-tertiary-octylphenol: 2003-2004. *Environmental Health Perspectives* 116(1): 39-44.

⁸ United States Environmental Protection Agency (EPA), Integrated Risk Information System. 1993. Bisphenol A. CASRN 80-05-7. Available: <http://www.epa.gov/iris/subst/0356.htm> [Accessed 2 July 2007].

⁹ vom Saal F, Hughes C. 2005. An extensive new literature concerning low-dose effects of bisphenol A shows the need for a new risk assessment. *Environmental Health Perspectives*, 113(8): 926-933.

¹⁰ vom Saal F, Akingbemi BT, Belcher SM, Birnbaum LS, Crain DA, Eriksen M, et al. 2007, Aug-Sep. Chapel Hill bisphenol A expert panel consensus statement: Integration of mechanisms, effects in animals and potential to impact human health at current levels of exposure. *Reproductive Toxicology* 24(2):131-8.

¹¹ Government of Canada. 2008. Bisphenol A research and monitoring activities. Available: www.chemicalsubstanceschimiques.gc.ca/challenge-defi/BPA_Research_fs_e.html (Accessed 5 March 2009).

¹² US National Toxicology Program (NTP) Center for the Evaluation of Risks to Human Reproduction (CERHR). 2008. *NTP-CERHR Monograph on the Potential Human Reproductive and Developmental Effects of Bisphenol A*. NIH Publication No. 08-5994. Research Triangle Park, NC: National Toxicology Program. Available: <http://cerhr.niehs.nih.gov/chemicals/bisphenol/bisphenol.pdf> [Accessed 18 March 2009].

¹³ Bucher JR. 2009. Bisphenol A: Where to now? *Environmental Health Perspectives* 117(3): A96-A97.

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- ¹⁴ Myers JP (Ed). Our Stolen Future: Scientists call for new risk assessment of bisphenol A and reveal industry biases in research. Available: <http://www.ourstolenfuture.org/NewScience/oncompounds/bisphenola/2005/2005-0413vomsaalandhughes.htm> [Accessed 10 September 2007].
- ¹⁵ Sugiura-Ogasawara M, Ozaki Y, Sonta S, Makino T, Suzumori K. 2005. Exposure to bisphenol A is associated with recurrent miscarriage. *Human Reproduction* 20:2325-2329.
- ¹⁶ Hunt PA, Koehler KE, Susiarjo M, Hodges CA, Ilagan A, Voigt RC, et al. 2003. Bisphenol A exposure causes meiotic aneuploidy in the female mouse. *Current Biology* 13:546-553.
- ¹⁷ Muñoz-de-Toro M, Markey C, Wadia PR, Luque EH, Rubin BS, Sonnenschein C, Soto AM. 2005. Perinatal exposure to bisphenol A alters peripubertal mammary gland development in mice. *Endocrinology* 146:4138-4147.
- ¹⁸ Lapensee EW, Tuttle TR, Fox SR, Ben-Jonathan N. 2009. Bisphenol-A at low nanomolar doses confers chemoresistance in estrogen receptor-alpha-positive and negative breast cancer cells. *Environmental Health Perspectives* 117(2): 175-180.
- ¹⁹ Wetherill YB, Petre CE, Monk KR, Puga A, Knudsen KE. 2002. The xenoestrogen bisphenol A induces inappropriate androgen receptor activation and mitogenesis in prostatic adenocarcinoma cells. *Molecular Cancer Therapeutics* 1(7):515-24.
- ²⁰ Kubo K, Arai O, Omura M, Wantanabe R, Ogata R, Aou S. 2003. Low dose effects of bisphenol A on sexual differentiation of the brain and behavior in rats. *Neuroscience Research* 45:345-356.
- ²¹ Leranath C, Hajszan T, Szigeti-Buck K, Bober J, MacLusky NJ. 2008. Bisphenol A prevents the synaptogenic response to estradiol in hippocampus and prefrontal cortex of ovariectomized nonhuman primates. *Proceedings of the National Academy of Sciences of the United States of America* 105(37): 14187-14191.
- ²² Alonso-Magdalena P, Morimoto S, Ripoll S, Fuentes E, Nadal A. 2006. The estrogenic effect of bisphenol-A disrupts the pancreatic β -cell function in vivo and induces insulin resistance. *Environmental Health Perspectives* 114:106-112.
- ²³ Lang IA, Galloway TS, Scarlett A, Henley WE, Depledge M, Wallace RB, et al. 2008. Association of urinary bisphenol A concentration with medical disorders and laboratory abnormalities in adults. *Journal of the American Medical Association* 300(11): 1303-1310.
- ²⁴ Grun F, Blumberg B. 2007. Perturbed nuclear receptor signaling by environmental obesogens as emerging factors in the obesity crisis. *Reviews in endocrine and metabolic disorders* 8(2): 161-171.
- ²⁵ Sutton R, Jackson J, Walker B, Tupper G, Horenstein B (eds.). 2007, July 12. Down the Drain: Sources of Hormone-Disrupting Chemicals in San Francisco Bay. Oakland, CA: Environmental Working Group. Available: <http://www.ewg.org/reports/downthedrain> [Accessed 10 September 2007].
- ²⁶ U.S. Food and Drug Administration. 2007. Cumulative Estimated Daily Intake/Acceptable Daily Intake Database. Available: <http://www.cfsan.fda.gov/~dms/opa-edi.html> [Accessed 10 September 2007].
- ²⁷ Lowell Center for Sustainable Production. 2009. US State level chemicals policy. Available: <http://www.chemicalspolicy.org/usstatelevel.shtml> [Accessed 18 March 2009].
- ²⁸ Kissinger M. 2009. US lawmakers move to ban BPA from food, beverage containers. *Milwaukee Journal Sentinel*. Available: www.jsonline.com/watchdog/watchdogreports/41215752.html [Accessed 24 March 2009].
- ²⁹ Maine Revised Statutes. 2008. Title 38, Chapter 16-D: Sections 1691-1699-B. Available: <http://www.mainelegislature.org/legis/statutes/38/title38ch16-Dsec0.html> [Accessed 18 March 2009].
- ³⁰ Health Canada. 2008. Government of Canada protects families with bisphenol A regulations. Available: www.hc-sc.gc.ca/ahc-asc/media/nr-cp/_2008/2008_167-eng.php [Accessed 5 March 2009].