Health Risks from Bisphenol-A in Polycarbonate Containers and Consumer Products

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Abstract

The use of toxins such as Bisphenol-A in the manufacturing of polycarbonate drinking bottles and the possibility of these and other toxins being ingested by humans has been in the news for the last few years. The possibilities of these chemicals migrating into drinking water and hot liquids will be investigated. The manufacturing processes of polycarbonate and polybutylene containers and the reasons for Bisphenol-A and other compounds being added will also be studied. The morphological behavior on humans and the health effects will be studied along with certain kinds of cancer risks. The final recommendations from both the author and the regulating agencies from both then and now will be determined.

There has been much discussion in the news and community in the last few years about the health risks of released manufacturing toxins in consumer products. This subject is especially true when talking about plastic drinking bottles. If there is any danger to the public from these toxins, then the causes and the ways to remedy these concerns should be explored and implemented.

In August 2006, CBS news releases an article "Study links plastics chemical with cancer". In this article they start with:

> **"In a growing debate, researchers have suggested a chemical additive used to make hard plastics — including toys, baby bottles and food storage containers — might promote breast cancer"**

This article cites a study done by Professor Theodore Widlanski of Indiana University that will be discussed later in this paper. (CBS News, 2006)

In February of 2008, an article in Science Daily "Plastic Bottles Release Potentially Harmful Chemicals (Bisphenol A) After Contact with Hot Liquids" was published. This article cites Dr. Scott Belcher of the

University of Cincinnati who has determined with his team of students that polycarbonate drinking bottles release the chemical Bisphenol-A fifty five times more rapidly with exposure to boiling water than before this exposure. According to the article, he also states ""Previous studies have shown that if you repeatedly scrub, dish-wash and boil polycarbonate baby bottles, they release BPA. That tells us that BPA can migrate from various polycarbonate plastics". Explaining further, he explains "There is a large body of scientific evidence demonstrating the harmful effects of very small amounts of BPA in laboratory and animal studies, but little clinical evidence related to humans ...There is a very strong suspicion in the scientific community, however, that this chemical has harmful effects on humans."(Science Daily, 2008)

The University of Cincinnati study also seemed to conclude that age of the bottle didn't have much effect on the amount of BPA released; well aged bottles of up to nine years seemed to produce roughly the same levels of the chemical as new bottles. (Science Daily, 2008).

As time went on, more and more stories were published, leading to a widespread belief that all plastic bottles were releasing toxins even the conventional PET bottles which 90% of all drinking water is bottled in, which isn't even related to the BPA controversy. Statements like ""We have only demonstrated a possible mechanism that explains what people have been speculating about for years," Widlanski said."It doesn't mean that your bottled water is any less safe today than it was yesterday. It just means that if it isn't safe, we might be able to explain why." (CBS News, 2006) gave the impression that standard bottled water was unsafe.

While Health Canada, the FDA and all the plastics associations and councils maintained that exposure to BPA posed no threat to consumers, more studies started to be performed and the beginning of the mountainous amount of information on the subject began to be amassed.

In response to these reports in the media, numerous state agencies started to take action against plastics that are manufactured with the chemical Bisphenol-A. In June of 2006, the San Francisco city council approved an ordinance that bans any toys or products manufactured with Bisphenol-A for use with children under three based on studies at the time. This ban takes effect on December 1, 2006 and prevents the sale, manufacture and distribution of these products.

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In April of 2008, the State of Connecticut put forth House Bill 5601: BANNING CHILDREN'S PRODUCTS CONTAINING LEAD, PHTHALATES OR BISPHENOL-A. According to an April 7th 2008, OLR Research Report proponents of the bill stated that their reasons for the ban were the issues of low pediatric IQ's, cancers, early puberty, and childhood obesity. Opponents of the bill expressed concern that these products have been in use for fifty years without any conclusive studies documenting any toxic effects. In an inquiry, Dr, Julie Goodman, a Gradient Corporation toxicologist stated that, in low doses, the chemical Bisphenol-A isn't harmful to humans. She brought up the fact that the European Union had set a safe limit on the chemical and raised it later upon further studies. She also testified that she was not aware of any synergistic studies on the suspected toxin and knew of no conclusive studies on the effects on fetal brain development, infant IQ's and behavior. She referenced a 1990 study that suggested that there might be a link between prostate weight and the chemical Bisphenol-A as the cause for the increased consumer awareness to this potential toxin (Reilly, 2008)

Consumer Product Advertising the Absence of BPA

In 2009, the Connecticut Legislature put forth House Bill 6572 which will phase out BPA from baby bottles and reusable food containers. It will also phase out the use of BPA as an epoxy resin liner of food cans and will prohibit any other toxic chemicals from taking its place. This bill was signed by Governor Jodi Rell in June of 2009. In a Coalition for a Safe and Healthy Connecticut fact sheet supporting the bill, it was listed that BPA has been found in 180 studies to be linked to many modern diseases (VomSall, 2005) and it is present in 95% of all Americans (Calafat, AM., et al. 2005)

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So what is Bisphenol A and how is it used in manufacturing plastic? Bisphenol A is a chemical compound that is composed of two phenol groups [C_6H_5OH] hence the prefix Bi and two methyl groups [CH_3] linked with a carbon atom ... $(CH_3)_2C(C_6H_4OH)_2$. It is produced with acetone and two equivalent phenols in a condensation reaction with an acid catalyst. The end product is Bisphenol A and water. The A suffix is because of the acetone involved. The chemical structure can be seen in Figure 1 below.

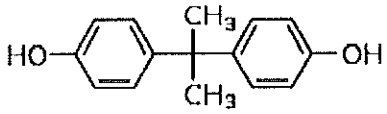

Figure 1: Bisphenol-A Chemical Structure

This process has been used for over 50 years now and its primary uses are in manufacturing polycarbonate plastics, polybutylene terephthalate, and epoxy resins. These polycarbonates use Bisphenol-A as their prime monomer and are linked with three oxygens and a carbon in a condensation reaction to form the repeating polymer. The chemical polymer structure of polycarbonate is shown in Figure 2 on the next page. The properties of this class of polymers and the properties of the individual monomer are the same as this is the only type of polycarbonate that has reached commercial success. You can see that the monomer's central portion is essentially the same as the polymer's central portion in Figure 2. The OH (hydroxyl) groups are changed with an initial reaction of the BPA and Sodium Hydroxide which deprotonates these and forms a chloroformate which then reacts with additional deprotonated BPA groups to form a carbonate linkage. This process repeats itself to form the long chains of polycarbonate.

Polycarbonate plastics have the properties of very high impact strength which is the reason many polycarbonate bottles and products are called "shatterproof". This mechanical property is due to the fact that this plastic has very large aromatic groups that are complex and tend to tangle the polymer chains together. Polycarbonate is also amorphous due to this property which gives it very good optical clarity. Its toughness can outdo some of the very crystalline nylon and acetals and it is nearly as strong. Some items that are made from polycarbonate are re-usable plastic drinking bottles, baby bottles, tool housings, safety helmets, hair dryers, electronics, and many, many more. It is also used in tough

optical applications such as eyeglass lenses, CD's, and the tough clear material sheet Lexan© made by General Electric.

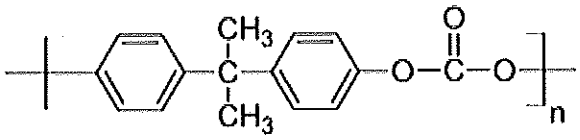

Figure 2: Polycarbonate Chemical Structure

Bisphenol-A is also used to make epoxy resins which line most every beverage and food can. This epoxy resin is produced from a reaction between Bisphenol-A and epichlorohydrin. The epoxides in the epichlorohydrin react with the amines in the BPA to form the heavily cross-linked material. The resulting material is called Bisphenol A diglycidyl ether or BADGE, and forms the hardened epoxy when a hardener that is comprised of polyamine monomers is mixed with it. A similar concern to the polycarbonate bottle BPA exposure has been expressed by many due to the possibility that some un-reacted BADGE may be present in these food containers exposing the consumer to BPA. In Japan, PET film has replaced epoxy coatings in most food linings because of the fears of BPA contamination.

The amount of BPA produced worldwide in 2003 has been estimated to around 2.3 million tons and the amount that is produced in the USA is roughly 800,000 tons or 1.6 billion pounds and from this about 72% is made into polycarbonate plastics and about 21% is used for the production of epoxy resins. Only about 5% of this production has any food contacting applications, though. This figure has grown since 2003 and is now around 5.75 million tons or 11.5 billion pounds of this chemical as of 2008 (Dow, 2010)

The main reason that this chemical is considered to be a potential health risk is that Bisphenol-A is classified, along with a number of other chemicals as an "endocrine disrupter" which is a compound that mimics one of the body's natural hormones and causes disruptions to the endocrine system. In the case of BPA, it is shown to mimic the estrogen hormones, estradiol and estrone. Since estrogen and estradiol have receptors, this BPA can be received by these receptors and then go on to reduce the synaptic response to the hormone estradiol therefore causing havoc with the body's ability to regulate its own hormone levels. While there are numerous studies that link the chemical to brain development and

reproduction in animals, there is little known about the effect on humans although the evidence is growing.

Some of the studies done on animals are as follows. A study was done on pregnant mice in that BPA was given to them in small doses and it altered sexual and fetal development. (Howdeshell. et al., 1999). Another study showed that BPA caused meiotic aneuploidy in these mice. Since this is one of the same symptoms that humans have for 40-70% of spontaneous abortions (Hunt et al., 2003), some OB GYN doctors began to suspect this relationship in humans. Many other studies followed such as "Bisphenol A prevents the synaptogenic response to estradiol in hippocampus and prefrontal cortex of ovariectomized nonhuman primates". This study notes that BPA in even small amounts "completely abolishes the synaptogenic response to estradiol. Because remodeling of spine synapses may play a critical role in cognition and mood, the ability of BPA to interfere with spine synapse formation has profound implications" This study also revealed that other hormone receptors such as the ones involving the thyroid and androgen groups can be affected (Leranth, Hajszan, eds. 2006). The list for animal testing continued with such findings until BPA began to draw some attention.

The chemical BPA has been definitely found to be present in measureable amounts in humans, though. The previous animal studies noted that the durability of polycarbonate isn't quite what people believed it was. Since polycarbonate's esther bonds are subject to losing its bonds through hydrolysis, everyday use of these materials is believed to release some BPA (Leranth, Hajszan, eds. 2006). In tests conducted in 2008, the first real study done on a large scale with 1500 people being tested for levels of BPA through urine analysis. The test showed that there was a significant connection between the levels of BPA and certain liver enzymes, heart disease and diabetes and was published by Iain Lang et al. in the September 2008 issue of the Journal of the American Medical Association.

A study done by Mayumi Sugiura-Ogasawara et al. in the Department of Obstetrics and Gynecology at Nagoya City University Medical School in Nagoya Japan showed one of the first links to recurrent miscarriage and immunoendocrine immunities. While his team just got done with doing studies on polychlorobiphenyls (PCBs), DDT and hexachlorobenzene and didn't find any association with recurrent miscarriage, they might have found something with BPA. They studied the relationship between immunological and endocrine abnormalities and serum levels of BPA present in patients who have had recurrent miscarriage problems. They did a study on 45 patients who had three or more consecutive first-trimester miscarriages in their medical history. They found that there were elevated levels of BPA

in a statistically significant amount of the subject who had multiple recurrent miscarriages. This was using a p-value of 0.05 as the level of confidence in their results. (Sugiura-Ogasawara, et al. 2005)

The study that probably got the most attention in the news, though, is the study done by Dr. Theodore Widlanski. In a Chemistry and Biology journal entry "A Role for Sulfation-Desulfation in the Uptake of Bisphenol A into Breast Tumor Cells", Dr Widlanski mentions the previously reported study on recurrent miscarriage and also addresses the fact that when the body first accepts the xenobiotic BPA, it is sought out by relatively promiscuous phenol-sulfotransferasing enzymes which are enzymes that are attracted to phenol compounds with the job of sulfating these compounds. The act of sulfating BPA helps its ability to circulate and makes it more water soluble. This sulfation makes the BPA bind poorly to the estrogen receptor cells but it seems to stimulate the growth of breast tumor cells that are receptor positive. (Widlanski et al. 2006)

In newer news, Dr Scott Belcher from the University of Indiana is continuing the research on BPA. In a news release from the University of Indiana in 2009 titled "BPA May Cause Heart Disease in Women, Research Shows", he states. "There is broad exposure to Bisphenol A, despite recognition that BPA can have harmful effects,"... "We had reason to believe that harmful cardiovascular affects can be added to the list". Dr Belcher and his team of scientists have found a correlation between the xenoestrogen BPA and abnormal heart activity in rats and mice. They found that this only occurs in females and the symptoms are irregular heart beat and abnormal arrhythmic behavior. This is due to the female's estrogen type receptor cells in the cardiac system. The effects of BPA are to increase the amount of free calcium inside the female only heart cells in the sarcoplastic reticulum which causes calcium spikes which affect the rhythm of the heartbeat. These effects are also seen with the natural estrogen hormones but since BPA is not natural it has the same effect. (University of Indiana, 2009)

There has been some controversy surrounding the disclosure of a lot of these scientific studies and articles. The American Plastics Association has been a key proponent of BPA manufactured polycarbonates. Since the manufacturing of polycarbonates is such a huge global business, it would only be natural that they would have an interest in not being critical of this material. According to the website of the SPI which is the plastics industry trade association "Polycarbonate plastics, including polycarbonate baby bottles and kitchen storage containers, are safe and convenient for the preparation and storage of all types of foods and beverages". They also state:

- "A raw material used in polycarbonate plastics, bisphenol A (BPA), has been the subject of recent news reports questioning its safety. The fact is that BPA has been extensively studied for decades. Based on numerous safety tests, the U.S. FDA permits the use of BPA in polycarbonate packaging for all types of food."
- One 1997 FDA study focused on BPA used to make polycarbonate baby bottles. The study concluded that, in conditions representing typical consumer use, there was no migration at all of BPA from the bottle into its contents. Another study conducted in 1997 by the U.K. Ministry of Agriculture, Fisheries and Food "conclusively demonstrated that there is no leaching of bisphenol A from polycarbonate baby bottles during use." (Safety, 2010)

This seems to be in contrast to the extreme amount of negative material that I can find on the subject of BPA when researching this paper. Most of this material has been done in the last three years, whereas most of the studies cited by the chemical companies tend to be older than five years and in some cases older than ten years. Very little scientific material is available other than the studies done by the plastics industry that shows no effects from BPA. They also reference a website, www.bisphenol-a.org which, of course, as it's referenced by them, paints a very rosy picture of this polycarbonate monomer. The first statement tells how this site is a comprehensive resource for everything involved with BPA; possibly a comprehensive resource for everything ***positive*** about this chemical. The first listing in the "What's New" section is an article that concludes no effect from BPA on the nervous system, and then there is a list of other positive approaches to the chemical. (www.bisphenol-a .org, May 2010)

There have been a few challenges to the plastics industry's stand on BPA. In a scathing review of the Plastics industry, Chemical and Industry Journal wrote an article "Low Dose BPA: Confirmed by Extensive Literature". This journal article starts out with "The Association of Plastics Manufacturers (APM) attempt to discredit scientific findings that threaten corporate products by invoking the concept of 'sound science' has failed in the past". It then goes on to compare this tactic to ones used by the tobacco companies to discredit scientific studies on second hand smoke which have turned out to be correct. The paper also describes how the APM's corporate sponsored research which finds that low dose BPA has no ill effects is largely overwhelmed by independent research that shows a uniform positive trend of effects from low dose BPA. It also mentions the studies by Howdeshell and others that say that in 94 studies, feeding mice doses of BPA at 2.4 µg/kg, causes effects to fetal development. This dose is 20 times lower than the accepted 50 µg/kg dose for humans. (Howdeshell et al., 1999). It also presents the fact that in 94 of 104 studies done by the government, low doses of BPA showed positive

for some sort of effect from the BPA (Chemistry, 2005). These criticisms of the plastics industry can be found in numerous journals and articles spread out through the last five years.

The Environmental Protection Agency (EPA), in its Environmental Risk Information System sheet, lists this chemical as "This substance/agent has not undergone a complete evaluation and determination under US EPA's IRIS program for evidence of human carcinogenic potential." but announced in September of 2009 that it will start to evaluate the chemical for action plan development.

What is the official stance of the FDA? In January 2010, the latest stance of the FDA is that standardized toxicity tests support the low levels of human exposure as safe. They write:

"Studies employing standardized toxicity tests have thus far supported the safety of current low levels of human exposure to BPA. However, on the basis of results from recent studies using novel approaches to test for subtle effects, both the National Toxicology Program at the National Institutes of Health and FDA have some concern about the potential effects of BPA on the brain, behavior, and prostate gland in fetuses, infants, and young children. In cooperation with the National Toxicology Program, FDA's National Center for Toxicological Research is carrying out in-depth studies to answer key questions and clarify uncertainties about the risks of BPA". (Bisphenol A, 2010)

The FDA does recognize that non-standard toxicity tests could have some merit and have released some guidelines for what they are going to do in the future.

- They state that they are taking steps to reduce the exposure of BPA to humans in the food supply.
- They will support the industry in trying to stop the production of polycarbonate baby bottles and infant cups.
- They will support the development of alternative linings for food cans, especially infant food cans.
- They will start to begin to develop a more robust framework for the regulation and oversight of BPA.

These new policies are posted on the FDA website (www.fda.gov, 2010).

If it's true that there is absolutely no risk from BPA as the plastics industry has claimed then it seems that there would be no need to make this list of recommendations from the FDA as shown on the website.

In conclusion, there was much work done researching this chemical in great detail for this paper. From the numerous journals on animal testing, human testing, medical association journals, government regulating agencies and the plastics industry, one can clearly see that just by the sheer volume of information being published that there is some merit to the claims that some concerns can be put forth over exposure to Bisphenol A.

It seems that the general consensus is that some problems can be seen in low doses of this chemical although this seems to be more of a concern in animal testing. One cannot really conclude that the low doses are a problem in humans, but it is suggested they might. Some have said that low doses are actually worse than higher doses when it comes to affecting fetal neural signaling (Zsarnovszky A. et al., 2005). Only the future will tell as human trials have to be done only by data due to exposure and not data obtained by administering the doses directly. It seems that the chemical is definitely much more of a problem and danger to pregnant women and women in general due to its xenobiological property of mimicking the female hormone estrogen. It does seem to be harmful to men also, but to a lesser degree. It also does seem to be a chemical that is absorbed, metabolized and purged from the body fairly quickly, but if absorbed on a regular basis as it's suggested it is by most, can stay in the body at a fairly regular level. I would assume the exposure to be widespread due to the amount of products that is used in and the morphological properties of polycarbonate, itself.

The regulating industries such as the FDA and the HHS seem to be cautious about reporting any harmful effects due to the huge industries it supports but seem to be in a general consensus that is not perfectly safe and could have some far reaching effects on pregnant women and infants, if not more. I suspect more such warnings and/or regulation will be forthcoming in the near future.

Based on all of the information, my recommendations would be to limit the use of BPA for food contact use, such as polycarbonate drinking bottles and baby bottles. I would also strongly warn that all pregnant women strongly avoid any type of polycarbonate bottle or utensils and would make all baby toys out of HDPE or some other chemical that doesn't contain BPA. In the end it's just going to take more time to completely understand the total effect BPA has on society.

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