Fact Sheet on Bisphenol A

Cancer Association of South Africa (CANSA)

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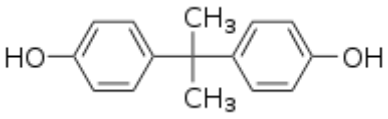
What is Bisphenol A? [1,2,3,4,5]

- Bisphenol A (abbreviated BPA) is a high-production volume, artificial, industrial, man-made molecule that was first synthesised in 1891 by AP Dianin.[1] It is an ever-present environmental contaminant with established endocrine disruptor properties. [10]

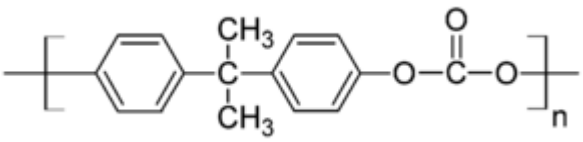
- It is a relatively small symmetric, organic compound (see below) with a molecular weight of 228. It is a white powder and surprisingly has been found to mimic the female hormone, oestrogen, by binding to the oestrogen receptor. It is one of the best examples of a so-called endocrine-disrupting compound (EDC) because it binds to oestrogen-receptors in the cell in a haphazard, uncoordinated way - disrupting the highly ordered working of the normal hormone, oestrogen, especially during pregnancy, and causing various health defects, i.e. it is a pseudo-oestrogen. [1,6]

- BPA was investigated in the 1930's as a possible synthetic oestrogen to be used for miscarriages. However, it was not developed further because another synthesized compound, diethylstilbestrol (DES), was found in 1940, which turned out to be a much more powerful oestrogen substitute in humans than BPA. Contrary to expectations DES was later taken off the market in 1970 when it was found to be linked to vaginal adenocarcinoma (cancer) and foetal malformations in daughters of 7 million mothers who used the drug while pregnant. This was a pharmaceutical disaster and in retrospect was an early warning signal for similar toxic properties confirmed for BPA 30 – 40 years later.[7]

- In 1953 Daniel Fox and Hermann Schnell synthesized polycarbonate for the first time using BPA and phosgen[8]. Bisphenol A is mainly used as a bifunctional monomer in the manufacture of polycarbonate plastic and epoxy resins and as an antioxidant in PVC.



BPA as a single molecule



BPA as part of a polycarbonate polymer[9]

WHY IS BPA A MATTER OF CONCERN?

- Exposure to BPA has been linked to increased breast cancer risk, early puberty, obesity, infertility in males and females, brain dysfunction, thyroid dysfunction, heart disease, diabetes and prostate cancer[9-19]

- Evidence has been found that BPA acts epigenetically, at low concentrations, to permanently silence critical genes during development in the womb with as yet unknown consequences[12,13]

- Substantial evidence indicates that exposure to BPA during early development may increase breast cancer risk. This is supported by studies showing that BPA activates genes involved in growth in mammary cells [12,14]

- Children may be particularly vulnerable to BPA[2]

- BPA was detected in the urine of 92% of the U.S. population in 2003-2004 and it is most likely to be in an average South African's urine as well[20]

- BPA is not essential and provides no known benefit to human health and appears to be harmful to human health

- In 2007 Prof Fred vom Saal of the University of Missouri-Columbia (World expert on BPA) found that very low level exposure of BPA (1 nM) harms the prostate[22]

- Between 1997 and 2008, over 100 publications linked very low level exposure of BPA with prostate damage, breast and prostate cells predisposed to cancer, decline in testosterone, changes in breast tissue that predispose cells to hormones and carcinogens, early puberty, behavioural problems and other effects[22,26]

- These effects have been found at BPA concentrations up to 25 times lower than the U.S. Environmental Protection Agency's (EPA) "safe" dose of 50 micrograms per kilogram (body weight) per day[22,23]

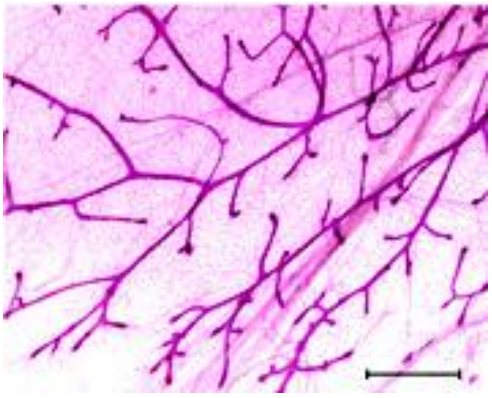
- 38 Independent BPA scientists (Chapel Hill Panel) completed an assessment of BPA safety in 2007 and concluded that BPA exposure at current levels presents a clear risk to human health[24]

- In a New York Times editorial (May 20th 2008), a ban on BPA in the U.S. is called for in terms of items such as baby bottles and cups[25]

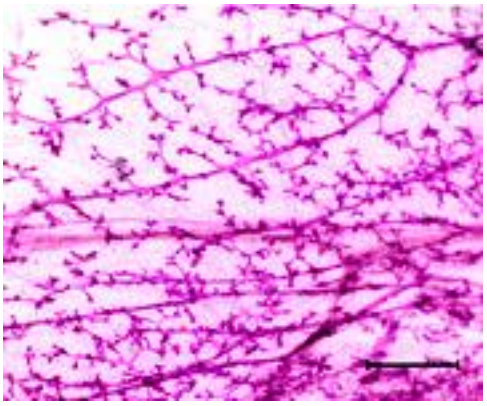
- BPA induces a profile of tumour aggressiveness in high-risk cells from breast cancer patients[12]

- Prenatal exposure to BPA induces early cancerous changes in the breast tissue of rats[10-14]

Effects of Low Dose BPA on Breast Tissue[3]



Control milk ducts in mouse breast tissue



Mice treated with 25 ng BPA/kg body weight per day.
Milk duct growth dramatically stimulated

How has the World Reacted?

- **Canada**. On April 18, 2008, the Canadian Government **moved to ban polycarbonate infant bottles** as it officially declared one of it's ingredients (bisphenol A) toxic[21]

- **Denmark**. From the 1st July 2010 all food contact materials for young children (ages 0-3 yrs), including baby bottles made of polycarbonate, will be banned in Denmark. This was due to concerns of food safety experts that BPA could inhibit learning capacity of children[41]

- **Belgium**. March 2010. Legislation to ban BPA in food contact plastics proposed

- **New York**. August 3, 2010. Sales of baby bottles, sippy cups, pacifiers and straws that contain plastic made from Bisphenol A will be banned in the state under law. Also banned in Minnesota, Chicago and Connecticut

- **United States**: April 2010. Annual report of President Obama's President's Cancer Panel states "..the available evidence argues for a precautionary approach to BPA". March 2010. The Environmental Protection Agency (EPA) declared BPA a chemical of concern". The FDA promises to respond by end November 2010 and so does European Food safety Authority (EFSA)

- **France**: 10 August 2010. 9 Senators call for BPA ban in food containers such as baby bottles[40]

- **China**: July 2011. China banned companies from manufactxuring, importing or selling baby bottles that contain Bisphenol A (BPA), a potentially dangerous chemical routinely added to everyday plastic products[43]

Reaction of the American Medical Association (AMA)

The American Medical Association (AMA) supports tighter restrictions on products containing BPA[44]

Where is Bisphenol A Found?

- Hard, clear, near shatterproof plastic – polycarbonate.
- Epoxy resin coating in metal food cans[30, 35]
- Plastic bottles and cups for babies. Heating these bottles releases up to 55-times more BPA[28,29]
- Precursor of flame-retardant – tetrabromobisphenol A
- Bicycle helmets
- Car safety seats
- Water coolers
- Medical devices
- CD's, credit cards, cell phones, computers, cars
- Sports equipment
- Household electronics
- Some drinking water[30, 33, 35,]
- Global production in 2003 was 2.2 million metric tones in 1999 (This is 2 200 000 000 kg or 328 grams for every man, women and child on earth per year!)[1]
- Recently BPA has been reported on cash receipts printed with the heat process such as those dispensed by ATM's. In some cases receipts contained 250 to 1000 times more BPA than is found in baby bottles[38]
- There is ever-present human exposure to BPA which is a pollutant across the whole planet only dropping to low levels over the poles[42,36]

BPA on receipts

What Source of BPA Poses the Greatest Threat?

- Exposure to boiling water increased the rate of BPA migration by up to 55-fold from polycarbonate drinking bottles, as especially those used by babies[28,29]

- BPA found in the liquid contents of various tinned food products[30,35]
- BPA rubbing of certain receipts
- Small amounts in the air, water and soil across the planet

How Can the Potential Cancer Risk of Bisphenol A be reduced?
CANSA advocates:

- Banning the production of BPA-containing products from which BPA can migrate into food and drink in concentrations known to cause adverse biological effects especially in children – 0-3 years old
- The developing of BPA-free alternatives for baby drinking bottles, the lining of tin cans and outdoor water bottles
- Finding an alternative for receipt paper containing BPA
- Ensuring that drinking water is BPA free
- The investigation of multiple uses of BPA and ascertaining which uses may pose a health threat to man
- Lobbying the government to protect citizens from untoward exposure to BPA
- Not putting polycarbonate plastic food containers in the microwave
- Avoiding plastic utensils with a number 7 in a triangle and the letters PC underneath the triangle. This indicates polycarbonate

Recent Publications Linking BPA to Breast Cancer
All of these publications are free on the internet, i.e. pubmed.

1. In utero exposure to diethylstilbestrol (DES) or Bisphenol-A (BPA) increases EZH2 expression in mammary gland: an epigenetic mechanism linking endocrine disruptors to breast cancer (Free on Pubmed). Taylor H et al., Hormone Research, 2010, 1, 146-155.

   Message:

   Mammary glands of mice exposed to BPA in utero at a concentration found in humans increased the expression of an enzyme known as EZH2. Similar exposures to BPA also increase the methylation of histone H3. These changes lead to epigenetic regulation and could be a precursor of breast cancer later.

2. Activation of the mTOR pathway by low levels of xenoestrogens in breast epithelial cells from high risk women. Dairkee et al., Carcinogenesis, Advance access published September 22, 2011.

3. Message:
Human high risk donor breast epithelial cells were exposed to BPA at concentrations that are detectable in human blood, placenta and milk. It was found that BPA stimulated the production of the mTOR proteins which help cells to survive. Such stimulation is also found in cells becoming cancerous.

Horm Mol Biol Clin Investig. 2011 Mar 1;5(2):45-52.

Exposure to the Endocrine Disruptor Bisphenol A Alters Susceptibility for Mammary Cancer.

Lamartiniere CA, Jenkins S, Betancourt AM, Wang J, Russo J.
Department of Pharmacology and Toxicology, University of Alabama at Birmingham, Birmingham, Alabama.

Abstract
Bisphenol A (BPA) is a synthetically made chemical used in the production of polycarbonate plastics and epoxy resins. Recent studies have shown over ninety percent of humans investigated have detectable BPA concentrations. Yet, the biggest concern for BPA is exposure during early development because BPA has been shown to bind to the estrogen receptors (ER) and cause developmental and reproductive toxicity. We have investigated the potential of perinatal BPA to alter susceptibility for chemically-induced mammary cancer in rats. We demonstrate that prepubertal exposure to low concentrations of orally administered BPA given to lactating dams resulted in a significantly decreased tumor latency and increased tumor multiplicity in the dimethylbenz[a]anthracene (DMBA) model of rodent mammary carcinogenesis. Our data suggested that the mechanism of action behind this carcinogenic response was mediated through increased cell proliferation, decreased apoptosis, and centered on an up-regulation of steroid receptor coactivators (SRCs) 1-3, erbB3, and increased Akt signaling in the mammary gland.Also, we demonstrate that prenatal exposure to BPA shifts the time of susceptibility from 50 days to 100 days for chemically-induced mammary carcinogenesis. Proteomic data suggest that prenatal BPA exposure alters the expression of several proteins involved in regulating protein metabolism, signal transduction, developmental processes, and cell cycle and proliferation. Increases in ER-alpha, SRCs 1-3, Bcl-2, epidermal growth factor-receptor (EGFR), phospho-IGF-1R, phospho-c-Raf, phospho-ERKs 1/2, phospho-ErbB2 and phospho-Akt are accompanied by increase in cell proliferation. We conclude that exposure to low concentrations of BPA during the prenatal and early postnatal periods of life can predispose for chemically-induced mammary cancer

Lack of Consensus

- There is no consensus in the world about the potential dangers of low dose BPA. The American Chemistry Council believes that BPA is a good product and safe.[37] The FDA has expressed ‘some concern’ but advocates no changes in the status quo at present. **Nevertheless, the public and the baby bottle industry are turning away from BPA in order to be safe, rather than sorry**

Selected Quotations

"We know a women's lifetime risk of breast cancer is directly linked to her lifetime exposure to estrogen – both natural and synthetic estrogen. It's outrageous that manufacturers of some baby bottles are exposing little girls to BPA, a synthetic plasticizer that mimics estrogen, and possibly increasing that little girl's risk of breast cancer later in life, especially when safe alternatives are available."

Janet Nudelman - Director, Program and Policy for the Breast Cancer Fund

BPA alone is "worth at least a million dollars every hour".

Wade Welshons - University of Missouri

"If a chemical is biologically active and interacts with our receptors, it's probably no good. Ban it."

Sheldon Krimsky - Tufts University

"If I were a pregnant woman, I would try hard to avoid exposure to BPA"

Randy Jirtle

Summary

Evidence that associates BPA with Breast Cancer;

BPA causes altered morphology of mammary tissue[45]
BPA causes altered timing of development[45]
BPA increases mTOR expression[46]
BPA causes increased cell proliferation[47]
BPA causes decreased apoptosis[47]
BPA promotes breast cancers in rats after exposure to known carcinogens at a dose that does not cause cancer in non-BPA treated mice[47].

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