

Bisphenol A: An update on Toxicity and Sources of Exposure

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Clean Med
5.19.09

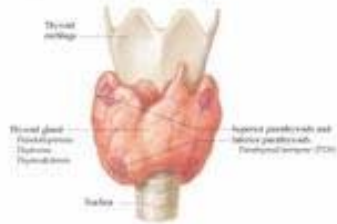


Increasing Incidence of Health Conditions

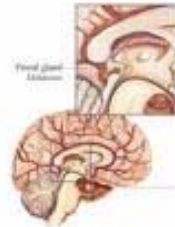
- Infertility
- Premature births
- Birth defects of genitalia
- Early onset of puberty
- Cancer - testicular
- Neurological conditions – ADHD, autism
- Insulin resistance/Diabetes
- Obesity

THE ENDOCRINE SYSTEM

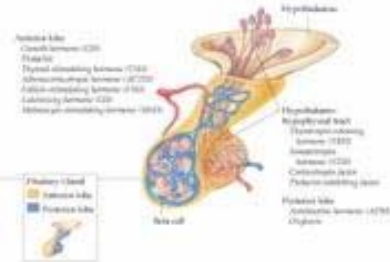
Thyroid and Parathyroid Glands



Pineal Gland



Pituitary Gland and Hypothalamus



Thymus Gland

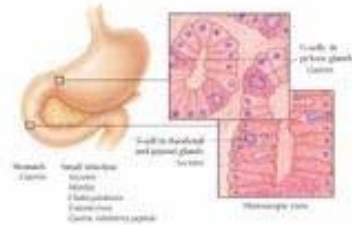


Heart



Coronary vessels (flow from the right atrium) (coronary sinus) (left)

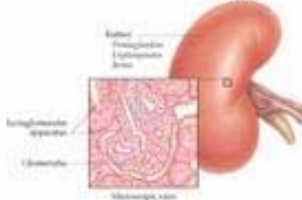
Stomach, Duodenum, and Jejunum



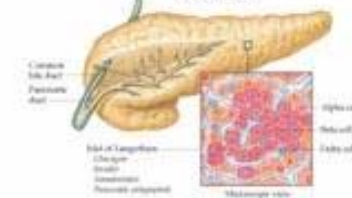
Adrenal Glands



Kidney



Pancreas



Ovary



Placental Hormones

Human chorionic gonadotropin (HCG)
Human chorionic somatomedin (HCS)
Human chorionic gonadotropin (HCG)
Human chorionic somatomedin (HCS)
Human chorionic gonadotropin (HCG)
Human chorionic somatomedin (HCS)

Testes



Endocrine Disruptor

- “An exogenous agent that interferes with the synthesis, secretion, transport, binding, action, or elimination of natural hormones in the body that are responsible for the maintenance of homeostasis, reproduction, development, and /or behavior.”

U.S. EPA, February 1997

- Or in simpler terms:

“A substance which interferes with natural hormones.”

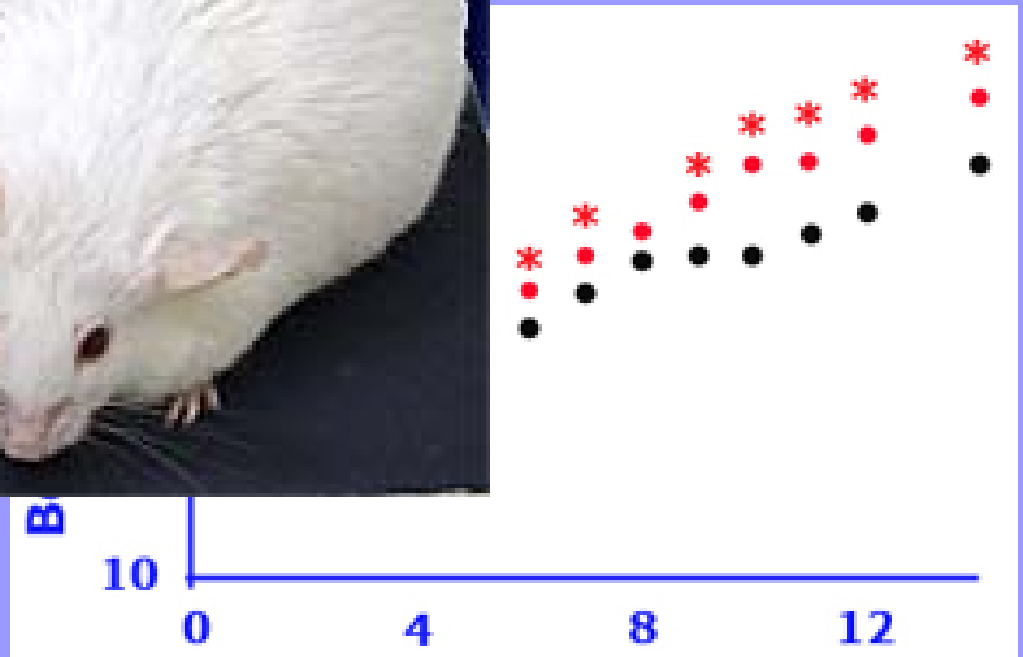
Endocrine disruptors and health

- Abnormal development of reproductive organs or neurological system
- Reduced fertility – male and female
- Poor birth outcomes – LBW/IUGR, SA
- Development of pre-cancerous/cancerous lesions
- Lower IQ/Behavioral abnormalities
- Obesity

Estrogenic agents and obesity



per billion DES

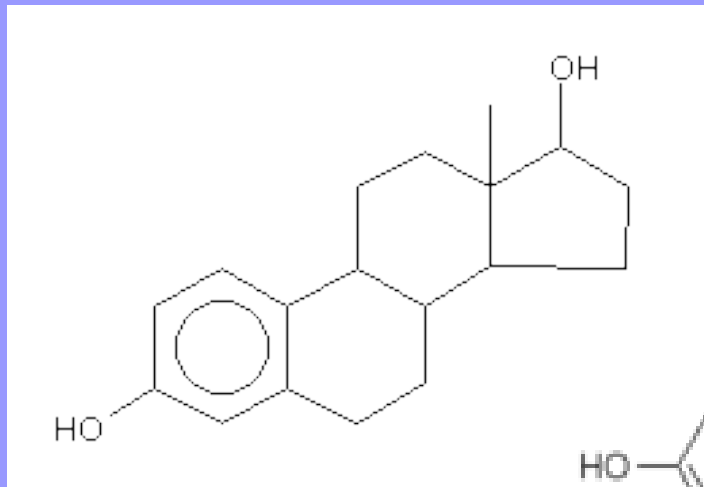


Newbold, et al. 2005.

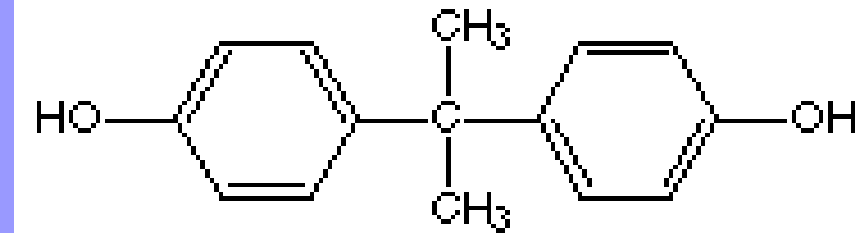
[Developmental Exposure to Estrogenic Compounds and Obesity](#). *Birth Defects Research (Part A)* 73:478–480.

Bisphenol A

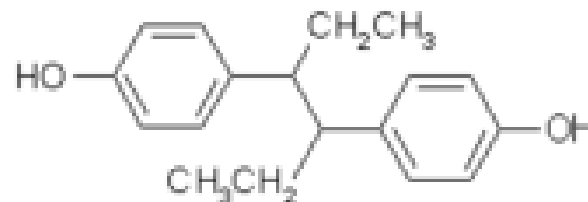
- > 6 billion pounds produced each year
- Developed as estrogenic drug 1930s



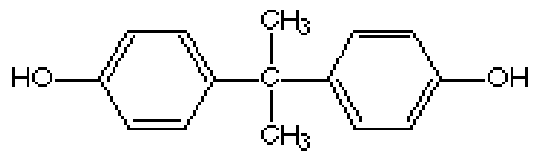
Estradiol



Bisphenol A



4,4'-(1,2-diethyl-1,2,ethene-diyl)bisphenol
diethylstilbestrol
DES



Bisphenol A

Bisphenol A

- Building block of polycarbonate plastic
- Epoxy resin – building materials, paints, food can lining
- Dental sealant
- Medical Devices
- Thermal paper receipts



PC



Human Exposures

- NHANES data – over 90% Americans have residues of BPA in their urine
 - young adults > older adults
 - NHB > Caucasian, Hispanic
- Breast milk, amniotic fluid, cord blood
- Exposure most likely oral, although dermal and inhalation also possible
- FDA estimates from food:
 - Infants 2 ug/kg bw/d (avg, range up to 13 ug/kg/d)
 - Adults 0.185 ug/kg bw/d

Recent studies of sources of exposure and metabolism

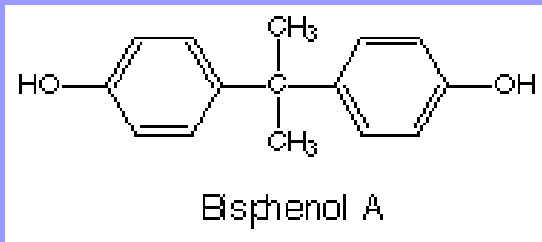
- **Polycarbonate beverage containers** - Drinking COLD beverages increased urinary BPA concentrations by two thirds- irrespective of exposure to BPA from other sources. (Carwile et al, EHP, 2009)
- **Premature Infants in ICU** – BPA levels 11x higher than general population. High exposure to medical devices correlated with higher levels of BPA (Calafat, EHP, 2009)
- Assumptions about metabolism and sources of exposure may be incorrect. (Stahlhut, EHP, 2009)

Route of Exposure

- In fetuses and infants, the detoxifying enzymes are not fully developed and exposures via mouth or injection result in similar circulating levels of BPA (Taylor, Repro Tox, 2008) .
- Oral exposure to low doses of BPA through breast milk has been shown to increase susceptibility to mammary tumors in rodents (Jenkins, EHP, 2009)

Good Laboratory Practice studies

- GLP studies ensure that the laboratory has passed inspections, keep accurate records and adhere to animal care protocols
- They do not mandate state of the art science, use of new techniques, or relevance of studies to human exposure levels
- They do not ensure that the right questions has been asked or that the study was designed properly.
 - » (Myers, JP. EHP, 2009)



Low dose Animal studies

- Reproductive toxin
 - Lower sperm counts
 - Prostate hyperplasia/cancer
 - Mammary cancer
- Developmental toxin
 - altered onset of puberty
 - decreased anogenital distance
 - oocyte aneuploidy
- Neurological toxin
- Obesogen/Insulin Resistance

Reproductive Toxicology, Aug 2007

NTP-CERHR Monograph on Bisphenol A. 2008 Sep;(22):i-III1.

Human/Non-Human Primates

- Normal breast tissue exposed to 22 ppb has gene expression patterns c/w high grade breast ca (Dairkee, 2008)
- Cross sectional analysis of BPA concentrations and health status of general US adult population using CDC data, 2003-2004. Found increase risk of CV disease and diabetes with evidence of BPA exposure (Lang, et al. *JAMA*. 2008).

Bisphenol A interferes with development of the brain

- Alters synaptogenesis in pre-frontal cortex and hippocampus of non-human primates (Leranth, 2008)
- Non-human primates exposed to BPA at low doses caused infant male monkeys to behave more like infant females. (Nakagami A, Psychoneuroendocrinology, 2009)
- **Confirms previous studies done in rodents**

Bisphenol A interferes with cancer treatment

- Bisphenol A interferes with androgen deprivation in the treatment of prostate cancer. (Hess-Wilson JK. Cancer Causes Control. 2009)
- BPA at environmentally relevant doses reduces the efficacy of chemotherapeutic agents in the treatment of breast cancer. (Lapensee, EHP, 2009)

Bisphenol A interferes with fat metabolism

- BPA decreases secretion of adiponectin from human adipose tissue (Hugo, EHP, 2008)
- BPA stimulates the release of inflammatory factors such as interleukin-6 (IL-6) and tumor necrosis factor alpha (TNFalpha) from human adipose tissue (Ben-Jonathon, Mol Cell Endocrinol, 2009)

BPA interferes with thyroid metabolism

- **Bisphenol A stifles thyroid hormone and slows frog development.**

(Heimeier RA, Endocrinology. 2009)

Confirms previous studies demonstrating BPA interferes with thyroid hormone and can alter development.

Conclusions

- We are highly exposed to BPA from multiple sources
- BPA has been associated with multiple health effects including cancer, neurological damage and abnormalities in fat metabolism
- Exposure to BPA should be reduced.
- Alternatives exist
- Public Policy decisions should be protective of public health