Bisphenol A (BPA)

CATEGORY: Endocrine disruptor

USED IN: Plastics, epoxy resins used in food cans

Bisphenol A (BPA) has been associated with increased risk for cardiovascular disease, miscarriages, breast and prostate cancer, reproductive dysfunction, metabolic dysfunction and diabetes, and neurological and behavioral disorders (Braun, 2009; Lang, 2008; Li, 2009; Sugiura-Ogasawara, 2005).

BPA is one of the most common chemicals to which we are exposed in everyday life. It is the building block of polycarbonate plastic and is also used in the manufacture of epoxy resins. According to Environment Canada (the Canadian equivalent of the EPA), more than 4 billion kilograms (4.4 million tons) of the chemical were produced globally in 2006, and more than 1 billion kilograms (1.1 million tons) were produced in the United States in 2007 (CEPA, 2009).

Present in many household products, BPA is also commonly found in the epoxy lining of metal food cans and in polycarbonate plastic food containers, including some baby bottles, microwave ovenware and eating utensils. Because BPA is an unstable polymer and is also lipophilic (fat-seeking), it can leach into canned foods (Noonan, 2011), infant formula and other food products (Schecter, 2010), especially when heated (Brotons, 1995). Once in food, BPA can move quickly into people—a particular concern for women of childbearing age and young children. Two recent studies have explored the effects of increased ingestion of food and drink packaged in EDC-containing sources. Both found rapid (within a few days to a week) increases in BPA levels in urine and/or blood samples taken from subjects who intentionally increased their intake of common foods and drinks packaged in BPA-containing products (Carwile, 2009; Smith, 2009).

Clearance rates for BPA are quite rapid, with a urinary half-life in the order of hours to days. A recent study of samples taken from fasting people indicate that sources other than foods may also be responsible for the pervasive exposure to BPA, as levels of the chemical did not decrease as rapidly as would have been predicted were food the only source of contamination (Stahlhut, 2009). However, a recent dietary study demonstrated that eating a diet free of packaging containing BPA contaminants led to an average 66 percent decrease in urinary BPA levels after only three days on the package-free diet (Rudel, 2011). Significant levels of BPA have also been measured in ambient air (Matsumoto, 2005), house dust (Rudel, 2003), and river and drinking water (Rodriguez-Mozaz, 2005) samples.

CDC researchers have measured BPA in 93 percent of about 400 urine samples from a broad national sample of adults (Calafat, 2005). BPA has been found in blood (Padmanabhan, 2008) and urine (Ye, 2009a) of pregnant women, and in breast milk soon after women gave birth (Kuroto-Niwa, 2006). BPA has also been found in blood samples from developing fetuses as well as the surrounding amniotic fluid (Ikezuki, 2002), and it has been measured in placental tissue and umbilical cord blood at birth (EWG, 2009; Schonfelder, 2002) as well as in the urine of premature infants housed in neonatal ICUs (Calafat, 2009).

That BPA is found so extensively in people, from prenatal to adult ages, is particularly impressive given the relatively short half-life of the chemical.

Several studies using both rat and mouse models have demonstrated that even brief exposures to environmentally relevant doses of BPA during gestation or around the time of birth lead to changes in mammary tissue structure predictive of later development of tumors (Maffini, 2006; Markey, 2001; Muñoz-de-Toro, 2005). Exposure also increased sensitivity to estrogen at puberty (Wadia, 2007). Recent data demonstrate that early exposure to BPA leads to abnormalities in mammary tissue development that are observable even during gestation and are maintained into adulthood (Vandenberg, 2007; 2008).

Interestingly, some of the long-term effects of neonatal exposure to BPA may be dose dependent, with low- and high-dose exposures resulting in different timing and profiles of changes in mammary gland gene expression. In one study, low-dose exposures had the most profound effect on rat mammary glands during the period just prior to animals reaching reproductive maturity, while higher doses had more delayed effects, altering gene expression in mammary tissues from mature adults (Moral, 2008).

Prenatal exposure of rats to BPA results in increases in the number of pre-cancerous lesions and in situ tumors (carcinomas) (Murray, 2007a), as well as increased number of mammary tumors following adulthood exposures to subthreshold doses (lower than that needed to induce tumors) of known carcinogens (Durando, 2007; Jenkins, 2009; Lozada, 2011). Exposures to BPA in adulthood also enhance the rate of growth and proliferation of existing hormone-sensitive mammary tumors, suggesting multiple mechanisms by which BPA may affect breast cancer development (Lozada, 2011).

Studies using cultures of human breast cancer cells demonstrate that BPA acts through the same response pathways as the natural estrogen estradiol (Rivas, 2002; Welshons, 2006). BPA can interact weakly with the intracellular estrogen receptor (ER), and it can also alter breast cell responsiveness and induce cell proliferation in vitro and in vivo. It affects cellular functions through interactions with the membrane estrogen receptor (Watson, 2005; Wozniak, 2005). Along with its many other effects on cell growth and proliferation, BPA has been shown to mimic estradiol in causing direct damage to the DNA of cultured human breast cancer cells (Iso, 2006).

Cell culture studies support animal evidence that BPA has dose-dependent effects. One recent study showed estrogen-like effects at extremely low concentrations; when somewhat higher concentrations were used, there were no effects on the cellular kinase pathway being studied. And at an even higher dose, the BPA inhibited the effects of estradiol. Despite the wide ranges of doses used in the study, even the very highest was in the nanomolar region; for all conditions, they were low and in the environmentally relevant range of concentrations (Jeng, 2011).

In the presence of BPA, cells from the non-cancerous breast of women diagnosed with breast cancer had a gene-response profile associated with the development of highly aggressive tumors (Dairkee, 2008). Two new studies indicate that BPA reduces the efficacy of common chemotherapy agents (cisplatin, doxirubicin and vinblastin) in their actions against proliferating breast cancer cells when tested in cell systems (LaPensee, 2009; 2010). Thus, not only does early exposure to BPA lead to an increased risk for development of breast tumors, but exposure to BPA during chemotherapy treatment for breast cancer may make the treatment less effective. Recent data further suggests that BPA leads normal human breast cells to behave like cancer cells, and indicates that BPA may also make cells less responsive to the cancer-inhibiting effects of the anti-estrogen tamoxifen (Goodson, 2011).