Bisphenol A in dental materials

Fact file

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What is bisphenol A?
Bisphenol A (BPA) is a chemical used primarily for the production of polycarbonate plastics and epoxy resins. Some 3 billion kilos of BPA are produced worldwide and the use of this chemical is so ubiquitous that it has been detected in the urine of 93 per cent of the population over 6 years of age (Welshons et al., 2006; Calafat et al., 2005). A recent study found that BPA was present in the saliva of all patients in the study group prior to the placement of a sealant and ranged from 0.07 to 6 ng/ml at baseline (Zimmerman et al., 2010).

A major source of BPA is believed to be polycarbonate water bottles (Hoa et al., 2008). For example, Nalgene™ water bottles were made with BPA until recently. These are being replaced voluntarily by bottles that are BPA-free. Other sources of polycarbonate are food and drink packaging, including infant bottles, toddler sipping cups, tableware, and food containers. Epoxy resins, which use BPA in their manufacturing process, are used to line metal products such as food cans, bottle tops and water supply pipes.

The highest estimated daily intake (exposure) for humans is:
- less than 14.7 µg/kg body weight (bw)/day for children
- less than 1.5 µg/kg bw/day for adults.

(Source: http://www.medicinenet.com/plastic/page4.htm#bisphenol.)

Why is BPA a concern?
BPA is one of a family of endocrine-disrupting chemicals (EDCs) and exposure to BPA and its potential effects on human health are receiving increasing attention, as studies on laboratory animals have shown that BPA can cause genetic damage. BPA stimulates cell proliferation and induces expression of oestrogen-responsive genes in vitro, albeit with a relatively low potency. In vivo, BPA increases prolactin release and stimulates uterine, vaginal and mammary growth and differentiation. BPA shares similarities in structure, metabolism and action with diethylstilbestrol (DES), a known human teratogen and carcinogen (Ben-Jonathan and Steinmetz, 1998).

Studies on laboratory rodents have shown that high doses of BPA during pregnancy and lactation can reduce survival, birth weight and growth of offspring early in life, and delay the onset of puberty (Richter et al., 2007). BPA has also been linked to cancer, diabetes, and obesity in animals. However, the doses given were considerably higher than the estimated human exposures shown above, being in the range of milligrams rather than micrograms:
- delayed puberty: greater than 50 mg/kg bw/day
- growth retardation: greater than 300 mg/kg bw/day
- survival: greater than 500 mg/kg bw/day.

This led the American Chemistry Council to state that, "consumers would have to eat more than 500 pounds of food and beverages in contact with polycarbonate plastic or epoxy resins every day of their lives to exceed exposure levels determined to be safe by the European Food Safety Authority and the US Environmental Protection Agency". (See: http://factsaboutbpa.org/what-are-the-bpa-myths.)

What are the recommended safe levels of BPA?
There is much confusion about the effects of BPA on the human body, and the greatest challenge seems to be in presenting irrefutable evidence that it is, in fact, harmless even at low levels. Correlations have been made between higher exposures to BPA in human adults and higher risks of heart attack and Type II diabetes. However, as long as adult exposures to BPA do not exceed acceptable levels, then there seems to be no impetus for change. (See: http://www.bisphenol-a.org/about/faq.html#j.)

In its risk assessment on BPA, published in January 2007, the European Foods Standards Agency (EFSA) set a Tolerable Daily Intake (TDI) of 0.05 mg/kg body weight (bw) for BPA. The TDI is an estimate of the amount of a substance, as a function of body weight, that can be ingested daily over a lifetime without appreciable risk. The EFSA has said that intakes of BPA through food and drink were well below the TDI, even for infants and children. A recent review (July 2010) by the EFSA, in which some 800 publications were considered (see: http://www.efsa.europa.eu/en/ceftopics/topic/bisphenol.htm), has for now decided that the EFSA will maintain the TDI for BPA at 0.05 mg/kg bw per day. However, some argue that this TDI is still some way above levels reported to have an effect in animals (Ginsberg and Rice, 2009), whereas the EFSA maintains that the TDI for BPA is some 200 times greater than that associated with adverse events reported in some rodent studies (Vandenberg et al., 2007).

Statement:
Current evidence suggests that only a very small and specific group of dental materials is susceptible to the release BPA, and then in only very small amounts. The majority of resin based dental materials appears not to release BPA, which should alleviate concerns regarding potential health risks.
The recommendations expressed by the EFSA are based on the concept of a toxic dose response, such that there is a toxic level and as long as this is not exceeded the product is safe. This relies on a monotonic dose-response curve, in which more of the chemical leads to a greater effect. Thus, by using a substantial safety factor, a recommended safe level (TDI) can be assumed. Endocrinologists have challenged this, in that very low doses that are outside the physiological range can produce quite different effects compared with what would be seen within the physiologically relevant dose range, especially during the critical periods of perinatal development (Myers et al., 2009a, Myers et al., 2009b). Thus endocrinologists make the case that non-monotonicity is a feature of endogenous hormones, hormonally active drugs and environmental chemicals with hormonal activity such as BPA and phthalates. Söderholm and Mariotti (1999), and more recently Welshons et al. (2006), have asked for a reassessment of the risks associated with current estimates of a safe daily exposure level for BPA. Myers et al., (2009a) go so far as to suggest that what is required is for “regulatory decision makers to fundamentally change the paradigm commonly used to assess the risk to human health posed by chemicals”.

BPA release from dental materials

From the perspective of the safety of dental materials, it is necessary to assess the contribution of dental materials to the overall body burden of BPA, and whether or not individual patients could be affected by exposure to dental materials that contain BPA or BPA-based compounds.

Concerns have been expressed about the possible exposure of patients to BPA from dental materials, in particular some fissure sealants. Bisphenol glycidyldimethacrylate (Bis-GMA) is one of the most commonly used monomers for both anterior and posterior resin restorative materials, fissure sealants and a range of other dental products. Bis-GMA is derived from the reaction of bisphenol A and glycidylmethacrylate. This resin is commonly referred to as Bowen’s resin, after its inventor. There are also several composites that use a urethane dimethacrylate resin (UDMA) rather than Bis-GMA. Bis-GMA and urethane dimethacrylate monomers are highly viscous fluids because of their high molecular weights; the addition of even a small amount of filler would produce a composite with a stiffness that is excessive for clinical use. To overcome this problem, low viscosity monomers known as viscosity controllers are added, such as methyl methacrylate (MMA), ethyleneglycol dimethacrylate (EDMA), triethyleneglycol dimethacrylate (TEGDMA) and bisphenol dimethacrylate (Bis-DMA). Thus, dental materials containing Bis-GMA or Bis-DMA could provide a potential source of BPA. It has been shown that BPA may be released from some resin composite restorative materials and fissure sealants (Olea et al., 1996). However, Hamid et al. (1997) and Nathanson et al. (1997) found no release of Bisphenol A from any of the sealants they tested. If BPA is found to be released from dental restorative materials then this may be for one of two reasons. The release may be due to residual BPA being present in the resin as part of the production process of Bis-GMA, i.e. as a contaminant. Manabe et al., (2000) reported that some unpolymerised materials may be contaminated with BPA, but they went on to say that the amount released from dental materials is less than 1/1000 of the dose required for xenoestrogenicity in vivo. Alternatively, the release of BPA may be a consequence of hydrolytic or enzymatic breakdown of the polymer with time in the oral environment. For example, BPA has been found to be released from Delton LC Opaque pit and fissure sealant™ (Joskow et al., 2006), which is believed to be due to the breakdown of Bis-DMA (Schmalz et al., 1999). Saliva levels of BPA reached a peak level of 9.08 ng/ml, compared with a baseline of up to 6ng/ml, whereas the blood serum did not contain BPA at any stage in the investigation and BPA levels returned to baseline levels within 24 hours (Zimmerman et al., 2010). This confirms the earlier work of Joskow et al., (2006), who also showed that the raised levels of BPA were transient. BPA has also been detected as being released from ScotchBond Multipurpose™ (3M/ESPE) and Delton™ sealant (Mazzaoui et al., 2002), and from Ceram X™ (Polydorou et al., 2009a). However, in another study, Polydorou et al. (2009b) were unable to detect BPA release from Clearfil Core™ (Kuraray), but did find up to 15 µg/ml of BPA being released from Clearfil DC Core Automix™. Kopperud et al. (2010) examined a range of orthodontic base plate materials and found no BPA in the eluates. However, the situation becomes more confusing when account is taken of the elution conditions used in the studies for the detection of BPA. In one study, Polydorou et al. (2009a) were unable to detect any release of BPA from Filtek Supreme XT, but when the resin composite was exposed to a bleaching regime BPA was detected as being eluted for Filtek Supreme XT (Polydorou et al., 2009c).

Is BPA release from dental materials a matter of concern?

It would appear that BPA is released from only a small number of resin-based dental materials. Thus the contribution of dental materials to the overall body/environmental burden of BPA is very small indeed. Also, where BPA release has been detected, the amounts involved have been very low and well within the TDI of 0.05mg/kg bw/day set by the EFSA. This has led the ADA to state, “The ADA believes any concern about potential BPA exposure from dental sealants or composites is unwarranted at this time. When compared with other sources of BPA, these dental materials pose significantly lower exposure concerns.” (Source: http://www.ada.org/2989.aspx?currentTab=1.) A systematic review of pit and fissure sealants (Azarpazhooh, 2008) also states that, “The evidence suggests that patients are not at risk for exposure to BPA from the use of dental sealants”. However, this recommendation is primarily based on the toxic effects of BPA.

Expert opinion currently suggests that BPA doses from dental materials are low and well within the safe exposure limits. Nevertheless, research should continue to determine whether human exposure to very low physiological levels of BPA associated with certain dental materials can cause adverse oestrogenic effects.
References:


Hoa H, Emily M et al. Bisphenol-A is released from polycarbonate drinking bottles and mimics the neurotoxic actions of estrogen in developing cerebellar neurons. Toxicol. lett., 2008; 176: 149-156.


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