Exposure to bisphenol A from bis-glycidyl dimethacrylate–based dental sealants

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ABSTRACT

Background. Bisphenol A (BPA) is a common component of composites and dental sealants. The potential exists for human exposure after sealant placement.

Methods. The authors prospectively enrolled 15 men in an exposure assessment study; 14 completed the study. After placement of clinically appropriate amounts of one of two sealants, the authors measured BPA in saliva and urine samples collected at prescribed intervals after the sealants were placed. They used selective and sensitive isotope-dilution mass-spectrometry–based methods for BPA measurements, thus providing the most reliable results.

Results. Helioseal F (Ivoclar Vivadent, Amherst, N.Y.) leached negligible amounts of BPA. Urinary and salivary BPA levels in subjects who received these sealants were similar to baseline levels. Delton Light Cure (LC) Opaque pit-and-fissure sealant (Dentsply/Ash, York, Pa.) leached more BPA, resulting in low-level BPA exposures similar to those used in laboratory animal testing. BPA exposure after Delton LC sealant placement was significantly higher than exposure after placement of Helioseal F. Patients treated with Delton LC had significantly higher doses of BPA (110 µg) than did those treated with Helioseal F (5.5 µg) ($P < .0001$).

Conclusions. Placement of clinically relevant amounts of Delton LC sealant resulted in low-level BPA exposure; however, exposure was negligible after placement of Helioseal F. Saliva collection after sealant placement likely reduced systemic absorption of BPA from dental sealants. Sealants should remain a useful part of routine preventive dental practice, especially those that leach negligible amounts of BPA.

Clinical Implications. Dental sealants may be a point source for low-level BPA exposure at levels that show health effects in rodents. Further research is required to determine whether human exposure to BPA at these levels causes adverse effects.

Key Words. Bisphenol A; dental sealants; mass spectrometry; urine; saliva.
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Bisphenol A (2,2'-bis[4-hydroxyphenyl]propane) (BPA) is a common ingredient in restorative resin-based composites and sealants used in dentistry.[1] The resin matrix initially is a fluid containing monomer that is "cured" or converted into a rigid polymer by a chemically or photo-initiated polymerization reaction.[2] Unpolymerized BPA can leach from the dental composite or sealant[3-9] or degrade chemically or mechanically[10,11] and may be absorbed systemically by the patient.

BPA exposures resulting from the placement of dental sealants or composites have been reported.[2,12-14] However, the magnitude of these exposures, the reliability of the analytical methods used, the long-term potential for sealant leaching and the potential for adverse effects have been debated hotly.[15-17] The American Dental Association (ADA) maintains that BPA-based dental sealants are an integral part of routine preventive dental care and that sealants carrying its Seal of Acceptance do not release detectable (> 5 nanograms per milliliter) amounts of BPA.[18-20]

Although dental sealants and composites represent a potential point source of exposure, only about one-third of the BPA produced in the United States is used in epoxy resins, including dental sealants.[21] BPA commonly is used to manufacture polycarbonate plastics used as protective coatings on food containers and in plastic baby

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bottles—applications accounting for about 63 percent of its use.[21] Furthermore, BPA can be released into the environment during the manufacturing process or by leaching from the manufactured products.[22-25] Thus, the potential for BPA exposure, not only from dental sealants and composites but also from other routinely encountered sources, is high.[26]

BPA is weakly estrogenic in in vitro screening assays.[2,27-30] However, because of its low protein-binding affinity, more unbound BPA may be available in vivo, potentially rendering it more estrogenic than observed in laboratory studies.[31] Toxicological studies in laboratory animals have shown estrogen-response mechanism-mediated effects after low-level in utero BPA exposures (20-400 micrograms per kilogram per day).[32] In males, low-dose BPA exposures of rodent fetuses produced postnatal estrogenic effects, including decreased sperm production[33] and increased prostate weight[34]; in females, it caused disruption of sexual differentiation in the brain,[35] alteration in mammary gland development,[36] altered vaginal morphology,[37] accelerated growth and puberty,[38] and alterations in estrous cyclicity.[39] Furthermore, low-dose BPA exposures disrupted meiosis in rats, leading to aneuploidy,[40] the chromosomal abnormality in humans most commonly identified as resulting in pregnancy miscarriage, or, if the pregnancy is taken to term, mental retardation in offspring.[41] BPA also has been shown to be a thyroid hormone receptor (THR) antagonist that disrupts THR-mediated transcription in rodents.[42,43] In humans, BPA concentrations have been associated with both polycystic ovary disease and obesity in women[44] and the disruption of secretion of gonadotrophic hormones in men.[45]

To our knowledge to date, four studies have reported the presence of BPA in saliva after placement of dental sealants or composites.[2,12-14] However, these studies were hampered by less sensitive and nonselective analytical procedures that, in some cases, required the use of larger amounts of sealant than clinically necessary. Furthermore, these studies did not evaluate urinary levels of BPA, which would have allowed an easy comparison with exposure data increasingly published in the literature.[45-50]

Therefore, we conducted a study to determine whether BPA exposure deriving from dental sealants occurred after placement of clinically appropriate, morphologically determined sealant amounts and to relate these exposures to urinary BPA concentrations that often are used for biological monitoring of exposure. We report salivary and urinary concentrations of BPA in 14 dental patients who received two different brands of dental sealants. Furthermore, we convert the biological concentrations to crude total BPA doses and relate them to the doses used in toxicological animal testing.

SUBJECTS, MATERIALS AND METHODS

Study population. Our study was a prospective cohort design. We recruited 15 healthy military personnel from the dental clinic at Dobbins Air Force Base/Naval Air Station (NAS) in Marietta, Ga. The participants already had been scheduled to receive dental sealants by the dentist at the dental clinic as a part of their routine dental care. We excluded people who had existing resin-based composite restorations, sealants or other resin materials on their teeth. We also excluded smokers, people who were taking antihistamines and people who reported having Gilbert syndrome. All eligible patients agreed to participate in the study and all participants provided written informed consent. The study complied with all national and international regulations for the protection of human research subjects and was approved by Centers for Disease Control and Prevention's institutional review board.

We administered no questionnaire and obtained only basic, self-reported demographic data (sex, age, race). We assigned each participant a number and collected samples from each in numbered collection containers. Right before receiving the sealant, we collected from each participant approximately 4 mL of saliva using two separate 2-mL saliva collection devices (Salivette, Sarstedt, Newton, N.C.) that were used consecutively. The devices contained a cotton plug on which the participant chewed on for two minutes to actively induce and collect saliva. In addition, we collected a single urine sample (approximately 10 mL) from each participant.

All dental care providers selected either Helioseal F (Ivoclar Vivadent, Amherst, N.Y.) or Delton Light Cure (LC) Opaque (Dentsply/Ash, Dentsply International, York, Pa.) from the three sealant brands available in the clinic. We weighed the sealant material and dispensing paper before and after treatment to determine the amount of sealant applied. We also recorded the brand used for each participant, number of sealants placed and teeth on which the dentists performed

occlusal adjustments of the dental sealant. The sealants were placed under cotton roll or dry angle isolation using an acid-etch, light-cured technique according to the manufacturers' instructions. Before each procedure, we used a light meter (Cure Rite, Efos, Mississauga, Ontario, Canada) to measure the intensity of each curing light and, therefore, ensure full curing of the sealant material. Readings taken were within acceptable limits to cure the sealant material (minimum-maximum: 534-803 milliwatts per square centimeter; mean: 678 mW/cm^2). We examined sealants for retention after each procedure.

TABLE 1

Data/sample collection strategy.

TIMING	DATA/SAMPLE COLLECTED
Pretreatment	Signed informed consent form Two 2-milliliter saliva samples (collected consecutively) Urine sample Preweighed sealant
Immediately After Treatment	Two 2-mL saliva samples (collected consecutively) Sealant weighed after treatment
One Hour After Treatment	Two 2-mL saliva samples (collected consecutively) Urine sample
24 Hours After Treatment	Urine sample

Immediately after sealant placement, we collected 4 mL of saliva in two consecutive 2-mL samplings from 13 of the 14 participants. One participant left before providing an immediate posttreatment saliva sample. One hour after placement of the sealant, we collected from each participant an additional 4-mL saliva aliquot in two samplings and another urine sample. Approximately 24 hours after placement, we collected a third urine sample from the 12 participants who returned. Thus, from each participant who completed sample collection, we obtained six saliva samples and three urine samples within a 24-hour period. Table 1 outlines the sample collection strategy. We froze all samples at –70 C without further processing until analysis.

Laboratory analysis. Saliva and urine samples (2 mL) were thawed before analysis. We centrifuged the saliva collection containers at 10,000 revolutions per minute for 10 minutes to remove the saliva from the collection device. We analyzed saliva and urine samples concurrently in batches of approximately 20 samples using a modification of the method of Brock and colleagues.[51] An aliquot (1 mL) of each sample was enriched with a 1.5-ng ring of -$^{13}C_{12}$-BPA (Cambridge Isotope Laborories, Andover, Mass.) and mixed well. We added β-glucuronidase (*Escherichia coli,* 5 microliters, 200 units per mL; Roche Biomedical, Mannheim, Germany) to each sample and incubated the samples at 37 C for 90 minutes to liberate glucuronide-bound BPA. We added 1 mL of 32 percent formic acid and 250 µL of 1 molar ammonium acetate (pH 6.5) to each sample. The treated samples were applied to preconditioned C_{18} solid-phase extraction columns (500 milligrams; Varian Analytical Services, Walnut Creek, Calif.) and pulled through with partial vacuum. The columns were washed with water and methanol in a ratio of 9:1 and eluted with 8 mL of methanol. We evaporated samples to dryness and reconstituted residues in dichloromethane. We added 0.1 millimoles per liter of tetrabutylammonium hydrogen sulfate (0.5 mL; Eastman Kodak, Rochester, N.Y.) and pentafluorobenzyl bromide (20 µL; Supelco, Bellefonte, Pa.) to each sample. The samples were kept at ambient temperature for 25 minutes to facilitate the conversion of BPA to its bis-pentafluorobenzyl ether. We centrifuged the reaction mixture, recovered the dichloromethane layer and evaporated it to dryness. We reconstituted the dried residue in 0.5 mL of 2,2,4-trimethylpentane resulting in a twofold concentration of the original sample.

We analyzed the derivatized extracts using a MAT-900 gas chromatograph-high resolution mass spectrometer (ThermoFinnigan, Bremen, Germany) set at 10,000 resolution (at 10 percent valley). Isobutane served as the reagent gas for negative chemical ionization. The transfer line temperature was 270 C, the electron energy was 130 electron volts and the emission current was 0.18 milliamperes. The BPA derivative was chromatographed using a DB-5 column ([5 percent phenyl]-methyl polysiloxane, 0.25 µm film thickness, 0.25 mm internal diameter) (J & W Scientific, Folsom, Calif.) with an injector temperature

of 250 C, an injection volume of 2 µL and a purge time of one minute. The gas chromatography oven temperature program was 75 C for one minute, ramped linearly to 200 C at 15 C/minute, ramped to 220 C at 10 C/minute, then ramped to 270 C at 15 C/minute and held for 12 minutes. The total run time was 27 minutes, and the BPA derivative eluted for approximately 24.5 minutes. We monitored monoisotopic mass ions at mass-to-charge (m/z) ratio 407.1070 and m/z ratio 299.0495 to quantify and confirm the presence of BPA, respectively. We monitored a monoisotopic ion at m/z ratio 419.1473 for $^{13}C_{12}$-BPA. Quantification was achieved using isotope dilution calibration with a limit of detection of 0.1 ng/mL. Using this technique, the isotopically labeled standard accurately and automatically accounts for losses in extraction recovery, reaction efficiency and human error, resulting in the most accurate and precise measurements possible. This calibration technique is considered the gold standard for quantification of trace amounts of chemicals in human samples.

The quality of measurements was further ensured by the simultaneous analysis of one negative and two positive control samples in concert with the specimens collected from the study. Furthermore, for a sample to be considered to have a detectable concentration of BPA, each BPA peak on the mass chromatogram had to coelute with the $^{13}C_{12}$-labeled BPA internal standard; have present both the quantification and confirmation ions; and have a ratio of the quantification-to-confirmation ion falling within ± 10 of a ratio predefined using analytical standards. In addition, we confirmed the presence of BPA in the urine samples, when adequate sample was available, using an independent method and laboratory.[52] This method used automated styrenyl-divinylbenzene copolymer-based solid-phase extraction, on-column pentafluorobenzyl derivatization and isotope dilution gas chromatography–low resolution mass spectrometry. The quantification and quality assurance techniques were similar to those used in the high-resolution mass spectrometry method described above. Laboratory personnel were blinded to the collection scheme, sample numbering system and sealant brand used to eliminate any potential bias in the reporting of laboratory results.

We corrected urinary concentrations for variable urine dilution by adjusting on the creatinine content in each urine sample.[53] We measured urinary creatinine using an automated colorimetric determination based on a modified Jaffe reaction using a clinical analyzer (Beckman Synchron AS/ASTRA, Beckman Instruments, Brea, Calif.) as in the method reported in Jaffe.[54] Approximately 10 to 15 percent of all samples consisted of negative and positive control samples.

The Health Care Finance Administration certified all laboratories and methods according to guidelines set forth in the Clinical Laboratory Improvement Amendment of 1988.[55]

Statistical analysis. We calculated geometric means (GMs) and percentiles of salivary and urinary BPA concentrations using the PROC UNIVARIATE procedure in SAS release 9.1 (SAS Institute, Cary, N.C.). We used the PROC TTEST procedure in SAS to determine BPA differences between the Delton LC- and Helioseal F-treated participants, assuming unequal variance. Using a paired PROC TTEST procedure, we evaluated differences in pretreatment and posttreatment samples for the same subjects. For the urinary concentrations, we performed analyses on both whole-volume and creatinine-adjusted measurements. We considered differences statistically significant when the two-sided P value was less than .05. Marginal significance was achieved when the P value was greater than .05 and less than .1.

RESULTS

Of the 15 subjects initially recruited, one withdrew just before dental treatment was rendered because of illness; however, his baseline saliva and urine samples had been collected. Of the 14 remaining subjects, nine reported their race as black and five reported their race as white. The subjects ranged in age from 19 to 42 years, with a mean age of 30 years. One subject was female and 13 were male.

Four dental practitioners provided the dental sealant treatment to their patients as scheduled by the clinic administration, and we observed no significant difference in results by dental provider. No patient received more than one brand of sealant. The 14 participants received sealants on a total of 84 posterior teeth, of which six were premolars. Thirty teeth were sealed with Helioseal F and 56 with Delton LC. The mean number of sealants placed per participant was six (range: two-12 teeth). The mean total weight of sealant material placed per participant was 40.35 mg, with a mean sealant weight of 7.36 mg per tooth. Neither the number of teeth treated

TABLE 2

Distribution of bisphenol A in saliva and urine samples of study participants receiving dental sealants.

MATRIX	COLLECTION TIME	ALL				DELTON LC*				HELIOSEAL F†				*P* VALUE‡
		N§	Mean	SD¶	Median	N	Mean	SD	Median	N	Mean	SD	Median	
Saliva#	Pretreatment	15	0.30	0.17	0.24	10	0.34	0.19	0.24	5	0.22	0.03	0.23	.055
	Immediately after treatment	13	26.5	30.7	22.7	8	42.8	28.9	38.9	5	0.54	0.45	0.35	.0022
	One hour after treatment	14	5.12	10.7	0.91	9	7.86	12.73	1.97	5	0.21	0.03	0.20	.0169
Urine**	Pretreatment	14	2.41 (0.64)	1.24 (0.40)	2.35 (0.55)	9	2.6 (0.77)	1.4 (0.45)	2.4 (0.71)	5	2.12 (0.42)	0.93 (0.14)	2.3 (0.40)	.6842 (.1787)
	One hour after treatment	14	20.1 (8.70)	33.1 (12.9)	6.75 (3.40)	9	27.3 (12.0)	39.1 (15.1)	12.9 (5.0)	5	7.26 (2.88)	13.5 (4.83)	1.5 (0.49)	.0847 (.0801)
	24 hours after treatment	12	5.14 (1.68)	3.96 (1.58)	3.75 (1.41)	7	7.34 (2.58)	3.81 (1.53)	7.60 (2.05)	5	2.06 (0.43)	1.04 (0.16)	1.5 (0.5)	.0013 (< .0001)

* Delton LC: Delton Light Cure Opaque, manufactured by Dentsply/Ash, Dentsply International, York, Pa.
† Helioseal F is manufactured by Ivoclar- Vivadent, Amherst, N.Y.
‡ *P* value from a *t* test assuming unequal variance between subjects treated with Delton LC and those treated with Helioseal F.
§ Number of samples tested.
¶ SD: Standard deviation.
\# Saliva concentrations are expressed in nanograms per milliliter.
** Urine concentrations are expressed in ng/mL with creatinine adjusted (micrograms per gram of creatinine) values shown in parentheses.

(six ± standard deviation three versus six ± two) nor the amount of sealant used (39.0 ± 1 mg versus 42.5 ± 1 mg) differed between Delton LC-treated and Helioseal F-treated subjects.

Table 2 shows the distributions of urinary and salivary BPA. Distributions are shown both collectively and stratified by sealant brand. We detected BPA in all of the samples tested. Salivary BPA concentrations ranged from 0.17 to 96.2 ng/mL. Salivary BPA concentrations in pretreatment or baseline samples were among the lowest found in the saliva samples tested. Example chromatograms for salivary and urinary BPA concentrations, as well as a blank and low-level fortified sample, are shown in Figure 1.

The BPA concentrations from the two consecutively sampled baseline saliva samples from each patient were indistinguishable ($P = .388$). However, baseline saliva samples collected from patients receiving Delton LC sealants had slightly higher BPA concentrations (0.34 ng/mL) than Helioseal F sealant recipients (0.22 ng/mL; $P = .055$). Immediately after sealant placement, salivary BPA concentrations in subjects who received Delton LC sealants were about 80 times higher than in the saliva of those who received Helioseal F sealants (42.8 ng/mL versus 0.54 ng/mL; $P = .0022$) (Figure 2A, page 359). A difference also was seen in the salivary BPA concentrations of Delton LC- and Helioseal F-treated patients one hour after sealant placement (7.86 ng/mL versus 0.21 ng/mL; $P = .0169$).

BPA concentrations in saliva samples collected immediately after sealant placement were more than 50-fold higher than their baseline BPA concentrations. When stratified by sealant brand, saliva BPA concentrations were an average 84-fold higher than those in baseline samples after Delton LC placement (confidence interval [CI] = 36.54 to 133.04, $P = .004$), but they demonstrated only a negligible nonsignificant increase after Helioseal F placement (CI = –0.45 to 1.75, $P = .177$).

Urinary BPA concentrations ranged from 0.6 to 112.2 ng/mL (0.17 to 45.4 mg/gram of creatinine). The highest urinary BPA concentrations were found in Delton LC-treated patients. Of the samples tested, concentrations of urinary BPA were highest one hour after sealant placement. On average, subjects treated with Delton LC had urinary BPA concentrations that were five times higher than their baseline levels, whereas subjects treated with Helioseal F had BPA concentrations similar to baseline levels. Baseline concentrations of urinary BPA were similar between both sealant groups ($P = .1787$). However, sub-

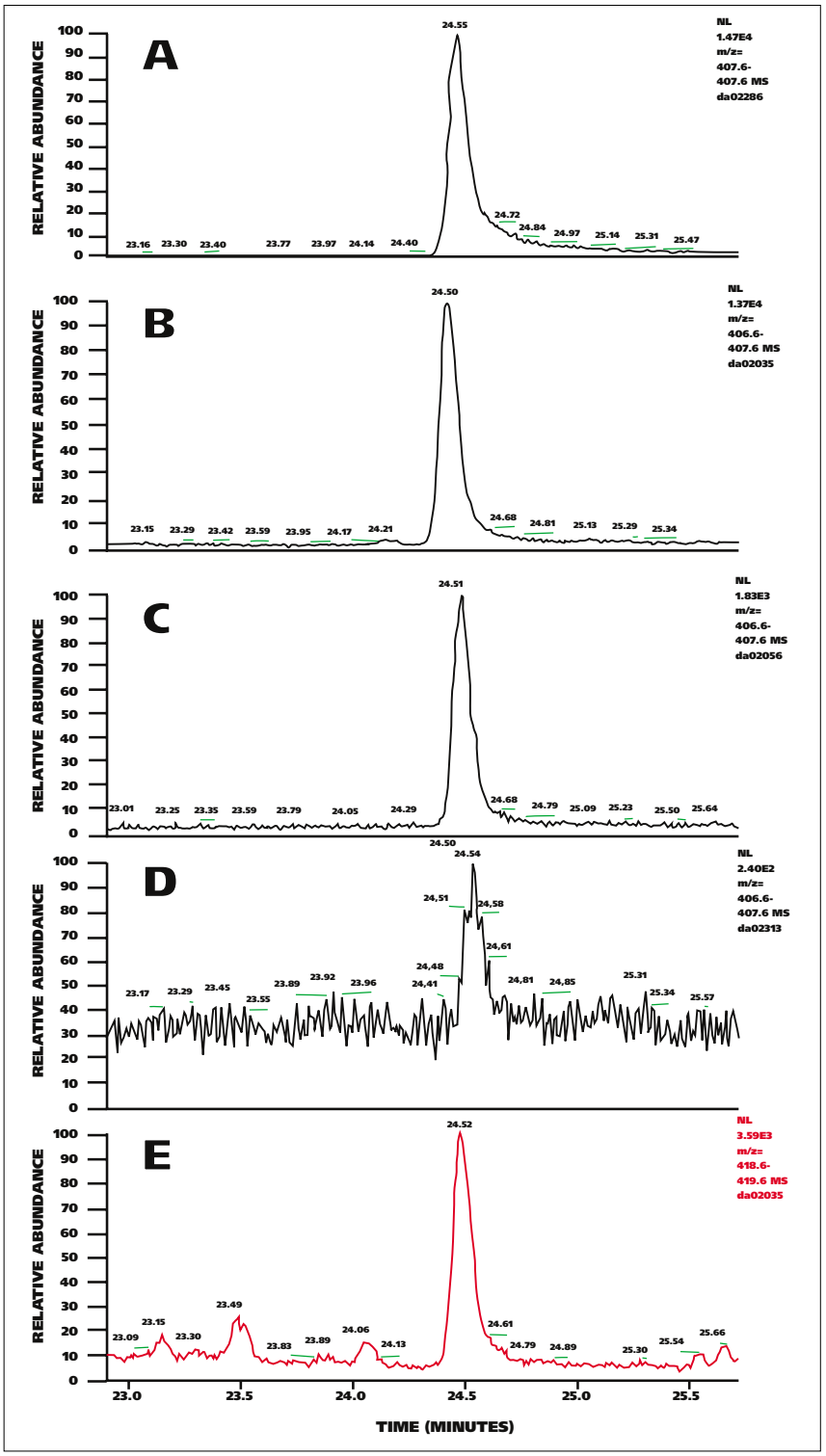

Figure 1. Mass chromatograms showing the elution of bisphenol A (BPA) extracted from various samples. **A.** A saliva sample (A) (2.1 nanograms per milliliter). **B.** A urine sample (B) (3.8 ng/mL). **C.** A spiked saliva sample (0.2 ng/mL). **D.** A water blank sample (< 0.1 ng/mL). **E.** The coeluting isotopically labeled internal standard. The blank sample has a discernible peak; however, the concentration was below our limit of detection and we subtracted its area from all quantified data as a laboratory background. Although the retention time varied up to six seconds among samples tested, the BPA peak always coeluted with the labeled internal standard.

jects treated with Delton LC had urinary BPA concentrations that were marginally significantly higher ($P = .0801$) than subjects treated with Helioseal F one hour after sealant placement and were significantly higher 24 hours after placement ($P < .0001$) (Figure 2B). Delton LC-treated subjects were about 12 times more likely than Helioseal F-treated subjects to have at least one urine sample taken after sealant placement that showed BPA concentrations exceeding the 95th percentile estimate (that is, 5.18 ng/mL) of urinary BPA concentrations for men in the general U.S. population.[47] One of the authors (A.M.C.) independently confirmed urinary BPA concentrations by means of another analytical method and laboratory (Figure 3, page 360).

After oral administration of BPA at low doses in humans, the BPA dose is recovered in the urine quantitatively as its glucuronide conjugate within 24 to 34 hours.[56] The half-life of elimination of BPA-glucuronide is 5.4 hours.[56] Using these pharmacokinetic data for BPA, and assuming a single point source exposure to BPA and an average daily urinary excretion volume of 1.5 L, we can obtain crude estimates of the acute dose of BPA after sealant placement. The background-adjusted dose estimates range from 0 to 239 µg with a GM of 52 µg. Delton LC-treated subjects had a GM estimated dose of 110 µg (range 49-239 µg); Helioseal F-treated subjects had a significantly lower GM estimated dose of 5.5 µg (range 0-9.5 µg; $P < .0001$).

We examined regression models to determine the relationships among covariates. The model that best accounts for the difference seen between pretreatment and immediate posttreatment saliva BPA concentration was adjusted for race, age, sealant brand, sealant weight and number of sealants ($P = .0211$).

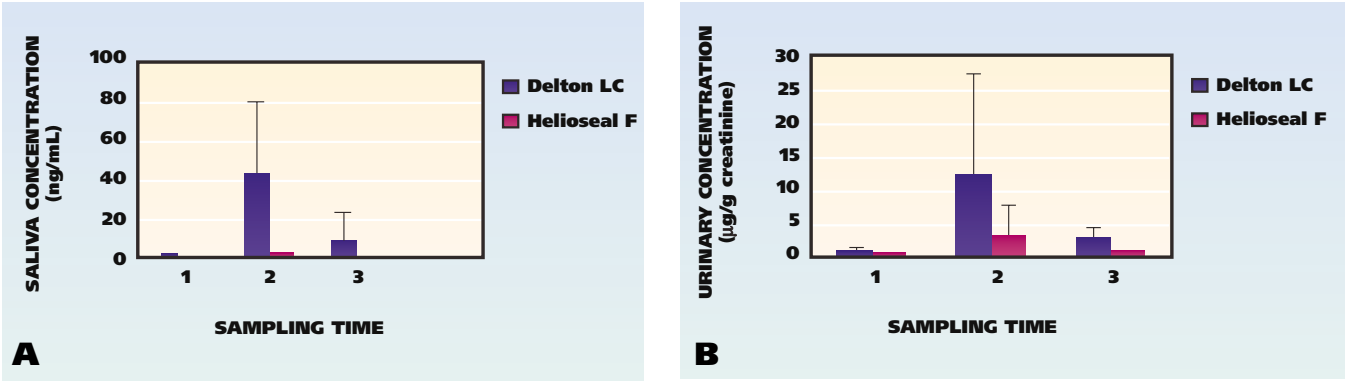

Figure 2.A. Salivary concentrations of bisphenol A (BPA) before sealant placement, immediately after sealant placement and one hour after sealant placement. **B.** Urinary concentrations of BPA before sealant placement (sample 1), and one (sample 2) and 24 (sample 3) hours after sealant placement. Delton LC: Delton Light Cured Opaque (LC), manufactured by Dentsply/Ash, Dentsply International, York, Pa. Helioseal F is manufactured by Ivoclar Vivadent, Amherst, N.Y. ng/mL: Nanograms per milliliter. µg/g: Micrograms per gram.

Urinary BPA concentrations one hour after treatment were significant when we adjusted them for the number of sealants placed (P = .0226), but not when we adjusted them for the weight of sealant or the amount of sealant use for each tooth. In addition, urinary BPA concentrations one hour after treatment were statistically significant when we adjusted them for the number of sealants placed and the brand of sealant (P =.0377), but it was not significant when we adjusted them only for the brand. Urinary BPA concentrations 24 hours after treatment were significant when we adjusted them for sealant type (P = .0045) and weight of sealant (P = .0301).

DISCUSSION

We detected BPA in all baseline (pretreatment) saliva samples tested. Detection of BPA in the saliva sample of a single dental patient before sealant placement[2] has sparked debate.[15] In 1996, Olea and colleagues[2] excluded a female patient from their study because BPA was detected in her saliva before sealant placement, even though she had had sealants applied two years earlier. Although they did not explicitly state so, the authors implied that the BPA had leached from the previously applied sealant.[15] Because BPA in the body is not appreciably protein-bound,[31] circulating BPA conceivably could be transferred from arterial plasma into saliva.[57-59] Furthermore, baseline concentrations of urinary BPA in our study are similar to those found in the general U.S.,[47] Japanese[46,60] and Korean[48] populations potentially resulting from environmental exposures, suggesting that the baseline salivary BPA concentrations in our subjects were derived similarly. Thus, the baseline saliva BPA concentrations likely reflect an integrated measure of environmental exposures to BPA including those from water and food packaging.

Immediately after placement, we observed a dramatic increase in the salivary BPA concentrations of subjects treated with Delton LC. Our findings regarding Delton LC sealants are consistent with the results reported by Arenholt-Bindslev and colleagues[14]; however, the sensitivity of our analytical method was much greater than that of their method, allowing us to detect BPA even one hour after treatment when saliva BPA concentrations approached baseline levels.

The saliva BPA concentrations we found after sealant placement are significantly—approximately 1,000 times—lower than those previously reported by Olea and colleagues[2] but are within the range reported by Fung and colleagues[12] and Sasaki and colleagues.[13] Two potential reasons exist for these discrepancies. The analytical methodology used by Olea and colleagues[2] involved high-performance liquid chromatography with ultraviolet detection. This technique is largely nonselective and prone to overestimation of results because of interfering components, inaccurate peak selection or underestimation of results owing to poor sensitivity. However, Fung and colleagues[13] used a method similar to that used by Olea and colleagues but obtained results that are more similar to ours. We independently confirmed our analytical measurements to avoid such controversy. Furthermore, Olea and colleagues placed a comparatively large amount of sealant (50 mg) to facilitate detection. The use of a larger amount of sealant than was clinically necessary could lead to an overestimation of the exposure potential for normal sealant placement,

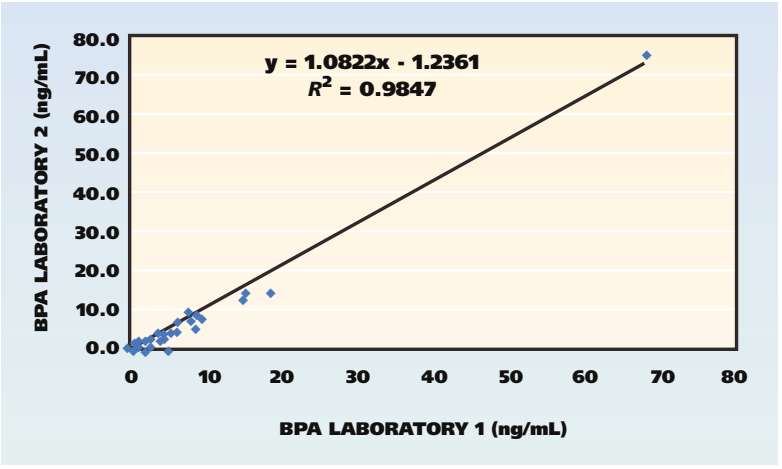

Figure 3. Comparison of urinary bisphenol A (BPA) concentrations measured in two independent laboratories using two separate analytical methods (N = 36). ng: Nanograms. mL: Milliliter.

in which a smaller amount of sealant may be used. However, Sasaki and colleagues[13] used twice the amount of sealant that Olea and colleagues[2] used, yet measured concentrations more similar to those we report here. Likely, salivary BPA measurements in our study and two previous studies[12,13] more realistically represent saliva concentrations after normal sealant placement than those reported by Olea and colleagues.[2]

Urinary excretion of BPA did not correspond directly with saliva levels; however, we usually observed the highest urinary BPA concentrations in the same patients with the highest saliva BPA concentrations. Furthermore, one-third of the urinary creatinine concentrations used to adjust urinary BPA concentrations were unusually large,[61] resulting in lower creatinine-corrected concentrations than would otherwise have been obtained. Because we eliminated a potentially significant amount of the exposure to BPA by taking saliva samples immediately after sealant placement, the urinary measurements likely underestimate the total exposure to BPA. In fact, the one participant who did not have a saliva sample taken directly after sealant placement had the highest urinary BPA concentrations observed in this study. Thus, our crude estimates of BPA dose for subjects treated with Delton LC probably were low. Helioseal F sealants did not appear to create significant BPA exposure.

BPA is completely eliminated from the body within 24 to 34 hours after low-dose exposures.[56] Because our results indicate that one hour after Delton LC sealant placement, salivary BPA levels are close to pretreatment levels, BPA exposures from Delton LC are likely acute, low-level exposures, with little or no exposure after the initial placement. Furthermore, active stimulation and elimination of saliva immediately after sealant placement, such as we did in our study, likely will reduce or eliminate BPA exposures resulting from Delton LC placements.

Our study has several limitations. The sample size is small, and we limited participants to military personnel, so caution should be used in any generalization of our findings. In fact, we documented that 73 percent of the creatinine concentrations in our study participants were higher than the 90th percentile for the U.S. population, regardless of race, sex and age,[61] highlighting the difference between our study population and the general U.S. population. Also, we did not collect urine samples at the time of peak urinary excretion and stopped collecting saliva samples one hour after sealant placement. Furthermore, the removal of BPA from the body through saliva sample collection immediately after treatment may have limited our ability to obtain statistical significance in the urinary BPA concentrations one hour after treatment in the group treated with Delton LC. Regardless, this study was prospectively designed, so we were able to determine the BPA solely on the basis of sealant placement and arrive at crude estimates of the total BPA exposure. Because health effects in rodents exposed to low doses of BPA have been reported increasingly in the literature,[32] human health-effect studies resulting from these low-dose exposures also should be conducted.

CONCLUSIONS

BPA leaches from Delton LC, a sealant without the ADA Seal of Acceptance, but negligible amounts leach from Helioseal F, which carries the ADA Seal of Acceptance. After Delton LC placement, saliva BPA concentrations increased dramatically. Furthermore, urinary BPA concentrations remained elevated for at least 24 hours after placement. Crude dose estimations show that acute BPA doses from Delton LC placement may result in low-dose exposures that are within the range at which estrogen receptor–mediated effects are seen in rodents. Further research is necessary to determine if human health effects can result from such exposures.

Dental sealants can remain an effective tool in

preventive dental care, especially if a sealant that leaches little or no BPA is used. Furthermore, BPA exposures can be effectively reduced by rubbing the sealant surface and removing the resultant stimulated saliva after dental sealant placement.

Dental sealants play an essential role in prevention of caries, especially in high-risk groups. The present study emphasizes the need for additional clinically relevant research to further identify sealants that may lead to exposure. It would be appropriate to reformulate the implicated sealants or modify handling procedures and guidelines for use to mitigate the leaching of components. ■

Dr. Joskow participated in this study while assigned to the Centers for Disease Control and Prevention, National Center for Environmental Health, Division of Environmental Hazards and Health Effects, Health Studies Branch.

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