Amalgam has been the material of choice for restoring posterior teeth for more than 100 years. The past 25 years have witnessed significant advances in restorative materials themselves and in the bonding systems for retaining a restoration in the prepared tooth. As a result, there has been a shift toward resin composite materials during this same period because of concerns about the esthetics and biocompatibility of dental amalgam. In addition, other materials such as glass ionomer cements, ceramic inlays and onlays, and gold alloys have been used as alternatives to amalgam. This article will review recent studies on the longevity and biocompatibility of these alternatives to dental amalgam.
Restoration Longevity

Assessment of Longevity

When comparing restoration choices, the issue of restoration longevity must be addressed. Ironically, assessing restoration longevity is not as straightforward as it might first appear, because there are many variables and various ways of addressing this issue. Two major systematic reviews of the literature on restoration longevity that have been published in the past few years3,4 (the Chadwick et al. report has been summarized in several other publications5,6,7). A systematic review is a special type of review article that methodically seeks out all the relevant studies on a particular subject of interest, evaluates the design and methodology of each study according to predetermined criteria, and summarizes the results of the highest quality studies. The authors of both of these systematic reviews have discussed the challenges encountered in synthesizing and drawing conclusions from the available literature.3,8

The types of studies that are useful in assessing restoration longevity are called “cohort studies.” A cohort study is designed to obtain information about a conceptual population — such as “all individuals that have restorations in one or more of their teeth” — over a long follow-up period. Cohort studies are also called “longitudinal studies.” A cohort study is conducted by sampling a subset of such individuals and drawing inferences about the entire population. Studies in which the study groups, or cohorts, are identified prior to the follow-up period and data are collected at intervals during the follow-up period, are referred to as prospective. Studies in which the cohorts are identified after a conceptual follow-up period and data are collected by recall on one occasion, are called retrospective. A prospective longitudinal study is generally referred to as a historical cohort study.9

Another type of epidemiologic study is the cross-sectional study. In contrast to cohort (longitudinal) studies, a cross-sectional study involves information pertaining to a single point in time. A cross-sectional study, as usually defined, provides a “snapshot” of conditions at a particular point in time.11 A cross-sectional study would be useful in assessing, for example, numbers of restorations of a given type are present in the mouths of people in different age groups — i.e., how many amalgams, how many resin composites, etc.12 The line between cross-sectional studies and retrospective (historical) cohort studies is blurred when retrospective longitudinal data are collected in a cross-sectional survey.13 The key factor that distinguishes whether such a study should be considered cross-sectional or historical cohort is whether records are available (as opposed to participants’ mere recollections) for the retrospective identification of study participants, the classification of the exposures of interest, and the follow-up of the participants for the relevant outcomes.10 If such records exist and are used in the study, it is considered a historical cohort (retrospective longitudinal). Many studies on restoration longevity that are classified (even by their authors) as cross-sectional, are perhaps more properly classified as historical cohort (retrospective longitudinal) studies. This distinction is important, because retrospective longitudinal studies are considered of greater validity and higher quality than cross-sectional studies in assessing restoration longevity.3 In fact, it would be virtually impossible to use a true cross-sectional study, as properly defined, to assess restoration longevity.

An example of a cohort (prospective longitudinal) study would be the study of restorations placed by one or a few practitioners, usually under controlled conditions (e.g., size of the restoration, placement technique, type of material). The restorations are then evaluated at periodic intervals thereafter. The advantages of prospective studies is the ability to control variables, including variables in placement and preparation techniques, types of materials, and variations in operators. One of the most important aspects of a prospective study is the ability to make random assignments of subjects to treatment group to avoid selection bias. In a prospective comparison of amalgam and composite materials, for example, the selection of the type of material to restore a given tooth would best be determined randomly. The reason is that restoration size has been shown to affect longevity, with smaller restorations lasting longer.3 If, for example, operators in a study of restoration longevity consciously or unconsciously tend to select amalgam rather than composite for larger cavities, then the study results will be biased against amalgam, because larger restorations tend to fail sooner than smaller ones. Random assignment of restoration type ensures that selection bias does not affect the study results. The disadvantages of prospective studies include the difficulty in recruiting and managing the large numbers of study subjects required, the expense of conducting a large clinical study, and the high dropout rate — which is typically more
Most studies have shown that resin composite restorations do not last as long as amalgam restorations. 

Resin composite

Retrospective Studies

Most studies have shown that resin composite restorations do not last as long as amalgam restorations. A 2001 study showed the median age of over 1,800 failed amalgam restorations was nearly 12 years but slightly less than five years for more than 1,500 failed resin composite restorations. A 2000 study of nearly 1,200 failed resin restorations was only eight years, with amalgam outlasting composite for Class 1, 2, 3, 4, and 5 restorations. A 1999 study of more than 9,000 restorations showed that amalgam outlasted resin composite for Class 1, 2, and 5 restorations, and a 1998 study showed the median age of a replaced amalgam restoration was 15 years versus only eight years for a replaced resin composite. A group of researchers in 2002 used an insurance claims database to study more than 207,000 replaced amalgam and more than 93,000 replaced composite restorations and found that resin composite restorations were significantly more likely to fail than amalgam restorations, but observed that “composite fared almost as well as amalgam.”

Prospective Studies

In a 2001 prospective study of 194 small Class 1 and 2 hybrid composite fillings, 46 fillings were available for review after 10 years. Failures were the result of total or partial filling loss, bulk fracture, or secondary caries. A minimum of 53.5 percent (and a maximum of 74.2 percent, based on the dropout of some patients in the study over the years) were clinically acceptable, confirming “the clinical safety of posterior composite restorations.” In a 1998 prospective study of 90 posterior resin composite restorations, Mair reported 56 were available for 10-year review, and none failed. Raskin et al. reported on 100 posterior resin composite restorations placed and reviewed after 10 years. At 10 years, 37 were available for review and 32 had failed, mostly because of loss of occlusal anatomic form or proximal contacts. The authors estimated the actual failure rate to have been between 40 percent and 50 percent.

Review Articles

Hickel and Manhart, in an 2001 comprehensive review article on longevity of posterior restorations, described annual failure rates of 0 to 7 percent for amalgam restorations, 0 to 9 percent for direct composites, 1.4 to 14.4 percent for glass ionomers, 0 to 5.9 percent for cast gold inlays and onlays, and 0 to 11.8 percent for ceramic or composite inlays. These results were similar to a 2000 review article they also published. The problem with pooled studies that give annual failure rate ranges for various restorations is that they tend to favor materials with shorter-term and/or smaller studies versus longer-term and/or larger studies. For example, a three-year study of 10 resin composite restorations with no failures will give a perfect 0 percent annual failure rate, even if three restorations failed over the following two years (30 percent failure after five years), which would have given a 6 percent annual failure rate. If five of the restorations fail over the following seven years (50 percent failure after 10 years), then the annual failure rate would have been 10 percent. On the other hand, a much larger, longer-term 10-year study of 100 amalgam restorations with 10 failures (10 percent failure after 10 years) would give a higher annual failure rate of 1 percent versus the perfect 0 percent failure rate of the short-term three-year study of 10 resin composite restorations cited above. Brunthaler et al. noted that “favorable results for composite mate-
Clinical Issues

Proximal Contacts

One challenge with posterior composites as compared to amalgam has been the operator’s ability to achieve acceptable proximal contacts in Class 2 cavity preparations. As an answer to this problem, packable composites were introduced to handle like amalgam. These composites can be “packed” into the cavity preparation, but they have not been shown to yield better proximal contacts than conventional composites.31 However, there are devices such as the Contact Pro, BiTine rings, and ceramic inserts that have been effective aids in achieving acceptable proximal contacts.32 After reviewing 24 prospective studies on posterior resin composite performance published between 1996 and 2002, Brunthaler et al. found that isolation method (rubber dam or cotton rolls) and packability of the composite material had no effect on restoration success.24

Wear

In the past, posterior composite materials were plagued by much lower wear resistance than amalgam,33 but improvements in posterior composite materials have led to clinically acceptable wear resistance.34-36 Even with the

Table 1

<table>
<thead>
<tr>
<th>Material</th>
<th># studies</th>
<th># short-term studies (≤15 years)</th>
<th># long-term studies (≥15 years)</th>
<th># small studies (≥100 restorations)</th>
<th># large studies (&gt;1000 restorations)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amalgam</td>
<td>34</td>
<td>5 (14 percent)</td>
<td>20 (59 percent)</td>
<td>4 (12 percent)</td>
<td>9 (26 percent)</td>
</tr>
<tr>
<td>Resin composite</td>
<td>24</td>
<td>14 (58 percent)</td>
<td>6 (25 percent)</td>
<td>7 (29 percent)</td>
<td>1 (4 percent)</td>
</tr>
<tr>
<td>Glass ionomer</td>
<td>16</td>
<td>12 (75 percent)</td>
<td>2 (12.5)</td>
<td>7 (44 percent)</td>
<td>0 (0 percent)</td>
</tr>
<tr>
<td>Cast gold</td>
<td>14</td>
<td>1 (7 percent)</td>
<td>9 (64 percent)</td>
<td>4 (29 percent)</td>
<td>5 (36 percent)</td>
</tr>
<tr>
<td>Ceramic or composite inlays</td>
<td>47</td>
<td>38 (81 percent)</td>
<td>2 (4 percent)</td>
<td>32 (68 percent)</td>
<td>1 (2 percent)</td>
</tr>
</tbody>
</table>
newest composite materials, however, greater wear than amalgam is apparent after two years.37

Postoperative Sensitivity

Postoperative sensitivity in Class 1, 2, and 5 resin composite restorations has been a problem and a cause of restoration failure. Christensen described several methods to prevent such sensitivity, including perfect use of the total-etch technique, tooth desensitizing solutions, flowable resins, high-viscosity bonding agents, resin-reinforced glass ionomer liners, and using multiple layers of bonding agent.38 He stated that the introduction of self-etching primers, which do not remove the smear layer, has virtually eliminated the problem of postoperative sensitivity.38 Two recent clinical studies that examined whether self-etching adhesives result in less postoperative sensitivity than total-etch adhesives were not able to demonstrate a difference between the two methodologies.39,40 Both studies found virtually no postoperative sensitivity with either technique, so if postoperative sensitivity is observed more often clinically with total-etch adhesives, it may be attributable to their greater technique sensitivity.40

Secondary Caries

Secondary caries has been the leading cause of resin composite restoration replacement in several studies.16,41,42 A five-year comparative prospective study showed a higher incidence of secondary caries in Class 2 composite restorations than in Class 2 amalgam restorations,43 possibly because composite resin components may contribute to plaque formation44 and the levels of cariogenic bacteria at the margins of composite restorations have been shown to be higher than at those of amalgam restorations.45

Although glass ionomer cements offer greater ease of placement than composites and have been advocated in caries-prone patients because of their fluoride-release, they have not been considered to possess adequate mechanical properties to function as long-term definitive restorations.22 Paradoxically, in spite of the fluoride release which occurs from glass ionomer restorations, studies have shown that the leading cause of failure of glass-ionomer restorations has been secondary caries. The most frequent reason for replacement of 278 glass ionomer restorations studied in 1997 was secondary caries.46 The median age of 309 failed glass ionomer restorations studied in 2001 was slightly more than four years, with secondary caries the leading cause of restoration failure.14 In a 2000 study of the replacement of 662 glass ionomer restorations in Norway, secondary caries was the most common reason for glass ionomer restoration replacement.47 The authors observed, “the anticariogenic effect of glass ionomer is limited and may be insignificant.” A systematic review of 28 papers on the putative secondary caries treatment effect of glass-ionomer restoratives did not reach any conclusion about the validity of such an effect.48 Despite the observation that glass ionomer appears to exert an anticariogenic effect in laboratory studies, Papagiannoulis et al. found that “no preventive effect was exerted in vivo from the glass-ionomer to protect the adjacent enamel wall from secondary caries attack.”49 The median age of 409 replaced glass ionomer restorations was only three years and two years for 156 replaced resin-modified glass ionomer restorations.15 The median age of 262 failed glass ionomer restorations in a 1999 study was three years, with secondary caries being the leading cause of failure.16 In all these studies where restoration longevity was analyzed, the median age of failed resin composite exceeded that of failed glass ionomer. Therefore, there is little or no advantage in sacrificing the esthetics of resin composite for the fluoride release of glass ionomer, even in caries-prone patients. Manhart et al. stated, “Glass ionomers can be considered only as long-term provisional restorations in stress-bearing posterior cavities.”34

Cost-effectiveness

Smales et al.50 calculated that amalgam fillings are 3.8 times more cost-effective than gold crowns, and Mjör51 has stated that amalgam is the most cost-effective dental restoration material. The authors of a systematic review of restoration longevity performed an economic evaluation and concluded that “amalgam clearly dominates composite and inlays across all time periods considered because it is cheaper and has better survival.”52 They estimated that composite “was between 1.7 and 3.5 times more expensive than amalgam to generate one tooth year.”5
Biological risks

Patient Risks

Estrogenicity Issue

The “estrogenicity issue” for resin composites and sealants was first raised in 1996 in work performed by Olea et al. at the University of Granada and Tufts University. The purpose of their work was to determine whether compounds derived from restorative resins or sealants based upon bis-GMA (bisphenol-A diglycidylether methacrylate, “Bowen’s resin”) could exhibit estrogenic activity — i.e., whether chemicals or breakdown products derived from these resins could mimic the activity of endogenous steroidal estrogens. Chemical compounds that mimic the activity of endogenous steroidal estrogens are called xenoestrogens. Xenoestrogens form the largest subset of the 48 endocrine-disrupting chemicals (EDCs) — compounds that can mimic or antagonize the actions of hormones — recognized by the Centers for Disease Control and Prevention. It is well established that EDCs can cause alterations in development, growth, and reproduction in wildlife that are exposed to them. Olea et al. suggested that xenoestrogens “are also being implicated in human infertility, genital tract malformations, and increased cancer rates in estrogen target tissues,” and concluded their paper by stating, “In view of the documented exposure to bis-GMA-based composites and sealants used in dental treatments for adults and children, the use of these xenoestrogens should be reevaluated.”

The publication of the Olea et al. paper generated considerable concern. The original focus of concern was on the compound bisphenol-A (BPA), and debate initially centered on whether BPA did or did not leach from dental resins. Bisphenol-A is an aromatic compound that is widely used in the plastics industry and that has been known for decades to be a xenoestrogen. It is present in some dental resins as an impurity residue from the manufacture of bis-GMA or as a breakdown product of other compounds. As this issue has been further investigated, other compounds besides bisphenol-A that leach from dental resins have also been found to be estrogenic. Even bis-GMA itself has been shown to exhibit modest estrogenic activity in a mouse animal model, although this observation may have resulted from impurities in the bis-GMA. Currently, there are no standard methods to determine whether a chemical is estrogenic or not.

Cytotoxicity and Other Effects

It has been known for some time that dental resin composites release substances which are toxic to cells and which alter cell function. Leaching from composites occurs as a result of two overlapping processes, 1) the short-term release of unpolymerized material from the composite after curing and 2) the long-term release of breakdown prod-
ucts of set polymer. Salivary enzymes (esterases) are thought to play a major role in the breakdown of the set polymer. Synergistic action of esterases has been shown to increase the biodegradation of dental resin composites beyond a simple additive effect. Many organic compounds can be extracted from set dental composites in water and/or methanol, even without the use of esterases. Composites and comomers have been shown to exhibit severe cytotoxicity even after aging in artificial saliva (aging times studied were 0, 7, and 14 days). As noted above, of particular note in this study was the discovery that cytotoxicity continues even when HPLC-UV shows no significant mass release versus Teflon controls. A study of flowable composites and core materials used a longer aging time in artificial saliva (aging times studied were 0, 1, 2, and 4 weeks), but all materials were found to be "severely cytotoxic" in cell culture at all aging times.

The cytotoxicity of five glass ionomer cements and resin-modified glass ionomer cements has been studied recently by de Souza Costa et al. They found that all of the materials were cytotoxic in cell culture, but that the conventional GICs were less so. They remarked that the RMGICs "caused intense cytopathic effects on the cultured cells decreasing significantly the cell metabolism as well as causing remarkable cell death." The adverse biological effects of UV light are well recognized, but the use of blue light has been regarded among dental personnel as having few effects on tissues other than the retina. However, Wataha et al. demonstrated that exposure of cells to blue light disrupted cell mitochondrial function (as assessed by succinic dehydrogenase activity), an effect that persisted for the entire 72-hour post-exposure observation period. They concluded that their results indicated "that dental photocuring lights pose at least some risk to oral cells" and that further study was warranted.

### Allergenicity

Several cases of allergic reaction to components of resin composites have been reported in the literature. One clinical report presented an unusual response of acute gingivostomatitis caused by contact sensitivity to the methacrylate compounds present in a dental restorative material. Another report described an intra-oral lichenoid lesion closely approximating anterior restorations. In a study of patients who had positive reactions to the standard Bis-A epoxy resin, 20 percent of these patients exhibited cross-reactivity with other epoxy acrylates. The most common reaction was to Bis-GMA.

A recent report of an adverse reaction unit for dental biomaterials in Norway examined the frequency of positive patch test results among 296 patients referred for clinical evaluation because of reaction to or concern about dental biomaterials. A surprising finding was that gold contact allergy was the second most frequent at 23 percent (after nickel at 28 percent). Interestingly, patients were slightly more likely to be allergic to one or more resin composite ingredients (8 percent), than to mercury (6 percent).

### Blue Light

The adverse biological effects of UV light are well recognized, but the use of blue light has been regarded among dental personnel as having few effects on tissues other than the retina. However, Wataha et al. demonstrated that exposure of cells to blue light disrupted cell mitochondrial function (as assessed by succinic dehydrogenase activity), an effect that persisted for the entire 72-hour post-exposure observation period. They concluded that their results indicated "that dental photocuring lights pose at least some risk to oral cells" and that further study was warranted.

### Occupational Risks

**Allergenicity**

In a Swedish study of dental personnel who were referred to the Department of Occupational and Environmental Dermatology in Stockholm, allergies to acrylates were the most common as determined by patch testing. Reactions to HEMA (2-hydroxyethyl methacrylate), EGDMA (ethylene glycol dimethacrylate) and MMA (methyl methacrylate) were most frequent. Hand eczema was the main manifestation of allergy, but one case of allergy to HEMA and other methacrylates produced asthma and rhinocon-
junctivitis that were sufficiently severe to force a cessation of work with methacrylates. Unfortunately, dental exam gloves do not tend to form an effective barrier against many of the allergens encountered in dental practice. One study measured the resistance of five types of dental gloves (latex, powder-free latex, coated latex, polychloroprene, and polyvinyl chloride) to permeation by six different dental monomers (methyl methacrylate [MMA], 2-hydroxyethyl methacrylate [HEMA], triethyleneglycol methacrylate [TEGDMA], ethyleneglycol dimethacrylate [EGDMA], urethane dimethacrylate [UDMA], and Bis-glycidyl methacrylate [Bis-GMA]). Four of the monomers tested (MMA, HEMA, TEGDMA, and EGDMA) permeated all the gloves tested. Another study found that the “protection of the poorest glove [against HEMA] was comparable to that of the positive control (no glove).” Andreasson et al. evaluated the permeability of various types of gloves to methyl methacrylate (MMA), 2-hydroxyethyl methacrylate (HEMA) and triethyleneglycol dimethacrylate (TEGDMA) and made recommendations regarding glove selection.

Respirable Dust

A study of the dust generated during finishing of composite restorations found that between 14 percent and 22 percent of the dust generated was respirable. Although some dental masks appear to be capable of filtering out a high percentage of respirable particles, the average is in the range of 40 percent to 50 percent. Concern has been expressed about the use of intra-oral air abrasion technology and its accompanying potential exposure to respirable particulates. However, two studies have demonstrated that the quantity of respirable dust generated is insufficient to pose a health hazard. The aggregate effect of all sources of particulates may be a concern in the dental office, however. A recent study of dental clinics found that respirable particulate matter exceeded ambient standards by a factor of 2 to 6. Of particular note was the observation of these elevated levels throughout the building, not merely in dental operatories. Thus, dental office personnel without masks would be exposed to respirable particles.

Summary and Conclusions

It has been argued for more than 20 years that when the variety of possible and actual systemic effects are considered along with local reactions at the implant site, no fully biocompatible material can be said to exist. Even gold alloys and ceramic materials — long considered the most biocompatible — have been shown to have significant biological liabilities in certain individuals. Over the past 20 years or so, various anti-mercury groups have fought to effect a ban on the use of dental amalgam. As no fully biocompatible material exists, this would appear to be a short-sighted objective. Not only would a ban on dental amalgam limit choices for the dentist and dental patient, but it would eliminate the only material that certain patients — those with allergies to components of resin composites and/or to gold alloys — may be able to tolerate.

For the vast majority of patients, amalgam still appears to be the most cost-effective and longest-lasting restorative material for posterior teeth. For those desiring a more esthetic alternative to amalgam, resin composites appear the best choice, although biocompatibility issues remain to be resolved. Glass ionomer cements offer greater ease of placement than composites and have been advocated in caries-prone patients because of their fluoride-release, yet they have not been considered to possess adequate mechanical properties to function as long-term definitive restorations. Because of the lack of definitive evidence for an anticariogenic effect of fluoride release from glass ionomer materials in vivo, there would appear to be no advantage in sacrificing the superior esthetics and greater durability of resin composite for the fluoride release of glass ionomer, even in caries-prone patients. Ceramic and
gold restorations have their place as amalgam alternatives under certain circumstances, particularly where the restoration is large, but both of these treatment modalities are considerably more expensive than a similarly sized amalgam.

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