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Contemporary Adhesive Bonding: Bridging the Gap between Research and Clinical Practice

Abstract: The dawn of minimally invasive dentistry has led to the development of materials which rely on the use of effective adhesion to bond to remaining tooth tissue. Successful adhesive bonding is dependent upon appreciating the quality of the dental substrate, appropriate clinical handling of the material and patient, together with an appreciation of the chemistry of the adhesive. This paper outlines the current status of contemporary bonding, with particular emphasis on translating laboratory-based evidence into clinical practice. Using laboratory-based evidence, the ability of a bond to achieve a seal to enamel appears to be the best predictor of clinical performance.

Clinical Relevance: This article discusses the issues raised when translating research data about adhesive bonding from the laboratory to clinical dental practice.

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The term adhesion is defined as 'the force that binds two dissimilar molecules together when they are brought into intimate contact'.

The evolution of restorative materials has seen the dentist's repertoire shift towards materials which are dependent on reliable adhesive bonding, inherent strength and aesthetics, namely the resin-based adhesive materials.² These require a mechanism to allow adhesion to remaining tooth tissue because they lack the inherent chemical self-adhesive capacity of materials like glass ionomer cements. In comparison to enamel bonding, dentine bonding has had a more problematic development, with clinically adequate adhesion achieved later than

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that to enamel. Despite making important advances, dentine bonding still has many hurdles to overcome with respect to the water content, structural heterogeneity of the substrate and the long-term stability of the bond. Nevertheless, the fact that adhesives can be placed at all in such a hostile environment and function with their intended purpose speaks wonders for the modern innovations and developments in the field of adhesive dentistry.

Successful bonding requires a full understanding and control of three intimately related factors illustrated in Figure 1:

- The dental substrate being adhered to;
- The chemistry of the adhesive being used: and
- The clinical handling of the bonding system and patient.

This represents the 'golden triangle' for successful bonding.

Dental substrate (Figure 2)

Healthy tissues

The primary factor within

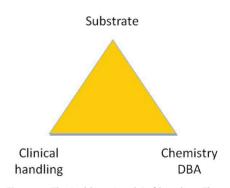


Figure 1. The 'golden triangle' of bonding. These three inter-connecting factors are necessary to achieve a satisfactorily performing bond.

the 'golden triangle' of bonding is the substrate being adhered to. This not only incorporates the dental hard tissues in their virgin states, but also their states as a consequence of the carious process, trauma or toothwear. Enamel and dentine present separate challenges to bonding. The heavily mineralized prismatic structure of sound enamel is in contrast to the tubular, organic and hydrophilic nature of dentine. The latter

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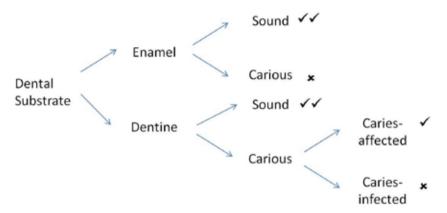


Figure 2. Potential dentine bonding substrates. Bonding to carious enamel is not recommended as the unsupported and often undermined prismatic structure prevents the formation of an adequate seal and often leads to cohesive failure with the enamel. The irreversibly damaged structure of caries-infected dentine also provides an inferior substrate for binding owing to the lack of its structural integrity and high risk of cohesive failure within the tissue, as well as a lack of sufficient hybrid layer formation. The reversibly damaged deeper caries-affected dentine can provide an adequate substrate for bonding, especially when surrounded by a periphery of more healthy dentine and enamel.

has ensured a more problematic bonding history, with generations of dentine bonding agents failing to achieve successful clinical performance.3 Dentine is a more complicated substrate to bind to because of its heterogeneous nature. Perdigão discussed not only the limitations of cariesaffected dentine as a substrate for bonding, but also other variables, including the physiological process of ageing producing intra-tubular hypermineralized dentine which makes adhesion more difficult.4 An increase in the number of tubules towards the pulp, coupled with an increased wetness due to pulpal pressure, means bonding to deeper sound dentine, closer to the pulp, can also be compromised.5

Carious enamel

The enamel and dentine substrates, as a result of the carious process, present very different bonding problems. It is accepted that adhesion to sound enamel is a prerequisite to successful bonding. Carious enamel with its unsupported prismatic structure prevents formation of an adequate seal. This weakened enamel structure is unable to withstand the shrinkage and stresses generated by the photo-curing of resin-based materials and, as a result, allows the ingress of the plaque biofilm through pores within the defective enamel structure, ie cohesive microleakage.

Further complications are associated with the potential of 'secondary' caries to develop along defective marginal interfaces where the plaque biofilm can stagnate and ultimately further compromise tooth structure.6

Carious dentine

Carious dentine can be subdivided into two distinct pathophysiological zones:

- The peripheral caries-infected zone (close to the enamel-dentine junction (EDJ), irreversibly damaged, necrotic and softened by long-standing bacterial contamination and proteolytic denaturation of collagen and acid demineralization of the inorganic component, and
- The deeper caries-affected zone, reversibly damaged by virtue of the carious process, which has the potential to repair under the correct conditions as the collagen is not denatured. The soft, wet necrotic nature of caries-infected dentine means it is an inferior chemical, ultrastructural and physical substrate for bonding, whereas the potentially repairable caries-affected dentine has been shown to exhibit adhesive bonding potential, especially when surrounded by a periphery of sound dentine and enamel. 8

It is important to appreciate that using the principles of minimally

invasive dentistry may often lead to less carious dentine excavation than past caries excavation rationales based on a mechanistic approach to maximize material retention within the cavity. Modern cavities will exhibit surfaces with different qualities of enamel and dentine histology within the same cavity and these tissues will require handling in different ways in order to optimize adhesive bonding. Indeed, delineating between the layers of caries infected and affected dentine within a carious lesion clinically is rather subjective at present. Caries-infected dentine is sticky and soft to a sharp dental explorer, whereas caries-affected dentine is a little more tacky (scratchy and sticky) in nature and blends down to the hard, scratchy consistency of sound dentine.6 Indicator dyes are being developed, using sulphurcontaining bacterial products to highlight the increased bacterial load present in caries-infected dentine, but these have yet to be validated in vivo.

Chemistry of dentine bonding agents (DBAs)

A common classification of dentine bonding agents is by way of describing their chemical composition through their generations of scientific research and development. This can be confusing as the classification sheds little light on the mechanism underlying how the bonding agent is working. In contrast, the simpler classification in Figure 3 assigns any commercial dentine bonding agent to one of four types, depending on the presentation of its chemical components:

- Etch;
- Primer;
- Bond; and
- Their handling of the smear layer.

Etch

Acid-etching with 37% orthophosphoric acid dissolves or modifies the smear layer, an adherent layer of organic/inorganic debris of 1–2 μm thickness caused by heat and frictional forces generated during cavity preparation.9 It demineralizes the hydroxyapatite structure in enamel and dentine unevenly, allowing micro-mechanical retention of the flowable resin adhesive into the pores

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| Туре | Smear layer | Etch | Primer | Bond | Clinical examples |
|---|----------------|------|--------|------|---|
| 1 3-step total etch (4 th generation) | Remove | | | | Adper Scotchbond MP, Optibond FL |
| 2 2-step etch- and-rinse (5th generation) | Remove | | | | Optibond Solo, Prime & Bond NT, XP Bond, iBond TE, Adper Scotchbond 1 XT |
| 3 Mild self- etch | Dissolve | | | | Liner Bond 2V, Clearfil SE Bond, Protect Bond |
| (6th generation) | | | | | Silorane SE (stronger self-etch primer) |
| 4 Strong self- etch (7 th generation) | Dissolve | | | | Fuji Bond LC, G Bond, Tri-S Bond (milder self-etch primers) |
| | | | | | Adper L-Pop Prompt, Xeno III, iBond, One Up Bond F Plus |

Figure 3. A classification of dentine bonding systems into four types, dependent upon the presentation and use of the etch, primer and bond components of the adhesive systems and their effect on the smear layer.⁶ A selection of UK clinical examples have been provided but this list is by no means exhaustive (current at the time of publication).

created and, as a result, increases the surface area for bonding to be achieved.

Primer

The primer's bi-functional chemical structure provides a mechanism to bond hydrophobic resin components to hydrophilic tooth substance, with a secondary component or 'carrying medium', often a solvent, allowing infiltration and diffusion of unfilled resin into the moist dentine collagen substrate.⁶

Bond

The bond (or adhesive), often similar chemically to the overlying resin composite matrix, diffuses into the demineralized enamel and dentine structure and, on polymerization, forms micro- or nano-mechanical interlocking by way of resin tags in mineral porosities, widened dentine tubule orifices and within the exposed collagen fibrillar network (hybrid layer). Dentine bonding is quite literally underpinned by the formation of

a hybrid layer; a 3–8 μm layer of exposed dentine collagen lattice which is infused with primer and resin monomer.¹⁰

Etch-and-rinse adhesives

Type 1 and 2 etch-andrinse DBAs are characterized by their separate etching stage in which 37% orthophosphoric acid is applied to sound enamel and dentine substrates (20 and 10-15 seconds, respectively) and then removed by thorough rinsing with water. This total-etch process removes the smear layer. The next steps consist of separate prime and bond stages for type 1 bonding systems and a simplified combined step for the type 2 systems. 11 The primer's function is achieved by manipulation of the monomer to allow it to function in both hydrophilic and hydrophobic environments. An example of such a bi-functional monomer is hydroxy ethyl methacrylate (HEMA) which, by virtue of its low molecular weight, is able to diffuse into the substrate more easily and surmount the hydrophilic barrier, enabling the unfilled resin to bond to tooth structure. Other bi-functional monomers used in a variety of commercial dentine bonding agents include 4-methacryloxyethyl trimellitate (4-MET),¹² 10-methacryloxydecyl dihydrogen phosphate (10-MDP) and 2-methacryloxyethyl phenyl hydrogen phosphate (phenyl-P).¹³

Self-etch adhesives

Type 3 and 4 DBAs endeavour to obtain a similar bond with enamel and dentine but present a different solution of how to deal with the smear layer. Instead of removing it in a separate etch step, the smear layer is instead penetrated, dissolved and incorporated into the final adhesive interface. These bonding systems consist of a combined self-etching primer with differing pHs and either a bond step, which is separate (type 3), or combined with the primer (type 4); UK examples of which have been given in Figure 3.

Unlike the etch-and-rinse adhesives, there is more scope for variation between bonding performance between systems, as there are variations in the

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acidity of the functional primer monomer. Briefly, the self-etch adhesives can be subdivided, based on their acidity, into strong (pH < 1), moderate (pH \approx 1.5) and weak (pH > 2). As expected, the degree of acidity has an impact on the amount of demineralization of hydroxyapatite and collagen network exposure. Strong acidic monomers resemble type 1 bonding systems, whereas milder ones cause less demineralization of hydroxyapatite, with potential clinical consequences (see later).

Clinical handling of DBAs

Type 1 – the 'gold standard'

As noted by Van Meerbeek et al., 2008¹⁵, type 1 bonding systems are described by many as the 'gold standard', especially in regards to enamel bonding often achieving a strong, stable bond with excellent marginal seal.¹⁶ The potential drawback of type 1 DBAs is the more complex clinical application procedure, both time consuming and open to contamination because of the number of separate steps involved (individual etch, primer and bond stages). However, evidence exists that the bond integrity is better maintained over time and is less prone to hydrolytic degradation.¹⁷

Type 2 – total etch/etch-and-rinse DBAs

A necessity in achieving adequate bond strengths with type 2 systems is to prevent the exposed dentine collagen scaffold collapsing after excessive air drying post-rinsing of the separate acid etch step. This technique is termed 'moist bonding'. The term 'wet bonding' is best avoided as this implies the substrate should be completely saturated with water. Clinical techniques that may be employed to remove the gross 'puddles' of water in the cavity, whilst leaving sufficient moisture within the outer layers of the etched dentine, may include blotting the cavity gently with cotton wool pledgets (or wide ends of paper points in smaller cavities) after an initial two second blast with the 3–1 air/water syringe. However, the difficulties in achieving this balance between complete desiccation and excessive moisture makes type 2 bonding particularly operator technique sensitive.18 It must be noted that this balance is also

an issue with type 1 bonding, but to a lesser degree, as the type 1 primer often contains water which has the ability to rehydrate over-dried dentine collagen. Furthermore, the solvent used to carry the type 2 primer into the moist environment needs to be fully evaporated before photocuring. Loguercio et al¹⁹ noted significantly higher bonding strengths after the removal of the solvent, with failure to remove it compromising ultimate bond strengths. The type of solvent also plays a role in the retention rate of the adhesive, with ethanol/ water-based systems possibly achieving better retention than acetone/water-based ones, shown in a study after 36 months.20 A possible explanation for this centres around the water content in some of these primer systems preventing excessive dessication by stabilizing the exposed collagen structure.

Types 3 and 4 - the 'self-etchers'

The intended benefits of selfetch adhesives are to reduce the number of bonding stages and facilitate the removal of operator-dependent clinical error. Yet, the intended benefits come at a price. It has been noted that some self-etch adhesives require more water to function as an ionization medium for the functional monomers.21 With more water comes the potential for insufficient polymerization, increased water absorption, increased longterm staining, decreased colour stability²² and more rapid hydrolytic degradation over time.23 These issues appear to be associated, especially with the type 4 bonding systems. It has been shown that type 4 DBAs are able to act as semi-permeable membranes, allowing water to move through the adhesive,^{24,25} with water trees present in the adhesive interface leading to the premature hydrolytic degradation of the bond. In vitro experiments have shown almost complete delamination of the adhesive layer at the substrate surface.26 Other observations have noted reduced bond strengths culminating in inferior mechanical properties, especially when associated with minimally invasive cavities.15,27

Mechanism of bonding

Enamel bonding

The mechanism by which bonding is achieved to enamel is by virtue

of the acid etch removal of the smear laver and demineralization of the surface layers of hydroxyapatite structure, leading to loss of prismatic and interprismatic structure. The introduction of hydrophobic resin or dentine bonding agent and its subsequent polymerization initiates the formation of micro-mechanical retention by way of resin tags within the surface porosities. The importance of the peripheral seal achieved to enamel has been described by many authors and reinforces the importance of binding to healthy enamel substrate. The positive seal also confers an element of medium-term protection to the more vulnerable dentine bond.15

Dentine bonding

The mechanism of bonding to dentine concerns either modification or removal of the surface smear layer. The priming stage bridges the gap between the hydrophobic monomer and hydrophilic substrate to form the hybrid zone, which consists of a network of interlocking monomer and hydroxyapatite-free collagen fibrils, which form the important nanomechanical retention zone. There is also some resin penetration of the partially opened dentine tubules, which contributes to an element of micro-mechanical retention. Neither the thickness of the hybrid layer, nor the penetration of resin tags into the dentine tubules, seem to play a significant part in the resulting strength of the bond, but the overall integrity and completeness along the full interface is of greater importance.28 There are 'milder' self-etch adhesives (eg Clearfil SE, Kuraray, Japan) which develop chemical interactions between the hydrophilic carboxylic and phosphate groups, which can bond ionically to calcium ions in the hydroxyapatite structure.29 It is suggested that nano/ micro-mechanical retention provides resistance to initial stresses associated with polymerization shrinkage and functional activity, whereas the chemical component of bonding may influence the medium- to long-term durability and survival of the adhesive in these materials.30

Glass ionomer cements

Glass ionomer cements (GICs) exhibit auto-adhesive chemical bonding, allowing them to bind to dentine and

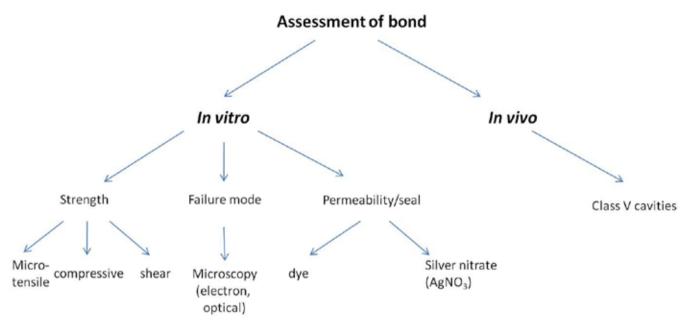


Figure 4. Methods used to assess/test adhesive performance. *In vivo* performance is assessed commonly using Class V cavities, where the lack of macromechanical retention and the presence of both sound enamel and dentine permits relevant assessment of how well the adhesive performs. The highly evolving nature of bonding agents mean *in vitro* experiments are often carried out to predict clinical performance. Experimentation ranges from analyses of bond strength, determining where the bond is likely to fail, to assessing the permeability of a bond using molecules that can diffuse through deficiencies within the adhesive/tooth interface.

enamel substrates by merit of their specific glass ionomer acid-base interaction. The weaker polyacrylic acid component causes limited demineralization of the enamel and dentine and results in minor micromechanical interlocking. The important retentive component is initiated by virtue of ionic chemical adhesion between calcium ions in hydroxyapatite and the backbone of polyacrylic acid.³¹ This multi-stage process takes minutes to set the material initially, but takes several weeks/months to achieve full maturity.

What causes a bond to fail?

The potential for ingress of water and saliva at the adhesive/tooth interface causes hydrolysis of the bond.³² Saliva, together with its constituent enzymes, water and bacterial enzymes may lead to plasticization of the resin bond, with subsequent leaching and degradation. A bond which resists permeability has the potential to resist this degradation. Endogenous dentine metallomatrix proteinases (MMPs) have been shown to be activated in the acidic environment of the carious process and possibly during

dentine bonding procedures.³³ These MMPs can degrade the hybrid layer over time and result in decreased longevity of resin-based restorations.³⁴ Management strategies have focused around inhibiting these enzymes by including MMP inhibitors in the primers of adhesives.³⁵ Brackett *et al* noted placing 2% chlorhexidine digluconate (an MMP inhibitor) after the etch-and-rinse step before the placement of adhesive inhibited degradation and did not affect immediate microtensile bond strength.³⁶ However, much research in this interesting field remains to be carried out.

Where is the evidence?

Promotional literature for DBAs frequently provides technical information on the performance of the product. This information can range from the strength of the bond to its permeability performance. These figures are predominately based on data extracted from *in vitro* laboratory studies and are interpreted as a means of illustrating or predicting long-term clinical performance. The fundamental question posed is what relationship exists

between this laboratory-based evidence and the real clinical performance of the adhesive? Figure 4 outlines the relationship of the investigatory procedures available to researchers for the assessment of the quality and longevity of the adhesive bond.

In vitro vs in vivo evidence

It is apparent that the true test of how an adhesive performs is to place it in its intended role, namely in the clinical setting, and assess the relative success of its outcome.37 Such tests will undoubtedly prove to be decisive in determining the performance of a bonding system as the bond is subjected to the full spectrum of onslaughts the oral environment has to offer. The contrasting argument for clinical in vivo experimentation is the highly evolving nature of bonding systems. Competition, in addition to advances in adhesive technology, means the commercial life expectancy of a bonding agent in the majority of cases is suggested to be 3-5 years.38 Therefore, by the time clinical longevity data is available, the adhesive is likely to have been surpassed by a newer product, rendering the original

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results obsolete. Further arguments against clinical studies are their time consuming nature, together with the cost implications of running such investigations.

In vitro studies – an ideal compromise?

In vitro studies are often the favoured method of assessing bond performance as they provide data rapidly and are less taxing logistically to perform. These studies, if designed appropriately, have been shown to be a successful predictor of clinical performance.16 However, laboratory experimentation is not a replacement for clinical studies as they are often restricted to studying only one or two tested variables. This is coupled to the fact that intra-oral conditions have to be simulated artificially, if at all. Problems also arise owing to the enormous variation in testing methods applied. Therefore, caution has to be taken when comparing data from different sources, as subtle differences between procedures can produce startling differences in results. Van Noort advised care when interpreting data from in vitro studies so as not to make unfounded extrapolations of clinical performance based on one type of laboratory experiment.38 Ideally, an array of in vitro data is needed to predict performance from diverse types of testing. Figure 4 illustrates the different methods used to assess adhesive bond performance. With a bewildering amount of in vitro information available, it is important to identify the relevant data and consider them in the correct context.

Bond strength

Arguably, the most familiar quality assessed when judging adhesive performance, the bond strength, seems a rational feature to quantify when considering the efficacy of an adhesive in the binding of two dissimilar molecules. The higher the strength of the adhesive the more tightly the two substrates are bound. However, the bond strength is often extrapolated directly and used alone incorrectly as a predictor of long-term clinical performance.

There is no standardized procedure to determine bond strength.³⁹ Methods vary on the basis of what aspect of strength is being tested, whether it

be microtensile, compressive or shear. Complications also exist with the origin of the bonding substrate. Hard tissues can be derived from human, bovine or artificial sources, all with potentially different properties affecting the bond strength. Additionally, the mechanical preparation of the substrate has been shown to have a profound effect on the bond strength. For example, carious dentine removed with hand-held spoon excavators exhibit reduced bond strengths when compared with those removed with Carisolv[™] gel.⁴⁰ The lack of standard protocols and array of variables mean wide variation in bond strengths have been recorded with the same adhesive from different laboratories around the world. What can be surmised from the resulting data of bond strength experiments, however, is that the higher the value, the lower is the probability of shortto medium-term failure.

Longevity/failure mode

The primary mode of failure for adhesive restorations has been described as the loss of marginal adaptation and loss of retention.14 Microscopy provides a mechanism whereby the failure mode of a material can be assessed. Scanning electron microscopy (SEM) can be used to assess at what interface failure has occurred in relation to tooth/adhesive interface, within the adhesive or within the restorative material or tooth itself. However, interpreting SEM images is difficult owing to the extensive sample preparation and artifact generation, meaning differentiating between the bond, composite, enamel and dentine can often only be achieved by very experienced researchers. Fluorescent optical confocal microscopy has the advantage of reducing and simplifying sample preparation and permitting samples to undergo sub-surface analysis, the depth dependent upon the translucency of the tissues being photographed. Use of a variety of trace fluorescent markers with differing excitation and emission wavelengths offers the potential to create images of the labelled adhesive interface through a cross-section of a tooth, so permitting analysis of the mode and locus of potential failure, either immediately after placement or after 6-month storage periods.41

Permeability/sealing ability

The longevity of the bond is affected by microleakage of oral fluid into the interface⁴² and thus has been described as a more clinically relevant predicator of bond survival.43,44 Microleakage can be observed using an array of trace dyes or silver nitrate (AgNO₃) photographed using fluorescence microscopy. The depth and pattern of penetration is then used as an indicator of the micropermeability of the adhesive. A degree of caution over data interpretation is required as, with bond strengths, there is no standard protocol in the experimental procedure.39 Furthermore, there are doubts regarding adequate sampling of the specimens. Conventional imaging techniques view a 2-D slice of a 3-D sample, and therefore maximum penetration of tracer dve may be underestimated or not representational.

The phenomenon of nanoleakage was identified by Sano et al45 where, by placing a sample in a solution of AgNO₃, it was noted that small molecules or ions were present in the hybrid layer without the presence of actual gap formation. The samples were photographed using transmission electron microscopy (TEM) and SEM to show areas of AgNO₃ infiltration.⁴⁶ The significance of this finding was that the presence of water molecules has the potential to degrade the bond by hydrolysis of the monomer components and collagen to a lesser degree.⁴⁷ Over a period of time this leads to the failure of the bond. Nanoleakage has been shown to increase in vitro when bonds are subjected to synthetic ageing processes.48

However, it has been argued that most, if not all, adhesive interfaces show some degree of nano-leakage, whilst exhibiting acceptable clinical longevity.⁴⁷ The importance nano-leakage has on bond longevity should not be discredited, but caution should be used when using it as a predictor of adhesive performance using methods in their current form.

Artificial ageing

Analysing 24-hour bond strength and permeability is important, but a fundamental requirement of any bonding system is to maintain its integrity over a prolonged time period. Methods have been developed to mimic the intra-

oral environment in a way to show how the bond performs. It should be noted that the array of variables an adhesive would experience *in vivo*, such as pH changes, wetness, heat and mechanical forces, are impossible to mimic entirely *in vitro*, in the correct combinations.

A common strategy is to place extracted teeth in a storage medium such as phosphate-buffered saline for a range of time periods (from 24 hours to 24 months at 37°C). Variables, including permeability, can then be measured and comparisons made over time. Monticelli et al identified that ageing increased the amount of dye penetration, with time indicating a breakdown at the adhesive interface and thus attenuation of the marginal seal. Dye permeability was most severe in the dentine substrate compared to enamel, highlighting that enamel bonding is more stable over time.49 It has been reported that, after 3 months, adhesives placed in water show similar correlation with the morphological changes observed in vivo.50

Alternative strategies for synthetic ageing include thermo-cycling mechanical wear/stress and degradation by enzymes. 14,51

In vivo tests

The true test of adhesion is how well it performs in its intended function, namely the retention of a restoration to tooth structure. As noted previously, the disadvantages of *in vivo* trials include their time consuming nature, high labour cost and lack of information with regards to the mode/locus of failure. Furthermore, it is impossible to control every patient-related variable, such as abrasion, occlusal wear, diet, coupled with the configuration factor of the cavity itself. 52

Non-carious Class V restorations are deemed to be the true test of adhesive performance as no macro-mechanical retention is available and the restoration margins exist in both dentine and enamel. 14 Retention, microleakage and marginal integrity are considered key factors in determining adhesive performance. 53 Clinical evidence has been compiled by Van Meerbeek *et al* regarding the long-term performance of adhesive systems, where it was concluded that the type 3 self-etching, two-bottle systems produce comparable,

if not better, longevity outcome data than type 1 adhesives, if coupled with an enamel pre-etching step to ensure an optimal bond to sound peripheral enamel.¹⁶

Conclusions

- Achieving an effective bond, no matter how advanced the chemistry, depends on the correct clinical handling, combined with bonding to the most suitable substrate. Carious enamel and caries-infected dentine are both inferior substrates for bonding and should be avoided wherever possible. Caries-affected dentine is a valid bonding substrate potentially, especially when surrounded by peripheral healthy enamel. The most stable bond is that achieved via bonding to healthy enamel.
- Evidence suggests that type 1 DBAs are still the gold standard for enamel bonding, whereas the adhesion achieved with milder self-etching type 3 DBA agents (including an enamel pre-etch stage), with their capacity to bond mechanically and chemically, are preferred for dentine bonding.
- It is possible to predict how DBAs will function *in vivo* through a variety of different test procedures. However, no test is completely conclusive and the large degree of variation in experimental procedure means caution is needed when interpreting data.
- The long-term integrity of an adhesive remains the Achilles' heel of adhesive bonding due to micro-/nano-leakage, enzymatic degradation and hydrolysis. In the future, methods will need to focus around attenuating these factors to improve the life expectancy of the adhesive bond and aim to extend the restorative life of resin-based materials.

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