

Abstract

Current concepts in dental adhesion

The use of restorative materials along with the adhesive techniques has become routine in today's dental practice. However, the longevity of the adhesive restorations mainly depends on good bonding between restorative material and tooth structure, which should be achieved *in situ*, within minutes. While bonding to enamel is reliable through micromechanical retention, bonding to dentin presents challenges due to the moist structure of dentin. Contemporary adhesive techniques are based on the removal of the smear layer, (etch-and-rinse adhesive systems), or incorporation of smear layer, (self-etch adhesive systems), into the bonded interface. There are also restorative materials with adhesive properties as glass-ionomer as well as newly introduced luting cements. Attempts to simplify the number of steps in adhesive systems have resulted in compromises in terms of bonding effectiveness, mechanical properties and shelf-life. Good resin encapsulation of the etched dentin is essential to minimize the degradation. Additional therapeutic agents such as chlorhexidine might increase the durability of resin-dentin bonds *in vitro*.

Key words:
Dental
restoration;
dental bonding;
adhesives;
longevity

Current concepts in dental adhesion

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Adhesive techniques have improved substantially during the last decades and are now involved in most dental restorative procedures. At the same time, it is not always easy to achieve a good seal due to the different properties of enamel and dentin. Enamel-resin bonds, produced after acid-etching with phosphoric acid, have shown to be satisfactory and stable over time (1). This is due to the absence of collagen and to the high mineral content (96 % hydroxyapatite by weight) in enamel, and to its dryness relative to dentin. Adhesion to dentin, on the other hand, has been difficult to achieve and is less durable (2-4). Dentin contains a significant amount of water and organic material, mainly type I collagen (5). Dentin, being organic and with a tendency to retain moisture, is difficult to bond.

Cavity preparation results in the formation of a loosely attached 1-5 μm thick debris, »smear layer«, on the tooth surface (6). As smear layer constitutes an unstable barrier the smear layer can be removed by acid-etching, or it can be made stable by adhesives that can penetrate through the smear layer in order to have a more stable bonding. The conventional adhesion strategy involves etch-and-rinse adhesives, which removes the smear layer and superficial hydroxyapatite through separate etching and relies on micromechanical interlocking. The second strategy involves self-etch adhesives, which makes the smear layer permeable without removing it (Table 1). The mechanical interlocking is shallower compared to etch-and-rinse adhesives, and additionally some of them chemically interact with residual hydroxyapatite similar to that of glass ionomers. A third strategy uses materials with an inherent capacity to bond to tooth structure, such as glass ionomer cements and newly developed self-adhesive luting cements (7).

Etch-and-Rinse adhesive system

Etch-and-rinse adhesive systems are the most commonly used for bonding and they include either three or two steps of application

Adhesive systems

Bonding strategy	Adhesive system name	Manufacturer
Three-step-etch-and-rinse adhesive systems - Acid etching with (usually) 37 % phosphoric acid - Rinsing; drying, with surface left slightly moist (shiny) - Application of primer - Evaporation of solvent - Application of adhesive resin - Air-thinning of adhesive resin - Light curing	Adper Scotchbond Multi-Purpose	3M ESPE, Seefeld, Germany
	All Bond 2/ All Bond 3	Bisco Inc., Schaumburg, IL, USA
	ProBond	Dentsply, Konstanz, Germany
	OptiBond/Optibond FL	Kerr, Orange, CA, USA
	Gluma Solid Bond	Heraeus Kulzer, Hanau, Germany
	Solobond Plus	VOCO, Cuxhaven, Germany
	Syntac	Ivoclar Vivadent, Schaan, Liechtenstein
	Clearfil Liner Bond	Kuraray Medical Inc., Tokyo, Japan
Two-step etch-and-rinse adhesive systems - Acid etching with (usually) 37 % phosphoric acid - Rinsing; drying, with surface left slightly moist (shiny) - Application of primer/adhesive resin - Evaporation of solvent - Light curing	Adper Scotchbond 1XT (Single Bond Plus)	3M ESPE
	One Step/ One Step Plus	Bisco
	Optibond Solo Plus/ Optibond Solo Plus Dual Cure	Kerr
	Gluma Comfort Bond	Heraeus Kulzer
	Prime and Bond NT/ Prime and Bond NT dual cure	Dentsply
	Solobond M	VOCO
	Clearfil New Bond	Kuraray
	HelioBond	Ivoclar
	Superbond C&B	Sun Medical Co., Shiga, Japan
Two-step self-etch adhesive systems - Application of an acidic primer - Evaporation of solvent - Application of adhesive resin - Evaporation of solvent - Light curing	Adper Scotchbond SE	3M ESPE
	All Bond SE	Bisco
	OptiBond Solo Plus self-etch	Kerr
	Clearfil SE Bond/ Clearfil Protect Bond Clearfil Liner Bond 2	Kuraray
	Peak Self-etch	Ultradent Products, Inc., Salt Lake City, UT, USA
One-step self-etch adhesive systems - Application of the acidic/primer adhesive resin - Evaporation of solvent - Light curing	Adper EASY Bond/ Adper Prompt L-Pop	3M ESPE
	Adhe SE One	Ivoclar Vivadent
	Optibond All-in-one	Kerr
	FuturaBond NR	VOCO
	iBond	Heraeus Kulzer
	Xeno V	Dentsply
	Clearfil S3Bond	Kuraray

Table 1. Examples of currently available etch-and-rinse and self-etch adhesive systems. The bonding strategies are described on a general level, and differences may occur e.g. in the number of recommended applications of primer and/or adhesive resin.



Smear layer removal

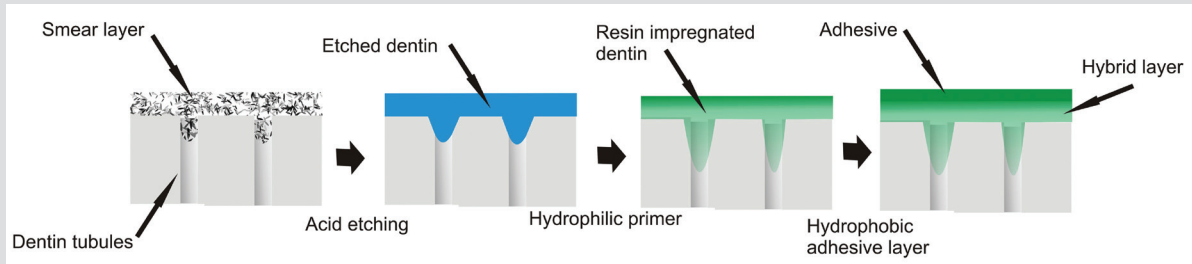


Fig. 1. In three-step etch-and-rinse adhesive systems, acid is used to remove the smear layer and smear plugs from the dentin and to remove peritubular dentin, increasing the diameter of tubules. The etched surface is then primed with methacrylate monomers in a solvent to expand and precoat the dentin matrix. Then a solvent-free, hydrophobic adhesive layer is applied that diffuses into the primed surface and down into the tubules, and light-cured.

(Fig. 1, Table 1). Dentin and enamel are treated first with an acidic gel to remove the smear layer and to demineralise the superficial hydroxyapatite crystals, and the remaining acid is rinsed away with water.

Etching step

Both three- and two-step etch-and-rinse adhesives rely on a similar adhesion mechanism. Enamel etching with 32-37 % phosphoric acid dissolves the apatite crystals and creates microporosities, increasing surface area and also surface energy, without any changes of the chemical composition of the surface (8,9). In dentin, acid treatment removes the smear layer and demineralises 5-8 μm of the intertubular dentin surface to expose the underlying collagen fibrillar matrix. However, in demineralised form dentin is very sensitive to drying, and when it collapses, it will prevent the adhesive permeation to create effective bonding (10). Therefore, a slightly moist environment was shown to increase the bonding and defined as wet-bonding technique.

Priming step

Conventional primers in etch-and-rinse adhesive systems consist of polymerizable monomers in an organic solvent such as ethanol or acetone (11). They include water and hydroxyethyl-methacrylate (HEMA)-rich solutions to ensure the expansion of the demineralised collagen matrix and wet the collagen with hydrophilic monomers. Re-expansion of the collagen matrix that has collapsed upon air-drying after acid-etching/rinsing step is essential to achieve a good bonding (12). The primer's function is to wet collagen fibril surfaces and to displace water to the full depth of demineralization.

The primer solvent is an important factor affecting the handling (13) and performance (12) of the adhesives. Water-based adhesives are believed to be the most forgiving regarding ap-

plicational errors, such as in the degree of dentin wetness or dryness. However, control of moisture may be difficult e.g. in deep dentin with wide open tubuli (14), and the water remaining in the interface (15) jeopardizes the durability. Therefore, water, or water-ethanol based primers require careful evaporation of the solvent (14). Acetone-based adhesives, on the other hand, have water-free formulations, but require challenging wet bonding technique. Due to the high vapour pressure of acetone, it may evaporate too quickly and may not be able to dehydrate the matrix.

Scanning electron microscopy

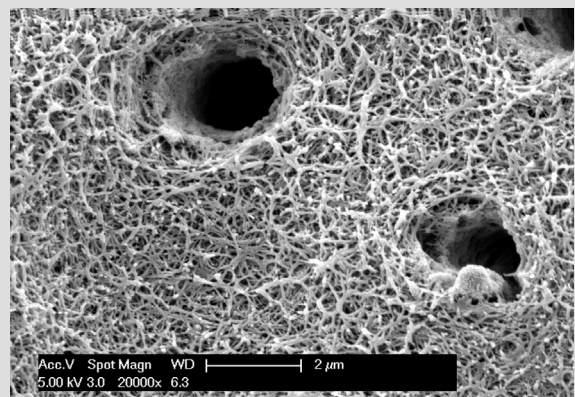


Fig. 2. Scanning electron microscope (SEM) image, showing the open dentinal tubuli and exposed collagen fibres after acid etching. This collagen matrix serves as a substrate for the hybrid layer formation (Photo: Dr. Franklin R. Tay, by permission).

Adhesive resin step

In three-step etch-and-rinse adhesive systems the bonding resin is normally solvent-free. A relatively hydrophobic adhesive layer covers the primed dentin encapsulating the exposed collagen fibrils (Fig. 2), resulting in the so-called hybrid layer. Solvent-free adhesives have water sorption and solubility values that are less than half that seen for two-step etch-and-rinse adhesives (16,17). In two-step etch-and-rinse adhesive systems, primer and adhesive resin are combined into the same liquid that therefore includes also solvated hydrophobic and hydrophilic monomers.

Problems related to etch-and-rinse adhesive systems

Despite the success of etch-and-rinse adhesive systems for enamel bonding, technique sensitivity in dentin bonding and inconsistency in collagen fibril encapsulation through the whole depth of the demineralisation zone led to the development of self-etch adhesive systems. Nevertheless, three-step etch-and-rinse concept adhesives are still today regarded as the »gold standard«.

Self-etch adhesive systems

Self-etch adhesive systems were developed to reduce the number of application steps in order to have more-user friendly adhesive systems (Fig. 3, Table 1). They are supposed to eliminate the risk of over-etching and over-drying. Self-etch adhesive systems do not require separate acid-etching and rinsing steps, since they are composed of aqueous mixtures of acidic monomers (such as phosphoric acid or carboxylic acid esters) that simultaneously etch and infiltrate enamel and dentin (11). As a result, the dissolved smear layer and demineralization products are not rinsed away, but incorporated in the hybrid layers (18,19).

CLINICAL RELEVANCE

Despite the increased number of simplified adhesives in the market, 3-step etch-and-rinse adhesives are still the »gold standard« for clinical use. Mild two-step self-etch adhesives show a clinically reliable bonding to dentin, selective etching of enamel is recommended for enamel bonding. One-step, (all-in-one), self-etch adhesives show often an ineffective clinical performance.

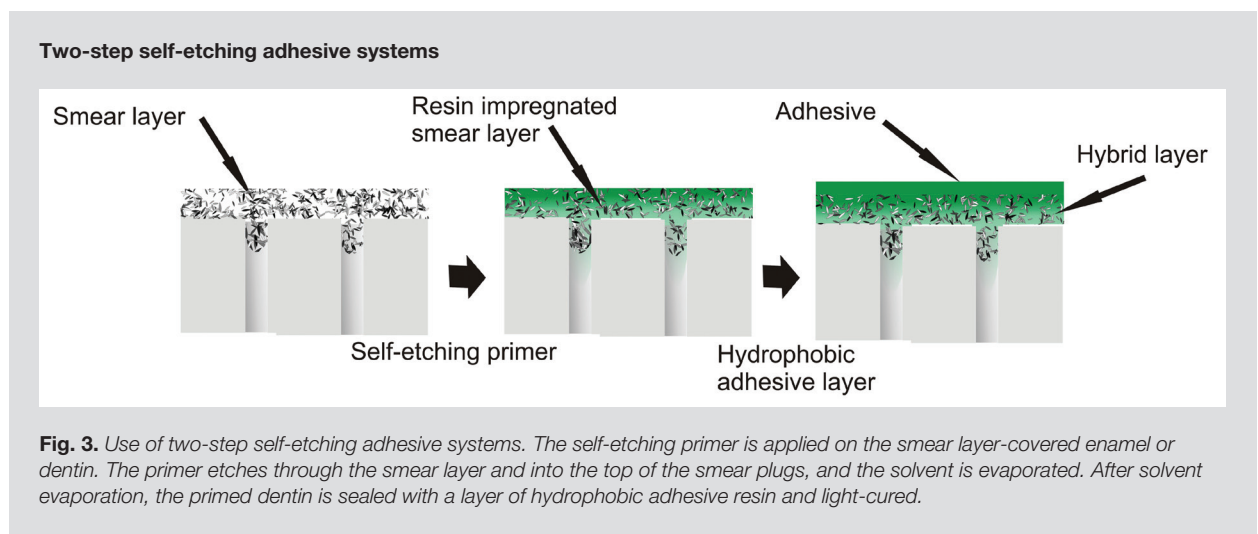
Two-step self-etch adhesive systems

In two-step self-etching adhesives, the first step includes acidic hydrophilic monomers that etch and prime the exposed collagen network. The second step includes a more hydrophobic adhesive resin. This second step makes the interface more hydrophobic and seals the bond more effectively.

One-step self-etch adhesive systems

In one-step (so-called all-in-one) adhesive systems, etching, priming and resin bonding components are all in the same mixture.

Water is an essential component of self-etch adhesives as it is needed in the ionization of acidic monomers. Total removal of water from the hybrid layer is unrealistic (20), raising concerns about the polymerization of the adhesive. This also applies to the high concentrations of solvent that may, in the case of incomplete evaporation, cause incomplete resin polymerization (21). The acidity of the self-etch adhesive systems range from pH 0.9 to 2.5; the self-etch adhesive systems can be classified as mild, moderate or strong according to the acidity (22). Therefore,



the etching effectiveness and pattern between these products may vary considerably. The use of strong (more acidic) self-etch adhesive is more favourable for the bond to enamel. Mild etching systems give better bonding to dentin, but demineralise enamel less effectively than traditional phosphoric acid. For some mild self-etch adhesive systems, the manufacturers also suggest selective enamel etching with phosphoric acid before the application of the adhesive.

Two-step and some one-step self-etch adhesive systems have relatively higher pH and result in shallower enamel demineralization compared to phosphoric acid. However, either roughening of enamel to remove prismless enamel or a separate phosphoric acid enamel-etching improves the enamel bonding ability of self-etch adhesives (23). While bonding to enamel might be a problem with mild agents, bonding to dentin with two-step self-etch adhesive systems has given results similar to those obtained by the »gold standard« three-step etch-and-rinse adhesives. Some two-step self-etch adhesives have shown an additional chemical interaction of carboxyl/ phosphate groups of functional monomer and hydroxyapatite (24). Good clinical results for some two-step self-etch adhesives have been reported (25,26). In general, selective enamel etching followed by a normal application of a two-step self-etch adhesive has been recommended for the best overall performance of the adhesives (26). Apart from the pH of the self-etch solution, other factors such as agitation during application, viscosity, thickness of the smear layer and wetting characteristics affect the resultant depth of demineralization and infiltration by self-etch adhesives (27,28).

Problems related to simplified etch-and-rinse and self-etch adhesives
Despite their user-friendliness and low technique sensitivity, simplified adhesive systems (two-step etch-and-rinse and one-step self-etch adhesive systems) have resulted in low bond strength in vitro (25,29) and less than ideal clinical outcomes (26). Due to their hydrophilicity, and lack of hydrophobic resin coating, cured adhesive layers may act as permeable membranes (30), permitting water movement across the adhesive layer when applied on wet dentin. Reticular patterns of nanoleakage (so-called 'water trees') have been found within the adhesive layer of simplified adhesives. They are considered as sites of incomplete water removal and subsequently suboptimally polymerised resins, which leads to lower bond strength and less durable bonding (30).

HEMA-containing formulations are prone to high water sorption, and upon polymerization, HEMA-water mixture forms hydrogel. On the other hand, HEMA-free formulations are prone to phase separations. This can lead to low bond strengths because of the formation of resin globules and poor resin tag formation and often results clinically in postoperative sensitivity. Additionally, the complex mixtures of hydrophilic and hydrophobic monomers and solvents in simplified adhesives, mainly in all-in-one adhesives, make them more technique sensitive. Air-drying is essential to remove the water and solvents as much as possible (31,32),

but might as well result in over-thinning of the adhesive layer at some parts of the cavity, and pooling of excessive adhesive layer in some other part (33). This results in non-uniform adhesive layers, and very thin areas are prone to the lack of polymerization due to the fast oxygen inhibition of thin layers (33). When restorative material is applied on top of this layer it might displace the adhesive, leaving the composite in direct contact with the hybrid layer. It is important to have a layer of cured adhesive between the restorative material and the hybrid layer to avoid the problems associated with thin oxygen-inhibited layers. Another consequence of the complex monomer mixtures is the in-the-bottle monomer degradation due to the hydrolysis of the ester groups of the resins (34), which limits their shelf life. To overcome this problem, some manufacturers use two-component one-step adhesives to keep water separated from the functional monomers until the time of application. These products thus require mixing of two components immediately prior to application (e.g. Adper Prompt-L-Pop, 3M ESPE, Futurabond NR, Voco).

Materials with adhesive properties

Restorative materials

Glass ionomer or resin-modified glass ionomer bonds to tooth structure through a specific chemical reaction combined with submicron hybridization (26). Glass ionomers are acid-base reaction cements containing a reactive ion-leachable glass base and an aqueous solution of polyalkenoic acid, usually polyacrylic acid. To improve the properties, resin-modified glass ionomers were developed with the addition of resin components into glass ionomer cements. Bonding of glass ionomer to tooth structure is mainly based on the chemical bonding through ion exchange, and the resin-modified version offers an additional micromechanical interlocking of the cement into dentin tubules. The adhesion depends both on a limited demineralization of enamel and dentin by polyalkenoic acid and infiltration, and on chemical adhesion between hydroxyapatite calcium and polyalkenoic acid. This results in a shallow hybrid layer formation (0.5-1 μ m) (7,26). The application of polyacrylic acid as a cavity conditioner improves the bonding through smear layer removal, demineralization of the tooth structure and also by chemical bonding with residual hydroxyapatite (35). The release, uptake and re-release of fluoride are thought to be important caries protective properties of glass-ionomers by preventing demineralization and in assisting remineralisation. So far, studies have shown over 90 % retention rates for up to five years in non-carious cervical restorations (36), and over 75 % survival even in load-bearing class II cavities (37).

Luting cements

Recently introduced luting cements with adhesive properties are considered as "self-adhesive materials" (26). Self-adhesive luting cements are relatively new and information on their compositions and adhesive properties are limited. They have multifunctional

monomers and phosphoric acid groups to achieve a simultaneous demineralization and infiltration of dentin and enamel. The reactions, (similar to those in glass-ionomer cements), of phosphoric acid with alkaline fillers result in a setting material, (38). However, interaction with dentin is superficial and no hybrid layer formation is observed (39). While adhesion to dentin seems still acceptable, enamel adhesion seems to be the much lower than in the conventional systems (38).

Degradation of resin bond to dentin

The limited durability of resin-dentin bonds is caused partially by hydrolysis of the hydrophilic resin components as a result of water sorption and swelling, and possible esterase attacks from saliva (17,40), and partly by the degradation of exposed collagen fibrils by endogenous matrix metalloproteinases (MMPs) derived from demineralised dentin (41,42). MMPs are a group of enzymes that collectively are able to degrade extracellular proteins, including collagen, and dentin contains several members of MMP family (43-45). They are normally inactive in the mineralised dentin matrix but acid-etching or application of self-etch adhesive systems uncovers and activates MMPs (41,46). Both *in vitro* and *in*

vivo studies have indicated that MMP inhibition in the hybrid layer with chlorhexidine is a promising approach to improve the durability of the resin-dentin bond with etch-and-rinse adhesives (47-49). However, clinical restoration survival data on the effect of such treatment is not available. Currently, only limited data is available on the long term effect of CHX, however, studies treating acid-etched dentin for 30-60 sec with 0.2 to 2 % chlorhexidine show around 1.9 % loss in bond strength compared to 5 % loss in no-treatment groups (Fig. 4). CHX has also been able to eliminate the reduction of bond strength *in vivo*: after 14 months in clinical service, bond strength of CHX-treated composite fillings reduced only 1.5 %, while in the control group the reduction was 35 % (49). While chlorhexidine is already in clinical use, other approaches to inhibit dentinal MMPs have also been studied with promising results (50,51).

Clinical recommendations

Bonding to enamel is still best accomplished using the etch-and-rinse approach. The *in situ* polymerization of adhesive resins in the etched pits creates a durable micromechanical interlocking. The enamel bond not only effectively seals the restoration margin but also protects the vulnerable dentine bond against degradation. Bonds formed to enamel with etch-and-rinse systems are strong and durable because their ability to wet and impregnate etched enamel is efficient.

In etch-and-rinse adhesive systems, evaporation of solvents is a critical step. Ethanol-water based primers applied on blotted-dry dentin, followed by proper evaporation of the solvent, may be the safest approach.

Both three-step etch-and-rinse adhesive systems and mild two-step self-etch adhesive systems show a clinically reliable bonding to dentin. In general the clinical performance of three-step etch-and-rinse adhesive systems are superior than that of two-step, and two-step self-etch adhesive systems are superior than one-step (all-in-one) self-etch systems. One-step (all-in-one) self-etch adhesive systems show often an inadequate clinical performance.

Effect of chlorhexidine on adhesive bond strength

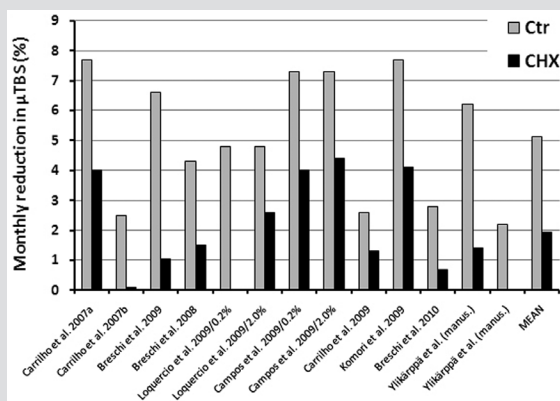


Fig. 4. The effect of chlorhexidine (CHX) on microtensile adhesive bond strength in studies with comparable study design. 10 *in vitro* studies and one *in vivo* study in humans (49) used the same adhesive (Adper™ Scotchbond™ 1, 3M ESPE) and similar CHX treatment (0.2 % or 2 % CHX solution applied on acid etched cavities prior to adhesive application). For the two studies using both 0.2 % and 2.0 % CHX concentrations the outcomes are presented separately. The bars indicate the percentage of loss of bond strength per month of the duration of the study (from six to 24 months) for the controls and CHX-treated samples. Mean values indicate the mean monthly bond strength loss of the controls (5.1 %) and CHX-treated samples (1.9 %).

Abstract (English)

Contemporary tooth-coloured filling materials

Tooth coloured materials dominate restorative treatments in the Nordic countries today. The most recent developments have concentrated on monomers and filler particles. The present article discusses composition of and results from laboratory studies on contemporary materials with specific focus on nano-composites and the clinical relevance of laboratory studies. Furthermore, polymerization by LED light curing units and the risk of release of hormone-like chemicals from composites are briefly discussed.

Referanser

1. Frankenberger R, Tay FR. Self-etch vs etch-and-rinse adhesives: effect of thermo-mechanical fatigue loading on marginal quality of bonded resin composite restorations. *Dent Mater* 2005; 21: 397-412.
2. Spencer P, Wang Y. Adhesive phase separation at the dentin interface under wet bonding conditions. *J Biomed Mater Res* 2002; 62: 447-56.
3. van Dijken JW. Durability of three simplified adhesive systems in Class V non-carious cervical dentin lesions. *Am J Dent* 2004; 17: 27-32.
4. Van Meerbeek B, Van Landuyt K, De Munck J, Hashimoto M, Peumans M, Lambrechts P et al. Technique-sensitivity of contemporary adhesives. *Dent Mater J* 2005; 24: 1-13.
5. Torneck CD. Dentin-pulp complex. In: Ten Cate AR, ed. *Oral histology: development, structure, and function*. 5th ed. St. Louis: Mosby Inc., 1998; 150-96.
6. Bowen RL, Eick JD, Henderson DA, Anderson DW. Smear layer: removal and bonding considerations. *Oper Dent Suppl* 1984; 3: 30-4.
7. Van Meerbeek B, De Munck J, Yoshida Y, Inoue S, Vargas M, Vijay P et al. Buonocore memorial lecture. Adhesion to enamel and dentin: current status and future challenges. *Oper Dent* 2003; 28: 215-35.
8. Fusuyama T. New concepts in operative dentistry. Chicago III: Quintessence Publishing Co. Inc, 1980.
9. Perdigão J. New developments in dental adhesion. *Dent Clin North Am* 2007; 51: 333-57.
10. Kanca J 3rd. Improving bond strength through acid etching of dentin and bonding to wet dentin surfaces. *J Am Dent Assoc* 1996; 123: 35-43.
11. Vaidyanathan TK, Vaidyanathan J. Recent advances in the theory and mechanism of adhesive resin bonding to dentin: a critical review. *J Biomed Mater Res B Appl Biomater* 2009; 88: 558-78.
12. Carvalho RM, Mendonça JS, Santiago SL, Silveira RR, Garcia FC, Tay FR, et al. Effects of HEMA/solvent combinations on bond strength of dentin. *J Dent Res* 2003; 82: 597-601.
13. Tay FR, Gwinnett AJ, Wei SH. Micromorphological spectrum from overdrying to overwetting acid-conditioned dentin in water-free, acetone-based, single-bottle primer/adhesives. *Dent Mater* 1996; 12: 236-44.
14. Spencer P, Ye Q, Park J, Topp EM, Misra A, Marangos O et al. Adhesive/Dentin interface: the weak link in the composite restoration. *Ann Biomed Eng* 2010; 38: 1989-2003.
15. Pashley DH, Ciucchi B, Sano H, Homer JA. Permeability of dentin to adhesive agents. *Quintessence Int* 1993; 24: 618-31.
16. Fabre HS, Fabre S, Cefaly DF, de Oliveira Carrilho MR, Garcia FC, Wang L. Water sorption and solubility of dentin bonding agents light-cured with different light sources. *J Dent* 2007; 35: 253-8.
17. Ito S, Hashimoto M, Wadgaonkar, B Svizero N, Carvalho RM, Yiu C et al. Effects of resin hydrophilicity on water sorption and changes in modulus of elasticity. *Biomaterials* 2005; 26: 6449-59.
18. Tay FR, Carvalho R, Sano H, Pashley DH. Effect of smear layers on the bonding of a self-etching primer to dentin. *J Adhes Dent* 2000; 2: 99-116.
19. Tay FR, Sano H, Carvalho R, Pashley EL, Pashley DH. An ultrastructural study of the influence of acidity of self-etching primers and smear layer thickness on bonding to intact dentin. *J Adhes Dent* 2000; 2: 83-98.
20. Ikeda T, De Munck J, Shirai K, Hikita K, Inoue S, Sano H et al. Effect of evaporation of primer components on ultimate tensile strengths of primer-adhesive mixture. *Dent Mater* 2005; 21: 1051-8.
21. Cadenaro M, Breschi L, Rueggeberg FA, Suchko M, Grodin E, Agee K et al. Effects of residual ethanol on the rate and degree of conversion of five experimental resins. *Dent Mater* 2009; 25: 621-8.
22. Pashley DH, Tay FR. Aggressiveness of contemporary self-etching adhesives Part II: etching effects on unground enamel. *Dent Mater* 2001; 17: 430-44.
23. Frankenberger R, Lohbauer U, Roggendorf MJ, Naumann M, Taschner M. Selective enamel etching reconsidered: better than etch-and-rinse and self-etch? *J Adhes Dent* 2008; 10: 339-44.
24. Yoshida Y, Nagakane K, Fukuda R, Nakayama Y, Okazaki M, Shintani H et al. Comparative study on adhesive performance of functional monomers. *J Dent Res* 2004; 83: 454-8.
25. Peumans M, Kanumilli P, De Munck J, Van Landuyt K, Lambrechts P, Van Meerbeek B. Clinical effectiveness of contemporary adhesives: a systematic review of current clinical trials. *Dent Mater* 2005; 21: 864-81.
26. Van Meerbeek B, Peumans M, Poitevin A, Mine A, Van Ende A, Neves A et al. Relationship between bond-strength tests and clinical outcomes. *Dent Mater* 2010; 26: 100-21.
27. Oliveira SS, Marshall SJ, Hilton JF, Marshall GW. Etching kinetics of a self-etching primer. *Biomaterials* 2002; 23: 4105-12.
28. Toledano M, Osorio R, de Leonardi G, Rosales-Leal JI, Ceballos L, Cabrerizo-Vilchez MA. Influence of self-etching primer on the resin adhesion to enamel and dentin. *Am J Dent* 2001; 14: 205-10.
29. De Munck J, Shirai K, Yoshida Y, Inoue S, Van Landuyt K, Lambrechts P et al. Effect of water storage on the bonding effectiveness of 6 adhesives to Class I cavity dentin. *Oper Dent* 2006; 31: 456-65.
30. Tay FR, Frankenberger R, Krejci I, Bouillaguet S, Pashley DH, Carvalho RM et al. Single-bottle adhesives behave as permeable membranes after polymerization. I. In vivo evidence. *J Dent* 2004; 32: 611-21.
31. Hashimoto M, Tay FR, Ito S, Sano H, Kaga M, Pashley DH. Permeability of adhesive resin films. *J Biomed Mater Res B Appl Biomater* 2005; 74: 699-705.
32. Hashimoto M, Tay FR, Svizero NR de Gee AJ, Feilzer AJ, Sano H et al. The effects of common errors on sealing ability of total-etch adhesives. *Dent Mater* 2006; 22: 560-8.
33. Van Meerbeek B, Inoue S, Perdigão J et al. Enamel and dentin adhesion. In: Schwartz RS, ed. *Fundamentals of operative dentistry. A contemporary approach*. Carol Stream, Ill: Quintessence Publishing Co, Inc 1996; 178-235.
34. Salz U, Zimmermann J, Zeuner F, Moszner N. Hydrolytic stability of self-etching adhesive systems. *J Adhes Dent* 2005; 7: 107-16.
35. Tyas MJ. Milestones in adhesion: glass-ionomer cements. *J Adhes Dent* 2003; 5: 259-66.
36. Tyas MJ, Burrow MF. Clinical evaluation of a resin-modified glass ionomer adhesive system: results at five years. *Oper Dent* 2002; 27: 438-41.
37. Scholtanus JD, Huysmans MC. Clinical failure of class-II restorations of a highly viscous glass-ionomer material over a 6-year period: a retrospective study. *J Dent* 2007; 35: 156-62.
38. Radovic I, Monticelli F, Goracci C, Vulicevic ZR, Ferrari M. Self-adhesive resin cements: a literature review. *J Adhes Dent* 2008; 10: 251-8.
39. Goracci C, Cury AH, Cantoro A, Papacchini F, Tay FR, Ferrari M. Microtensile bond strength and interfacial properties of self-etching and self-adhesive resin cements used to lute composite onlays under different seating force. *J Adhes Dent* 2006; 8: 327-35.
40. Lin BA, Jaffer F, Duff MD, Tang YW, Santerre JP. Identifying enzyme activities within human saliva which are relevant to dental resin composite biodegradation. *Biomaterials* 2005; 26: 4259-64.
41. Pashley DH, Tay FR, Yiu C, Hashimoto M, Breschi L, Carvalho RM, et al. Collagen degradation by host-derived enzymes during aging. *J Dent Res* 2004; 83: 216-21.
42. Carrilho MR, Tay FR, Donnelly AM, Agee KA, Tjäderhane L, Mazzoni A et al. Host-derived loss of dentin matrix stiffness associated with solubilization of collagen. *J Biomed Mater Res B Appl Biomater* 2009; 90: 373-80.
43. Martin-de Las Heras S, Valenzuela A, Overall CM. The matrix metalloproteinase gelatinase A in human dentin. *Arch Oral Biol* 2000; 45: 757-65.
44. Mazzoni A, Mannello F, Tay FR, Tonti GA, Papa S, Mazzotti G et al. Zymographic analysis and characterization of MMP-2 and -9 forms in human sound dentin. *J Dent Res* 2007; 86: 436-40.
45. Sulkala M, Tervahartiala T, Sorsa T, Larman M, Salo T, Tjäderhane L. Matrix metalloproteinase-8 (MMP-8) is the major collagenase in human dentin. *Arch Oral Biol* 2007; 52: 121-7.
46. Nishitani Y, Yoshiyama M, Wadgaonkar B, Breschi L, Mannello F, Mazzoni A et al. Activation of gelatinolytic/collagenolytic activity in dentin by self-etching adhesives. *Eur J Oral Sci* 2006; 114: 160-6.
47. Hebling J, Pashley DH, Tjäderhane L, Tay FR. Chlorhexidine arrests subclinical degradation of dentin hybrid layers in vivo. *J Dent Res* 2005; 84: 741-6.
48. Carrilho MR, Carvalho RM, de Goes MF, Di Hipólito V, Geraldelli S, Tay FR et al. Chlorhexidine preserves dentin bond in vitro. *J Dent Res* 2007; 86: 90-4.
49. Carrilho MR, Geraldelli S, Tay F, de Goes MF, Carvalho RM, Tjäderhane L et al. In vivo preservation of the hybrid layer by chlorhexidine. *J Dent Res* 2007; 86: 529-33.
50. Breschi L, Martin P, Mazzoni A, Nato F, Carrilho M, Tjäderhane L et al. Use of a specific MMP-inhibitor (galardin) for preservation of hybrid layer. *Dent Mater* 2010; 26: 571-8.
51. Tezvergil-Mutluay A, Agee KA, Hoshida T, Tay FR, Pashley DH. The inhibitory effect of polyvinylphosphonic acid on functional matrix metalloproteinase activity in human demineralized dentin. *Acta Biomater* 2010; 6: 4136-42.