MMPs

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Dentists who conduct research have known for some time that, when it comes to bonding to tooth structure, all things are not equal. Both clinical and laboratory studies have revealed that the resin bond to properly etched enamel is strong and durable. In contrast, the bond to dentin deteriorates over time. Restorations that are bonded to dentin depend on a stable hybrid layer, which is the region in which bond failures occur.

Understanding the subtleties of this problem requires a basic review of how the hybrid layer is formed. Bonding procedures use acidic conditioners such as phosphoric acid to effect superficial dissolution of dentin mineral and a resultant exposure of the dentin matrix. This matrix is predominantly composed of the fibrillar protein collagen but also contains other non-collagenous proteins. Adhesion to dentin is established as spaces between and around the collagen fibrils are infiltrated with resin monomers that are subsequently polymerized. Thus, the hybrid layer should be considered a mixture of dentin proteins (collagen and non-collagenous matrix proteins) and resin. The collagen component of the hybrid layer remains attached to the mineralized dentin, and the adhesive resins in the hybrid layer are bonded to and retain the overlying resin-based restorative material. We observe that, as time passes, both components (the collagen matrix and the resin polymers) of the hybrid layer begin to deteriorate.

The collagen matrix is covered with various proteins that were necessary for the initial mineralization of the dentin during dentinogenesis. Included among them are proteins capable of collagen degradation. These are called *matrix metalloproteinases* (MMPs) because zinc and calcium ions are required for them to degrade the collagen matrix. MMPs become active during the steps of creating the resin bond to dentin and are able to degrade the collagen component of the hybrid layer. Collagen degradation causes a loss of hybrid layer integrity that results in deterioration of the resin bond to dentin.

Agents that bind zinc and calcium ions inhibit the ability of MMPs to degrade the matrix. For example, 2 wt% solutions of chlorhexidine gluconate (placed on etched dentin for 30–60 seconds prior to use of primer and adhesive) have proved effective for preserving the hybrid layer and overall resin–dentin bond strengths in Class I restorations, at least for 12 to 14 months. It is unknown whether this promising technique will result in MMP inhibition and dentin bond preservation over the long term. An alternative approach to stabilizing the collagen in and below the hybrid layer is to use a collagen cross-linking agent such as 5% glutaraldehyde after the dentin has been etched. Cross-linked collagen is much more difficult for MMPs to degrade. Active research is underway to identify agents that are optimally able to inhibit dentin MMPs and/or cross-link the collagen matrix.

Dentin is saturated with water. Dentin bonding agents contain solvents designed to penetrate the moist surface of the etched dentin so as to foster resin infiltration of the collagen matrix. Water inclusion during hybrid layer formation can result in chemical degradation (hydrolysis) of the resin molecules in the hybrid layer. Therefore, efforts have been made to create adhesive

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resins that are less hydrophilic and to use solvents that displace water more effectively, thus improving the resin infiltration of the collagen matrix.

It is important to understand that the MMPs in mature dentin are inactive as long as the dentin remains mineralized. Acidic conditions that result in mineral dissolution will increase the potential for MMP activity and resultant degradation of the supporting collagen matrix. Etching procedures used in restorative dentistry result in mineral dissolution. In addition, acidogenic bacteria (*mutans streptococci* and *lactobacilli*) produce acids that result in tooth mineral dissolution (dental caries). MMPs have been identified as part of the host response to dental caries, a disease that includes acid-induced mineral loss as an initial step.

Oral conditions that fail to buffer acids from bacterial, dietary, or gastric sources result in increased likelihood of developing dental caries (high caries risk). Recent clinical research has shown that high caries risk individuals have an increased risk of secondary caries adjacent to composite resin than to amalgam restorations. The problem does not lie with the physical properties of contemporary composite resins, as these materials are more than adequate to survive the rigors of the oral environment. The growing sense among researchers is that the increased failure of composite restorations in high caries risk patients is related to deterioration of the hybrid layer and is secondary to increased MMP activity as the balance of mineralization—demineralization is pushed toward demineralization. Deterioration of the hybrid layer allows rapid development of secondary caries along the composite-tooth interface**.** Establishment of an effective and stable hybrid layer is an essential step in limiting the risk of secondary caries adjacent to composite resin restorations.

Other sources of MMPs include the odontoblasts in the dental pulp via the dentinal tubules, gingival crevicular fluid, and saliva itself. Continued research is essential to gain further understanding into the careful balance of MMP activity and inhibition that occurs in health and means by which to limit MMP activity stimulated by bonding procedures.

SUGGESTED READING

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