Dental Remineralization: Simplified

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Throughout our patients’ lives we interact at regular intervals, assessing and treating as their oral condition requires. The ongoing progression of disease in dental hard and soft tissue is often a multifactorial downward spiral. It does not have to be. The dental team must fully understand the disease process and then proactively intervene to slow or preferably stop its progress. This is the concept of Proactive Intervention Dentistry. Tools and techniques are needed to provide these services. These tools are readily available and can be easily incorporated into daily practice. This article focuses on dental hard tissue and the various products and systems demonstrated to be beneficial in reversing and controlling the caries process. These systems should be used proactively when the patient requires extra help in maintaining hard tissue health.

DEMINERALIZATION
Dental caries is a multifactorial disease caused by the interaction of dietary sugars, dental biofilm and the host’s dental tissue within the oral environment. It is the cumulative result of consecutive cycles of demineralization and remineralization at the interface between the biofilm and the tooth surface. Oral bacteria excrete acid after consuming sugar, leading to demineralization. Upon this acid challenge, the hydroxyapatite crystals are dissolved from the subsurface. Remineralization is the natural repair process for non-cavitated lesions. It relies on calcium and phosphate ions, assisted by fluoride, to rebuild a new surface on the existing crystal remnants in the subsurface. The remineralized crystals are less acid soluble than the original ones.

Remineralization is the natural repair process for non-cavitated lesions. Under normal physiological conditions (pH7), saliva is supersaturated with calcium and phos-
phate ions, making caries progress slow. However, as the bacteria in the biofilm continue to produce acid with sugar consumption, plaque pH falls to 4.5-5.5. This shifts the driving force within the tooth to mineral dissolution.\(^1\) As the pH is lowered, the saturation point of the minerals in the surrounding fluid is changed. The lower the pH, the higher the concentrations of calcium and phosphate required to reach saturation with respect to hydroxyapatite. This is called the “critical pH”, the point where equilibrium exists. There is no mineral dissolution and no mineral precipitation. The critical pH of hydroxyapatite is around 5.5 and that of fluorapatite is around 4.5. This varies with individual patients. Below critical pH, demineralization occurs while above critical pH, remineralization occurs (Figs. 1 & 2).

The critical pH is significantly higher for children than adults. Children have a greater driving force for demineralization in a more acidic oral environment and a decreased driving force for remineralization at normal oral pH. This puts children at greater risk for demineralization than adults.\(^4\)

**FLUORIDE**

It has been known since the 1980s that fluoride controls caries predominantly through its topical, not systemic, effect.\(^1\) Four mechanisms are involved:

1. **Fluoride inhibits demineralization.**
   If fluoride is present in the plaque fluid when bacteria produce acids, it will penetrate along with the acids at the subsurface, adsorb to the apatite crystal surface and protect the crystals from dissolution.\(^5\) This coating makes the crystals similar to fluorapatite (critical pH of 4.5) ensuring that no demineralization takes place until the pH reaches this point. Fluoride present in solution at low levels among the enamel crystals can markedly inhibit dissolution of the tooth mineral by acid.\(^6,7\) This fluoride comes from topical sources such as drinking water, and fluoride products like toothpastes and varnishes. The fluoride, which is incorporated systemically into the tooth, is insufficient to have a measurable effect on its acid solubility.\(^7,8\)

2. **Fluoride enhances remineralization.**
   When the pH returns to pH 5.5 or above, the saliva which is supersaturated with calcium and phosphate, forces mineral back into the tooth.\(^7\)
Fluoride adsorbs to the surface of the partially demineralized crystals and attracts calcium ions. This new surface veneer takes up fluoride preferentially from the solution around the crystals and excludes carbonate.7

Fluoride speeds up the growth of the new surface by bringing calcium and phosphate ions together and is also preferentially incorporated into the remineralized surface. This produces a surface which is now more acid resistant.

3. **Fluoride may inhibit essential bacterial activity.**
Fluoride cannot cross the bacterial cell wall in its ionized form (F⁻). However in an acid environment, F⁻ combines with H to form HF which easily diffuses into the bacterial cell.9,10 Inside the cell HF breaks up and releases fluoride ions that interfere with the essential enzyme activity of the bacterium.

4. **Fluoride is retained in intraoral reservoirs after the application of a fluoride treatment such as toothpaste, varnish or restorative material and is then released into the saliva over time.**11,12
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Fluoride can remain on dental hard tissue, the oral mucosa or within the dental plaque. Fluoride retention, especially in dental plaque, is clinically beneficial since it can be released during cariogenic challenges to decrease demineralization and enhance remineralization.¹

**OTHER REMINERALIZATION THERAPIES**

The action of fluoride in remineralization is the gold standard to which newer therapies are compared. The requirements of an ideal remineralization material are as follows:¹³,¹⁴

- Must diffuse into the subsurface or deliver calcium and phosphate into the subsurface
- Does not deliver an excess of calcium
- Does not favor calculus formation
- Works at an acidic pH
- Works in xerostomic patients
- Boosts the remineralizing properties of saliva
- Shows a benefit over fluoride

The major remineralization technologies that are available in the dental marketplace are Recaldent,
NovaMin, and Tricalcium Phosphate (TCP) (Table 1). They are discussed below:

**Recaldent (CPP-ACP)**

Recaldent combines phosphoproteins from milk with amorphous calcium phosphate (ACP). ACP on its own simply produces a thin surface coating of hydroxyapatite when applied topically. This is a surface phenomenon that is fundamentally different from the remineralization of enamel subsurface lesions which require the actual penetration of ions into enamel. With the addition of casein phosphopeptide (CPP), Recaldent is more effective than ACP alone.

The CPP in milk stabilizes the calcium and phosphate ions through the formation of complexes which are more readily absorbed by the intestine. The same concept has been applied to Recaldent. The bioavailable complexes of calcium and phosphate are created in the appropriate form for optimal remineralization of subsurface lesions in enamel, not just on the enamel surface. CPP also localizes the ACP in the dental plaque biofilm. The resulting high calcium and phosphate ion concentration gradient drives the ions into the subsurface lesions and achieves high rates of remineralization. Recaldent is available in solutions, gums, lozenges and creams.

**NovaMin**

NovaMin (GlaxoSmithKline, Brentford, United Kingdom) is technically described as an inorganic amorphous calcium sodium phosphosilicate (CSPS). It belongs to a class of materials which are known as “bioactive glasses”. NovaMin as well as other CSPS materials were originally developed as bone regenerative materials in the early 1970s. Prior to the invention of bioactive glass, all biomaterials were designed to be as inert as possible in the human body. The discovery that a synthetic biomaterial could actually form a chemical bond with bone proved that biomaterials could be engineered to interact with the body. This meant that it was not necessary or advantageous to minimize interactions. It could even be beneficial to encourage them. Bioactive glasses facilitate hydroxyapatite deposition when exposed to fluids containing calcium and phosphate. The mechanism of action is as follows:

In the presence of water or saliva NovaMin rapidly releases sodium ions. This increases the local pH and initiates the release of calcium and phosphate. Many studies have shown NovaMin particles to act as reservoirs and continuously release calcium and phosphate ions into the local environment. This may continue over many days. The calcium-phosphate complexes crystallize into hydroxyapatite, which is chemically and structurally similar to biological apatite. NovaMin has been incorporated into toothpastes, gels and prophy pastes.

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A novel delivery system for NovaMin is through an air polishing unit (Fig. 3). This procedure has been developed as an improved cleaning method with the added benefit of tooth desensitization and smoothing of surface irregularities. Using the Sylc (Oral Science, Montreal, Quebec) technique significantly reduces dentin permeability and completely occlude exposed dentinal tubules. NovaMin powder also has positive remineralization effects on partially and completely demineralized models of dentin. The treatment decreases surface roughness, promoting a smoother, less plaque and stain retentive surface (Fig. 4).
Tri-Calcium Phosphate (TCP)

TCP (3M ESPE, London, Ontario) is a bioactive formulation of tri-calcium phosphate and simple organic ingredients. It works synergistically with fluoride to produce superior remineralization of enamel subsurface lesions when compared to using fluoride alone.\textsuperscript{25,26} When it is used in toothpaste formulations, a protective barrier is created around the calcium, allowing it to coexist with the fluoride ions. During toothbrushing, TCP comes into contact with saliva, causing the barrier to dissolve and releasing calcium, phosphate and fluoride. When TCP is incorporated into a 5\% NaF varnish, microhardness and acid resistance improve.\textsuperscript{27} Studies are currently underway to demonstrate the clinical advantages of TCP in rinse form.

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The above remineralization therapies work directly to enhance the concentration of calcium, phosphate and fluoride. The ingredient discussed below, xylitol, works indirectly to promote remineralization by decreasing bacteria and bacterial function and creating the environment where reparative remineralization is optimized.

Xylitol

Xylitol is one of a number of non-sugar sweeteners permitted for use in foods throughout the world. It is found naturally in some foods but is produced primarily from hardwood sources such as birch and beech wood. It is a sugar alcohol that has been shown to have non-cariogenic as well as cariostatic effects.\textsuperscript{28} More recently it has been shown that the habitual use of xylitol is associated with a significant reduction in caries incidence and increased tooth remineralization.\textsuperscript{29} Cariogenic bacteria process xylitol very poorly, producing little acid or plaque. This decreases caries incidence and promotes colonization of less virulent strains of bacteria that can ferment xylitol.

Dental caries is an infectious, transmissible, bacterial disease. Most children acquire the bacteria (predominantly Streptococcus mutans) from their mothers/caregivers by salivary contact during the emergence of the primary teeth between the ages of 6-30 months.\textsuperscript{30,31} This is called the “discrete win-
dow of infectivity”. After the initial colonization of S. mutans, the successful establishment of other bacteria on the tooth surfaces is impaired. It has been demonstrated that a reduction of S. mutans in the saliva of mothers has resulted in the delayed acquisition of S. mutans in their children. And most remarkably, studies have shown that the habitual chewing of xylitol gum by mothers can decrease the caries incidence in their children by preventing the transmission of S. mutans (Fig. 5).

In fact, chewing xylitol gum decreases caries incidence significantly up to at least five years after the xylitol therapy has been discontinued. Children who chew xylitol gum exhibit a significantly lower caries progression and a significant number of caries lesion reversals, suggesting that remineralization has occurred. The efficacy of xylitol candies has been shown to be equivalent to that of xylitol gum. The dental literature suggests that a minimum of 5-6 grams and three exposures per day (from chewing gum and/or candies) is required for clinical effect.

A novel method of delivering remineralizing ions (calcium and phosphate) in combination with xylitol has been developed using a NaF varnish (Embrace Varnish, Pulpdent). This varnish contains calcium and phosphate salts that have been nano-coated with xylitol (cXp technology). The xylitol coating prevents early reaction and produces a sustained release of the remineralizing ions. Saliva exposure dissolves the xylitol and frees the calcium and phosphate ions. They then react with the fluoride in the varnish to form protective fluorapatite on the teeth (Fig. 6).

**BIOACTIVE RESTORATIVE MATERIALS**

When the enamel and dentin no longer have adequate structure to maintain their mineral framework, cavitation takes place and remineralization is an insufficient treatment. Tooth preparation and restoration are now required. Although most restorative materials are inert with respect to the biological tissues of the tooth, some are bioactive. Bioactive restorative materials actually interact with or affect the biological tissues. They effectively work with the dental hard tissues to harden and “heal” them (Table 2). Three bioactive restorative materials are discussed below.

**Glass Ionomer Cements**

Glass ionomer cements were developed in the early 1970s. They are especially valuable for initial carious lesions, abfractions/erosions/abrasions and for caries control in a high caries risk patients.
Glass ionomers have a true chemical bond with dental tissue. They are bioactive; they encourage remineralization of the surrounding tooth structure and prevent bacterial microleakage through the ion-exchange adhesion that they develop with both enamel and dentin. This creates a new, ion-enriched material at the tooth-glass ionomer interface. The material consists of phosphate and calcium ions from the dental tissues, and calcium (or strontium), phosphate and aluminum from the glass ionomer cement. The remineralization process creates a harder dentin surface (Fig. 7). Restoration failure is usually cohesive, leaving the ion exchange layer firmly attached to the cavity wall. The dentinal tubules are sealed and protected from bacterial penetration.

Fluoride is the catalyst for remineralization, aided by calcium (or strontium) and phosphate. The pattern of release for all the ions in the glass ionomer cement is similar. A low pH actually enhances the process.

The bioactive remineralizing effect of glass ionomer cements occurs in two distinct regions of the tooth:

1. **The outer surface** of the restoration is exposed to oral fluids and plaque with which it has a continuous exchange of ions. While wear resistance of the restoration is low at placement, it steadily increases with time and ion uptake.

2. **The inner surface** of the restoration, adjacent to the preparation, is isolated from the oral environment. The continuous flow of dentinal fluid creates a wet environment that is conducive to the exchange of ions. At placement, there is a significant release of ions from the cement which combine with similar ions from the dentinal fluid to promote remineralization. After the glass ionomer sets, there is a continuous low-level ion exchange which accounts for the remineralization of the tooth surface that is found clinically.

**Giomers**

Giomers (Shofu Dental, San Marcos, CA) are the latest category of hybrid restorative materials and they are bioactive as well. Giomer technology represents the true hybridization of glass ionomers and composite resins. There is an ideal combination of the properties of these two distinct restorative categories: the fluoride release and recharge of glass ionomers and the esthetics, physical properties and handling of composite resins.

The Giomer concept is based on PRG (Pre Reacted Glass) technology: a glass core, surrounded by a glass ionomer phase enclosed within a polyacid matrix (Fig. 8). Studies show dentin remineralization occurs at the preparation surface adjacent to the giomer.

The ions within the pre reacted glass particles have distinct biological effects. The fluoride, as discussed above, improves acid resistance through the formation of fluorapatite, remineralizes decalcified tooth substance and is antibacterial. The strontium ion improves acid resistance by forming stontiumapatite, inhibits dentin hypersensitivity and has been shown to accelerate the formation of bone. The aluminum ion inhibits dentin hypersensitivity. The silicate ion aids in the calcification of bone while the borate ion accelerates bone formation and is bactericidal.

**Giomers**

Giomers are also able to take up extra fluoride (after fluoride toothpaste, rinse or varnish are applied) from the oral fluids and then act as a reservoir until the fluoride is needed. This is called “fluoride release and recharge” (Fig. 9). Giomers release and recharge fluoride efficiently and significantly better.
than composites and composite resins although not as well as glass ionomers. Giomer fissure sealants have superior recharge and release of ions when they are compared to resin sealants. Hence, they work actively to decrease demineralization and increase remineralization in young teeth at their most caries susceptible stage.

Giomers resist plaque formation. A “material film layer” forms on the surface of the giomer with salivary contact. It consists of aluminum, silica, strontium and other ions which originate from the PRG fillers and act to inhibit bacterial adhesion. The clinical performance of giomers has been tested against those of high quality hybrid resin composites. Giomers have been found to compare favorably for all criteria.

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**Biodentine Tricalcium Silicate Cement**

Biodentine (Septodont, Cambridge, Ontario) is a new bioactive calcium silicate based product that has been designed as an all-around “dentin replacement” material. It can be used in endodontic repair (root perforations, apexification, resorptive lesions), pulp capping, as well as a dentin replacement in restorative dentistry. It was formulated by taking the MTA-based endodontic repair cement technology, improving its physical and handling properties, and creating a dentin replacement material with significant reparative qualities.

Biodentine penetrates the dentinal tubules forming tag-like structures that create a micromechanical lock with the tooth. It then begins to stimulate reparative dentin (Fig. 10).

Biodentine has been shown to enhance the formation of reparatory dentin and to create a dense dentin barrier after direct pulp capping as well as healing damaged pulp fibroblasts. Clinical trials confirm Biodentine’s ability to preserve pulp vitality even in very difficult cases. Biodentine has the potential to heal pulps, avoiding what may have been inevitable endodontic treatment in the past.

**CONCLUSION**

The medical model of Proactive Intervention is becoming the paradigm in dental care. This should be an integral part of daily practice and not relegated to the “preventive” side of the office. The multifactorial disease process of demineralization and caries can be slowed or even stopped before more extensive treatment becomes necessary. The oral care provider has simple remineralization tools, techniques and products that have been found effective in reversing and controlling the caries process. They can and should be used proactively to maintain hard tissue health throughout the patient’s life.

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Oral Health welcomes this original article.

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