Strategies for Noninvasive Demineralized Tissue Repair

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KEYWORDS

• Tissue repair • Remineralization • Fluoride
• Calcium-based strategies • Sealants • Infiltration • Lasers

Traditional management of a caries lesion primarily was focused on operative treatment. This often started an irreversible, restorative cycle, leading to several replacements over time with increasing restoration size and every so often iatrogenic damage. The last two decades have seen a growing insight about the process of lesion development and its causal and continual factors. This awareness changed the paradigm of Black's "extension for prevention" into the motto "extension of prevention".[1] The effect of caries disease in the tissue sets off/prompts lesion formation. Once the first clinically visible signs have been discovered, the detection should be followed by diagnosis of severity and extent of the lesion and whether it is an active process or not. Presence of tissue damage alone is not sufficient for management decisions as the present lesion might be rather a scar than a sign of current activity.

Fortunately, recognition of caries as a multifactorial disease process involving the biofilm has received more and more attention. The first step in contemporary caries management is focused on the various options to cope with the locally out-of-balance oral biofilm and stop progression of the disease (see the articles by Philip D. Marsh; and Svante Twetman elsewhere in this issue for further exploration of this topic). After the caries process has been halted, causative factors need to be evaluated and individual treatment regimens installed that will prevent new occurrence of the caries disease. Caries lesions develop by dissolution of minerals from the tooth tissues, leaving behind a more porous structure. Therapies that focus on rebalancing the interplay between demineralization and remineralization (see the article by Young and Featherstone elsewhere in this issue for further exploration of this topic), tipping the balance toward an overriding mineral uptake in the tissue, not only result in repair of the damage done, but concurrently assist in preventing new lesions of forming.

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This article focuses on the repair of affected hard tooth tissues using noninvasive management strategies. Such an approach takes into account the dynamic nature of the caries disease process (see the article by Hara and Zero elsewhere in this issue for further exploration of this topic). For successful noninvasive management, the lesions have to be detected early on, so they can be managed in a nonoperative way.[2] This type of early caries management requires special clinical attention, detection, and diagnostic skills (see the article by Braga and colleagues elsewhere in this issue for further exploration of this topic). It is time-consuming, but reestablishing the integrity of the tooth surface early on in the caries process will bring great rewards for patients. Their tooth structures will be preserved, and costly, extensive restorative treatments in the future prevented.

THE DISEASE—A SLOW-PACED PROCESS

The equilibrium that exists between plaque fluids and apatite crystals at the tooth surface is constantly overwhelmed by pH fluctuations at the plaque–tooth interface. In a healthy mouth, this is a normal physiologic process that takes place at a subclinical level numerous times a day. During periods of neutral pH, lost minerals are replaced by calcium and phosphates from saliva, forming a hard outer surface. A continual ion exchange, in both directions across the tooth surface interface, attempts to reestablish the mineral balance. The caries lesion is a result of loss of mineral from the dental tissues. Caries is not a disease process that develops rapidly, but it takes time for the effect (ie, lesion) to develop. Initial lesions undergo a constant daily battle between progression and regression. It may take 3 to 4 years to develop a cavitation.[3] Not all initial lesions, however, develop to cavities at the same rate.[4] The progression rates are not the same for each site,[5] and they are independent of the patient's decayed, missing or filled surfaces (DMFS).[3]

In general, there is ample time—between lesion initiation in enamel and subsequent progression into dentin involvement—to interrupt this process using preventive and repair strategies. Preventive management strategies can effectively arrest and even completely reverse the caries process. It is therefore important to detect lesions in their early stage. Reasons for slower pace of lesion progression in the last three decades are not clearly defined, but increased use of fluoride may have attributed to lower progression rates of fissure caries for example. Some lesions may have become arrested. This will lead to clinically undetected carious dentin at the base of occlusal fissures. This phenomenon, reported since 1931,[6] received renewed attention in the 1990s.[7,8] When initial lesions are taken into account, however, the percentage of clinically undetected carious dentin lesions dropped dramatically to less than 2%[9] and were in the same order of magnitude as pre-eruptive lesions.[10]

A critical period for rapid caries development occurs when a tooth erupts in the oral environment and the enamel is not yet fully matured. Continuous exposure to saliva promotes full maturation. This maturation and the continuing demineralization/remineralization processes lead to a more acid-resistant outer enamel. The time during eruption and immediately after is the most vulnerable period for caries development. Caries initiation and progression rates of permanent molars are highest during this early posteruptive period.[11] Additional fluoride during the first few years after eruption will encourage full maturation of the enamel. To counteract plaque stagnation and provide fluoride ions, it is crucially important to teach parents to brush erupting surfaces of first molars with special attention using fluoride toothpaste.

Another exception to the usually slow pace of lesion development occurs in high-risk patients (eg, those with compromised salivary flow). Patients who suffer from

hyposalivation or a reduced quality of saliva are missing the protective clearance and buffering effects of saliva (see the article by Hara and Zero elsewhere in this issue for further exploration of this topic). This may lead to rapid and rampant lesion development. The calcium and phosphates from the saliva are the primary source for the recrystallizing minerals and thus for remineralization. Therefore, also in healthy individuals, stimulation of salivary flow by daily use of sugar-free chewing gum assists in caries management.

Changes in tooth structure

Teeth are composed of calcium phosphate minerals (hydroxyapatite) that dissolve when the pH drops below the critical value. The drop in pH necessary for demineralization in cementum and dentin (pH 6.2 to 6.7) is less than that required for enamel (pH 5.4 to 5.5).[12,13] Therefore, given the proper environment, both the initiation and progression of root surface caries lesions will occur more rapidly than in an enamel surface.[14] As the environmental pH recovers, the minerals precipitate on the remaining mineral crystals. Remineralization is slower than the dissolution process, but is still able to eliminate the damage done to tooth tissues by demineralization. If no or limited remineralization takes place, however, the demineralization will proceed, and a caries lesion will develop.

The dental caries process starts in the outer enamel and, as it proceeds, also involves and demineralizes dentin to a significant depth, even when the outer layer is still noncavitated. Low levels of fluoride are adequate for enamel remineralization but insufficient to facilitate dentin remineralization. The effect of the caries process in dentin is similar to that in enamel, except that dentin demineralizes at a higher pH and proceeds about twice as fast, because dentin has only half the mineral content of enamel. Even very deep lesions, extending through enamel into dentin, can be remineralized.[15] Although this is a slow process, it enlarges the window for noninvasive management and postponement of operative intervention for lesions that have passed the enamel–dentino junction.

Both initiation and progression of root surface caries lesions occur more rapidly in dentin than in coronal enamel.[4] Surface irregularities, collagen degradation, longer periods of acid challenge, and lower saliva clearance all aggravate the process of root caries. Taking the multitude of changes associated with aging into account, and the fact that root dentin is more prone to acid dissolution, it will be obvious that this will lead to differences in management strategy. Combating root caries may need greater fervor.

LESION ARREST AND REPAIR

Treatment and management strategies should be based on interpretation of activity of the lesion and future caries risk of the patient. Caries is a disease, caused by a multifactorial process, and contemporary caries management takes this into account. Current management approaches call for control of disease activity and tissue repair by reversal of mineral loss. Restorative treatment options are advised only when the caries disease process has resulted in more extensive damage (ie, cavitations), and form, function or esthetics need to be restored. The only (complementary) role restorations play in a patient's caries management plan is that they partially assist disease management by eliminating plaque stagnation spots and facilitate plaque control in case of clinically detected, frank cavitations.

In the very early active caries lesion (the *initial demineralized lesion*), only the external enamel microsurface is dissolved by plaque acids. After plaque removal, the ultrathin superficially eroded area will wear and become polished, changing its

appearance from rough and chalky-white into a hard, shiny surface. When the lesion has progressed a little further and resulted in a deeper surface and subsurface dissolution, it is called an *active noncavitated caries lesion*. Intervention in the caries process will now, in addition to the previously described initial process, also result in a slow remineralization of the subsurface defect. Although such remineralized lesions show a decrease in size (depth and width), they may remain visible as shiny, white lesions. The caries process has ceased, but the lesion is not completely recovered and may remain forever visible as white or brown scar tissue. Although they have not been reversed completely, these areas are more resistant to a subsequent caries attack than sound enamel. This will be explained in more detail subsequently when the mechanism of topical fluorides are discussed.

Special care must be taken with interpretation of radiographic evidence of demineralized tissue. An arrested, nonactive lesion may still present itself as a demineralized, radiolucent area on a radiograph. Such an arrested lesion, however, does not need any management and should be considered a tissue scar. Greater awareness of this phenomenon will help to reduce the perceived need for operative intervention and avoid overtreatment.

Assisting natural processes

The question now becomes how one can help naturally occurring processes to arrest lesion activity, respond to mineral dissolution by remineralization effort, and thus potentially reverse early caries lesions. Lesion activity can be halted with several means by taking the infectious part out of the equation. Diet modification, general or targeted antibacterial strategies, plaque-removal and plaque-reducing strategies, stimulation of salivary flow, and sealing of lesions, all lead to reduction or elimination of acid attacks on the tooth surface. This changes the dynamics of the ion exchange between the hard tissues and the ambient plaque fluids. In the presence of normal saliva, a reduction in demineralization automatically will result in remineralization, halting the caries process (see the article by Hara and Zero elsewhere in this issue for further exploration of this topic). An arrested lesion does not require treatment.

Basic Preventive Steps for Moderate/High Risk Patients		Special Needs
Patient motivation	Emphasize behavioral change	R + H
Diet counseling	Reduction of fermentable carbohydrate intake and frequency	R + H
	Reduction of softdrink consumption and frequency	R + H
Tooth brushing	Twice daily with fluoride toothpaste (preferably 3x/day)	R + H
Flossing	Daily, few times a week	R + H
Sugar-free gum	Chew 2 pieces for $\geq$5 min, 3 $\times$/d (after each meal preferred)	R + H
Sealants	All at-risk surfaces (sound or noncavitated)	H

Abbreviations: H, hyposalivation; R, root caries.

Plaque Reduction/Removal

The average speed of lesion progression on different surfaces has been determined.[16] Caries proceeds slowly on smooth surfaces (proximal and buccal/labial/lingual). Therefore, restorative intervention always should be postponed, and active preventive management and monitoring are indicated. This includes modifying the caries environment by improvement of oral hygiene (ie, twice-daily effective plaque removal and use of floss, diet modification, and provision of fluoride) (see the article by Hara

and Zero elsewhere in this issue for further exploration of this topic). Although no good evidence exists for caries-preventive effect of tooth brushing alone, the conventional health wisdom keep your mouth clean is not only a social and cosmetic strategy. This tooth-cleaning advice will continue to be an important step in caries management for the foreseeable future, in particular when using fluoride toothpaste.

When lesions show cavitation, the caries process has not only reached the enamel–dentino junction, but the dentin is always involved.[17] Such lesions contain many cariogenic microorganisms and thus are by definition active lesions.[18] It is difficult to effectively remove plaque from these lesions, because access to the cavitation is problematic. Simply removing undermined and overhanging enamel margins from cavitated lesions will assist in keeping the lesion free from plaque. Open, accessible cavities, cleaned twice daily with fluoridated toothpaste, can be arrested and converted into a leathery or even hard lesion and lead to decreased activity and an arrested caries process.[19] This type of basic caries management, successful in the primary dentition, might be applicable to the permanent dentition as well when rampant caries require immediate and simple, noninvasive management. Carious dentitions can be managed so that the caries process is arrested, and the balance between physiologic de/remineralization processes has been reinstated.

Because cariogenic microflora thrive in bacterial plaque communities (ie, biofilm), reducing or disturbing their living environment is a sensible approach. Basic tooth cleaning is helpful in keeping the biomass of acidogenic and acid-tolerant microflora under control. Limiting available substrate for cariogenic bacteria by use of xylitol, for example, is another approach. Xylitol chewing gum is considered an adjunct preventive therapy that results in transient effect on the biofilm. The lack of well-designed randomized control trials (RCTs) results in a lack of definitive evidence for a caries-preventive effect of xylitol.[20]

The use of antibacterials like chlorhexidine (CHX) for caries prevention has been a controversial topic. The caries-inhibiting effect was not greater than fluoride, while CHX administration has several drawbacks (see the article by Svante Twetman elsewhere in this issue for further exploration of this topic). There is lack of consensus on evidence-based treatment protocols, and the evidence using different CHX modes and concentrations or a combined CHX-fluoride therapy is "suggestive but incomplete."[21] A recent meta-analysis on CHX-varnishes for targeted patient groups stated that there was either a nonsignificant effect or the effect was only shown in few studies.[22] Based on current inconclusive evidence, CHX rinse (0.12%) or varnish (1% CHX), the only products available in the United States, are not recommended for caries prevention. Even so, in spite of lacking wide consensus regarding efficacy, CHX use for short periods aiming to temporarily eliminate or reduce bacterial plaque may provide a complementary strategy in noninvasive management for high-caries risk individuals.

Nowadays, antibacterial strategies are no longer only wide spectrum therapies (eg, CHX) reducing biofilm and plaque formation. Promising, emerging research findings show positive effects of herbal and novel approaches targeting or modifying only the major cariogenic species in the biofilm communities. Probiotic approaches that retain the healthy benign plaque may define future strategies (see the article by Svante Twetman elsewhere in this issue for further exploration of this topic).

Brushing with fluoride toothpaste

Brushing teeth is still an excellent way to combine mechanical plaque removal with a therapeutic treatment. Brushing the plaque exposes the tooth surface to an environment that might mediate the initial caries process. Exposure of the surface to mineral-rich

saliva may prevent mineral loss and induce mineral uptake if there are caries lesions in development. The use of fluoride toothpaste enhances the plaque removal effect by introducing fluoride ions at the clean surface during lesion development phase.

The effectiveness of fluoride increases when elevated levels are maintained throughout the day by frequent applications of small amounts of fluoride. The current understanding from numerous clinical trials, although of great complexity due to the number of variables, resulted in the widely accepted recommendation that *brushing at least twice daily with fluoride toothpaste* is appropriate for all age and risk groups. It is recommended to brush just before going to bed (to reduce plaque, remove remaining fermentable carbohydrates, and boost fluoride levels) and at one other time during the day at a mealtime. The recommendation for young children is supervised brushing and the use of a pea-size amount of fluoridated toothpaste (only when they can spit). Supervised brushing with 1000 ppm fluoride toothpaste resulted in 56% fewer decayed and filled surfaces in children compared with unsupervised children.[23]

Tooth Brushing	Special Needs
Tooth brushing (adults)	
Use over-the-counter fluoride toothpaste (approximately 1100 ppm fluoride)	
Brush at least twice a day (preferably 3×/d), including immediately before going to bed	
"Spit—don't rinse" should be the motto	
Tooth brushing in children:	
Supervise and check amount of toothpaste (pea-size) on brush, if at risk for fluorosis	
Finish-off brushing with special attention for occlusal surfaces of erupting teeth	Erupting surfaces

Special attention is needed when patients have appliances, and plaque removal becomes more difficult. Fixed and removable orthodontic appliances and partial dentures will encourage plaque retention and require special attention and motivation for plaque removal. The unbelievably high incidence of 73% of new white spot lesions during fixed orthodontic treatment presents a dire iatrogenic shortcoming in the profession.[24] In addition to motivational oral hygiene instruction and supplementary fluoride administration, monitoring compliance of these high caries risk patients (and intervene, when necessary) is a 'must' and a professional ethical responsibility.

Modifying ambient plaque/oral fluids

Increasing the amount of bioavailable ions in the saliva also will drive the remineralization process. Several caries management strategies rely on providing additional fluoride, calcium, or phosphate ions to saliva, with the intent to deliver an ample supply of ions to the immediate caries-active environment: the plaque–tooth interface.

Fluorides

Enamel crystals, the building blocks for enamel, consist of hydroxyapatite (HA). Therapeutic use of fluoride is aimed at substituting the HA crystals in the enamel with fluoroapatite (FA) and inhibition of the carbohydrate metabolism in the biofilm. When fluorides are present, the enamel crystals in the incipient lesion will be repaired or replaced with FA or fluorohydroxyapatite. These crystals are relatively insoluble.

Therefore repeated cycles of de/remineralization in the presence of fluorides result in a more caries-resistant enamel.[25] Presence of fluorides in the ambient solution effectively protects enamel during acid challenges. Therefore a frequent availability of fluoride ions in the oral fluids is important. In the early stages of a caries lesion, the bacterial acids in the surface biofilm penetrate through the eroded crystal spaces and form a porous mineral structure: the subsurface lesion. The mechanism by which fluoride inhibits demineralization is facilitating re-precipitation of dissolved calcium and phosphate ions on the remaining crystals. This mechanism prevents the tissue ions from being leached out to the environment into the plaque and saliva. Precipitated ions at the tooth surface decrease the pores in the enamel, obstruct the diffusion pathways for plaque acids, and hamper acid penetration into the enamel. When ambient pH is higher than approximately 5.5, fluoride will facilitate remineralization, promoting lesion arrest and enhancing repair.[26] On the other hand, a lack of fluoride constitutes a caries risk. The loss and incorporation of minerals in enamel is a continual dynamic process that takes place with and without fluoride. Frequent presence of fluorides at the tooth surface enhances this dynamic toward effective remineralization. To ensure high frequency of ion availability, the fluorides need to be replenished.

Retention of fluoride in the mouth is site-specific, and there is minimal transport of fluoride ions between left and right sides of the mouth or between arches. This explains also why localized lesions can occur while patients use fluoride toothpaste. A strong, off-label advice is thus to discourage vigorous rinsing with water after tooth brushing. Instead: encourage patients to only spit out the excess toothpaste, so that what remains will continue to facilitate remineralization processes. This no-rinse method resulted in 26% reduction in approximal caries incidence.[27]

Topical home fluorides: tooth pastes, mouth rinses, and gels

The use of fluoride toothpaste that retains a sufficient concentration of bioavailable fluoride is a cost-effective means of caries control. A recent summary of Cochrane systematic reviews on fluoride[28] concluded that the benefits of daily tooth brushing with fluoride toothpastes for preventing dental caries were firmly established, based on a sizeable body of evidence from randomized controlled trials. Although long-term studies in adults were still lacking,[29] a clear and similar effectiveness of topical fluoride toothpastes, mouth rinses, gels, and varnishes for preventing caries was confirmed.[30] The size of the reductions in caries increment in both the permanent and primary dentitions emphasizes the importance of including topical fluoride delivered through toothpastes, rinses, gels, or varnishes in any caries preventive program.[28]

After assessing the individual caries risk and fluoride exposure of a patient, the appropriate fluoride concentration should be considered. As a basic caries-preventive method, the concentration in over-the-counter (OTC) fluoride toothpastes in the United States is approximately 1100 ppm fluoride (for 7 years and older). The caries-preventive effect of regular use is typically 20% to 40% over 2 to 3 years.[31] In caries-active patients, it is essential to increase fluoride therapy until the caries is under control. This can be achieved by more intensive (at least three times per day) use of OTC fluoride toothpaste, asking the patient to refrain from rinsing after brushing or adding fluoride mouth rinses. Another therapeutic use of toothpaste is to apply the paste locally (with finger or brush) directly onto the cleaned active caries lesion before going to bed (taking advantage of the decreased salivary secretion at night). Alternatively, a prescription high-fluoride containing toothpaste (5000 ppm fluoride), fluoride rinses, or various professionally applied applications may be chosen. Compared with a conventional OTC toothpaste of 1100 ppm fluoride, a study in elders using 5000 ppm fluoride showed almost twice as much rehardening of noncavitated root lesions.[32]

A summary of seven systematic reviews concluded that additional caries reduction can be expected when another topical fluoride as mouth rinses, gels, and varnishes is combined with fluoride toothpaste.[29] Home fluoride rinses may benefit adults with active caries who have difficulty cleaning their teeth adequately. Rinses with 0.02% NaF (US market) should be used daily for a full minute. Prescription solutions with 0.2% NaF may be used daily or weekly, depending on the caries risk of the patient. Products without alcohol are preferred to avoid dry-mouth effects.

Adjunct Topical Therapies for Moderate/High Risk Patients	Special Needs
Home fluoride options:	
Prescription fluoride toothpaste: 5000 ppm F	R + H
Brush at least twice a day (preferably 3x/day), incl. immediately before going to bed	
"Spit—don't rinse" should be the motto	
Daily (in tray – radiation hyposalivation)	H
Fluoride rinses	
Twice daily/daily/weekly (depending on need and product)	R + H
In-office fluoride options:	
Fluoride gels/foams: 1.23% APF or neutral 2% NaF	
4 min, 2–4× per year	
4× over 2–4 weeks (root caries)	R + H
Fluoride varnishes:	
Isolate each quadrant with cotton rolls	
Apply to lesions and other surfaces at risk	
2–4× per year depending on subject's risk	R + H

Abbreviations: H, hyposalivation; R, root caries.

Professionally applied/in-office topical fluoride applications

To further assist the body's response to caries attacks and address mineral imbalances, several professionally applied preventive measures are available, such as topical application of concentrated fluoride solutions, gels, or varnishes. To achieve optimal caries-preventive effect, the more frequent elevated fluoride levels are offered, the better. Thus, the intensity of home-used fluoride may have to be stepped up for a while by adding a third fluoride boost per day through extra brushing with high-concentration fluoride toothpaste, a fluoride rinse, or other forms (ie, tablets, gels).

Professional application of topical fluorides is an effective approach to caries control, as supported by strong evidence from many clinical trials. The American Dental Association (ADA) Council on Scientific Affairs developed evidence-based clinical recommendations for professionally applied topical fluoride, summarized in this paragraph and in the **Table 1**.[33] Strong evidence (grade A) supports its use for moderate and high caries risk children and adolescents (younger than 18 years). Although there are no clinical trials with adults, there is reason to believe that fluoride gels and varnishes work similarly for adults in these risk categories (grade D). As can be seen in the table, low-risk individuals may not receive additional benefits from professionally applied topical fluoride application (grade B). Fluoride gels and foam should be applied for 4 minutes. A 1-minute fluoride application was not endorsed, as clinical equivalence was not proven. The Council on Scientific Affairs found insufficient evidence to address

whether there is a difference in efficacy between sodium fluoride (NaF) and acidulated phosphate fluoride (APF) gels.

Based on systematic reviews, an evidence-based protocol for the use of fluoride varnish in children and adolescents recommends that fluoride varnishes (in the United States 5% NaF) should be applied twice a year, unless the individual has no risk of caries.[34] There is also good evidence of the complementary efficacy of preventive strategies such as sealants and varnish, as well as tooth brushing.[34] Fluoride toothpastes in comparison to mouth rinses or gels appear to have a similar degree of effectiveness for the prevention of dental caries in children. Fluoride varnish was not more effective than mouth rinses, and the evidence for the comparative effectiveness of fluoride varnishes and gels, and mouth rinses and gels is inconclusive.[29]

Caries-active patients In addition to a fluoride regimen at home, the caries-active patient may benefit from topical fluoride applications, which may be repeated every 2 to 3 months until caries activity is under control. In-office applications, however, are time-consuming and thus not as cost-effective, unless used in high caries-active patients.

Erupting teeth *Mineralization of erupting teeth*, following exposure of immature enamel to saliva, is a natural physiologic process.[35] Maturation can be stimulated by providing an oral environment that is supersaturated with ions. Hence, at times of tooth eruption (5 to 6 years of age; and 12 to 13 years of age) special attention is warranted for cleaning erupting surfaces and providing additional topical fluorides.[36] In addition to application of topical fluorides, erupting surfaces also may be protected by a transitional glass ionomer sealant. In contrast with resin sealants, glass ionomer may be used when moisture control is a problem. Recent meta-analysis found no conclusive evidence that either glass ionomer or resin-based sealant was superior to the other in preventing dental caries.[37] Glass ionomer sealant is indicated for erupting occlusal surfaces with overlying operculum where continued mineralization is needed. Upon setting, glass ionomer introduces an acidic cariostatic environment and provides a fluoride boost to the underlying maturing enamel. Serving as a semipermeable membrane, and replenished by fluoride toothpaste, it may continue to provide fluoride ions to the enamel during the eruption period while concurrently protecting the surface from acidic plaque fluids.

Root caries *Active root caries lesions* can be arrested by effective daily plaque removal with fluoride toothpaste.[38,39] The quality of plaque removal, and thus exposure of incipient lesions to saliva, is crucial for arresting active caries root lesions; buccal and lingual surfaces showed about 50% success rate, with less favorable outcome for approximal root lesions.[38] Application of topical fluoride, independent of the mode chosen, is appropriate management for root lesions.[40] This can be complemented with a 2-week regimen of twice-daily 0.12% chlorhexidine rinse, or in-office CHX varnish (currently in the United States only available as 1% CHX/1% thymol varnish). Patients also may be advised to use daily xylitol chewing gum (see the article by Svante Twetman elsewhere in this issue for further exploration of this topic).

Hyposalivation *Patients with a dry mouth*, or those who have been exposed to radiotherapy of salivary glands inevitably develop rampant, raging caries, unless following a strict caries-control program. As soon as radiotherapy begins, daily self-applied 5 minute topical applications with a 1% NaF gel in individually fitted trays[41] are advised in addition to meticulous daily plaque removal (brushing, flossing). Disclosing

Table 1
In-office topical fluorides

Evidence-Based Clinical Recommendations for Professionally Applied Topical Fluoride

Risk Category	Age Category for Recall Patients					
	<6 years		6 to 18 years		18 + years	
	Recommendation	Strength[a]	Recommendation	Strength[a]	Recommendation	Strength[a]
Low	May not receive additional benefit from professional topical fluoride application[b]	B	May not receive additional benefit from professional topical fluoride application[b]	B	May not receive additional benefit from professional topical fluoride application[b]	D
Moderate	Varnish application at 6-month intervals	A	Varnish application at 6-month intervals or Fluoride gel application at 6-month intervals	A A	Varnish application at 6-month intervals or Fluoride gel application at 6-month intervals	D[e] D[d]

High	Varnish application at 6-month intervals or Varnish application at 3-month intervals	A D[c]	Varnish application at 6-month intervals or Varnish application at 3-month intervals or Fluoride gel application at 6-month intervals or Fluoride gel application at 3-month intervals	A A[c] A D[d]	Varnish application at 6-month intervals or Varnish application at 3-month intervals or Fluoride gel application at 6-month intervals or Fluoride gel application at 3-month intervals	D[e] D[e] D[d] D[d]

Laboratory data demonstrate foam's equivalence to gels in terms of fluoride release; however, only two clinical trials have been published evaluating its effectiveness. Because of this, the recommendations for use of fluoride varnish and gel have not been extrapolated to foams.

Because there is insufficient evidence to address whether there is a difference in the efficacy of sodium fluoride versus acidulated phosphate fluoride gels, the clinical recommendations do not specify between these two formulations of fluoride gels. Application time for fluoride gel and foam should be 4 minutes. A 1-minute fluoride application is not endorsed.

[a] Strength of recommendation ranges from A (highest level of evidence from systematic reviews of randomized controlled trials) to D (lowest level of evidence from expert committee reports or opinions or clinical experience of respected authorities).

[b] Fluoridated water and fluoride toothpastes may provide adequate caries prevention in this risk category. Whether to apply topical fluoride in such cases is a decision that should balance this consideration with the practitioner's professional judgment and the individual patient's preferences.

[c] Emerging evidence indicates that applications more frequent than twice per year may be more effective in preventing caries.

[d] Although there are no clinical trials, there is reason to believe that fluoride gels would work similarly in this age group.

[e] Although there are no clinical trials, there is reason to believe that fluoride varnish would work similarly in this age group.

Adapted from American Dental Association Council on Scientific Affairs. Professionally applied topical fluoride: Evidence-based clinical recommendations. J Am Dent Assoc 2006;137(8):115–9.

remaining plaque, every day after brushing, to complete its removal may assist in achieving this meticulous daily plaque control that is so crucial for a positive outcome. If plaque control is insufficient, twice-daily fluoride (0.05% NaF) rinses could be added. Alternatively, in an attempt to temporarily boost plaque control, a dual rinsing strategy of fluoride and CHX-gluconate (0.05% NaF with 0.2% CHX) rinse could be advised to concurrently suppress the oral microflora. However, it is recommended to separate the application of an anionic product such as fluoride and a cationic product like CHX by at least a few hours to avoid binding of the active ingredients, and they should never be mixed together for the same reason. It is wise to provide regular professional tooth cleaning to these patients followed by high-concentration in-office topical fluoride application. Calcium phosphate-based compounds also may have a beneficial effect for patients with hyposalivation.[42,43]

Potentially Helpful Adjuncts to Home Fluoride (Emerging)	Special Needs
Antimicrobial boost: 4–6 ×/year	
Xylitol chewing gum: xylitol as first ingredient	
Chew 2 pieces for ≥5 min, 3×/day (after each meal preferred) for 2 weeks	
CHX rinse: 0.12% CHX-gluconate	Hyposalivation
Rinse ½ oz for 30 s, 2×/day for 2 weeks	
Calcium-based therapy:	
Calcium-based products (eg, paste, toothpaste, mints) with/without fluoride	Hyposalivation
Depending on product	

Calcium-Based Strategies

Fluoride alone cannot achieve remineralization; calcium and phosphate ions are necessary for remineralization to occur. The calcium and phosphates in saliva are the primary source for recrystallizing minerals. When salivary flow is hampered, rampant caries is the effect of the lack of these minerals. Remineralizing agents seek to promote remineralization through increase of bioavailable calcium and phosphate ions that become incorporated in tooth structure. Supplementing calcium and phosphates is likely to have a positive effect, in particular when effective fluoride levels are available at the same time. Although various formulations and modes have been tested in vitro, the complexity of the oral environment with/without saliva might lead to different results. With normal salivary flow, sufficient amounts of mineral will be readily available, and additional minerals may not be helpful. On the contrary, too much calcium, phosphate, or fluoride may contribute to limited remineralization.[44] With hyposalivation, however, supplementing fluorides with home applications of amorphous and reactive calcium phosphate complexes may greatly assist remineralization.

Potential benefits have been shown for casein phosphopeptides, amorphous calcium phosphates, and other approaches. Inhibition of enamel and dentin demineralization, promotion of remineralization, and a slow-down of the caries process as well as regression of subsurface lesions have been reported for casein phosphopeptide–amorphous calcium phosphate (CCP-ACP).[45] Although a remineralizing effect is reported for chewing gum and mints with CPP-ACP, solid evidence to support clinical efficacy for specific delivery modes remains lacking. More well-designed and

independent studies investigating clinically relevant conditions are needed. A recent systematic review reported that the quantity and quality of clinical trial evidence were insufficient to make conclusions regarding the long-term effectiveness of casein derivatives, specifically CPP-ACP, in preventing caries in vivo.[46] Clinical studies investigating the clinical benefits of CCP-ACP paste with and without fluoride are promising and emerging.[47] Although persuasive scientific evidence from randomized clinical trials (RCTs) is not yet available,[48] the off-label use of CPP-ACP technology may hold potential as an adjunct to fluoride treatment in the noninvasive management of early caries lesions.

Calcium sodium phosphosilicate bioactive glass is another new agent that reacts with an aqueous environment and releases calcium and phosphate ions. It is used as a desensitizer and approved as hypersensitivity agent. Off-label use as remineralizing agent is promoted, but simultaneous delivery of the right amounts of calcium, phosphate, and fluoride ions at the same time and location might be problematic and cause undesired adverse effects (eg, rapid precipitation). More research is needed to provide scientific evidence supporting claims of caries prevention and remineralization.[44]

Other emerging calcium-based strategies are entering the market. These include calcium phosphate solutions to reduce root caries and ACP technologies that can remineralize hard tooth tissues or at a minimum slow down the demineralization process.[49] Second-generation ACPs and multimodal approaches are being developed to prevent caries. These include new compounds with antimicrobial and remineralization potential.[50] In addition, a new experimental product employing synthetic HA in an acid paste is said to repair defects and replace crystals within a matter of minutes.[51] These strategies, however, are only recently available, too recent to be supported by solid evidence of their anticaries efficacy.

Summarizing, at this moment the scientific evidence to support the claim of caries-preventive efficacy from calcium-based products available in the US market has not been provided. Although promising in some cases and potentially beneficial, few studies have confirmed calcium-based agents have actually resulted in an anticaries benefit. Combinations of fluoride and calcium-based ingredients may involve potential formulation and compatibility challenges, and their mechanisms of action are likely difficult to demonstrate.[52] The level of evidence for calcium-based strategies reported in the literature remains incomplete and insufficient to substantiate claims by manufacturers or researchers. Application of these products cannot yet be recommended as evidence-based caries-preventive measures.

THE PROVEN AND THE NEW

Resin Sealants—A Proven Effective Management Strategy

An increasing body of evidence indicates that arrest of lesions is possible, even when dentin is involved. Sealants protect the underlying surface by blocking renewed and continuous attacks by plaque acids. Sealants prevent plaque accumulation and dissolution of minerals from the tooth tissues. They have been used successfully for many years[53,54] and have shown a clear benefit even when partially lost.[55,56] In particular when caries risk is moderate to high, teeth with caries-susceptible pits and fissures will greatly benefit from sealing. The ADA Council on Scientific Affairs assessed the available body of evidence, which led to clinical recommendations.[57] The effectiveness of sealants in managing noncavitated and cavitated caries lesions was overwhelming.[58] The recommendations were based on six systematic reviews, and no matter how studies were grouped, the effect of sealants was strong and

consistent. Sealed noncavitated lesions consistently had better outcomes than unsealed lesions, while the percentage of sealed carious surfaces that progressed was low. Sealants resulted in a caries reduction of about 71% up to 5 years after placement.[58]

Concerns about placing sealants over undetected dentin caries are ungrounded, as there is ample evidence that caries lesions do not progress as long as the fissures remain sealed.[59,60] It also has been reported that sealed teeth with fissures showing a partial sealant or a lost sealant over a 3-year period still showed caries reduction, and thus were more protected than unsealed teeth.[61] The caries risk in formerly sealed teeth appeared to be not higher than teeth that never were sealed.[56] Sealing of cavitated lesions significantly reduced bacteria levels (50% to 99% of mean bacteria counts), and this effect increased with time.[62] Caries lesions under intact sealants may even regress. Cavitated, but sealed frank dentin caries lesions also have been shown not to progress over a period of 10 years.[63] Additionally, sealed restorations placed over caries lesions arrested the caries progression in these lesions.[64] Recently, updated evidence-based recommendations were published by a Centers for Disease Control and Prevention (CDC) work group, recommending to seal sound surfaces and noncavitated lesions and to provide sealants to children even if follow-up cannot be ensured.[65]

Because even active dentin lesions that are covered by a well-applied sealant do not progress, there is no good reason to be hesitant in promoting sealants in caries-prone patients. Sealant protection is in particular indicated during periods of tooth eruption (ages 5 to 6 years and 10 to 12 years). When moisture control is a problem, glass ionomer sealants may be indicated for erupting first molars. Also older high-risk patients with suspect fissures will benefit from sealants. A third category of high-risk patients, those with appliances, also will benefit greatly from sealing tooth areas with a high potential of future caries activity (eg, around orthodontic brackets and removable partial denture clasps).

As strongly evidenced, both sealing of the caries process and sealing of restorations appear to be highly effective in conserving sound tooth tissue and providing protection to the hard tooth tissues against caries progression. Where indicated (patients with moderate and high caries risk), sealant application is an essential part of an effective and preventive caries management plan. Only when previous attempts to arrest the lesion have failed and there is evidence of lesion progression is a restorative treatment approach warranted.

Resin infiltration of lesions

Resin infiltration of early lesions is a recent development by which subsurface porosities in the lesion are being filled with a resin to strengthen this area.[66] Due to the concurrent sealing of the caries lesion from the oral environment, progression of the lesion is halted. Once the porous demineralized enamel is filled with resin, it has been claimed that its refractory index changes also. The lesion may become less opaque and thus less visible as it regains translucency. After erosion of the superficial surface layer using hydrochloric acid, the underlying pores are opened up, and a low-viscosity resin is able to penetrate into the demineralized tissues. A drawback of this technique is the need for erosion of the intact surface layer, which ultimately is replaced by the resin and the fact that the resin, once placed, will make natural remineralization therapy impossible (similar to a sealant). Short-term results from the first clinical studies that used this enticing concept for approximal and smooth surface lesions are emerging, and judgment about its clinical efficacy is still out. Until proper clinical trials have been presented, this novel approach should be used wisely and in conjunction with other preventive strategies.

Alternative Treatment Options

In the last decade, laser ablation has been applied in caries research. Lasers have been used to coalesce enamel fissures[67] and to provide greater caries resistance to the outer enamel surface. Increased attention for this technology has led to research aiming to optimize the laser parameters to achieve an optimal ablation effect. The large variability in lasers and laser parameters used has not yet led to consensus about their use.[67,68] CO_2 laser irradiation in combination with fluoride treatment is more effective in inhibiting caries-like lesions than CO_2 laser irradiation or fluoride alone.[69] These technologies are still emerging, and evidence of clinical anticariogenic efficacy is not yet available or scarce at best. No evidence of anticaries efficacy in controlled clinical studies has been reported so far. Laser treatments for caries inhibition are still considered experimental and cannot be recommended.

An interesting discussion of other novel preventive management options that are currently under investigation includes promising treatments already applied in clinical practice.[70] The authors conclude that many of the techniques mentioned show considerable promise, and dentists should be aware of these developments and follow their progress. The evidence, however, for each of these novel preventive treatment options is currently insufficient to make widespread recommendations, and more research needs to be done to show clinical efficacy for effective caries control.

SUMMARY

At the individual patient level, there is a great variation in the complex interplay between all known and unknown factors that are involved in lesion development. Assessment of caries risk of the individual patient is an important prerequisite for an appropriate and successful management strategy. Therefore, clinical recommendations have to be balanced with the clinician's professional judgement and the patient's history and preference.

Available strategies for noninvasive tissue repair are summarized in **Table 2**. By providing repair options that encourage remineralization, the damage of the initial caries process may be healed. Vulnerable tissues may be protected and strengthened.

Noninvasive Management Strategies—Implications for Clinical Care

Evidence-based management strategy should be tailored to the individual, with due regard to negative risk factors.

Find out which major causal factors led to the patient's caries problem. To prioritize and address these factors should be the main goals when assisting the body's response toward caries control.

Table 2
Protection and remineralization of damaged enamel

Noninvasive Demineralized Tissue Repair		
Mode	**Mechanism**	**Strategy**
Remineralize	Replenish ions (F, Ca, P)	Heal + increase acid resistance
Remineralize + protect	Seal lesion area (glass ionomer)	Heal + seal
Protect	Seal lesion area (resin)	Seal
Strengthen + protect	Resin infiltrant	Strengthen + seal

Sealants are strongly recommended for all at-risk surfaces (sound or noncavitated)

Management strategies should be based on interpretation of lesion activity and future caries risk of the patient.

Active monitoring of lesion activity and the patient's compliance with behavioral modifications (oral hygiene, adjunct therapies, and diet) are essential parts of a successful caries management and maintenance plan.

Preventive noninvasive strategies demand and rely on patient cooperation. Regular recall visits to assess and discuss cooperation are important for long-term results. Motivating the patient is key to success!

Although there are increasing numbers of technologies aimed at enhancing tooth remineralization, fluoride remains the most widely used agent for managing the caries process, supported by strong levels of evidence.

The primary modes of action of fluorides are enhancing remineralization, inhibiting demineralization, and inhibition of the biofilm. The most important effect, enhancement of remineralization, only can occur in the presence of calcium and phosphate ions.

When saliva flow is inadequate, topical fluorides might be assisted by additional supply of calcium and phosphates to enhance remineralization.

In individuals with a high caries challenge, fluoride therapy is not always enough to overcome the challenge. In high-risk individuals, an effective management strategy may call for increased and frequent fluoride delivery together with an antimicrobial therapy to take advantage of the synergy and complementary effect of both modes of action.

New emerging technologies should be considered adjuncts to fluoride treatments until their caries-preventive and therapeutic efficacy is sufficiently evidenced in well-designed RCTs.

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