Remineralisation – the buzzword for early MI caries management

B. T. Amaechi[1]

In brief

Highlights that minimal intervention dentistry aims to preserve dental tissues first and restore only when indicated.

Emphasises non-operative treatment of initial caries lesions as an integral part of comprehensive caries management.

Discusses the strategies available to aid in arrestment/remineralisation of initial caries lesions on root and coronal surfaces.

Points out that all caries remineralisation treatment be complemented with general behaviour modification advice.

Minimal intervention (MI) dentistry aims to preserve dental tissues first and restore only when indicated, thus remineralisation of initial (non-cavitated) caries lesions, an integral part of caries management, is an essential treatment strategy in MI. With this understanding, dental practitioners are increasingly embracing the principle of non-operative treatment of initial caries lesions. The purpose of this review was to summarise the most recent literature published in non-operative management of dental caries. Three electronic databases (MEDLINE, EMBASE, Cochrane CENTRAL) were searched, and clinical studies, systematic reviews and meta-analysis were included. This report outlines the strategies and numerous therapeutic materials available to aid in arrestment/remineralisation of initial caries lesions on root and coronal surfaces. However, the level of evidence of effect is variable, as well as the availability in different parts of the world. Options available to practitioners will vary when placing emphasis on the level of evidence supporting them. Strong clinical evidence support the effectiveness of pits/fissure sealants for therapeutic management of active initial caries on occlusal surfaces, and fluoride varnishes for remineralisation of caries lesions on root and coronal smooth surfaces, including proximal surfaces. Other materials formulated to enhance the effectiveness of any chosen remineralisation strategy were discussed. However, it is absolutely necessary that all caries remineralisation treatment be complemented with general behavioural modification in oral health through motivational interviewing directed towards change in oral hygiene to control plaque, dietary attitude modification to reduce the frequency of intake of fermentable sugars, and establishment of risk-based recall visits.

Introduction

Traditionally, radiographic evidence of demineralisation in enamel or to the dentino-enamel junction led to the immediate decision to place a restoration. Although such management is still an accepted part of some licensing board examinations, the advent of minimal intervention dentistry, which is based on contemporary researches has shown that this is not the right approach. Minimal intervention (MI) stresses a preventive philosophy, with individualised risk assessment; accurate and early detection of caries lesions; and efforts to arrest and then remineralise non-cavitated lesions with the prompt provision of preventive care in order to minimise operative intervention.[1,2] A MI approach to caries management is the cornerstone of the modern comprehensive personalised caries care plan (Fig. 1), aimed to maintain health by preserving tooth structure and restoring only when indicated, of which remineralisation of initial stage caries lesions is an essential component.[3] Remineralisation is the delivery and deposition into the caries lesion of the mineral elements, mostly calcium and phosphate, lost through demineralisation of the tooth tissue, which results in growth by apposition of hydroxyapatite crystals (or partially fluoridated crystal structure when fluoride is present in the environment). The aim of remineralisation as the treatment of choice for an active initial stage (non-cavitated) caries is to reverse the caries lesion or arrest the progression of the lesion to cavitation. It is well established that early caries lesions are more prevalent than cavitated tooth surfaces,[4] especially in children aged 18 months and below,[5] thus the need for remineralisation strategies. Even for an active cavitated lesion, when operative intervention is unequivocally required, remineralisation can be used as an interim treatment to arrest the caries lesion progression when caries control is necessary before placement of definitive restorations or when traditional operative care is not feasible, especially in primary teeth that will exfoliate with time.

Before discussing how to accomplish remineralisation, it is important to remember that caries initiation and progression is a dynamic process involving alternating periods of demineralisation (caused by bacteria acids from fermentable dietary sugars) and remineralisation (facilitated by saliva). Caries

[1]Professor and Director of Cariology Department of Comprehensive Dentistry University of Texas Health Science Centre at San Antonio, 7703 Floyd Curl Drive, San Antonio, Texas
Correspondence to: Bennett Amaechi
Email: amaechi@uthscsa.edu

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lesions develop and progress when the cumulative, negative mineral balance (net demineralisation) exceeds the rate of remineralisation over an extended period.[6] This situation occurs when the pathological factors (salivary dysfunction, poor plaque control, frequent intake of simple dietary sugars) that increase caries risk outweigh the protective factors (good oral hygiene, reduced intake of simple dietary sugars, adequate saliva flow/its component mineral ions) that decrease caries risk, tilting the caries balance towards caries development.[6] Thus remineralisation is a natural process, which can be accomplished unaided by changing the local biochemistry of the oral environment to one that reduces the proliferation of cariogenic bacteria, neutralises plaque acid and provides the required minerals for lesion remineralisation, through alteration in oral hygiene and dietary behaviour of the patient, in addition to fluoride application and saliva stimulation. In situations where the caries is due to a medical condition causing salivary gland dysfunction, the remineralisation process should unequivocally be aided, while in cases where the risk factors are behavioural such as poor dietary and oral hygiene attitude, the compliance of the patient to behavioural modification advice is required to achieve remineralisation, otherwise the remineralisation process has to be aided. In general, for remineralisation to be successful it should be preceded by caries control at various levels: at the patient level by engaging the individual to reduce the frequency of intake of simple dietary sugars and maintain adequate plaque control; at the local level by establishing and maintaining a neutral pH and state of supersaturation of calcium and phosphate ions on the tooth surface; and at the lesion level by prolonged mineral ions' access to the lesion body.[7] The control at local and lesion levels can be aided using a plethora of technologies described later.

Fig. 1 The Caries Management Cycle of the International Caries Classification and Management System (ICCMS™).3 (Courtesy: ICCMS™ & the Global Collaboratory for Caries Management)

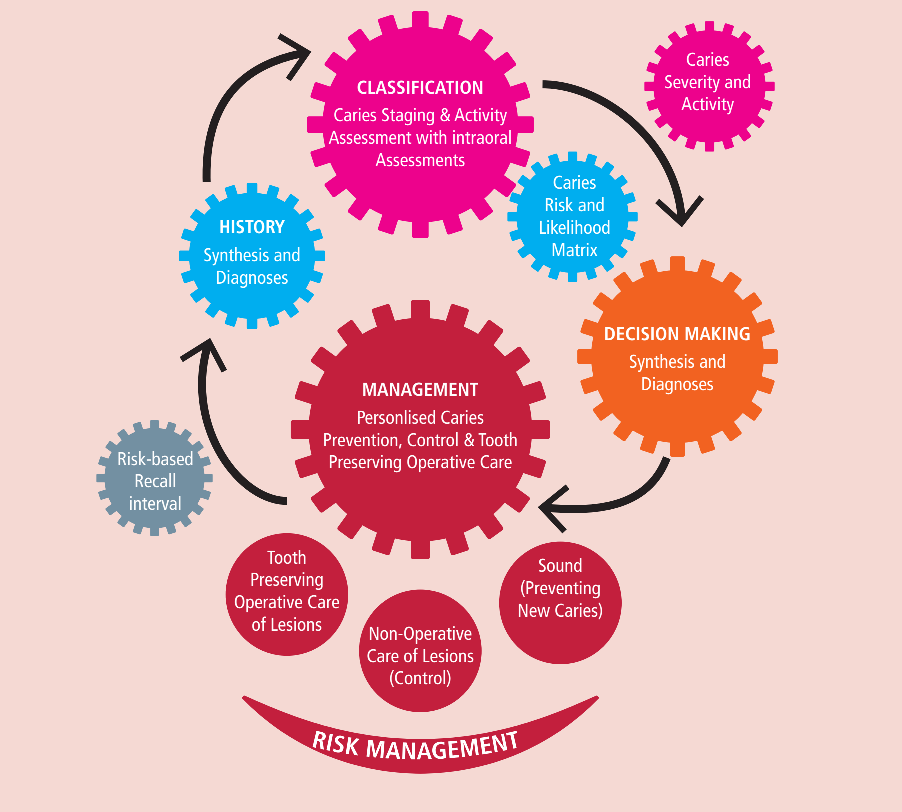
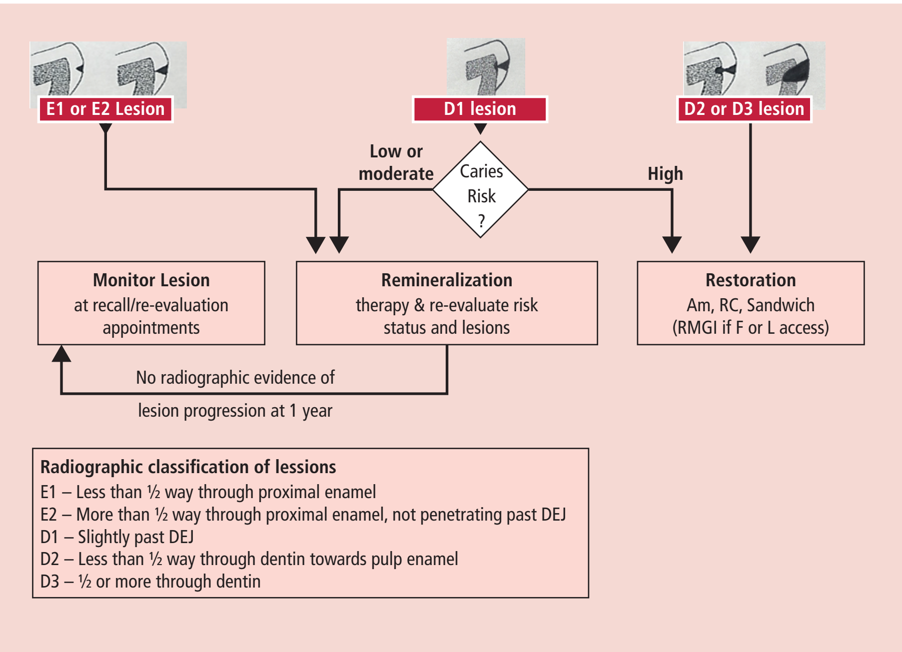


Fig. 2 Decision tree for management of caries lesions on proximal coronal surfaces. (Courtesy of the Department of Comprehensive Dentistry, University of Texas Health Science Centre at San Antonio, UTHSCSA)



Remineralisation

When and what level of lesions do we remineralise?

A crucial step in the development of a caries care plan involving non-operative care of lesions is caries diagnosis, which would distinguish the cavitated and non-cavitated lesions. Among the non-cavitated lesions, considering that their whitish appearance (white spot lesion) is due to changes in the optical properties of enamel consequent to demineralisation or hypomineralisation, the initial caries lesions should be differentiated from the developmental hypomineralisations through accurate diagnosis. Diagnosis, unlike detection, does not consider only the clinical signs of caries, but takes into account the dynamics and determinants of the caries process. Furthermore, among the initial caries

Table 1 Differences between white spots due to caries and developmental hypomineralisation. ourtesy of ICCMS™ & the Global Collaboratory for Caries Management

Factors	Initial caries lesion	Developmental hypomineralisation
Appearance	Opaque, chalky and dull (matt) surface when air-dried (>5 seconds)	Glossy and smooth surface like a sound enamel when air-dried (>5 seconds)
Discoloration	May be discoloured by extrinsic stain	No extrinsic discolouration except in mottling due to severe fluorosis
Texture	Feels rough when the ball end of a CPITN probe or blunt tip of the explorer is moved gently across the surface	Feels smooth when the ball end of a CPITN probe or blunt tip of the explorer (probe) is moved gently across the surface
Location	Located in plaque stagnation areas (areas diffi-cult-to-reach by toothbrush)	At any point on the tooth surface but more definite if in self-cleansing areas
distribution	May occur on multiple teeth without any resemblance to each other	May occur with similar shape on corresponding sites on all the four identical teeth (for example, all first premolars, canines, etc.) in the four quadrants of the dentition

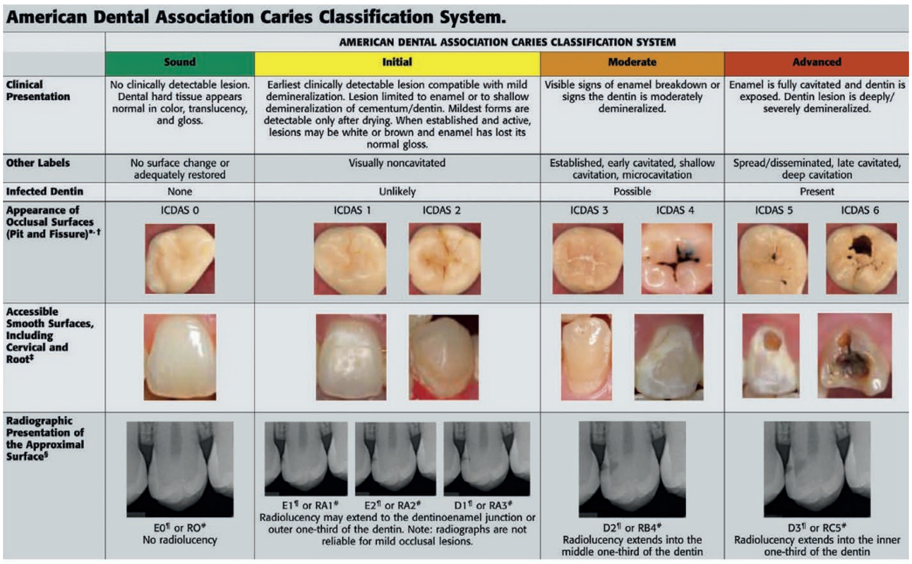


Fig. 3 ADA Caries Classification System 2015. Reprinted from *J Am Dent Assoc*, 146, Young D A *et al*. The American Dental Association Caries Classification System for clinical practice: a report of the American Dental Association Council on Scientific Affairs, 2015, with permission from Elsevier

lesions, the active lesions need to be distinguished from the inactive (arrested) lesions. The conventional caries diagnostic methods are visual and radiographic examinations. For proximal surfaces, bitewing radiograph is the most accurate method for detecting initial caries when there is contact between proximal surfaces, though it is less sensitive for very early stage lesions.[8] The radiograph should be examined carefully to determine the depth of the radiolucency (caries lesions) in relation to the enamel, dentino-enamel junction and dentin since this is crucial to remineralisation decision (Fig. 2). Although considered subjective, less sensitive and of poor specificity on the occlusal pits and fissures, visual inspection is the most often used method for diagnosing initial caries on the accessible (smooth and occlusal) surfaces of the tooth. Radiographic evaluation of these surfaces has been found to be of minimal diagnostic value for detecting initial caries because of the large amounts of surrounding sound enamel.[8] However, the accuracy of the visual examination for diagnosis of initial caries can be improved when the tooth surface is cleaned (no plaque), thoroughly dried (>5 seconds) and the practitioner is equipped with air-water syringe, good lighting, a Community Periodontal Index of Treatment Need (CPITN) probe (ball-ended), and when possible, a magnification device. The accuracy of visual caries detection can be improved by 50% by the use of magnifying devices such as a head-worn prism loupe or a surgical microscope.[9] With these tools, a white or brown spot lesion detected on tooth surface can be diagnosed as either an initial caries lesion or a developmental hypomineralisation using the criteria outlined in Table 1.

Before the decision to remineralise should be taken it is important to assess the activity status of the lesion since it is an active lesion that has the tendency to progress. There are some features of individual lesions that indicate whether a lesion is active or arrested. Some of these features will be obvious the first time a dentist and patient meet. Active initial enamel lesions, which are commonly located in plaque stagnation areas, present a chalky white and dull (matte) surface when air-dried, feels rough when the blunt tip of the probe is moved gently across the surface, and are usually covered by visible plaque.[10,11] An inactive or arrested enamel lesion may be white or brown with a plaque-free shiny surface that is mainly smooth but sometimes rough.[10,11] A caries lesion on a root surface is seen as a clearly demarcated, light brown, dark brown or black discoloured area on the root surface or at the cemento-enamel junction.[12] While an active root caries may feel soft or leathery with a rough and matte surface, an arrested/inactive root lesion feels hard in texture with smooth and shiny surface.[12] Early root caries is considered clinically cavitated if there is loss of surface integrity (anatomical contour) with a depth equal or greater than 0.5 mm when measured with the ball of the CPITN probe.[12] The ball is 0.5 mm in diameter, so if the cavity accommodates the ball, then the depth is ≥0.5 mm. If there is no loss of surface integrity or depth of loss is less than 0.5 mm (not accommodating the ball), it is considered non-cavitated.[12]

Even when an initial lesion is diagnosed as an active lesion, the decision to remineralise an active initial caries lesion depends on the clinical stage of the lesion and the radiological extent (when information is available) of the demineralisation in enamel or dentin (Fig. 3)[3,13] as well as the caries risk status of

Table 2 ICCMS™ Risk analysis to assess likelihood of new lesions or progression of existing caries.[3] *Sound surfaces/or inactive lesions. Courtesy of ICCMS™ & the Global Collaboratory for Caries Management

Risk status	Current caries activity status at the patient level		
	No active caries lesions*	Initial stage active caries lesions	Moderate-or advanced-stage active caries lesions
Low risk	Low likelihood	Moderate likelihood	Moderate likelihood*
Moderate risk	Low likelihood	Moderate likelihood	High likelihood
High risk	Moderate likelihood	High likelihood	High likelihood

Table 3 Diagnostic stages of caries based upon clinical and radiographic status[3]

Clinical caries classification (C) for a tooth surface	Radiographic caries classification (R) for a tooth surface			
	R_{sound}	$R_{initial}$	$R_{moderate}$	$R_{Advanced}$
C_{Sound}	Sound	Initial	Moderate	Advanced
$C_{Initial}$	Initial	Initial	Moderate	Advanced
$C_{Moderate}$	Moderate	Moderate	Moderate	Advanced
$C_{Advanced}$	Advanced	Advanced	Advanced	Advanced

Fig. 4 Decision tree for management of caries lesions on occlusal pits and fissure. (Courtesy: Department of Comprehensive dentistry, UTHSCSA)

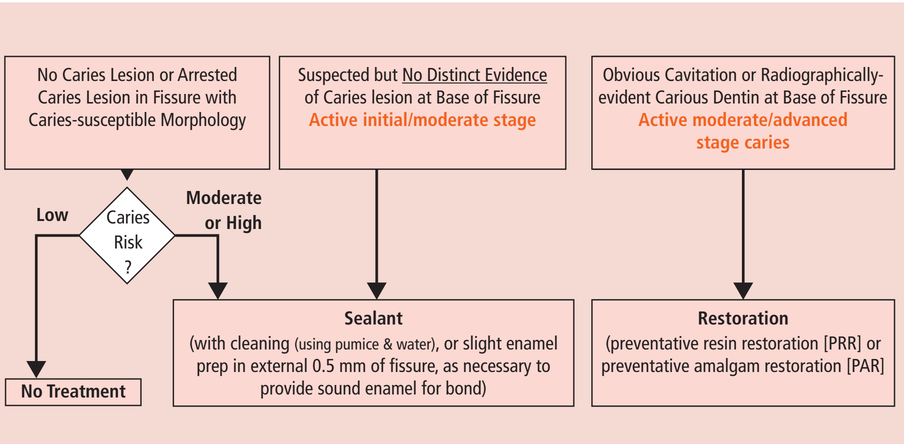
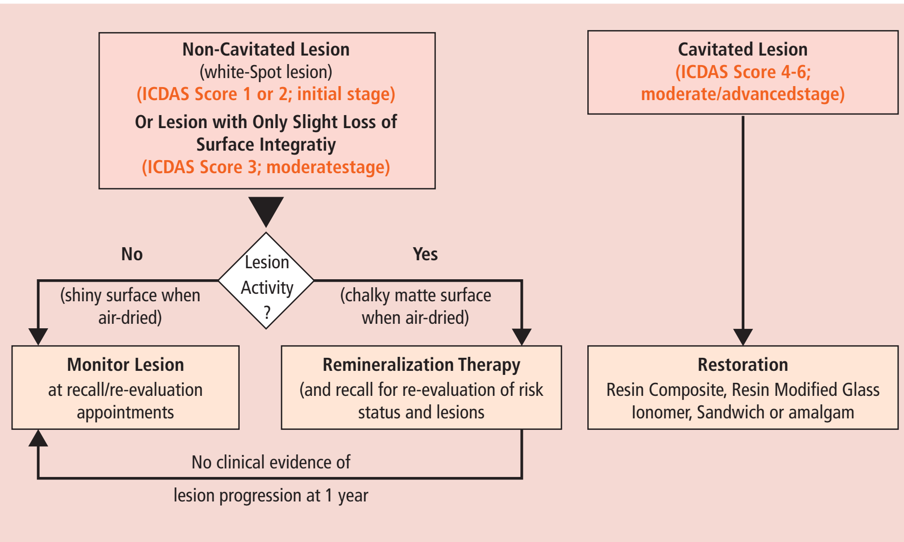


Fig. 5 Decision tree for management of Caries Lesions on Non-Proximal Coronal Smooth Surfaces. (Courtesy: Department of Comprehensive dentistry, UTHSCSA)



the patient, all of which determine the likelihood of the lesion progressing to cavitation (Table 2). However, the diagnostic staging of caries lesions for treatment decision should be based upon both the clinical and the radiographic presentations of the lesion as shown in Table 3.[3] Establishment of the right protocols can guide the practitioner to a better treatment decision as well as help protect the patients. The decision trees depicting treatment decisions based on the caries risk status of the patient are shown in Figures 2, 4, 5 and 6. Although the decision tree shown in Figure 2, which is based on the review of the best available evidence,[3] suggests remineralisation for initial caries with radiolucency reaching the outer one-third of dentin, this recommendation can be locally modifiable provided that the lesion is confirmed not cavitated. It is appreciated that proximal lesion cavitation is difficult to diagnose by conventional clinical or radiographic means; however, the probability of having a cavity is greater for deep dentinal lesions than for small enamel lesions (Fig. 7),[14] but considerable uncertainty exists for lesions at the dentino-enamel junction.[15]

What to use and How to accomplish remineralisation.

The selection of strategies for remineralisation of a caries lesion should be based on the best available evidence while taking into account the dentist's knowledge and expertise and focusing on the caries risk status of the patient, but at the same time not neglecting the needs and desires of the patient. However, considering that a patient with an active initial caries is at a high caries risk and a high likelihood of his/her lesions progressing to cavitation, the remineralisation strategies and materials discussed here are tailored for such category of patients. The use of any remineralisation product for such individuals should always be accompanied with active preventive measures of good oral hygiene, dietary modification, a daily use of high fluoride containing toothpaste/or mouthrinse with frequent reviews

Fig. 6 Decision tree for management of caries lesions on root surfaces. (Courtesy: Department of Comprehensive dentistry, UTHSCSA)

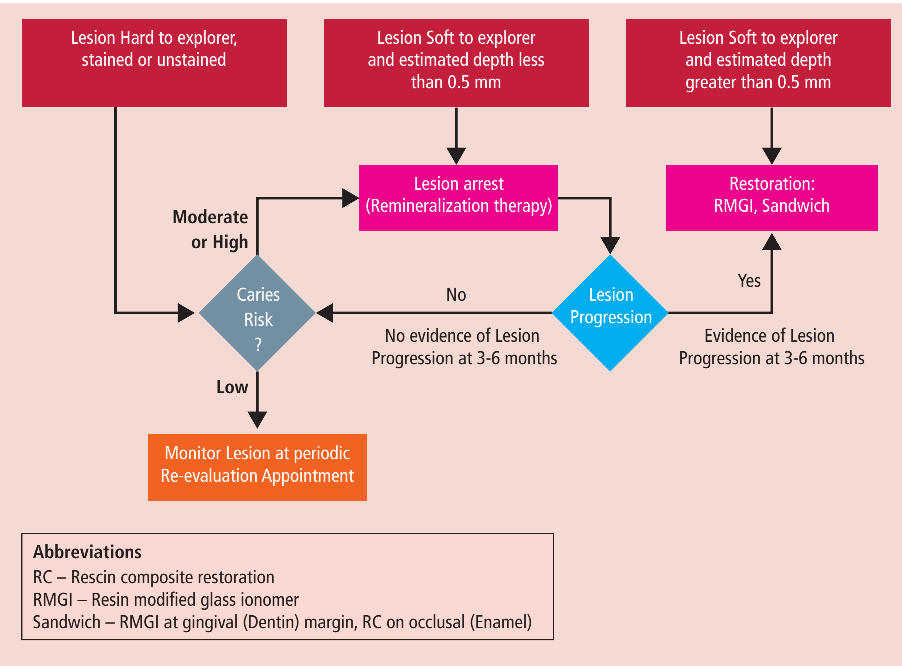
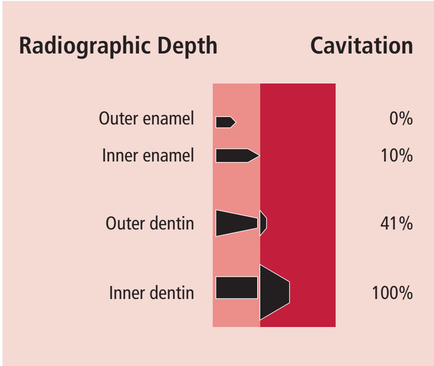


Fig. 7 Prediction of proximal caries lesion cavitation based on the depth of radiolucency in bitewing radiograph[15]



and recall visits.[3] Thus, before discussing the available materials to aid remineralisation, behavioural modification and recall visits need to be discussed as crucial components of remineralisation strategies.

Behavioural modification

Empowering the patient to adopt healthy behaviour should be incorporated as part of the caries care plan for patients. The primary objective of behavioural modification, as a crucial component of any remineralisation strategy, is to encourage patient behaviours that maintain adequate plaque control and reduce frequency of intake of simple dietary sugars as well as influence his/her compliance with the use of self-applied home-use materials prescribed to aid the remineralisation process. Counselling in behavioural modification should be individualised, and directed to getting the patient to doing the minimum necessary to restore balance in the oral environment. It has been demonstrated that motivational interviewing is the most effective and successful way to deliver information and advice that translate into sustained changes in behaviour.[16–18] Motivational interviewing is a patient-centred method for enhancing intrinsic motivation to change by exploring and resolving ambivalence. Individuals assess their own behaviours, present arguments for change, and decide what behaviour to focus on; while the counsellor helps to create an acceptable resolution that triggers change. Factors that might influence the patient's compliance such as the desire and willingness to change, the ability/skill to carry out the involved tasks, the financial costs to the patient, cultural issues, and other personal factors, must be considered and discussed with the patient. The ultimate aim is to empower the patient to adopt and sustain a behaviour that will improve and maintain their oral and general health.

Recall visits

An important component of the remineralisation strategy is the recall visits, which is a continuing care regime. This is particularly needed in remineralisation therapy of initial lesions as it offers the practitioner the opportunities to: (1) assess the status of the previously diagnosed and treated lesions; (2) enable the clinician to consider altering the treatment regimen (if necessary) to obtain a more favourable outcome; (3) monitor patient compliance with previous advice and treatment; (4) encourage patient behaviour that will improve and maintain their oral and general health; and (5) measure the outcomes of the treatment, including the impact on the patient's quality of life.[19] The UK National Institute of Health and Clinical Excellence (NICE) recommended that the individual patient's age and caries risk status should inform his/her recall interval, and as such should be personalised.[20] According to the recommendation, the interval should vary from three to 24 months, with patients at high caries risk starting with three months interval irrespective of their age. As previously stated, a patient with an active initial caries is at a high caries risk and a high likelihood of his/her lesions progressing to cavitation, and as such should be started with three month interval. Following a review of the patient's caries risk status at each recall visit, the previously recommended recall interval should be reviewed for possible alteration according to the prevailing caries risk status and patient compliance to previous advice. The patient's compliance with the visits could be facilitated by prior discussion with the patient, regarding the recommended recall interval, the patient's ability or desire to visit the dentist at the recommended interval, the financial costs to the patient, including any possible insurance coverage issues, and any subsequent treatments. However, the longest recall interval between visits should be 12 months for patients younger than 18 years, and 24 months for patients aged 18 years and older.[19,20]

Materials available to aid remineralisation therapy

Choosing the right products is the key to better remineralisation outcomes. Ideal remineralisation material should diffuse or deliver calcium and phosphate into the lesion or boost the remineralisation properties of saliva and oral reservoirs without increasing the risk of calculus formation.[21] However, before discussing the wealth of materials and strategies currently available to practitioners to aid remineralisation of active initial caries lesions, it is pertinent to look into the strengths and limitations of fluoride as a remineralising agent since the caries remineralisation ability of fluoride is considered the 'gold standard' against which other remineralisation systems have to compete, either alone or in combination with fluoride.[22] Fluoride is currently recognised as the main active ingredient in different fluoridated products tailored for remineralisation and arrestment of progression of existing caries.[7] However, the reversal of early lesions by fluoride vehicles is most effective at the surface of the lesion,[23] and in many cases, especially at high fluoride concentration, causes lamination.[24] Lamination is a phenomenon in which remineralisation occurred mainly at the porous surface layer of the lesion, causing the blockage of enamel pores and thereby reducing the mineral ions' access to the lesion body, and hindering the full remineralisation of the underlying lesion body.[25] Thus strategies that could work either better than or synergistically with fluoride to provide a fuller remineralisation of lesions should be ideal, some of which are discussed below. Numerous caries remineralisation therapies available today are discussed below in relation to different surfaces of the teeth in a way that is relevant to clinical practice. The level of evidence of effect is variable, as well as the availability in different parts of the world. Two remineralisation strategies have the highest level of supporting evidence, pit/fissure sealants for occlusal surface lesions, and topical fluorides for proximal and smooth surface lesions.

Remineralisation therapy for active initial caries lesions on occlusal surfaces

When active initial fissure caries has been diagnosed, sealants should be indicated, preferably fluoridated or fluoridated/antimicrobial sealants (Fig. 4). After acid etching, (for lightly filled resin fissure sealant or a flowable resin composite), or conditioning (for glass ionomer cements), the sealant material is used to penetrate the fissures, rendering it self-cleansing to prevent plaque accumulation. There is strong evidence that, regardless of lesion severity, sealants were 100% effective in controlling initial caries lesions on occlusal surfaces, and if sealant is intact, caries lesions will not progress.[26–31] Consequently, the American Dental Association and the Centres for Disease Control and Prevention support the sealing of non-cavitated caries lesions.[32,33] It is appreciated that one of the barriers to universal acceptance of this evidence-based clinical recommendation is the difficulty in monitoring the progression of the lesions underneath the sealant,[34] considering that the effectiveness of resin-based sealants depends on long-term retention.[35,36] However, it has been demonstrated that these lesions, when sealed with a clear sealant, can be monitored by visual examination using the criteria of the International Caries Detection and Assessment system (ICDAS) or electronically using devices such as quantitative light-induced fluorescence (QLF) and DIAGNOdent, which may aid in predicting the need for sealant repair over time.[26] Some clinicians wonder the fate of bacteria entrapped within the pits/fissures; it has long been established that following sealant, there is a major reduction in viable microorganisms within the first two weeks, and a gradual reduction in the total count thereafter, with a 2,000-fold decrease in the number of cultivable microorganisms after 2 years, and there was no progression of the caries lesions.[37,38]

A formulation of pits/fissure sealants contains surface pre-reacted glass-ionomer (SPRG) filler (GIOMER products; SHOFU Inc., Kyoto, Japan), in which a ligand exchange mechanism within the pre-reacted hydrogel endows the SPRG fillers with the ability to release and recharge fluoride ions, and as such can achieve a sustained fluoride release, in addition to the release of multiple other ions such as Sr^{2+}, Na^{+}, BO_3^{3-}, Al^{3+}, and SiO_3^{2-} at high concentrations.[39] This multiple ion-releasing capacity endows this material with several therapeutic effects, including reduction of the pathogenicity of the cariogenic plaque,[40,41] shifting the pH of the surrounding medium to weak alkaline regions,[39] enhancing the formation of apatite in the presence of mineralising oral fluid, such as saliva,[42] and conversion of hydroxyapatite to strontium apatite that enhance the acid resistance of teeth surrounding enamel.[42] Although commercially available, clinical evidence of its efficacy is lacking.

Remineralisation therapy for active initial caries lesions on root, proximal and non-proximal smooth surfaces

Remineralisation/arrestment of active initial caries lesions can be achieved successfully with a combination of improved oral hygiene and application of topical fluoride materials and/or other caries remineralising agents. The selection of materials and the regimen to follow for remineralisation of active lesions on the proximal, non-proximal coronal smooth, and root surfaces should depend on the nature of the materials and the likelihood of caries progression in an individual patient (Table 2). These materials are available either for professional topical application or self-applied home-use. Combination of both professional and home-use materials enhances the remineralisation process. Materials available to practitioners for remineralisation, which may vary in different parts of the world, are discussed below.

Fluoride varnishes

It has long been established that fluoride varnish (FV) application is effective in reversing and arresting active enamel lesions,[43–45] including proximal caries,[46] and therefore reduces the need for restorative intervention. Several *in vivo* studies demonstrated that sodium fluoride varnishes professionally applied at least once every three months were 67-80% effective in arresting initial root caries and reducing the numbers of cariogenic bacteria.[47–51] At least four times per year is required for patients at high likelihood of lesion progression, and this regimen should be accompanied with a daily use of high fluoride containing toothpaste and acidulated mouthrinse or gel. The varnish can be dragged onto the proximal surfaces with dental floss using forward and backward strokes. FV application takes less time, creates less patient discomfort, and achieves greater patient acceptability than does fluoride gel, especially in preschool-aged children.[52] Professional prophylaxis is not necessary before varnish application, thus reducing the application time.[53] Although FV comes in varying concentrations ranging from 1.1–5% NaF, and fluoride uptake by enamel was greatest with the most concentrated varnish,[54] the efficacy of the FV in remineralising initial caries is not proportional to the fluoride concentration, but rather to the number of applications.[55,56] FV application on tooth surfaces results in formation of a deposit of calcium fluoride globules that can act as a reservoir for the slow release of fluoride and calcium over time under acid challenge, thus the rate of fluoride release is enhanced at lower pH levels.[56–58] As previously described, FV with its high fluoride concentrations may cause lamination of the porous surface layer of the lesion, and this may imply that the fluoride varnishes only arrest the progression of the lesion by stabilising (remineralising) the surface layer of the lesion while still retaining the subsurface demineralisation. This effect could be mitigated by combining its use with daily home-use of either an acidulated dentifrice (mouthrinse or gel) or stannous fluoride dentifrice for reasons described later.

Some special technologies, such as casein

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phosphopeptide stabilised amorphous calcium phosphate (CPP-ACP)[59] and functionalised βtricalcium phosphate (*f*TCP),[60] have been incorporated into certain brands of FV, but the advantages of FV with these added technologies over the fluoride-only varnishes has not been proven in randomised clinical trials. In *f*TCP, by milling βtricalcium phosphate (TCP) with organic materials (functionalisation) the calcium oxides in TCP become 'protected' by the organic materials (fumaric acid or sodium lauryl sulphate), thus allowing the calcium and phosphate ions of the TCP to coexist with fluoride ions in an aqueous dentifrice base (toothpaste or varnish) without premature TCP-fluoride interactions.[60] When applied intraorally saliva degrades the protective coating, releasing calcium at the tooth surface, resulting in high fluoride and calcium ions bioavailability on the lesion surface, and subsequent diffusion into the lesion to promote remineralisation.

Self-assembling peptides

Self-assembling peptides (P_{11}-4) monomers for regenerative treatment of initial caries lesions (Curolox Technology) is a new technology that is commercially available in Europe as a monomer (Curodont Repair, Credentis AG, Windisch, Switzerland). The monomeric low-viscosity peptide solutions, when applied to an initial caries lesion, diffuse into the subsurface micropores of the lesion and assemble under high ionic strength into a 3D-matrix (scaffold), which attracts mineral ions, mainly calcium, phosphate and fluoride, from saliva and triggers *de novo* nucleation of hydroxyapatite nanocrystals around the matrix, resulting in biomimetic mineralisation that enables the regeneration of enamel and dentin.[61,62] The safety and clinical efficacy of this monomer was demonstrated in a clinical study in which a single application resulted in significant enamel regeneration.[63] However, the success of initial caries treatment with self-assembling peptides monomer depends strongly on the diffusion of the monomers into the lesion body, thus the application requires prior prophylaxis to remove biofilms and mineral deposits that may inhibit diffusion. Also, the application requires prior etching of the lesion surface to open the pores to facilitate diffusion. The process, which may take several weeks to accomplish full remineralisation of the treated lesion, is enhanced by the use of other fluoride containing caries therapeutic materials (toothpastes, varnishes, gels and foams).[63,64] The fluoride ion acts in a catalytic manner to favour the deposition of calcium hydroxyapatite within the matrix in tooth tissue.

38% Silver diamine fluoride

Thirty-eight percent silver diamine fluoride (SDF) is composed of 25% silver that serves antimicrobial function and inhibits biofilm formation, 5% fluoride ions promotes remineralisation and 8% ammonia stabilises high concentrations in solution.[65,66] Application simply involves drying the surface, then applying sparing amounts of the liquid to the caries lesion, with no special instructions for post-application care. Without any excavation of soft dentin, silver diamine fluoride reacts with dentin protein and lays down a layer of silver protein that is resistant to bacterial acids and promotes the formation of hydroxyapatite and fluorapatite.[67] Thus, the treated surfaces increase in hardness,[68] and are less susceptible to biofilm formation due to its antimicrobial effect.[69] Annual applications of SDF arrested more active initial caries and reduced more new caries formation than three-monthly application of NaF varnish,[70] although increasing the frequency of application to every six months can increase the caries arrest rate of SDF application.[71] Although it has the drawback of black staining of the arrested lesion due to the reduction of silver ions to metallic silver and silver oxide, SDF has received considerable attention as a caries-preventive agent.[72,73] Thirty-eight percent SDF has been shown to be effective in arresting root caries[74–76] and coronal caries, including proximal caries lesions in adults,[77] as well as preventing secondary caries.[78] Studies have established the effectiveness of 38% SDF in arresting cavitated caries lesions in young children with early childhood caries (ECC), particularly for apprehensive children.[70,79,80] In these children, SDF has been used in place of operative treatment under general anaesthesia since the cavitated caries may be kept arrested until the tooth exfoliates or to arrest cavitated caries lesions in young children with ECC while on a waiting list for an operating room for definitive operative management.[67] It has also been employed as an alternative to traditional care of cavitated lesions, such as stainless steel crowns, pulpotomies and extractions.[79,81] While being used as an alternative treatment to children with special healthcare needs, cavitated lesions treated with SDF are sometimes covered with self-curing glass ionomer cements to mask the staining effect, in which case the technique has been referred to as silver modified atraumatic restorative treatment (SMART).

A new strategy to reduce the black staining by silver diamine fluoride was introduced into the dental market recently (Riva Star, SDI Ltd, Victoria, Australia). Reduction of black staining was to be accomplished by chemical modifications through an immediate application of potassium iodide (KI) solution following SDF application. However, randomised controlled clinical studies demonstrated that while this SDF/KI combination does not affect the caries arresting[76,82] and dentin desensitising[83] abilities of SDF as well as its speed of arresting caries, the immediate application of KI after SDF application does not reduce the black staining of arrested caries in the long term (30 months of the study).[76] Studies have also shown that the application of SDF/KI solutions does not affect the biofilm inhibitory effect of SDF,[69] and that silver and iodine ions were present in the dentin treated with SDF/KI,[84] and iodine can inhibit oral bacteria.[85]

Acidulated fluoride products

The idea of acidulating fluoride products to enhance their effectiveness is growing as well as the number of products. Sodium fluoride gels, mouthrinses and foams are acidulated with phosphoric acid to a pH range of 3.0–4.0. Reducing the pH of the fluoridated vehicle may prolong the ingress of mineral ions into the lesion body by keeping enamel micropores open and preventing fluoride-induced lamination of surface layer of the initial caries lesions, thus enabling full remineralisation of the lesion. In intact sound enamel, acidulated dentifrices, through mild etching, increase the enamel micropores and enhance the uptake of mineral ions (mainly fluoride) into the tooth tissue.[4,86] In addition, at a low pH, there is release of calcium and fluoride associated with bacteria, particularly bacterial lipoteichoic acid, as well as the calcium-fluoride-like and other calcium salts deposits in plaque matrix and tooth surfaces.[4] These processes would provide calcium and fluoride at the site of action when needed most, thus potentiating the remineralisation process. Thus the use of acidulated products either alone or in combination with materials, such as fluoride varnishes and self-assembling monomers, would greatly facilitate the remineralisation of initial caries lesions.

However, due to the low pH and high

titratable acidity, there is potential for erosive damage of glass-ionomer restorations and the glass-based fillers in composite resin, loss of glaze of porcelain restorations, and dentin hypersensitivity, particularly when used frequently. Furthermore, its strong acidic taste provokes marked salivation, and this may raise the risk of ingestion from inadvertent swallowing by children, so fluoride varnish is preferred for the younger age group.

Stannous fluoride-containing products

Stannous fluoride has been used for arresting proximal enamel and cervical root surface caries, although problems with stability and discoloration have occurred with it, which has required formulation changes, such as addition of sodium hexametaphosphate, to prevent this problem. Besides its antimicrobial effects and provision of fluoride that promotes remineralisation, stannous ions (Sn^{2+}), as a crystal growth inhibitor, are valuable agents in controlling the lamination effect of fluoride during the remineralisation of initial caries lesions. Sn^{2+} adsorbs to active growth and dissolution sites on enamel crystals, and prevents their remineralisation as well as further dissolution, and as such increases the resistance of the apatite to dissolution.[24] By this mechanism, it slows down the rate of remineralisation of the surface layer of the caries lesions, keeping the enamel micropores open for gradual and prolonged ingress of mineral ions into the lesion body, thus preventing lamination, facilitating increase in fluoride uptake and promoting full remineralisation of the lesions.[24] Combining the application of other high fluoride concentration material (for example, fluoride varnishes) or self-assembling peptide monomers with daily use of stannous fluoride dentifrice may enhance the remineralisation process.

Prescription dentifrices (toothpastes, gels, foams, pastes)

As stated previously, patients with active initial caries lesions are actively producing new caries, and as such are at high caries risk with a high likelihood of progression of their existing initial caries (Table 2). Thus, high fluoride concentration dentifrices (toothpastes, gel, foams) are often recommended to those categories of patients, not only for their daily home-use for prevention of new caries formation,[87] but also to enhance the effectiveness of any remineralisation therapy (FV, self-assembling peptide monomer, etc.) applied for control of existing active initial caries.[88,89] While prescription toothpastes and gels with fluoride concentration ranging from 2800 to 5000 ppm are recommended for daily use in adults, fluoride gels and foams, such as 1.23% NaF acidulated phosphate fluoride or neutral 2% NaF are professionally applied with custom-made trays for four minutes, 2-4 times per year (or 4 times over 24 weeks for root caries). The cariostatic benefits of these high fluoride vehicles, including remineralisation of primary root caries, have been demonstrated in various clinical trials.[89–94] Functionalised tricalcium phosphate described earlier has also been added into prescription toothpastes containing 5000 ppm (USA) or 850 ppm (Asia) fluoride to enhance their caries preventive and remineralising efficacy.

Some dental creams are available to enhance the remineralising capacity of the daily home-use fluoride dentifrices. A body of clinical evidence supports the caries remineralising efficacy of dental cream (paste) containing casein phosphopeptide-stabilised amorphous calcium phosphate (CPP-ACP) or casein phosphopeptide-stabilised amorphous calcium fluoride phosphate (CPP-ACFP).[59] Casein phosphopeptide (CPP) is a milk-derived phosphoprotein that stabilises high concentrations of calcium and phosphate ions in a soluble amorphous calcium phosphate at acidic and basic pH as well as in the presence of fluoride ions, forming nanoclusters of CPP-ACP or CPP-ACFP (with 900ppm fluoride).[95] When applied intraorally, these nanocomplexes bind onto the tooth surfaces and dental plaque to create a state of supersaturation of calcium and phosphate ions in the oral biofilm, providing high levels of bioavailable calcium and phosphate ions to facilitate remineralisation, and modifying the dynamics of the demineralisation-remineralisation events when cariogenic challenge occurs, to prevent caries development.[96]

Arginine-containing toothpaste

Toothpaste containing 1.5% arginine, insoluble calcium carbonate, and 1450 ppm fluoride as sodium monofluorophosphate is available for remineralisation of initial caries lesions and prevention of new lesion development when used at least twice daily for routine oral hygiene. When applied intraorally, the amino acids (arginine) is deaminated by the arginine deaminase (enzyme) system in saliva, producing ammonia, which is highly alkaline and causes a rise in pH within the oral environment, thus presenting an ideal condition for remineralisation, with the sodium monofluorophosphate providing the fluoride ions and the calcium carbonate serving as the calcium source.[97] Randomised clinical studies demonstrated reduction of the pathogenicity of the cariogenic plaque, consistent with significantly enhanced efficacy in arresting and reversing enamel and root caries when compared with toothpaste containing fluoride alone.[97]

Fluoridated bioactive glass products

Recently, a fluoride-containing bioactive glass (BioMinF; http://www.biomin.co.uk) was introduced as a caries remineralising and preventive additive in toothpastes. Fluoridated bioglass (f-BG) has fluoride, strontium, potassium and zinc incorporated within the glass itself, thus enabling simultaneous delivery of Sr^{2+}, Ca^{2+}, PO_4^{3-} and F^- ions into the initial caries lesions to promote remineralisation by formation of a partially fluoridated crystal structure, zinc ions for bactericidal function, and potassium as a desensitising agent. Having the fluoride incorporated within the glass prevents the risk of premature reaction of fluoride and calcium ions to calcium fluoride (CaF_2), which reduces the bioavailability of the two ions.[98,99] However, current lack of clinical studies does not permit any firm conclusions on their effectiveness.

Conclusion

Minimal intervention dentistry aims to preserve dental tissues first and restore only when indicated, thus remineralisation of initial (non-cavitated) caries lesions, an integral part of caries management, is an essential treatment strategy in minimal intervention. With this understanding, coupled with growing emphasis on preventive and minimal intervention dentistry, dental practitioners are increasingly embracing the principle of non-operative treatment of initial caries lesions. The adoption of MI dentistry is currently stimulating the development of various caries remineralising and preventive materials by innovators and industry. Different strategies are also being developed for management of different categories of caries lesions. Strong clinical evidence supports the effectiveness of pits/fissure sealants for therapeutic management of active initial caries on occlusal surfaces, and fluoride varnishes for remineralisation of caries lesions on root and coronal smooth surfaces,

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including proximal surfaces. Numerous other therapeutic materials such as self-assembling peptides, 38% silver diamine fluoride, acidulated fluoride products, stannous fluoride containing products, prescription dentifrices (toothpastes, gels, foams, pastes), arginine-containing toothpaste, and fluoridated bioactive glass products are available today for arrestment/remineralisation of initial caries lesions on root and coronal smooth surfaces; however, the level of evidence of effect is variable, as well as the availability in different parts of the world. Options available to practitioners to aid in caries management will vary when placing emphasis on the level of evidence supporting them. It is absolutely necessary that all caries remineralisation treatment be complemented with general behavioural modification in oral health through motivational interviewing directed towards change in oral hygiene to control plaque, dietary attitude modification to reduce frequency of intake of fermentable dietary sugars, and establishment of risk-based recall visits starting with three-monthly intervals to assess the status of previous treated lesions and monitor the patient's compliance with previous advice.

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