

# White spot lesions: A literature review

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## ABSTRACT

There has been a paradigm shift from Black's "extension for prevention" to a minimal intervention approach in the recent time. To diagnose earliest stages of enamel demineralization, accurate and reliable detection of white spot lesions is very important. The newer diagnostic aids would enable the dentist to detect and diagnose early such lesions and direct appropriate preventive measures to promote remineralization and conservation of the tooth substance. A high level of caries experience necessitates preventive strategies which are more cost-effective than surgical intervention and restorative procedures. The goal of modern dentistry is to manage white lesions non-invasively through remineralization in an attempt to prevent disease progression, and to improve strength, esthetics, and function of teeth.

**Key words:** Demineralization, Remineralization, White spot lesions

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## INTRODUCTION

The initial carious lesions are the so-called "white spot" lesions, which implies that there is a subsurface area with most of the mineral loss beneath a relatively intact enamel surface.<sup>[1]</sup>

Clinically, early caries lesion in enamel is initially seen as a white opaque spot and is characterized by being softer than the adjacent sound enamel and is increasingly whiter when dried with air. A cross-section of the white opaque spot reveals the features of carious enamel and suggests that dental caries is essentially an enamel defect with a relatively intact surface layer (SL) and some subsurface damage due to acid formed from plaque on tooth surface.<sup>[2]</sup> Downer's criteria for detection of caries include: Enamel caries-if there is destruction of the enamel surface or a white area in enamel extending up to, but not including the ADJ, and there is no cavity or discolored area beneath the ADJ. Dentinal caries — if there is destruction of the enamel extending up to and including the ADJ or a cavity or discolored area beneath the ADJ extending into dentine.<sup>[3]</sup>

The main types of enamel demineralization include incipient lesions and "surface-softened defect" which

are the other names used to describe white spot lesions.<sup>[4,5]</sup> It is essential to differentiate incipient lesion from arrested lesions. Incipient lesions are active lesions which continue to progress under acid attack whereas an arrested lesions does not progress. *In vivo* ultrastructural studies done by Thylstrup and Fredebo concluded that there were wide variations between active and arrested lesions.<sup>[6]</sup> "Micro-scars" were seen on active lesions while micro-cavitation was usually seen on arrested lesions.<sup>[2]</sup>

Dental caries is now being increasingly considered as a dynamic disease process wherein equilibrium exists between pathological factors causing demineralization and protective factors causing remineralization. The major pathological factors involve frequent ingestion of fermentable carbohydrates, inhibition of salivary function, and acidogenic bacteria while the protective factors include antibacterial agents which are both natural and applied, composition and rate of salivary flow, fluoride from extrinsic sources and diet. Caries intervention can be natural, or by some mode of treatment or procedure. The disease process is believed to be a continuum beginning with the first atomic level of demineralization, and then the early lesions of the enamel are followed by the dentinal involvement and finally cavitation. However,

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the early lesion is known to remineralize and is, therefore, regarded as reversible.<sup>[7]</sup>

## SUBSURFACE WHITE SPOT LESION FORMATION

The caries process takes place slowly which requires repeated episodes of prolonged exposure to acidic conditions consistently below the critical pH for enamel dissolution (pH 5.5, demineralization) with intervening periods of return to the resting pH of plaque (pH 7.0, remineralization period).<sup>[8-11]</sup> In case of failure to remove plaque from retentive tooth areas, a diet rich in refined carbohydrates, and frequent carbohydrate ingestion, the dynamic equilibrium between demineralization and remineralization will be tipped toward demineralization with the development of clinically detectable white spot lesions. The early enamel lesion is characterized by four distinct histopathologic zones.<sup>[12,13]</sup> Two zones of demineralization are present:

1. The translucent zone (1% pore volume) along the advancing front of the lesion; and
2. The body of the lesion (>5-25% pore volume) representing the majority of the lesion and situated approximately 15-30  $\mu\text{m}$  beneath the overlying intact enamel surface.

Two zones of remineralization are also present:

1. The dark zone (2-4% pore volume) situated near the advancing front just superficial to the translucent zone; and
2. The surface zone (1 to <5% pore volume) forming the intact surface overlying the lesion.

The initial formation of the lesion is due to the dissolution of hydroxyapatite (HAP) from the enamel prisms forming the enamel surface.<sup>[8,12,13]</sup>

The initial dissolution results in the loss of a small amount of mineral within the enamel and would have a similar appearance to the translucent zone (negative birefringence in quinoline). With continuing demineralization without the benefit of remineralization of this initial lesion, a surface zone that resembles the surrounding sound enamel, with respect to its negative birefringence (water imbibition) is formed. With ongoing removal of mineral from the underlying enamel, a positively birefringent body of the lesion (water imbibition) develops and separates the overlying surface zone from the translucent zone at the advancing front. If lesion development occurs over a relatively long period, a zone of remineralization (the dark zone, positive birefringence in quinoline) with reciprocation of mineral phases from the translucent zone will occur. If lesion formation is over a short period of time, the dark zone will not form and there will be rapid advancement

of the front with a large, heavily demineralized body of the lesion and a surface zone of minimum thickness. Once a certain degree of demineralization has occurred the lesion will take on a white spot appearance and become clinically detectable. The maintenance of an intact surface during caries formation is quite remarkable. At first, this was considered to be unique to surface enamel. Later, it was proven that an intact surface can be reproduced even when the surface enamel is ground away, and artificial caries is created in the remaining abraded enamel.

The subsurface white spot lesion with an intact surface occurs due to the physicochemical parameters of demineralization of HAP. The mechanistic approach to demineralization of enamel is based upon the primary driving force being hydrogen ion transport from the dental plaque at a pH of 5.0 into the underlying enamel at a pH of 7.0. The concentration gradient for hydrogen is much less in enamel than that in dental plaque, during episodes of acidogenesis by mutans streptococci and lactobacilli. Hydrogen ions are transported to the advancing front of the lesion. Once the hydrogen ions encounter susceptible tooth mineral, dental HAP undergoes dissolution with the resultant dissolved mineral transported from the advancing front to the dental plaque. Of interest is the fact that the fluid phase at the advancing front has a much lower calcium and phosphate concentration (0.1 mmol/L) than that at the enamel surface (5-8 mmol/L). This implies that calcium and phosphate are being transported against their concentration gradient, and this requires energy input to accomplish this. The energy for this active transport of solubilized mineral phase from the advancing caries front is supplied by the influx of the hydrogen ions driven by a 100 fold concentration gradient. In the plaque compared with enamel along the advancing front. Mineral phases may become entrapped in the zones of remineralization if the caries process is a slow process. During the intervening periods of remineralization and return to a resting neutral plaque pH, partially demineralized crystals may be repaired, or new crystals formed from the available dissolved mineral phases within the lesion and dental plaque. Demineralization may be markedly decreased in individuals with high plaque levels of calcium, phosphate, and fluoride. The increased calcium and phosphate in plaque would require a lower pH between plaque and the advancing front to allow for active transport of calcium and phosphate from the advancing caries front into the plaque. This effectively would result in a lower critical pH in order to induce demineralization. The presence of increased levels of fluoride in plaque favors reprecipitation of dissolved mineral and also allows for the incorporation of fluoride into reconstituted HAP. Likewise, increased fluoride content of native enamel in the form of fluoro-hydroxyapatite would lessen the extent of demineralization and favor mineral reprecipitation.<sup>[14]</sup>

## DETECTION OF WHITE SPOT LESIONS

Over the last two decades, there has been a drastic change in the prevalence and pattern of dental caries with a decrease in smooth surfaces caries and with more lesions being detected on the occlusal surfaces of the tooth. Thus, it is important to identify early and institute preventive measures for the control of dental caries. The traditional methods of detecting early lesions include visual inspection and radiography. In visual observation, reflected light is used to detect changes in color, texture, and translucency of the tooth substance. However, these traditional methods for early caries diagnosis have been found to be inaccurate and insensitive. Unfortunately, radiographs have the added risk of exposure of ionizing radiation to the patient.<sup>[3]</sup> As the present-day caries lesion progresses slowly, it is advisable to have a method which misses some of the shallow lesions, but yet has a high positive predictive value for deeper lesions.<sup>[2]</sup> It is hard to diagnose occlusal caries in teeth without a macroscopic breakdown of the outer enamel surface.<sup>[15]</sup> Enamel approximal caries lesions are poorly detected by radiography since demineralization in excess of 40% must occur for the radiographic detection to be possible although dentinal lesions in occlusal surfaces may be detected with some accuracy.<sup>[16,17]</sup> In a study by Yassin on *in vitro* mechanical damage of early carious lesion (enamel lesion) in artificial U-shaped grooves caused by a sharp dental explorer, it was seen that when a force of 500 g was used there was no damage to the sound enamel grooves. However, the probing by a sharp dental explorer in demineralized enamel grooves resulted in cavitation of white spot lesion with apparently a sound SL. The dentist should, therefore, be cautious while using a sharp dental explorer to examine early carious lesions in pits and fissures.<sup>[18]</sup> The newer available methods for caries detection include auto-fluorescence (such as quantitative light-induced fluorescence [QLF]) of teeth, electrical resistance (such as ECM), and imaging techniques like conventional and digital bitewing radiography.<sup>[19]</sup> Transillumination, DIAGNOdent, and DIFOTI devices comprise the other supplemental methods to aid in the diagnosis.<sup>[20]</sup> QLF which measures enamel autofluorescence can detect differences in remineralization of early enamel caries.<sup>[21]</sup> A new fiberoptic diagnostic tool enabling dentists to identify early caries lesions with greater sensitivity and specificity is the fibre-optics-based confocal imaging system which can record axial profiles through caries lesions using single-mode optical fibers.<sup>[22]</sup> A novel technology involving optical coherence tomography (OCT) imaging of tooth which shows greater light backscattering intensity at sites of carious lesions than the sound enamel could be used for screening carious sites and determining lesion depth, in combination

with Raman spectroscopy for biochemical confirmation of caries.<sup>[23]</sup> Polarization-sensitive optical coherence tomography (PSOCT) system has also been used to study the spatially resolved scattering and polarization phenomena of teeth which are known to have strong polarization effect. PSOCT is another tool that has been used for *in vitro* dental caries assessment of remineralized lesions.<sup>[24]</sup> Digital Imaging Fiber-Optic Transillumination (DIFOTI) uses images of teeth obtained with a digital CCD camera, which are sent to a computer for analysis with dedicated algorithms for location and diagnosis of carious lesions by the operator in real time, thereby providing a quantitative characterization for monitoring of approximal, occlusal, and smooth-surface caries.<sup>[25]</sup> Frequency-domain photothermal radiometry (FD-PTR or PTR) and modulated luminescence have also been used to detect early interproximal demineralized lesions. However, PTR provides more accurate diagnosis than the modulated luminescence.<sup>[26]</sup> Laser fluorescence device DIAGNOdent has been used to detect occlusal caries and has more sensitivity and specificity than radiographic examination.<sup>[27]</sup> In a study on Digital Imaging Fiber-Optic Trans-Illumination (DIFOTI), F-speed radiographic film, and depth of approximal lesions, it was observed that the histologic lesion depth determined by F-speed radiographic film was identical to that evaluated by polarized light microscopy while DIFOTI did not measure the depth. However, DIFOTI could detect surface changes associated with early demineralization as early as 2 weeks. The investigators of this study suggested that surgical or chemical treatment strategies should take into account cavitation rather than histologic lesion depth.<sup>[28]</sup> Data evaluating the accuracy of enamel demineralization detection using conventional, digital, and digitized radiographs, and evaluation of radiographs and logarithmically contrast-enhanced subtraction images show that Den-Optix<sup>®</sup> system represents the advances in the development of photostimulable phosphor plates and is a plausible alternative to conventional radiographs. It was observed that radiographs taken with InSight<sup>®</sup> film were cheap and accurate and that digital subtraction enhanced approximal enamel caries lesion detection.<sup>[16]</sup> According to Gimenez *et al.* fluorescence-based methods had similar accuracy in detecting occlusal and approximal caries lesions, on both primary and permanent teeth, and they performed better in detecting more advanced caries lesions.<sup>[29]</sup> Gomez *et al.* concluded that electrical conductance (EC) and QLF seemed to be promising for the detection of early lesions. Visual methods remained the goal standard for clinical assessment in dental practice keeping in mind both cost and practicality considerations.<sup>[30]</sup> Twetman *et al.* reported in his study that electrical methods and laser fluorescence could be useful adjuncts to visual-tactile and radiographic examinations, especially on occlusal surfaces in permanent and primary molars.<sup>[31]</sup>

## CHARACTERISTICS OF WHITE SPOT LESIONS IN ENAMEL

The enamel demineralization defect has a lower mineral distribution in the SL in comparison to the adjacent sound enamel and also a lower interprismatic mineral content. The first stage of enamel demineralization is characterized by removal of interprismatic mineral content and in the subsequent stages a well-defined SL formation occurs which constitutes early caries lesion.<sup>[2]</sup> These studies have demonstrated that a porous and mineral-rich SL covers an enamel lesion and the morphology differs a little from that of sound enamel while body of the lesion which comprises the subsurface area has low mineral content (10-70 vol.%). The early caries lesion in enamel is characterized by a prominent perikymata pattern and focal holes.<sup>[32-34]</sup> The main drawback of the numerous experimental techniques is that they are static measurements of caries progression at a particular time period whereas the carious process is time-dependent and is in a constant state of dynamic equilibrium wherein a balance is struck between demineralization and remineralization.

## SURFACE LAYER COVERING WHITE SPOT LESIONS

The early investigators who observed the white opaque spots attributed the presence of these lesions to artifacts. They believed that the SL could be due to sound enamel which has a higher mineral content. These explanations were proved false by subsequent investigations by Langdon et al.<sup>[35]</sup> Their studies on pressed pellets of HAP demonstrated that subsurface lesion could occur in an acidic gel system with 2 ppm fluoride. They also concluded that organic matrix is not important for subsurface lesion formation, and that neither a preferred crystallite orientation in the enamel prisms nor an uneven ion/mineral distribution in enamel were essential for the formation of a subsurface lesion since these are absent in pressed apatites. This is in contrast to earlier reports by Brudevold et al.<sup>[36]</sup>

## REMINERALIZING AGENTS FOR TREATMENT OF WHITE SPOT LESIONS

### Complex of casein phosphopeptides-amorphous calcium phosphate

Complex of casein phosphopeptides-amorphous calcium phosphate (CPP-ACP) is an acronym for a CPPs and ACP. Caseins are a heterogeneous family of proteins predominated by alpha 1 and 2 and b-caseins. CPPs are phosphorylated casein-derived peptides produced by tryptic digestion of casein.

The CPP containing the amino acid cluster sequence - Ser (P)-Ser (P)-Ser (P)-Glu-Glu has the ability to bind and stabilize calcium and phosphate in solution, as well as to bind dental plaque and tooth enamel. Through their multiple phosphoryl residues, the CPPs bind to form clusters of ACP in metastable solution, preventing their growth to the critical size required for nucleation and precipitation. The proposed mechanism of anticariogenicity for the CPP-ACP is that it localizes ACP in dental plaque, which buffers the free calcium and phosphate ion activities, thereby helping to maintain a state of supersaturation with respect to tooth enamel depressing demineralization and enhancing remineralization. The CPPs have been shown to keep fluoride ions in solution, thereby enhancing the efficacy of the fluoride as a remineralizing agent.<sup>[37,38]</sup>

Complex of casein phosphopeptides inhibits adherence of oral bacteria to saliva-coated hydroxyapatite beads (S-HA). By selectively inhibiting the streptococcal adhesion to teeth, it can modulate the microbial composition of dental plaque and favor establishment of less cariogenic species such as oral actinomyces. This could also control acid formation (buffering) in dental plaque, in turn reducing HAP dissolution from tooth enamel.<sup>[39,40]</sup>

It can be incorporated into the pellicle in exchange for albumin and thus inhibits the adherence of *Streptococcus mutans* and *Streptococcus sobrinus*, causing both neutralization and enhancement of remineralization.<sup>[41]</sup>

The Recaldent Technology was developed by Prof. Eric Reynolds of the University of Melbourne. CPP-ACP has been trademarked Recaldent and has been launched in sugarless chewing gum and confectionery. More recently, a sugar-free, water-based cream containing RECALDENT™ (CPP-ACP) (GC Tooth Mousse/Prospec MI Paste) has been made available to dental professionals.<sup>[42]</sup>

Azarpazhooh and Limeback concluded that the long-term effectiveness of CPP-ACP in preventing caries *in vivo* is unknown due to lack of clinical trial evidence.<sup>[43]</sup>

### Amorphous calcium phosphate

The ACP technology requires a two-phase delivery system to keep the calcium and phosphorous components from reacting with each other before use. The current sources of calcium and phosphorous are two salts, calcium sulfate and dipotassium phosphate. When the two salts are mixed, they rapidly form ACP that can precipitate onto the tooth surface. This precipitated ACP can then readily dissolve into the saliva and can be available for tooth remineralization.<sup>[44]</sup>

It can be considered a useful adjuvant for the control of caries in orthodontic applications. Experimental ACP



composite has shown to efficiently establish mineral ion transfer throughout the body of the lesion and restore the mineral lost due to acid attack.<sup>[45]</sup>

The ACP technology was developed by Dr. Ming S. Tung. In 1999, ACP was incorporated into toothpaste called *Enamelon* and later reintroduced in 2004 in *Enamel Care* toothpaste by Church and Dwight. It is also available as Discus Dental's Nite White Bleaching Gel and Premier Dental's Enamel Pro Polishing Paste. It is also used in the Aegis product line, such as Aegis Pit and Fissure Sealant, produced by Bosworth.<sup>[46]</sup>

### Sodium calciumphosphosilicate (bioactive glass)

When bioactive glass comes in contact with saliva, it rapidly releases sodium, calcium, and phosphorous ions into the saliva that are available for remineralization of the tooth surface. The ions released form hydroxycarbonate apatite (HCA) directly. They also attach to the tooth surface and continue to release ions and remineralize the tooth surface after the initial application. These particles have been shown to release ions and transform into HCA for up to 2 weeks. Ultimately, these particles will completely transform into HCA.<sup>[47]</sup>

Novamin adheres to exposed dentin surface and forms a mineralized layer that is mechanically strong and resistant to acid. There is a continuous release of calcium over time, which maintains the protective effects on dentin.<sup>[48]</sup>

The *NovaMin Technology* was developed by Dr. Len Litkowski and Dr. Gary Hack. Currently, available products in the market are NovaMin: SootheRx, DenShield, NuCare-Root Conditioner with NovaMin, NuCare-Prophylaxis Paste with NovaMin, and Oravive.<sup>[49,50]</sup>

### Calcium carbonate carrier-SensiStat

The SensiStat technology is made of arginine bicarbonate, an amino acid complex, and particles of calcium carbonate, a common abrasive in toothpaste. The arginine complex is responsible for adhering the calcium carbonate particles to the dentin or enamel surface and allows the calcium carbonate to dissolve slowly and release calcium that is then available to remineralize the tooth surface.<sup>[51]</sup>

The SensiStat Technology was developed by Dr. Israel Kleinberg of New York. The technology was first incorporated into Ortek's Proclude desensitizing prophylaxis paste and later in Denclude.<sup>[52]</sup>

### Xylitol carrier

The use of chewing gum carrying xylitol increases salivary flow rate and enhances the protective properties of saliva. This is because the concentration of bicarbonate and phosphate is higher in stimulated saliva, and the resultant

increase in plaque pH and salivary buffering capacity prevents the demineralization of tooth structure. Moreover, the higher concentration of calcium, phosphate, and hydroxyl ions in such saliva also enhances remineralization.<sup>[53]</sup>

Miake *et al.* observed that xylitol can induce remineralization of deeper layers of demineralized enamel by facilitating  $\text{Ca}^{2+}$  movement and accessibility.<sup>[54]</sup>

### Nano-hydroxyapatite

A study was done to determine the effect of nano-HAP concentrations on initial enamel lesions under dynamic pH-cycling conditions. It was concluded that nano-HAP had the potential to remineralize initial enamel lesions. A concentration of 10% nano-HAP may be optimal for remineralization of early enamel caries.<sup>[55]</sup>

### The trimetaphosphate ion

The potential mode of action of trimetaphosphate ion (TMP) is likely to involve in adsorption of the agent to the enamel surface, causing a barrier coating that is effective in preventing or retarding reactions of the crystal surface with its fluid environment, and hence reducing demineralization during acid challenge.<sup>[56]</sup>

Gu *et al.* highlighted the role of sodium TMP as a templating analog of dentin matrix phosphoproteins for inducing intrafibrillar remineralization of apatite nanocrystals within the collagen matrix of incompletely resin infiltrated dentin.<sup>[57]</sup>

### Alpha-tricalcium phosphate

It is used in products such as Cerasorb, Bio-Resorb, and Biovision. Tricalcium phosphate (TCP) has also been considered as one possible means for enhancing the levels of calcium in plaque and saliva. Some small effects on free calcium and phosphate levels in plaque fluid and in saliva have been found when an experimental gum with 2.5% alpha-TCP by weight was chewed, when compared to a control gum without added TCP.<sup>[58]</sup>

### Dicalcium phosphate dihydrate

Inclusion of dicalcium phosphate dehydrate (DCPD) in a dentifrice increases the levels of free calcium ions in plaque fluid, and these remain elevated for up to 12 h after brushing, when compared to conventional silica dentifrices.<sup>[59]</sup>

Calcium from DCPD was incorporated into enamel and detected in plaque 18 h post-treatment after brushing with a DCPD dentifrice which fosters improved remineralization of teeth in combination with fluoride.<sup>[60]</sup>

The reaction of DCPD and fluoride forming fluorapatite may provide a potentially promising treatment for remineralization of caries lesions *in vivo*.<sup>[61]</sup>

## CONCLUSION

The dynamic balance between demineralization and remineralization determines the progression of white spot lesion. The diagnostic armamentarium includes novel technologies and non-invasive techniques like fiber-optic transillumination and electrical resistance methods which are very useful in detecting posterior approximal dentinal caries and occlusal caries. Radiographs and direct digital imaging are still important tools in estimation of caries. A clear understanding of the mechanism of subsurface lesion formation and progression, possibilities, and limitations of newer methods and their clinical applications need to be recognized by the dentist to direct preventive strategies to the high caries risk individuals. The emphasis currently is being given to new technologies for enamel remineralization which suggest the changes in the understanding of dental caries. Recent investigations have primarily focused on various calcium phosphate-based technologies which are designed to supplement and enhance fluoride's ability to restore tooth mineral.

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