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The Development and Utilization of Fluoride Varnish

A Peer-Reviewed Publication
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Educational Objectives

The overall goal of this course is to provide the reader with information on caries prevention and the use of fluoride varnishes. Upon completion of this course, the reader will be able to do the following:

1. Review the development of in-office topical fluorides.
2. List and describe the anti-caries efficacy of available in-office topical fluorides.
3. Review the current recommendations for the use of in-office topical fluorides for caries prevention.
4. List and describe risk assessment and the individualization of patient treatment.
5. List and describe recent developments in in-office topical fluorides.

Abstract

For several decades, the use of fluoride has been a mainstay in controlling dental caries. Preventing and treating dental caries requires an individualized approach that must consider a patient's risk level, determined through a risk assessment. In-office topical fluorides were developed between the 1950s and 1970s, with considerable research conducted on ways to enhance the duration of contact and uptake of fluoride. Based on available clinical trials and evidence-based data, the American Dental Association Council of Scientific Affairs developed recommendations for the use of in-office topical fluorides. In addition, antimicrobials and calcium and phosphate technologies are available for use.

Introduction

The possible beneficial effects of fluoride on the dentition were first recognized well over one hundred years ago. As early as the 1840s, fluoride lozenges were distributed in some European communities with the intent of preventing dental caries, albeit based only on observations of the local population.¹ By the late 1930s and early 1940s, a considerable amount of research was focused on the possible effects of fluoride on the prevention of dental caries,^{2,3,4} with water fluoridation first being introduced in the 1940s.⁵ Home-use and professional topical fluoride agents were introduced later and, following clinical trials, the first dentifrice with active fluoride was commercially available in 1954. This was rapidly followed by the introduction of other fluoride formulations (sodium fluoride, sodium monofluorophosphate, stannous fluoride and amine fluoride). Since these early beginnings, it has been recognized globally that fluoride has an anti-caries benefit, with one meta-analysis concluding an average reduction of 24% in DMFS with appropriate fluoride dentifrice use.^{6,7,8,9}

Higher concentrations of fluorides were investigated during the 1950s and 1960s, with various chemistries and application techniques. These included a 4% sodium fluoride rinse and 8% stannous fluoride applied once per year,¹⁰

1.23% acidulated phosphate fluoride (APF) and 2% neutral sodium fluoride topical gels. Five percent sodium fluoride varnish was first investigated by Schmidt, a discovery that was reported in *Stoma* in 1964, when it was described as "a new application method with a special long-lasting intensive fluoridating effect."¹¹ This was followed by the first reported clinical trial on its efficacy in 1968, by Heuser and Schmidt.¹² In the 1970s, a second type of fluoride varnish was introduced based on difluorosilane, which was later changed to a lower concentration difluorosilane formulation in the late 1980s.

Much of the early research on in-office applications was focused on developing formulations that would increase the concentration of fluoride available for uptake or prolong its contact with the tooth surface. Currently available in-office topical fluorides include 5% sodium fluoride varnish, 1.23% APF gels and foams, 2% sodium fluoride gels, foams and rinses, difluorosilane varnish, and a rinse containing a combination of fluorides. (Table 1) Efficacy has been conclusively demonstrated for some, but not all, currently available in-office topical fluoride options.

Table 1. Currently available in-office topical fluorides

1.23% acidulated phosphate fluoride gels and foams
2% sodium fluoride gels, foams and rinses
5% sodium fluoride varnish
1% difluorosilane varnish
Combination rinses

Based on available clinical trials and evidence-based data, the American Dental Association Council of Scientific Affairs developed recommendations that were published in 2006.¹³ These recommendations address risk-based treatment modalities and efficacy for professional (in-office) topical fluorides.

Much of the early research on in-office applications was focused on developing formulations that would increase the concentration of fluoride available for uptake or prolong its contact with the tooth surface.

Caries Prevention: Risk-Based Therapy

In order to provide appropriate preventive therapy and intervention, knowledge of the individual patient's current risk level is necessary. The use of in-office and home-use fluorides should be tailored to an individual patient's risk level, age, and the efficacy and safety of the proposed treatment. For patients at low risk of caries, it has been determined that no additional topical fluoride may be required beyond use of a fluoride dentifrice, with a further recommendation to use clinical judgment in determining

appropriate therapy for a given patient.¹⁴ A patient at low risk of caries is defined as one who has no factors that could increase caries risk and who has had no carious lesions in the prior three years (incipient, cavitated primary or secondary).¹⁴ For these patients, use of fluoride dentifrice may suffice, depending on clinical judgment for the individual patient.

All other individuals are at moderate or high risk of caries; for these patients, in-office topical fluoride treatment is recommended, and home-use fluoride therapy may also be required (in addition to fluoride dentifrice use). In order to individualize therapy, it is therefore necessary to first know a patient's level of risk. In the presence of carious lesions – indicative of a moderate or high risk level – performing a risk assessment helps determine which modifiable risk factors are present, to then help a patient reduce his or her risk level and optimize treatment.

The use of in-office and home-use fluorides should be tailored to an individual patient's risk level.

Determining Risk: Risk Assessment Tools

Risk level is determined by assessing the presence of caries risk factors, including carious lesions. Given that caries is a multifactorial disease, this requires a thorough medical and dental history, familial history and clinical examination. A number of formal risk assessment tools are available with the primary goal of helping the clinician determine risk level prior to individualizing treatment. Cariogram was developed in Sweden and CAries Management By Risk Assessment (CAMBRA) was developed in the United States. CAMBRA is one of the most frequently used formal risk assessment tools in the United States, utilizing 25 data points to determine risk level and with several objectives.¹⁵ (Table 2) CAMBRA is also a tool for caries management, providing recommendations on the use of fluorides, calcium and phosphate products, antimicrobials and salivary testing by risk level and age. Since a patient's risk level is not static, a risk assessment must be repeated at regular intervals. The American Academy of Pediatric Dentistry recommends that a child receive his or her first dental examination when the first tooth erupts and at the latest by 12 months of age.¹⁶

Table 2. Objectives of Caries Management By Risk Assessment

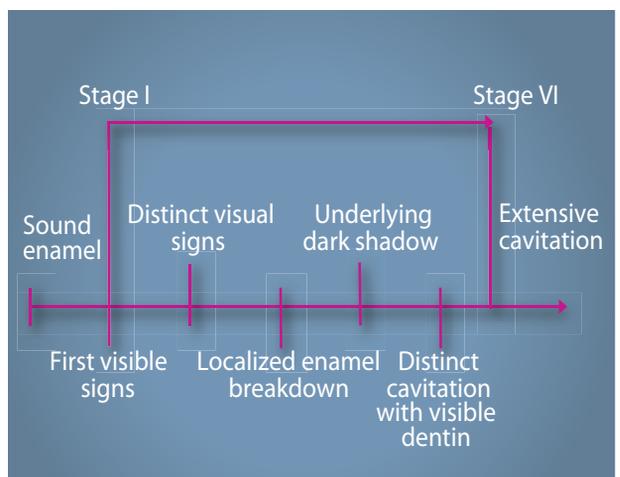
Determine, manage and reduce risk
Educate and manage patients
Provide chemotherapeutic intervention
Prevent demineralization
Minimal intervention to restore cavitated lesions

Since a patient's risk level is not static, a risk assessment must be repeated at regular intervals.

Detection and Assessment of Carious Lesions

In the last decade, several technologies have become available that aid in the diagnosis of carious lesions. The overall goal of diagnosis is to identify carious lesions at an early stage when they are still susceptible to remineralization and to be able to differentiate between active and inactive lesions as well as whether they are at a reversible or irreversible stage. Technologies that have been incorporated in recent years, in addition to the pre-existing and continuing use of radiographs, include the use of laser fluorescence, LED fluorescence, fiberoptic transillumination and digital fiberoptic transillumination. In addition to these new diagnostic aids, new criteria have been developed to aid in categorizing the severity and activity of carious lesions at all stages of development. The International Caries Detection and Assessment System (ICDAS) was developed during the last decade and agreed upon at an international symposium in Scotland. ICDAS provides guidelines for classifying carious lesions. The severity is determined under this classification system by the depth of penetration. This classification system with guidelines has been found to be reliable and accurate.¹⁷ Direct probing into lesions or suspected lesions is not recommended as this can detrimentally affect the area, promoting breakdown of enamel as well as greater introduction of cariogenic bacteria.¹⁸

Figure 1. Carious lesion classification under ICDAS



Source: Criteria Manual; International Caries Detection and Assessment System

“...the use of sharp explorers in the detection of primary occlusal caries appears to add little diagnostic information to other modalities and may be detrimental.”

Bacterial tests that can be performed chairside or in a laboratory to measure bacterial load are also available, as are chairside salivary tests that will provide an assessment of salivary flow, salivary pH and buffering capacity, and quality of the saliva. These tests are important to consider in patients suspected of having xerostomia and other high risk patients.

Risk Factors

Risk factors may be behavioral, environmental or biological/anatomical (Table 3) – some of these are modifiable, and if modified can reduce a patient’s level of caries risk. Risk factors include poor oral hygiene, whether due to inability to perform oral hygiene or unwillingness to do so, resulting in a high load of cariogenic bacteria. Since cariogenic bacteria are essential for dental caries to occur, local conditions that enhance the ability of a thick biofilm and heavy bacterial load to develop, or that impede its removal, also increase caries risk – these include deep and complex fissures, the surface characteristics of the enamel, overhanging margins, defective restorations, restorations with rough surfaces, crowded teeth, fixed multiunit restorations and orthodontic appliances. A diet or regularly used oral medications that are high in sugars and fermentable carbohydrates, as well as high frequency of intake, are also well-recognized risk factors.^{19,20,21,22} Exposed root surfaces are at greater risk than enamel, given that dentin contains a lower proportion of inorganic mineralized tissue and is more easily demineralized than enamel.²³ In addition, degradation of exposed collagen fibers occurs rapidly after these are exposed following demineralization of the dentin.

Xerostomia is one of the major risk factors for caries, has a number of etiologies, and is estimated to occur in a significant percentage of adults, as well as occurring in children.^{24,25} In addition to resulting in greater accumulation of biofilm and bacteria, and specifically with respect to directly influencing caries control, xerostomia also results in reduced (or no) availability of calcium and phosphate from saliva as well as a loss of buffering capacity and an absence of other protective factors.²⁶ A reduced level or lack of saliva also results in reduced levels of (or no), proline-rich proteins (PRPs), statherin (a phosphopeptide) and histatins, which are believed to play a role in reducing susceptibility to caries due to their high affinity to hydroxyapatite, binding to calcium, and role in remineralization.^{27,28} Xerostomia also results in other clinical signs and symptoms not directly related to caries control.

The importance of xerostomia in the progression of dental caries and the high caries risk and rampant caries observed in patients with dry mouth can easily be understood when looking at the process by which dental caries occurs, the functions of saliva,²⁹ and factors that influence the balance between demineralization and remineralization. Table 4 contains a list of the functions of saliva with relevance for caries control.

Table 3. Caries risk factors

Poor oral hygiene – inability or unwillingness to perform adequate oral hygiene
Xerostomia
Orthodontic appliances
Crowded teeth
Deep and complex fissures
Defective restorations and overhanging margins
Enamel surface characteristics
Restorations with rough surfaces
Fixed multiunit restorations
Exposed root surfaces
Diet high in fermentable carbohydrates
High frequency of intake of fermentable carbohydrates (foods, drinks, snacks)
Tobacco use
Substance abuse
Genetics

Table 4. Functions of saliva for caries control

Prevention of demineralization (supply of calcium, phosphate, fluoride, statherin, PRPs and other substances)
Promotion of remineralization (supply of calcium, phosphate, fluoride, statherin, PRPs and other substances)
pH buffering (against intraoral acids)
Removal of debris (physical action)
Removal of bacteria (physical action)
Clearance of carbohydrates (physical action)
Antibacterial activity (chemicals and enzymes, including lactoferrin and lactoperoxidase)

Other risk factors include substance use and abuse. Smokeless tobacco contains sugar and is linked to dental caries, while smoking tobacco has now also been found to be a risk factor for caries.^{30,31,32} Methamphetamine use and alcohol combined with drug abuse are additional risk factors.^{33,34} Interestingly, renewed interest in a possible genetic role for caries has led to the conclusion that genetics does indeed play a role in caries risk level. As examples, Slayton et al. found that 27% of the dmfs measured in their study was due to interaction of the gene tuftelin with *Streptococcus mutans*; in an earlier study reported in 2004, Luo concluded that overexpression of tuftelin in the extracellular enamel matrix during tooth development resulted in imperfections in enamel prisms and crystals.^{35,36}

Xerostomia is one of the major risk factors for caries, resulting in reduced (or no) availability of calcium and phosphate from saliva as well as a loss of buffering capacity and an absence of other protective factors.

Once risk has been determined, it is time to educate and manage the patient, help the patient change behaviors that are modifiable risk factors, remove risk factors such

as defective restorations or overhanging margins, and provide chemotherapeutic intervention as well as minimally invasive treatment where required. Chemotherapeutic intervention typically involves the use of fluorides, and may also include the use of calcium and phosphate technologies, and antimicrobials such as chlorhexidine or xylitol to reduce the cariogenic bacterial load.³⁷ Chlorhexidine is available as an alcohol-free rinse and as an alcohol-containing rinse; it is also available as chlorhexidine/thymol and chlorhexidine varnishes. In a rinse formulation as chlorhexidine gluconate, it has been used in early childhood caries prevention programs as part of a prevention and treatment protocol that also includes fluoride varnish applications. However, with respect to anti-cariogenicity, results for chlorhexidine are equivocal - a highly concentrated chlorhexidine varnish was found in one study to result in only a 'weakly significant' reduction in *mutans streptococci* 2 weeks after use in orthodontic patients, while another study found that chlorhexidine varnish was effective in reducing the level of these bacteria.^{38,39} Other antimicrobials include cetylpyridinium chloride, triclosan and povidone-iodine. Using xylitol gum has been shown in some studies to reduce microbial load, and in one study of a xylitol and fluoride dentifrice to incrementally reduce caries beyond the influence of fluoride dentifrice without the addition of xylitol.^{40,41} Chewing gum also helps to stimulate saliva where salivary gland function is still present, providing an added benefit.

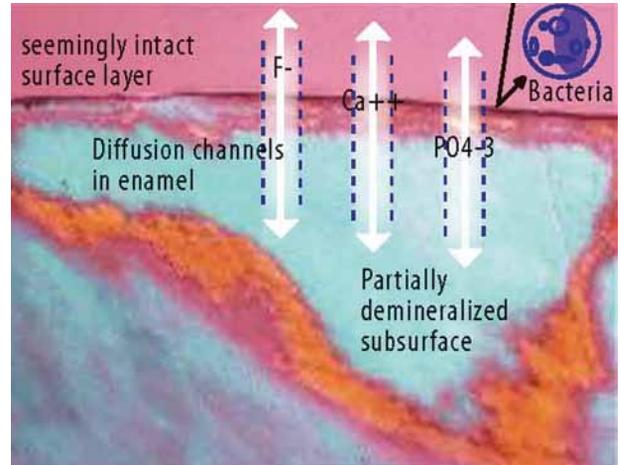
The Caries Process

Dental caries is a process by which mineral transfer occurs from the dental hard tissues during demineralization and to the dental hard tissues during remineralization, with the results depending on the relative balance of these.⁴² Demineralization associated with dental caries occurs in response to the diffusion into the enamel (or dentin) of acid following its production by cariogenic bacteria (primarily *mutans streptococci*) as they metabolize fermentable carbohydrates. Minerals – primarily calcium and phosphate – leach out from the hydroxyapatite crystals during demineralization, and in situations where demineralization outpaces remineralization this leads to the development of subsurface lesions. These initially involve only the enamel and often result in the appearance of white spots where sufficient subsurface mineral content has been lost to alter the optical properties of the dental hard tissues. Ultimately, if not halted or reversed, cavitation ensues.

Saliva is supersaturated with calcium and phosphate, which helps to prevent demineralization until the critical pH is reached during an acid attack. Remineralization occurs once the pH rebounds following the acid attack, at which time calcium and phosphate (and fluoride) are taken up into the demineralized areas and reverse the destructive phase of the caries process. The rebound of pH takes from 20 minutes to 40 minutes following an acid attack, depending on the individual's salivary flow and buffering capac-

ity and the density of the plaque. When considering these facts, the importance of reducing intake of carbohydrates and healthy salivary flow become obvious.^{43,44}

Figure 2. Caries process of demineralization and remineralization



Courtesy of www.ineedce.com

In patients with xerostomia, the pH remains below the critical pH level for longer and remains below pH5 for at least 30 minutes or longer. In other patients, by 30 minutes the pH is rebounding to neutral.⁴⁵ Reduced salivary flow significantly lengthens the period of time during which teeth are exposed to low pH levels following acid attacks.

Calcium and phosphate in saliva help to prevent demineralization and promote remineralization.

Current ADA Recommendations for Professionally Applied Topical Fluorides

Primary chemotherapeutic intervention includes using professionally applied (in-office) topical fluorides in moderate- and high-risk patients. Whether or not to use professionally applied topical fluorides in a low risk patient depends on clinical judgment. Antimicrobial agents may also be used chemotherapeutically.

With the recent attention given to fluorosis and the new recommendation to reduce the level of fluoride in drinking water to 0.7 ppm, it is important to stress with patients, parents and guardians that professionally applied topical fluorides are only periodically applied, and are safe and effective. Fluorosis results from excessive levels of ingested fluoride from all sources on a regular, ongoing basis, and only during tooth development. It presents in the case of a mild excess of fluoride as light mottling of the teeth, which may or may not be of esthetic concern depending on location and severity. At highly excessive levels of fluoride, severe fluorosis can result in brown, gray and mottled areas as

well as structural and morphological changes that include brittle, pitted and malformed enamel. This occurs where water is obtained from wells and contains high levels of fluoride, again during tooth development. *It should be noted that professional topically applied fluorides are used intermittently, and no link or association has been found between their use and fluorosis.*⁴⁶

The current recommendations on professional topical fluorides from the Council for Scientific Affairs of the American Dental Association are for the use of only fluoride varnish in children under 6 years of age. For children age 6 and above, and adults, either fluoride varnish or fluoride gel is recommended for use two to four times a year (six-monthly or three-monthly applications) depending on risk level. For these recommendations, a high-risk patient in the under-6 age group is defined as one with an incipient or cavitated lesion within the past three years or who has multiple risk factors, suboptimal fluoride exposure, xerostomia or a low socioeconomic status. A moderate risk patient is one who has had no incipient or cavitated carious lesions within this time period and has at least one risk factor. In the age 6 and above group, three or more incipient or cavitated lesions or multiple risk factors, xerostomia or suboptimal fluoride exposure define a high-risk patient, while one or two incipient or cavitated lesions or at least one caries risk factor defines a moderate-risk patient.¹⁴

Table 5. Current recommendations for in-office topical fluorides

	< 6 years of age	6-18 years of age	18+ years of age
Low-risk patients	May be of no benefit	May be of no benefit	May be of no benefit
Moderate-risk patients	Fluoride varnish 2 times per year	Fluoride varnish or gel 2 times per year	Fluoride varnish or gel 2 times per year
High-risk patients	Fluoride varnish 2-4 times per year	Fluoride varnish or gel 2-4 times per year	Fluoride varnish or gel 2-4 times per year

Adapted from: Evidence-based Clinical Recommendations: Professionally Applied Topical Fluoride. ADA Council of Scientific Affairs.

The recommendation to use fluoride varnish or gel (depending on the age of the patient) is based on available evidence of efficacy. The Council found that available clinical data indicate that 4-minute fluoride gel is effective in school-age children, and 4-minute fluoride foam for the primary dentition as well as freshly erupted first permanent molars. Clinical studies have demonstrated the efficacy of 4-minute gel and foam.^{47,48} It was found that 1-minute gels may be effective based on laboratory data,^{49,14} and a recent *in situ* study found that a 4-minute and 1-minute APF gel application were equivalent in inhibiting enamel demineralization and increasing fluoride concentrations.⁵⁰ However, there is a lack of clinical data on 1-minute treatments. The Council for Scientific Affairs does not endorse the use of 1-minute professional topical fluorides.¹⁴ No evidence exists to support the efficacy of dual rinses.

The large number of clinical studies on 5% sodium fluoride varnish provides proof of its efficacy and safety, while numerous public health initiatives in Europe and the United States also provide evidence-based support for its use. The effectiveness of 5% sodium fluoride varnish for caries prevention has been demonstrated for young children up to 6 years of age, older children, adolescents and adults. Meta-analyses by Marinho et al. of 5% sodium fluoride varnish and 1.23% APF gels led to the conclusion that the caries preventive effect of the fluoride varnish was superior (46% pooled average reduction in DMFS vs. 28%). In addition, Marinho et al. found a 33% pooled average reduction in the primary dentition for 5% sodium fluoride varnish.^{51,52} Another meta-analysis, by Helfenstein and Steiner, resulted in the conclusion that 5% sodium fluoride varnish is efficacious in the prevention of dental caries, finding an average 38% reduction in caries.⁵³ In recent years, 5% sodium fluoride varnish has been used in a number of public health settings and open trials, together with early screening, anticipatory guidance, and counseling for parents and caregivers in both dental and medical settings and for underprivileged communities.⁵⁴ One 2-year randomized clinical trial found a significant reduction in early childhood caries in disadvantaged children between 6 and 44 months of age who were initially caries-free and received either one or two varnish treatments annually in addition to anticipatory guidance and counseling of the parent. The same study showed an incremental benefit with twice-yearly applications.⁵⁵

Five percent fluoride varnish is effective in reducing caries in young children, adolescents and adults; for the prevention of coronal caries on all surfaces of the teeth; and for the prevention of root caries.⁵⁶⁻⁶³ It has also been used as a cavity liner, as well as for desensitization (the indications for which fluoride varnish is cleared by the Food and Drug Administration) and to strengthen enamel against dental erosion.⁶⁴⁻⁶⁶ A small number of caries clinical trials have also been conducted on the efficacy of the current difluorosilane varnish formulation.⁶⁷⁻⁶⁹ Petersson et al. found it to be effective on the proximal surfaces of primary teeth.⁶⁹ (Note that any trials conducted prior to the late 1980s involved use of a higher concentration of difluorosilane.)

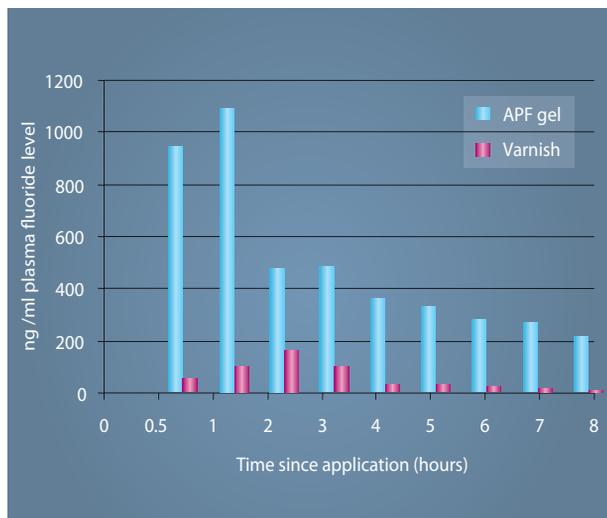
With respect to occlusal caries, it has been found that pit and fissure sealants are superior to fluoride varnishes for the prevention of occlusal caries, although a recent Cochrane review concluded that there is limited data on this.^{70,71} Pit and fissure sealants are available as resin-based sealants (with or without fluoride) and glass ionomer cements. One study found that use of a glass ionomer sealant was more effective for reducing caries and caries progression of incipient lesions, and for caries prevention, than either resin-based sealants or fluoride varnishes.⁷² Resin-based sealants generally have greater longevity than glass ionomer sealants, however in partially erupted teeth glass ionomers enable early prevention since they are moisture tolerant, can

be placed even in the presence of moisture and will release fluoride on an ongoing basis. Therefore, sealant selection must consider whether or not the product contains fluoride and will release fluoride, and the relative benefit of moisture tolerance versus longevity.

Fluoride Varnish Application and Fluoride Release

The recommended dose for application of 5% sodium fluoride varnish is 0.25 ml for the primary dentition, 0.40 ml for the mixed dentition and 0.50 ml for the permanent dentition. For infants, 0.10 ml is required. The ingestion of fluoride is significantly lower in children receiving a 5% fluoride varnish treatment compared to fluoride gel.⁷³ It was also found that the highest level of plasma fluoride obtained with the varnish (Figure 3), was similar or slightly higher compared to that resulting from the use of a regular fluoride dentifrice, and significantly lower than with professional application of APF gel.

Figure 3. Fluoride ingestion



Source: Ekstrand et al.

A professional prophylaxis is not essential prior to topical fluoride application, and in fact more alkali-soluble (loosely bound) fluoride is retained as calcium fluoride-like globules in the presence of plaque; large quantities of plaque, however, should be removed (and can be achieved using gauze, a toothbrush or a professional prophylaxis).^{74,75} Fluoride varnish is typically left on the teeth undisturbed for 4 to 6 hours for fluoride release. This is also a practical length of time for patients to follow the instructions to avoid brushing and flossing, as well as to avoid imbibing hot drinks or alcohol (or rinsing with alcohol-containing products), or eating crunchy foods that respectively could dissolve or chip away some of the varnish. During this period of time, considerable protective fluoride release occurs. However, the varnish can be left on for up to 24 hours⁷⁶ if wished and will still release fluoride. In fact, one

in vitro study of two 5% sodium fluoride varnishes conducted in 2001 found that varnish coated on enamel slabs that were then immersed in buffered calcium phosphate solution (to mimic the intraoral environment) continued to release fluoride for five to six months.⁷⁷

5% sodium fluoride varnish can be left on for up to 24 hours if wished and will still release fluoride.

Chemotherapeutic Intervention: The Mechanism of Action for Topical Fluoride

Fluoride has been found to be effective in controlling dental caries through mechanisms of action that include inhibiting demineralization and promoting remineralization, as well as by reducing the production of acid by cariogenic bacteria (believed to occur due to the inhibition of the metabolism of fermentable carbohydrates, primarily through the inhibition of the enzyme enolase).^{78,79} The inhibition of demineralization and the promotion of remineralization both require the presence of sufficient quantities of calcium, phosphate and fluoride. If a higher level of these minerals can be maintained at the tooth surface prior to and during an acid attack, their increased concentration helps prevent migration of calcium and phosphate from the tooth; it is known that supersaturation with calcium and phosphate ions intra-orally results in increased resistance to demineralization and that saliva is supersaturated with these ions. During remineralization, fluoride is present on the surface of the demineralized enamel crystals and attracts calcium and phosphate ions, thereby aiding remineralization of the crystals. In early carious lesions, remineralization occurs while demineralization is limited.

Following the application of topical fluorides, calcium fluoride-like globules are formed on the tooth surface. In addition, the surface coatings of phosphates on these calcium fluoride-like deposits have been found to reduce their solubility in saliva. The calcium fluoride-like globular deposit is believed to create a fluoride reservoir, with the subsequent release of calcium, phosphate and fluoride. A higher concentration of topical fluoride and a more prolonged application increase the amount of fluoride released as well as the deposition and availability of these globules.⁸⁰⁻⁸² The amount of calcium fluoride-like deposit has also been found to be related to the availability of calcium and fluoride ions on the tooth surface. Tenuta et al. investigated the influence of the calcium fluoride-like globular layer deposited following use of professional topical fluorides on the level of fluoride contained in plaque that later developed. They concluded that fluoride concentrations in the plaque fluid were significantly related to the amount of calcium fluoride-like deposits present at the tooth surface prior to plaque development and reduced enamel demineralization during subsequent acid attack.⁸³

Loosely Bound and Firmly Bound Fluoride

Loosely bound fluoride is also known as KOH-soluble or alkali-soluble fluoride, and inhibits demineralization of the enamel crystals. The calcium fluoride-like globules and ionic fluoride available intraorally are loosely bound fluoride. The other category is firmly bound fluoride, which is also known as alkali-insoluble fluoride, KOH-insoluble fluoride or apatitically bound fluoride – the fluoride that is incorporated into the apatite crystals. Cruz et al. found this to be minimal in sound enamel during *in vitro* testing following brief exposures with topical fluorides.⁸⁴ In an *in vivo* study on sound enamel in premolars slated for orthodontic extraction, prepared enamel was treated with 2% sodium fluoride and then either left protected or first treated with an alkali solution to remove the KOH-soluble fluoride and then protected. The paired premolar served as an untreated control. Following extraction, it was found that the lesion depths for the control teeth and those with only KOH-insoluble fluoride were similar and significantly greater than for the teeth with KOH-soluble and KOH-insoluble fluoride. The conclusion from this research on sound enamel was that it was the KOH-soluble fluoride (loosely bound fluoride) that “reduced mineral loss and lesion depths significantly compared with the untreated teeth.”⁸⁵

However, it is also known that demineralized lesions will absorb more minerals than sound hard tissue. This results in the uptake of fluoride into the crystals, which are more resistant to acid dissolution and contain more calcium as well as fluoride compared to the original hydroxyapatite crystals (which also contained carbonates and other ions in lieu of some calcium).^{86,87} Attin et al. found that demineralized samples treated with 5% sodium fluoride varnish in one study acquired both KOH-soluble and KOH-insoluble fluoride subsequent to fluoride application, at the fluoridated sites.⁸⁸ Firmly bound fluoride also requires time for its acquisition, which first involves diffusion of available fluoride into the enamel.

It is known that demineralized lesions will absorb more fluoride than sound hard tissue.

Recent Developments in Fluoride Varnishes

Since their introduction, 5% sodium fluoride varnishes have evolved with the addition of clear and white varnishes that are more acceptable to patients, a variety of flavors, the use of syringe tips and unit doses, and in some cases the addition of calcium and phosphate technologies. Single-use unit doses enable the clinician to mix the varnish within the small unit dose to make sure it is homogenous prior to application; make it quick to apply straight from the unit dose; and, since the unit doses are disposable, also can help with infection control.

Calcium and Phosphate Technologies

Calcium and phosphate technologies currently incorporated into dental products include amorphous calcium phosphate (ACP), casein phosphopeptide-amorphous calcium phosphate (CPP-ACP), calcium sodium phosphosilicate (CSPS) and tricalcium phosphate (TCP). The overall intent of these technologies is to increase the amount of available calcium and phosphate, typically together with fluoride.^{89,90} The indications for products incorporating these technologies are caries control and sensitivity reduction, depending on the product.⁹⁰⁻⁹³ Over the last decade, all of these calcium and phosphate technologies have been incorporated and are currently available in home-use dentifrices or crèmes, while ACP has been incorporated into a tooth whitener and CPP-ACP into a chewing gum. In the case of professional products, ACP, CSPS and TCP technologies have variously been incorporated and are currently available in restorative materials, sealants, orthodontic cement, prophylaxis pastes, in-office fluoride varnishes and in-office fluoride gel. In-office fluoride varnishes with *in vitro* testing are currently available containing ACP, CSPS and TCP; these are addressed below.

Table 6. Products containing calcium and phosphate technologies

	Professional products	Home use products
ACP	5% sodium fluoride varnish	Dentifrice
	1.23% fluoride gel	Desensitizer
	Prophylaxis paste	Bleaching agent with desensitizer
	Sealant	
	Orthodontic cement	
CPP-ACP	Dental crème	Dental crème
	Dental crème with fluoride	Dental crème with fluoride
		Chewing gum
CSPS	5% sodium fluoride varnish	5,000 ppm fluoride prescription dentifrice
	Prophylaxis paste	Dentifrice
TCP	5% sodium fluoride varnish	5,000 ppm fluoride prescription dentifrice

Calcium sodium phosphosilicate (CSPS)

Calcium sodium phosphosilicate (NovaMin®) is a bioactive glass that has been shown to release calcium and phosphate ions (as well as sodium) that are then deposited and form hydroxycarbonate apatite. This has been researched both for hypersensitivity relief as well as remineralization therapy.⁹⁴ Five percent sodium fluoride varnish with Novamin has been found to result in relief of hypersensitivity for up to 6 months.⁹⁵ In addition, a 48-hour *in vitro* study comparing 5% sodium fluoride varnish containing CSPS with a control varnish (no CSPS) found significantly greater release of fluoride, calcium and phosphorus from the CSPS-containing varnish.⁹⁶

Table 7. Cumulative fluoride and calcium ion release

	1 hour	4 hours	24 hours	48 hours
Fluoride release (µg/g)				
with CSPS	97.8	1,134.9	9,835.80	10,346.80
without CSPS	71.4	130.4	301.7	513.1
Calcium release (µg/g)				
with CSPS	31.3	378.10	1,166.70	2,521.90
without CSPS	13.3	52.1	71.9	65.4

Tricalcium phosphate (TCP)

Tricalcium phosphate consists of fine-milled particles that are incorporated into 5% sodium fluoride varnish. When exposed to saliva, the barrier coating around the particles dissolves and the calcium and phosphate ions are released. *In vitro* data is available on this varnish demonstrating greater fluoride release than in the absence of TCP, higher average salivary fluoride levels and the release of calcium. It is claimed that the varnish flows longer and more interproximally and over the teeth than other varnishes. It is also claimed that the TCP-containing varnish releases fluoride and calcium continuously over a 24-hour period. (In this regard, as mentioned previously, 5% fluoride varnishes continue to release fluoride for up to 24 hours and longer based on *in vitro* testing.)

Amorphous calcium phosphate (ACP)

Amorphous calcium phosphate was developed by the American Dental Association Foundation and consists of an unstructured form of calcium phosphate molecules. Its amorphous structure allows for the incorporation of fluoride and other ions into it, and *in vitro* tests show increased bioavailability of fluoride.⁹⁷ Intraorally, ACP has the fastest rate of formation and dissolution of the calcium phosphate compounds, and has been shown in SEMs to precipitate onto the tooth surface as globules that release calcium and phosphate on dissolution. ACP has also been found to increase fluoride release and uptake.⁹⁸⁻¹⁰⁰

In fluoride varnish, ACP has been found to result in greater fluoride release compared to a fluoride varnish without the addition of calcium and phosphate technology, and to result in greater fluoride uptake into sound enamel slabs.¹⁰⁰ In a recent *in vitro* study comparing ACP-containing varnish with TCP-containing varnish, standardized sound enamel cores were treated with the fluoride varnishes and untreated demineralized enamel cores were placed adjacent to the respective test samples. After immersing all the enamel cores in artificial saliva for 24 hours and then removing the alkali-soluble (loosely bound) fluoride from the treated samples, fluoride uptake (firmly bound fluoride) and the lesion depth resulting from exposure to acid were measured. Samples demonstrated greater fluoride uptake, and less lesion depth in response to exposure to acid, with the use of ACP.¹⁰¹

Table 8. Fluoride uptake and depth of etch

	ACP varnish	TCP varnish	Water
Fluoride uptake (ppm) in demineralized enamel	5567	2126	49
Etch depth in demineralized enamel	17.8	19.46	21.14

Source: Comparison of fluoride uptake into tooth enamel from two fluoride varnishes containing different calcium phosphate sources. J Clin Dent. May, 2011.

Summary

Fluoride has proven to be beneficial for the control of caries over many years. Professional topical fluorides are recommended for at-risk patients, with the use of fluoride gel recommended for age 6 and over and 5% sodium fluoride varnish recommended for all age groups. The efficacy and safety of fluoride varnish are supported by extensive trials and studies, with recent developments in fluoride varnishes including the use of unit doses, white and clear varnishes, and the addition of calcium and phosphate technologies.

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Questions

- _____ were distributed in some European communities during the 1840s with the intent of preventing dental caries.
 - Fluoride dentifrices
 - Fluoride lozenges
 - Xylitol lozenges
 - all of the above
- The first dentifrice with active fluoride intended for topical application was commercially available in _____.
 - 1934
 - 1944
 - 1954
 - 1964
- Higher concentration fluorides investigated during the 1950s and 1960s included _____.
 - 8% stannous fluoride
 - 1.23% acidulated phosphate fluoride
 - 4% sodium fluoride
 - all of the above
- The use of 5% sodium fluoride varnish was first described in the _____ publication.
 - British Dental Journal
 - Journal of the American Dental Association
 - Stoma
 - none of the above
- The first clinical trial on the efficacy of 5% sodium fluoride varnish was reported on in _____, by Heuser and Schmidt.
 - 1958
 - 1963
 - 1968
 - 1973
- Much of the early research on in-office topical fluorides was focused on formulations that would _____.
 - prolong the contact of the topical fluoride with the tooth surface
 - provide an alkaline environment
 - increase the concentration of fluoride available for uptake
 - a and c
- Efficacy has been conclusively demonstrated for _____ currently available in-office topical fluorides.
 - some
 - all
 - none of the
 - none of the above
- The use of in-office and home-use fluorides should consider _____.
 - an individual patient's risk level
 - an individual patient's age
 - the efficacy and safety of the proposed treatment
 - all of the above
- For patients at low risk of caries, it has been determined that the use of additional topical fluoride _____.
 - is never required
 - is always required
 - depends on the clinician's determination based on clinical judgment
 - a or c
- In the presence of carious lesions, it is still important to perform a risk assessment to _____.
 - determine which modifiable risk factors are present
 - help a patient reduce his or her risk level
 - optimize treatment
 - all of the above
- The American Academy of Pediatric Dentistry recommends that a child receive his or her first dental examination _____.
 - when the first tooth erupts
 - at the latest by six months of age
 - at the latest by 12 months of age
 - a and c
- _____ is a caries diagnostic that has been developed in recent years.
 - Digital fiberoptic transillumination
 - LED fluorescence
 - Laser fluorescence
 - all of the above
- The International Caries Detection and Assessment System (ICDAS) _____.
 - provides guidelines for classifying carious lesions
 - has been found to be reliable and accurate
 - was developed during the last decade
 - all of the above
- Direct probing into lesions or suspected lesions can _____.
 - promote breakdown of enamel
 - result in a greater introduction of cariogenic bacteria
 - detrimentally affect the area
 - all of the above
- Chairside salivary tests are available that can provide an assessment of _____.
 - salivary flow
 - salivary pH and buffering capacity
 - saliva quality
 - all of the above
- _____ is an example of a local condition that enhances the ability of a thick biofilm and heavy bacterial load to develop.
 - Deep and complex fissures
 - Overhanging margins
 - Crowded teeth
 - all of the above
- Dentin contains _____.
 - a lower proportion of inorganic mineralized tissue compared to enamel
 - collagen fibers that degrade rapidly after their exposure
 - a greater proportion of organic tissue compared to enamel
 - all of the above
- A reduced flow or lack of saliva results in no, or reduced levels of, _____ from saliva.
 - calcium
 - phosphate
 - proline-rich proteins
 - all of the above
- _____ is/are believed to play a role in reducing susceptibility to caries due to their high affinity to hydroxyapatite, binding to calcium, and role in remineralization.
 - Proline-rich proteins
 - Statherin
 - Histatins
 - all of the above
- _____ is a risk factor for dental caries.
 - The use of smokeless tobacco
 - Methamphetamine use
 - Alcohol combined with drug abuse
 - all of the above
- The gene tuftelin _____.
 - influences tooth development
 - interacts with *Streptococcus mutans*
 - has been researched for its influence on caries susceptibility
 - all of the above
- Chemotherapeutic intervention can involve the use of _____.
 - fluorides
 - calcium and phosphate technologies
 - antimicrobials
 - all of the above
- Chlorhexidine gluconate rinse _____.
 - has been used in early childhood caries prevention programs
 - is available as an alcohol-free formulation and alcohol-containing formulation
 - is unequivocally the best antibacterial for caries prevention
 - a and b
- Using xylitol _____.
 - was shown in one dentifrice study to incrementally reduce caries
 - has been shown in some studies to reduce the microbial load
 - as a gum results in the gum stimulating saliva
 - all of the above
- In situations where demineralization _____ remineralization, subsurface lesions develop.
 - increases
 - involves
 - outpaces
 - decreases
- Professional topically applied fluorides _____.
 - are used intermittently
 - have not been found to be linked to or associated with fluorosis
 - are available in several forms
 - all of the above

Questions

27. The current recommendations on professional topical fluorides from the Council for Scientific Affairs of the American Dental Association are for the use of only _____ in children under 6 years of age.
- fluoride foam
 - fluoride gel
 - fluoride varnish
 - all of the above
28. A recent in situ study found that a 4-minute and 1-minute _____ were equally effective in inhibiting enamel demineralization and increasing fluoride concentrations.
- APF gel application
 - APF foam application
 - fluoride varnish
 - all of the above
29. Marinho et al. concluded from meta-analyses that the use of 5% sodium fluoride varnish was _____ the use of 1.23% APF gels.
- as effective as
 - inferior to
 - superior to
 - none of the above
30. 5% sodium fluoride varnish has been used in a number of _____.
- public health settings
 - open trials in dental settings
 - open trials in medical settings
 - all of the above
31. Petersson et al. found difluorosilane varnish to be effective on the _____.
- proximal surfaces of primary teeth
 - occlusal surfaces of primary teeth
 - proximal surfaces of permanent teeth
 - all of the above
32. With respect to occlusal caries, it has been concluded from evidence that pit and fissure sealants are _____ fluoride varnishes for the prevention of occlusal caries.
- inferior to
 - as effective as
 - superior to
 - none of the above
33. In partially erupted teeth, glass ionomers enable early prevention since they _____.
- are moisture tolerant
 - will release fluoride on an ongoing basis
 - can be placed even in the presence of moisture
 - all of the above
34. The recommended dose for application of 5% sodium in infants is _____.
- 0.25 ml
 - 0.20 ml
 - 0.15 ml
 - 0.10 ml
35. The ingestion of fluoride is _____ in children receiving a 5% fluoride varnish treatment compared to receiving fluoride gel.
- the same
 - significantly higher
 - significantly lower
 - none of the above
36. Following application of sodium fluoride varnish, patient instructions include to avoid _____.
- brushing and flossing
 - imbibing hot drinks or alcohol
 - eating crunchy foods
 - all of the above
37. The inhibition of demineralization and the promotion of remineralization require the presence of sufficient quantities of _____.
- calcium
 - fluoride
 - phosphate
 - all of the above
38. Saliva is supersaturated with _____.
- calcium
 - fluoride
 - iodine
 - all of the above
39. Fluoride concentrations in the plaque fluid were found by Tenuta et al. to _____.
- be significantly related to the amount of calcium fluoride-like deposits
 - reduce enamel demineralization during subsequent acid attack
 - be related to bacterial promotion
 - a and b
40. A _____ of topical fluoride increases the amount of fluoride released as well as the deposition and availability of calcium fluoride-like globules.
- higher concentration
 - lower concentration
 - more prolonged application
 - a and c
41. Loosely bound fluoride _____.
- is also known as KOH-soluble fluoride
 - is also known as alkali-soluble fluoride
 - inhibits demineralization of the enamel crystals
 - all of the above
42. Calcium fluoride-like globules deposited on teeth are a form of _____.
- loosely-bound fluoride
 - firmly-bound fluoride
 - apatitically-bound fluoride
 - all of the above
43. Demineralized lesions will absorb _____ minerals compared to/as sound hard tissue.
- fewer
 - more
 - the same amount of
 - all of the above
44. Attin et al. found in one study that demineralized samples treated with 5% sodium fluoride varnish acquired _____.
- alkali-soluble fluoride
 - alkali-insoluble fluoride
 - a and b
 - none of the above
45. Single-use unit doses of fluoride varnish _____.
- enable the clinician to mix the varnish within the small unit dose
 - make it quick to apply straight from the unit dose
 - can help with infection control
 - all of the above
46. Fluoride varnishes have been shown to release fluoride for _____.
- up to 4 hours
 - up to 6 hours
 - at least 24 hours
 - at least nine months
47. Calcium sodium phosphosilicate _____.
- is a bioactive glass
 - results in greater release of fluoride from fluoride varnish
 - results in greater release of calcium from fluoride varnish
 - all of the above
48. Amorphous calcium phosphate _____.
- was developed by the American Dental Association Foundation
 - has the fastest rate of formation and dissolution of the calcium phosphate compounds
 - has been shown to increase bioavailability of fluoride in in vitro testing
 - all of the above
49. Amorphous calcium phosphate _____.
- has an amorphous structure allowing for incorporation of ions
 - in varnish has been shown to increase fluoride release
 - in varnish has been shown to increase fluoride uptake
 - all of the above
50. 5% sodium fluoride varnishes have evolved with _____.
- the addition of clear and white varnishes
 - a variety of flavor choices
 - the inclusion of calcium and phosphate technologies
 - all of the above

The Development and Utilization of Fluoride Varnish

Name: _____ Title: _____ Specialty: _____

Address: _____ E-mail: _____

City: _____ State: _____ ZIP: _____ Country: _____

Telephone: Home () _____ Office () _____ Lic. Renewal Date: _____

Requirements for successful completion of the course and to obtain dental continuing education credits: 1) Read the entire course. 2) Complete all information above. 3) Complete answer sheets in either pen or pencil. 4) Mark only one answer for each question. 5) A score of 70% on this test will earn you 3 CE credits. 6) Complete the Course Evaluation below. 7) Make check payable to PennWell Corp. **For Questions Call 216.398.7822**

Educational Objectives

- List and describe the development of in-office topical fluorides.
- List and describe the anti-caries efficacy of available in-office topical fluorides.
- List and describe the current recommendations for the use of in-office topical fluorides for caries prevention.
- List and describe risk assessment and the individualization of topical fluoride treatments.
- List and describe recent developments in in-office topical fluorides.

Course Evaluation

Please evaluate this course by responding to the following statements, using a scale of Excellent = 5 to Poor = 0.

- | | | |
|---|----------------------|----------------------|
| 1. Were the individual course objectives met? | Objective #1: Yes No | Objective #3: Yes No |
| | Objective #2: Yes No | Objective #4: Yes No |
| | Objective #5: Yes No | |
- To what extent were the course objectives accomplished overall? 5 4 3 2 1 0
 - Please rate your personal mastery of the course objectives. 5 4 3 2 1 0
 - How would you rate the objectives and educational methods? 5 4 3 2 1 0
 - How do you rate the author's grasp of the topic? 5 4 3 2 1 0
 - Please rate the instructor's effectiveness. 5 4 3 2 1 0
 - Was the overall administration of the course effective? 5 4 3 2 1 0
 - Do you feel that the references were adequate? Yes No
 - Would you participate in a similar program on a different topic? Yes No
 - If any of the continuing education questions were unclear or ambiguous, please list them.

- Was there any subject matter you found confusing? Please describe.

- What additional continuing dental education topics would you like to see?

If not taking online, mail completed answer sheet to
Academy of Dental Therapeutics and Stomatology,
 A Division of PennWell Corp.

P.O. Box 116, Chesterland, OH 44026
 or fax to: (440) 845-3447

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| 2. (A) (B) (C) (D) | 27. (A) (B) (C) (D) |
| 3. (A) (B) (C) (D) | 28. (A) (B) (C) (D) |
| 4. (A) (B) (C) (D) | 29. (A) (B) (C) (D) |
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| 14. (A) (B) (C) (D) | 39. (A) (B) (C) (D) |
| 15. (A) (B) (C) (D) | 40. (A) (B) (C) (D) |
| 16. (A) (B) (C) (D) | 41. (A) (B) (C) (D) |
| 17. (A) (B) (C) (D) | 42. (A) (B) (C) (D) |
| 18. (A) (B) (C) (D) | 43. (A) (B) (C) (D) |
| 19. (A) (B) (C) (D) | 44. (A) (B) (C) (D) |
| 20. (A) (B) (C) (D) | 45. (A) (B) (C) (D) |
| 21. (A) (B) (C) (D) | 46. (A) (B) (C) (D) |
| 22. (A) (B) (C) (D) | 47. (A) (B) (C) (D) |
| 23. (A) (B) (C) (D) | 48. (A) (B) (C) (D) |
| 24. (A) (B) (C) (D) | 49. (A) (B) (C) (D) |
| 25. (A) (B) (C) (D) | 50. (A) (B) (C) (D) |

AGD Code 258, 430

PLEASE PHOTOCOPY ANSWER SHEET FOR ADDITIONAL PARTICIPANTS.

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